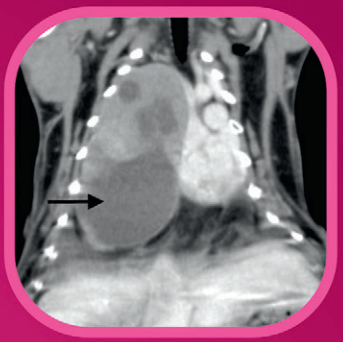
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I dedicate this fourth edition of the "Pink Book" to the younger generations of veterinarians who are at the beginning of their careers and are pursuing their interest and passion in exotic animal medicine and surgery. I have been privileged to meet and work with so many bright and dedicated young veterinarians during my career at the Animal Medical Center, my travels while lecturing, and my work as a journal and book editor. You have made my career journey so worthwhile. I am grateful for all that I have learned from every one of you, and I hope that I have been able to pass on some of my knowledge and experience to you. I thank all of my friends and colleagues who have worked with me on this book for so many editions and for so many years—you have truly made this book what it is. I am grateful for my co-editors of this edition, Connie J. Orcutt and Christoph Mans, who put so much time and effort into this book, and especially Jim Carpenter, who has worked with me on three editions of this book—we could not have done this without you. I thank my children, Zachary and Chelsea Messinger, who are forever the center of my life, and my sister, Marcia Quesenberry, for always being there for me and encouraging me to move forward. Lastly, I thank John Harris for being so patient and loving while I worked on this book and for always reminding me to enjoy life.

Katherine E. Quesenberry

With immense gratitude, I dedicate this book to the professional colleagues I've worked with over the years. First among them is Kathy Quesenberry, who introduced me to both exotic pet medicine and medical writing. As a mentor and friend, she has always modeled professionalism, intellectual curiosity, and compassion. I also thank the extremely talented and dedicated clinicians, technicians, and great friends with whom I've shared professional and personal successes and struggles; they include my "exotic" colleagues, Jennifer Graham, Flo Tseng, Wendy Emerson, Deborah Kennedy, Jenny Hayes, and Lauren Skeens, as well as the "nonexotic" clinicians at Angell Animal Medical Center, who always pushed the envelope for my unusual patients. Finally, I offer my deep thanks and admiration to the veterinarians who authored these chapters—those searchers who attempted and accomplished things that had not been tried before and then generously shared their discoveries with the rest of us.

Connie J. Orcutt

I would like to dedicate this book to all the kind and generous people who have supported me throughout my career. From the staff at the Avian Exotic Service at the Animal Medical Center in 2005 (welcoming the German veterinary student who just got off the boat and barely spoke any English) to all the great people I met and worked with at many institutions since, including the University of Tennessee, the Ontario Veterinary College, the Vetsuisse Faculty Zurich, the Tai Wai Small Animal and Exotic Hospital, the Milwaukee County Zoo, and University of Wisconsin-Madison—thank you. I particularly would like to thank Kathy Quesenberry for inviting me to be a co-editor of the fourth edition of the "Pink Book," which has been a great honor. I would like to thank Tom Donnelly and Cyndi Brown for their mentorship, which had a profound impact on my career. Special thanks go to Penny Rudolph for the many opportunities provided over the years. Most importantly, I would like to thank and dedicate this book to my wife for her support while I was editing the "Pink Book" and to my children, without whom this book likely would have been published two years earlier.

Christoph Mans

I wish to acknowledge all of our colleagues who contributed their knowledge and time to this edition of Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery. *I also thank Dr. Kathy Quesenberry for her friendship and for once again inviting me to collaborate on this edition of the Pink Book. I also wish to thank the 42 interns and residents whom I have helped train in zoological/exotic pet medicine at Kansas State University and who have inspired my professional life. I am indebted to Drs. Bonnie Rush, Dean, and Elizabeth Davis, Department Head, for their strong support of me and for my professional/academic growth. I also wish to thank veterinary students Sarah Wilson, Karissa Severud, Elizabeth Loos, and Danielle Windle for their assistance in the preparation of this text.*
I would like to dedicate this book to my family (wife, Terry; son, Michael; and daughter, Erin, and her family—husband, Steve, and my grandkids, Kylie, Hayden, and Asher) who have supported me as I pursued my passion for zoological and wildlife medicine for the past 45 years.

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FERRETS, RABBITS, and RODENTS
CLINICAL MEDICINE and SURGERY

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PREFACE

In this fourth edition of *Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery*, we have gathered together an experienced, international team of authors to provide our readers with a comprehensive source of the clinically relevant information on topics concerning the medicine and surgery of common small mammals kept as pets. The knowledge base of small mammal medicine has advanced rapidly with each edition of this book, so much so that it is difficult to capture and filter the most relevant and timely information into one source. As in the previous three editions, our goal remains to present the most relevant information in a succinct format that is easily readable and user friendly. With the hard work and dedication of all four editors, Connie J. Orcutt, Christoph Mans, James W. Carpenter, and myself, as well as the many talented authors who have contributed to this fourth edition of the "Pink Book," we feel we have accomplished our goal.

This edition continues in the tradition of the previous three editions in presenting separate sections on the medicine and husbandry of ferrets, rabbits, rodents, and other small mammals. In this edition, as in previous editions, we also have included dedicated chapters on sugar gliders and African pygmy hedgehogs, and we have added chapters on degus, prairie dogs, and skunks. We have consolidated a separate section titled "Surgical Techniques and Dentistry," which includes specific chapters on soft tissue surgery of ferrets, rabbits, and rodents, as well as chapters on general principles, orthopedics in small mammals, diagnostic and surgical endoscopy, and small mammal dentistry. In the "General Topics" section, we have a new chapter on hematology and biochemistry, which discusses specific information on and interpretation of clinical pathology in small mammals.

As in the previous editions, this book would not have been successful without the expertise and team effort of the editors. We have collaborated in all aspects of this book to bring the pieces together, including author selection, chapters, photos, and editing. We are extremely grateful to our support team at Elsevier, namely Jennifer Catando, Kathryn DeFrancesco, and Karthikeyan Murthy, who have been patient and supremely helpful as we worked through the roadblocks we encountered. Their professionalism and expertise has been invaluable. As with the previous three editions, we are confident that the format, presentation, information, and reliability of this fourth edition of the "Pink Book" will continue to set it apart as the standard in this subspecialty of veterinary medicine.

Katherine E. Quesenberry

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Basic Anatomy, Physiology, and Husbandry of Ferrets

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NATURAL HISTORY AND DOMESTICATION

The domestic ferret (*Mustela putorius furo*) belongs to the family Mustelidae, the largest family within the mammalian Order Carnivora. Along with ferrets, the Genus *Mustela* includes polecats, mink, weasels, and ermines (also called stoats). The domestic ferret is most likely a direct descendant of the European polecat (*M. putorius*) but may also be descended from the steppe (or Siberian) polecat (*M. eversmannii*).[8,16,31,52] The domestic ferret is also closely related to the black-footed ferret (*M. nigripes*) but is likely not a direct descendant.

Free-ranging ferrets and polecats are found throughout Europe, Asia, and North America. Black-footed ferrets nearly became extinct due to habitat destruction and the deliberate depopulation of prairie dogs (*Cynomys* species), their main food source.[25,36] Captive breeding and reintroduction programs for the black-footed ferret have reestablished populations in some areas of North America; however, the species continues to be listed as endangered under the US Endangered Species Act.

Ferrets likely have been domesticated for more than 2000 years, probably first being domesticated in southern Europe.[8,11,16,25,31] They may have been introduced into the United Kingdom by the Romans or Normans.[8,11,25] In the late 1800s, domestic ferrets were intentionally introduced into New Zealand to depopulate feral colonies of European rabbits (*Oryctolagus cuniculus*).[25] Because of the lack of predatory species, feral populations of ferrets were established and are still present, raising concerns for the spread of infectious

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diseases (e.g., *Mycobacterium bovis* in livestock and zoonotic diseases, such as rabies), and preying on native bird populations.[16,25] Similarly, ferrets were released in Australia in the 1800s to depopulate feral colonies of introduced rabbits; however, predators prevented the establishment of feral populations of ferrets.[25] The domestic ferret was introduced into the United States approximately 300 years ago, most likely for pest depopulation and hunting.[16,25,31] There are currently no established feral populations of domestic ferrets in North America.[31]

USES

In the early 1900s, tens of thousands of ferrets were bred in the United States to help rid granaries, barns, and warehouses of rodents.[16] Ferrets were also used for pest control on ships.[11,16,25] In some areas of the world, ferrets are still used for rodent and rabbit control.

Ferrets have long been bred to hunt European rabbits, and ferrets are still used to hunt in some areas of the world.[16,25,31] In the past, domestic ferrets were used to hunt rabbits in the United States; however, most states now prohibit this practice, primarily to protect native rabbit species.[16,25]

Ferrets were farmed for fur in North America in the early 1900s and even earlier in Europe.[16] Ferret fur farming was popular in New Zealand as late as the 1980s and still exists in a few areas of Northern Europe.[16,25] Ferret fur has also been used in artists' paint brushes.[25]

"Ferret-legging" is a type of English pub game in which two ferrets are placed into each competitors' trousers before the leg openings and waist are securely closed. The competitor who withstands the presence of the ferrets the longest is the winner.[16]

Because of their elongated, narrow body and willingness to travel through long, narrow tunnels, domestic ferrets have been used to string cable and wire through long stretches of conduit for the oil, aviation, and telephone industries.[16]

Ferrets have been used in biomedical research since the early 1900s, when they were used to study human influenza and other viral diseases, and are now widely used for experimental studies in numerous biomedical fields.[16,19,31] Ferrets are popular as research models because of their small size, high fecundity, biologic similarities to humans, and susceptibility to many human pathogens and diseases.[16,19,23,31,43]

Ferrets are popular as companion animals worldwide.[25] Domestic ferrets bred for today's pet market are docile, curious, intelligent, playful, and interactive with humans.[6,11,17] Their small size and relatively quiet nature makes them popular pets for smaller homes. Because of large-scale commercial breeding (eg, Marshall Farms Group Ltd., North Rose, NY), ferrets are readily available in pet stores in the United States. Commercially bred ferrets typically undergo surgical sterilization and anal sacculectomy and receive their initial canine distemper vaccination before shipment to pet stores. Ferrets are also available from small-scale commercial breeders and hobby breeders, but they may not have undergone surgical sterilization or anal sacculectomy before purchase.

Ferrets were banned in many states until the availability of a rabies vaccine licensed by the US Department of Agriculture for use in this species.[25] Ferret ownership is still prohibited or restricted in some cities and states, such as New York City and California, because of concerns regarding rabies exposure, attacks on people (particularly infants), and establishment of feral populations.[16,17] Such concerns are now less warranted due to the availability of a licensed rabies vaccine and to genetic selection and routine surgical alteration of ferrets. In the European Union, only domestic ferrets, cats, and dogs are eligible for pet passports and free travel among member countries, provided they are microchipped and current on rabies vaccination. Although keeping ferrets is popular in other parts of the world, ownership is restricted or prohibited in some areas to protect native wildlife.

ANATOMY AND PHYSIOLOGY

The basic anatomy and physiology of the domestic ferret is similar to that of other carnivores. The following is a brief review of clinically relevant features. Skeletal anatomy is depicted in Fig. 1.1, visceral anatomy in Fig. 1.2, and normal radiographic anatomy in Figs. 1.3 and 1.4. Selected physiologic values are detailed in Table 1.1. The reader is directed to other publications containing more extensive reviews of ferret anatomy and physiology.[10,12,15,23,48]

Integument

Coat

The pelage of the domestic ferret consists of long, coarse guard hairs and a fine, white to yellow undercoat, which results in excellent insulation.[10,26] There are no specific breeds of domestic ferrets; instead, ferrets are often classified according to the color and pattern of their coat (Fig. 1.5).[26] The two predominant varieties of domestic ferret are the fitch (also known as sable, or wild-type) and the albino.[19] Some of the color standards recognized by the American Ferret Association are sable (warm, deep brown), black, black sable, champagne, and albino (white guard hairs and unpigmented eyes). Some standardized patterns for white markings include mitt (white paws), panda (nearly completely white head), and blaze (white blaze from the forehead down the back of the neck). Other recognized color patterns include solid, standard, and point (with a distinct color difference between the color of the body and the points). The dark-eyed white is a combination of any solid white ferret with pigmented eyes. The color and pattern of the coat and mask can change over time. Ferrets living outdoors tend to be darker in color.[26]

Ferrets undergo a heavy shed in the spring and fall along with seasonal weight changes.[12] The coat may be shorter in summer months and longer in the fall, and lighter in color in the winter and darker in the fall.[12,26] Some intact females (jills) in estrus can become dramatically alopecic and completely lose the undercoat, exposing bare patches of skin.[12] Sexually altered ferrets of either sex have a less dramatic molt and color change. Warn clients that shaved fur may not regrow for weeks to months, and that before erupting, the fur may cause the skin to appear bluish. Regrown fur may have a different color or texture than surrounding fur.

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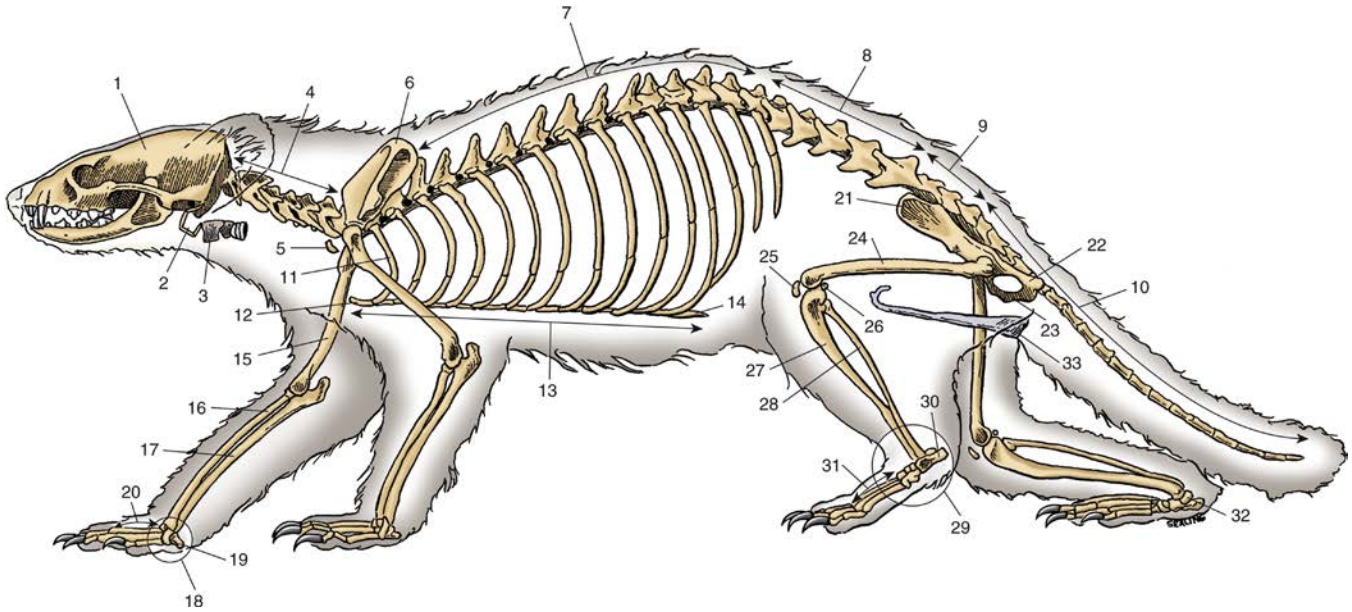


Fig. 1.1 Skeletal Anatomy of a Ferret *1,* Calvaria; *2,* hyoid apparatus; *3,* larynx; *4,* seven cervical vertebrae; *5,* clavicle; *6,* scapula; *7,* 15 thoracic vertebrae; *8,* five lumbar vertebrae; *9,* three sacral vertebrae; *10,* 18 caudal vertebrae; *11,* first rib; *12,* manubrium; *13,* sternum; *14,* xiphoid process; *15,* humerus; *16,* radius; *17,* ulna; *18,* carpal bones; *19,* accessory carpal bone; *20,* metacarpal bones; *21,* ilium; *22,* ischium; *23,* pubis; *24,* femur; *25,* patella; *26,* fabella; *27,* tibia; *28,* fibula; *29,* tarsal bones; *30,* calcaneus; *31,* metatarsal bones; *32,* talus; *33,* os penis. (Adapted from An NQ, Evans HE. Anatomy of the ferret. In: Fox JG, ed. *Biology and Diseases of the Ferret*. Philadelphia: Lea & Febiger; 1988:14.)

Skin and Associated Glands

Ferrets have very active sebaceous glands that produce a strong musky odor.[19] During the breeding season, intact ferrets have increased sebaceous secretions, resulting in a more intense odor, yellow to orange discoloration of the undercoat, and oily fur.[19] Ferrets lack sweat glands, making them very susceptible to heat prostration.[20,33]

Anal Glands

Ferrets have a well-developed pair of anal glands, which produce a serous yellow liquid with a strong odor. Frightened or threatened ferrets can express their anal glands but cannot project the fluid over long distances.[19,20] The anal glands typically measure 10 mm × 5 mm, and the ducts open into the anal canal at about 4 o'clock and 8 o'clock positions.[26] External anal sphincter muscle encloses each duct.[10,20,26] Although most of a ferret's odor arises from its sebaceous glands and not its anal glands,[19] domestic ferrets raised at large commercial breeding facilities in the United States are routinely descented between 5 and 6 weeks of age. This practice is being increasingly questioned on ethical grounds. Therefore, in other countries, and increasingly in the United States with small-scale breeders, ferrets may be descented later or not at all.

Gastrointestinal System

Teeth and Salivary Glands

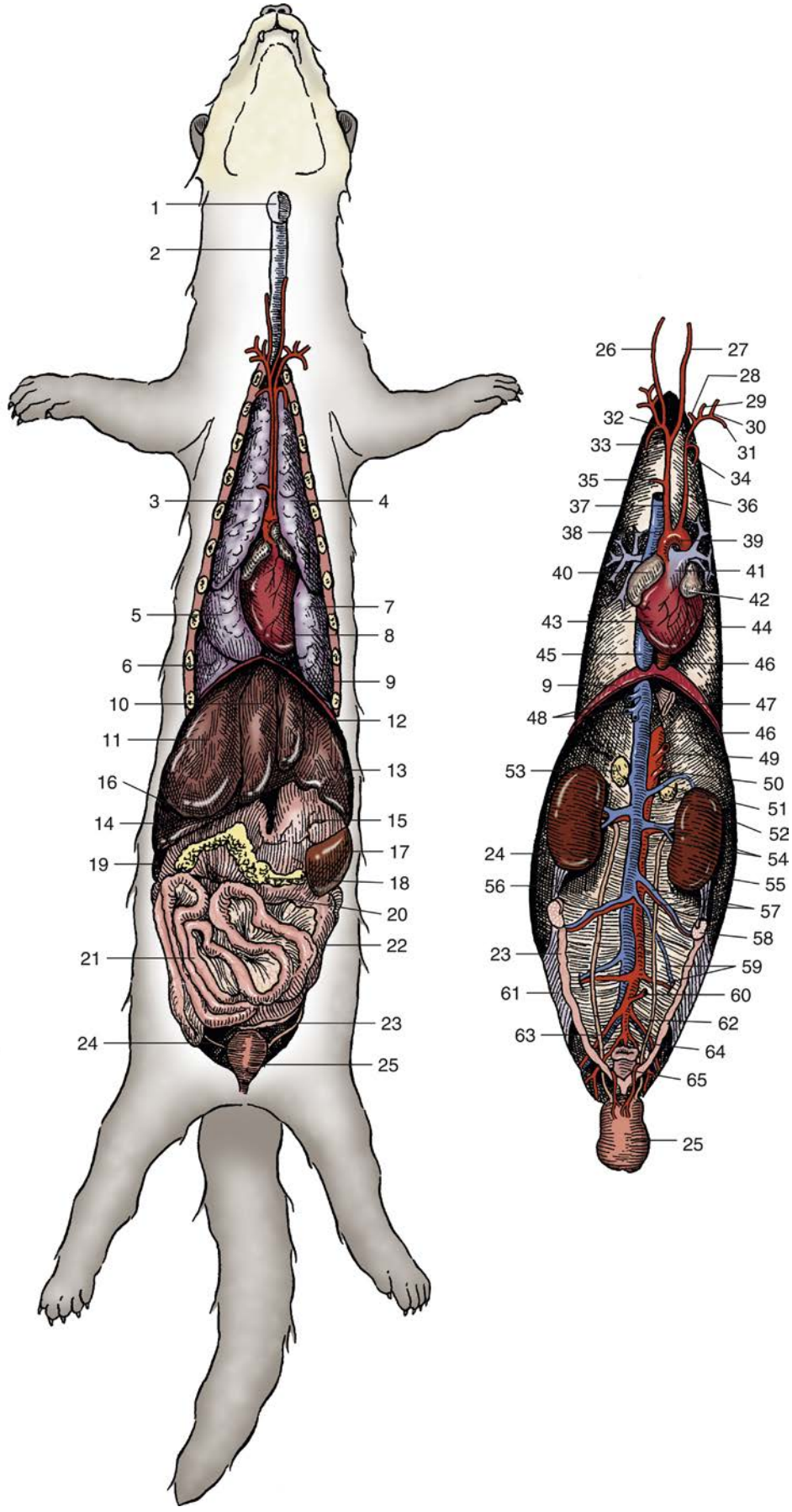
Ferret dentition is typical of carnivores, with long, curved canine teeth and shearing and crushing premolars and molars (See also Chapter 36). Permanent teeth erupt between 50 and 74 days of age.[31] Ferrets have 34 permanent teeth, and the dental formula of the adult ferret is $2(I^3_3\ C^1_1\ P^3_3\ M^1_2)$.[19,20,26,27] Note that ferrets have three rather than four premolars, and the maxillary carnassial tooth is likely the fourth premolar.[10] Incisors and canine teeth each have a single root. The premolars have one to two roots each, except for the carnassial tooth, which has three roots. The maxillary first molar and mandibular first molar have three roots, and the tiny mandibular second molar has only one root.[10,34] Supernumerary incisors are common.[4,19,26,34] Ferrets have five major pairs of salivary glands: the parotid, mandibular, sublingual, molar, and zygomatic glands.[10,20,26]

Esophagus, Stomach, and Intestines

Similar to the dog, the muscle of the ferret esophagus is striated along the entire length cranial to the diaphragm.[15,44] There is no true gastroesophageal sphincter, and ferrets are readily able to vomit.[20,26,27,38] Although domestic ferrets are popular experimental research models for the study of emesis, ferrets with gastrointestinal (GI) obstruction rarely vomit.[26] The ferret's simple monogastric stomach is similar in shape to that of the dog, consisting of the cardia, fundus, body, and pylorus.[10,19,26,31,38] The stomach contacts the diaphragm and left liver lobes cranially, the ascending colon dorsally, and the spleen and left pancreatic limb caudally.[38] The stomach is joined to the spleen by the gastrosplenic ligament and is separated from the papillary process of the caudate liver lobe by the lesser omentum.[10,38] A full stomach is readily palpable and displaces the intestines to the right.[26,27,38]

The small intestine is comparatively short; therefore the adult ferret has a comparatively short GI transit time of 3 to 4 hours.[5,10,20,27,38,40] The duodenum consists of three

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Fig. 1.2 (A) Ventral aspect of the viscera of a ferret in situ. (B) Anatomy of the viscera and most important blood vessels as seen after removal of the lungs, liver, and gastrointestinal tract. *1,* Larynx; *2,* trachea; *3,* right cranial lobe of lung; *4,* left cranial lobe of lung; *5,* right middle lobe of lung; *6,* right caudal lobe of lung; *7,* left caudal lobe of lung; *8,* heart; *9,* diaphragm; *10,* quadrate lobe of liver; *11,* right medial lobe of liver; *12,* left medial lobe of liver; *13,* left lateral lobe of liver; *14,* right lateral lobe of liver; *15,* stomach; *16,* right kidney; *17,* spleen; *18,* pancreas; *19,* duodenum; *20,* transverse colon; *21,* jejunoileum; *22,* descending colon; *23,* uterus; *24,* ureter; *25,* urinary bladder; *26,* right common carotid artery; *27,* left common carotid artery; *28,* vertebral artery; *29,* costocervical artery; *30,* superficial cervical artery; *31,* axillary artery; *32,* right subclavian artery; *33,* right internal thoracic artery; *34,* left internal thoracic artery; *35,* branch to thymus; *36,* left subclavian artery; *37,* brachiocephalic (innominate) artery; *38,* cranial vena cava; *39,* aortic arch; *40,* right atrium; *41,* pulmonary trunk; *42,* left atrium; *43,* right ventricle; *44,* left ventricle; *45,* caudal vena cava; *46,* aorta; *47,* esophagus; *48,* hepatic veins; *49,* celiac artery; *50,* cranial mesenteric artery; *51,* left adrenolumbar vein; *52,* left adrenal gland; *53,* right adrenal gland; *54,* left renal artery and vein; *55,* left kidney; *56,* suspensory ligament of ovary; *57,* left ovarian artery and vein; *58,* left ovary; *59,* left deep circumflex iliac artery and vein; *60,* caudal mesenteric artery; *61,* broad ligament of uterus; *62,* left external iliac artery; *63,* right common iliac vein; *64,* left internal iliac artery; *65,* rectum. (Adapted from An NQ, Evans HE. Anatomy of the ferret. In: Fox JG, ed. *Biology and Diseases of the Ferret*. Philadelphia: Lea & Febiger; 1988:14.)



Fig. 1.3 (A) Ventrodorsal radiograph of a 1-year-old, spayed female ferret. Note normal positioning of thoracic and abdominal viscera. (B) Same radiograph as (A): *1,* trachea (endotracheal tube within lumen); *2,* lung; *3,* cranial mediastinum; *4,* left primary bronchus; *5,* heart; *6,* liver; *7,* stomach; *8,* spleen; *9,* left kidney; *10,* urinary bladder; *11,* right primary bronchus; *12,* small intestine; *13,* right kidney. (Silverman S, Tell LA. *Radiology of Rodents, Rabbits, and Ferrets: An Atlas of Normal Anatomy and Positioning*. St. Louis: Elsevier Saunders; 2005:233.)

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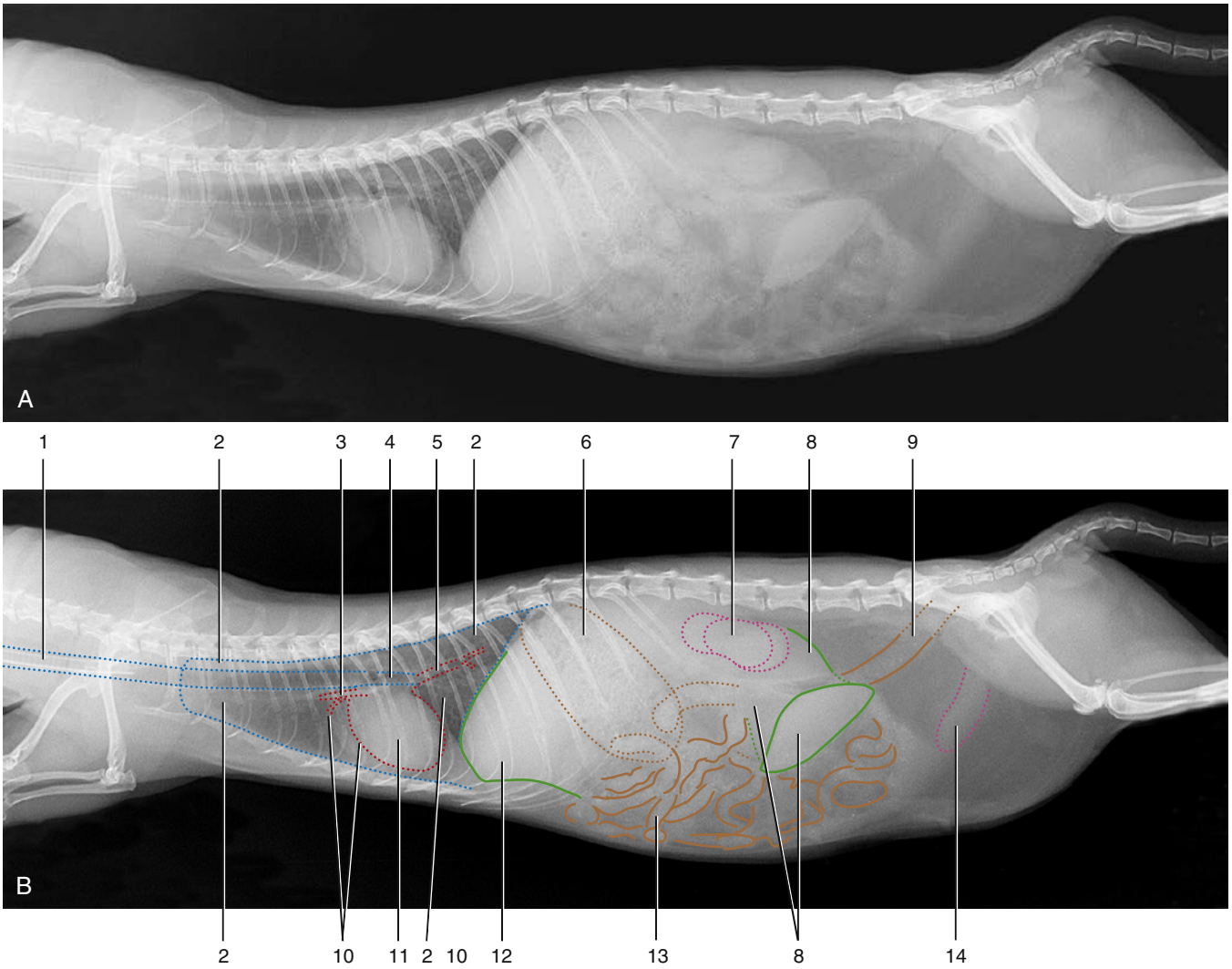


Fig. 1.4 (A) Lateral (right lateral recumbency) radiograph of a 1-year-old, spayed female ferret. Note normal positioning of thoracic and abdominal viscera. (B) Same radiograph as (A): *1,* trachea (endotracheal tube within lumen); *2,* lung; *3,* pulmonary vasculature; *4,* bronchus; *5,* pulmonary vein; *6,* stomach; *7,* kidney; *8,* spleen; *9,* colon; *10,* intrathoracic adipose tissue; *11,* heart; *12,* liver; *13,* small intestine; *14,* urinary bladder. (Silverman S, Tell LA. *Radiology of Rodents, Rabbits, and Ferrets: An Atlas of Normal Anatomy and Positioning.* St. Louis: Elsevier Saunders; 2005:232.)

portions: the shorter, sigmoid-shaped cranial portion; the descending portion, in contact with the right kidney caudally; and the ascending portion.[38] A hairpin turn separates the descending and ascending portions. The mesoduodenum encloses the right limb of the pancreas and a portion of the lesser omentum.[10] The jejunum and ileum are macroscopically indistinguishable, creating a jejunoileum.[20,38] The ferret lacks a cecum, ileocecal valve, and appendix; therefore the ileocolic junction is indistinct and is typically defined as the region where the ileojejunal and colic arteries join.[20,27,38] The jejunoileal mucosa is flat, whereas the colonic mucosa forms longitudinal folds.[38] The large intestine consists of the colon (with ascending, transverse, and descending regions), rectum, and anus.[10,38]

Liver, Gallbladder, and Pancreas

The ferret's liver is relatively large and consists of six lobes: left lateral, left medial, right lateral, right medial, quadrate, and caudate.[10,20,26,27] The gallbladder lies between the quadrate and right medial lobes and measures approximately 2 cm by 1 cm.[10,20,26] Although variable in pattern, the cystic duct usually joins the left, right, and central hepatic ducts to form the common bile duct.[10]

The pancreas is V-shaped and divided into right and left lobes connected by a body that lies close to the pylorus and is contained within the mesoduodenum.[10] The left lobe extends along the dorsal caudal stomach and medial to the spleen, and the right lobe follows the descending duodenum. Ducts from the left and right lobes connect to form the common pancreatic

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TABLE 1.1 Selected Biologic Values for the Domestic Ferret[15,19,20,26,45]

Parameter	Sex	Value
Body weight	Intact male (hob) Intact female (jill) Neutered, both sexes	1–2 kg 0.6–0.95 kg 0.8–1.2 kg
Life expectancy		5–11 years
Rectal temperature		Mean 101.8°F [38.8°C] (Range 100°–104°F [37.8°–40°C])
Heart rate		200–400 beats/min
Blood volume	Male Female	60 mL 40 mL
Noninvasive blood pressure (high-definition oscillometry, n = 63; sedated with 0.2 mg/kg butorphanol and 0.2 mg/kg midazolam)[45]		Systolic: 95–155 mmHg Diastolic: 51–87 mmHg Mean: 69–109 mmHg
Respiratory rate		33–36 breaths/min
Tidal volume		10–11 mL/kg
Stomach capacity		50 mL/kg when distended
Gastrointestinal transit time		2.5–3.6 hours (meat); liquids may reach rectum within 1 hours
Urinary output		1 mL/h (range 0.33–5.8 mL/h)
Bladder capacity		Approximately 5 mL/kg (higher under increased pressure)
Urine pH		6.5–7.5
Puberty	Male Female	9 months (as early as 23 wk with photoperiod manipulation) 8–12 months (as early as 16 wk with photoperiod manipulation)
Reproductive life span	Male Female	Throughout life 2–5 years
Gestation		41 days (range 39–42 days)
Litter size		8 kits (range 1–18 kits)
Birth weight		6–12 g
Eyes and ears open		28–34 days
Weaning age		6–8 weeks
Water intake		75–100 mL/d
Maintenance fluid needs		Unknown, estimated at 60 mL/kg/day
Maintenance caloric needs		200–300 kcal/kg/day

duct that joins the bile duct before opening into the duodenum about 3 cm caudal to the cranial duodenal flexure at the major duodenal papilla.[10,38] The minor duodenal papilla is often absent in ferrets.[38]

Urogenital System

Kidneys, Ureters, and Urinary Bladder

The ferret's kidneys are retroperitoneal and average 2.4 to 3.0 cm in length, 1.20 to 1.35 cm in width, and 1.10 to 1.35 cm in thickness.[10] The cranial margin of the right kidney sits in a fossa of the caudate lobe of the liver.[10] The ureters pass from the renal pelvises and extend caudally along the ventral aspect of the psoas muscle, entering the dorsolateral urinary bladder just caudal to its neck.[10] The urinary bladder sits ventrally in the abdomen just cranial to the pelvic inlet. Although the bladder is small, it can easily hold 10 mL of urine at low pressure.[20,48]

Male Reproductive Tract

The reproductive tract of the intact male (hob) ferret resembles that of the dog, with a palpable os penis.[19,20] Unlike the dog, however, the tip of the os penis is J-shaped, making urethral catheterization somewhat challenging (see Chapter 2).[20] The preputial opening lies just caudal to the umbilical area along the ventral abdomen. The scrotum lies just caudal to the os penis.[10] The prostate gland is the single accessory reproductive gland in male ferrets. It completely surrounds the proximal urethra and measures approximately 1.5 cm by 0.6 cm.[10,21] Each ductus deferens opens into the urethra at the level of the prostate gland.[10]

Female Reproductive Tract

The reproductive tract of the jill closely resembles that of other carnivores, containing two long uterine horns, a short uterine body, and a single cervix.[10,20,41] Paired ovaries are located just caudal to the kidneys. Each ovary attaches to the abdominal wall by the suspensory ligament cranially and to the uterine horn by the proper ligament caudally. The uterus is suspended by the broad and round ligaments. The urethra opens into the vaginal floor.[10] The vulva is located in the perineum ventral to the anus. In the nonestrous jill, the urogenital opening appears as a small slit. During estrus or with adrenocortical disease, the vulva can swell considerably and resemble a pink doughnut. Both female and male ferrets have three to five pairs of nipples.[19,20]

Cardiovascular and Lymphatic Systems

Heart and Major Blood Vessels

The ferret's heart lies in the caudal thoracic cavity, between the sixth and eighth ribs, with the apex to the left.[20,26,27] The cardiodiaphragmatic ligament can contain varying amounts of fat,[20] causing the cardiac silhouette to lift dorsally from the sternum on a lateral radiographic projection. A single brachiocephalic artery exits the aorta just proximal to the left subclavian artery; at the level of the thoracic inlet, it divides into the right and left common carotid arteries and the right subclavian artery.[10,27] This anatomic variation is believed to aid cerebral blood flow during extreme head and neck rotations.[51]

Lymphatic Structures

The thymus is located in the cranial mediastinum and can vary in size with age.[10] The mediastinum is believed to be complete in ferrets, and it contains mediastinal lymph nodes.[20] The palatine tonsil is a flattened, ovoid structure that can be seen lateral to

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Fig. 1.5 Examples of Various Colors and Patterns of the Domestic Ferret (A) Albino. (B) Sable. (C) Dark-eyed white. (D) Blaze. (Photography subjects for Fig. 1.5A–B provided by J. Ball. Photography subjects for Fig. 1.5C–D provided by P. Ogle.)

the ventral sulcus of the soft palate during a thorough oral examination.[10,20] The mandibular lymph node lies just rostral to the mandibular salivary gland and can easily be confused with this structure. The abdominal cavity has several major lymph nodes, including a prominent, palpable node at the root of the mesentery that can be mistaken for a mass or foreign body on exam.[10,37]

The spleen, which normally measures 5.1 cm × 1.8 cm, lies in the left hypogastric region and parallels the greater curvature of the stomach.[10] Splenic size reportedly increases slightly as ferrets age.[47] When enlarged, the spleen can extend diagonally from the upper left to the lower right abdomen, crossing the midline. Splenic size can increase dramatically with use of certain anesthetics from splenic sequestration of blood; this may result in a reduced hematocrit.[30] Splenomegaly is common in ferrets and is associated with benign extramedullary hematopoiesis of undetermined origin, as well as numerous disease conditions.[20,30] Use caution when palpating an enlarged spleen, as iatrogenic splenic rupture has been reported in ferrets.[49]

Respiratory System

The lungs are comparatively long in ferrets and have a filling capacity of about three times the predicted value for body size.[19,27,46] The right lung is divided into cranial, middle, caudal, and accessory lobes, whereas the left lung has a cranial and caudal lobe.[10,19,20,26, 27] Pinpoint yellow foci on the lung surface are typically foci of alveolar histiocytosis, the significance of which is unknown.[19] The trachea is wide and very long, bifurcating at the fifth intercostal space.[20]

Endocrine System

Adrenal Glands

An adrenal gland is embedded in fat and covered by peritoneum near each kidney.[10] Each gland lies ventral to the ipsilateral adrenolumbar artery. The right gland lies in close apposition to the caudal vena cava and is draped by the caudate lobe of the liver. Adrenal gland length in female ferrets is 5.0 to 10.0 mm for both glands, whereas in males, measurements are 7.0 to 10.5 mm for the left gland and 7.5 to 13.5 mm for the right. Blood is supplied to the adrenal glands from the renal artery, with branches arising directly from the aorta, as well as the right adrenolumbar artery for the right adrenal gland.[18] Accessory adrenal tissue can occasionally be found.[10,20]

Thyroid and Parathyroid Glands

The thyroid gland is located ventrally along the neck, with each lobe positioned lateral to the trachea between the third

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and eleventh tracheal rings.[10,20] The parathyroid glands are small pinkish structures that lie along the medial surface of the cranial thyroid, contacting the fourth to fifth tracheal ring.[10,20] The glands may be paired or occasionally single on either side.[10]

Musculoskeletal System

The ferret's skeleton is lightweight but very flexible and strong.[10,27] The vertebral formula is C7, T15 (14), L6 (5 or 7), S3, Cd18.[10,20,27] The thorax is comparatively large with a narrow thoracic inlet and small first ribs.[10,26,27] There are 15 pairs of ribs (occasionally 14), the first 10 of which are attached to the sternum and the last 5 comprising the costal arch.[10,27] The spine is very flexible, facilitating 180-degree turns in a narrow passage. Despite having short legs, ferrets can climb remarkably well. Each foot has five digits with nonretractable claws.[19]

Neurologic System and Special Senses

Brain and Spinal Cord

The ferret brain has a typical mammalian design, which resembles that of other carnivores.[23] The cerebral cortex is folded into several gyri and sulci, unlike many rodent species used as research models.[23] The ferret's spinal cord and peripheral nerves are similar to those of other carnivores.[20] The cauda equina begins at about the level of the last lumbar vertebra.[20]

Special Senses

Vision. The ferret eye appears to be less well developed than in other carnivores, including other mustelids such as mink.[50] The ferret is adapted to nocturnal living, and its eyesight is relatively poor compared to its olfactory and auditory senses.[27,50] However, the ferret is a skilled hunter and can track rapid object movements in the range of 25 to 45 cm/sec. Ferrets appear to track moving objects with movements of the head rather than pronounced ocular movements.[11,20] The eyes are widely spaced, allowing for a field of view of about 270 degrees.[50] The eye has a prominent third eyelid, proportionately large cornea, horizontal elliptical pupillary opening, and large, spherical lens.[27,32,50] Dorsal and ventral nasolacrimal puncta are present, although the dorsal punctum is smaller.[20] The retina is similar to that of the dog, and pigmented ferrets have a well-defined tapetum lucidum.[50] Ferrets have scotopic (dim-light) vision, and the retina is primarily comprised of rods.[50] Ferrets are believed to have limited color discrimination at best.[20,27,32] Albino ferrets have impaired motion perception and contrast sensitivity.[31]

Hearing. The structure of the middle and inner ear is similar to that in the dog, although the ferret lacks a distinct tubular ear canal.[27] Auditory function in the ferret is similar to that in the cat, although the auditory response may be more primitive.[27,35] The hearing range is about 20 Hz to 44 kHz.[50] Ferrets with white markings, such as pandas and blazes, are prone to deafness associated with a congenital Waardenburg-like syndrome.[39]

Taste and Olfaction. Ferrets rely extensively on their sense of smell.[27] Domestic ferrets appear to develop their olfactory and taste preferences for food items during the first few months of life, which may explain why diet changes in pet adult ferrets can be quite challenging.[2,11] Feeding kits a variety of foods during their first 6 months of life may help broaden dietary selectivity later in life.[11]

PHYSIOLOGY AND REPRODUCTION

Life Expectancy and Physiology

Ferrets typically live about 6 to 8 years but can occasionally live as long as 11 to 12 years.[12,31] Normal physiologic values of the domestic ferret are presented in Table 1.1.

Body Size and Seasonal Weight Variation

Domestic ferret kits weigh approximately 6 to 12 g at birth and around 300 to 450 g at weaning.[12] Ferrets typically reach adult size by 6 months of age.[12] Normal adult weights are 1 to 2 kg for hobs and 0.6 to 1 kg for jills.[27,29,41] If ferrets are surgically altered before weaning, females (sprites) tend to become comparatively larger and males (gibs) comparatively smaller, with weights of 0.8 to 1.2 kg for the two sexes. Gibs lack the pronounced muscular neck and shoulders characteristic of hobs. Ferrets tend to gain weight as winter approaches and lose weight in the spring, with seasonal weight fluctuation approaching 40% in some individuals.[12,19,20] This weight variability is far less pronounced in surgically altered animals and those living indoors under altered photoperiods.

REPRODUCTION

Jills become sexually mature at 8 to 12 months of age, usually during the first spring after birth, whereas hobs reach puberty at about 9 months of age.[12,19,28,41] Ferrets are seasonally polyestrous, requiring alternating periods of long and short days for a normal reproductive cycle.[12,19,28] In both sexes, fertility increases as the days get longer. Spermatogenic activity in the hob occurs from December to July, during which testicles enlarge.[12] If not bred, jills may remain in persistent estrus from late March into early August, although this depends on the geographic area.[12,28,41] To an inexperienced observer, copulation appears violent, with the hob biting and dragging the jill by the neck.[19,41] A receptive jill will remain limp and not fight back. For successful mating, it is suggested to wait until the jill has been in estrus for 10 days before placing her with the hob. The jill and hob can be left together for up to 48 hours or can be bred for shorter periods on 2 consecutive days.[28,37] Jills are induced ovulators, requiring neck restraint and intromission, and ovulation generally occurs 30 to 36 hours after copulation.[12,19,28,41] If ovulation is not induced mechanically or chemically, the jill may remain in estrus until the photoperiod changes. Prolonged estrus carries the risk of severe anemia and thrombocytopenia because of bone marrow suppression caused by persistent hyperestrogenism.[27,42] In one report, 55% of jills with prolonged estrus were thrombocytopenic, and the mortality rate reached about 40%.[42]

Gestation length in the ferret is 39 to 42 days. In the absence of fertilization, a pseudopregnancy of 40 to 42 days may result.[12,19,20,28] The typical litter size is 8 to 18 kits, although litters of 20 kits have been recorded.[26] Kits are born blind and deaf with a thin coat of white fur.[12,19,28] Jills raise the kits alone. Kits

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begin eating soft food by 21 days of age, often before their eyes open, and are generally weaned by 6 to 8 weeks of age.[12,19,27]

BEHAVIOR

Domestic ferrets are highly social and often enjoy playing, exploring, and sleeping with other ferrets. Their play is often very rough and can resemble true aggression. Ferrets tend not to form social hierarchies, although they may fight with each other, especially when introduced to a new ferret.[6,7,11] They are highly inquisitive and show little fear of heights or open spaces.[11]

Ferrets typically engage with humans and do not normally show fear of people or unfamiliar objects.[8,11] They generally do not bite unless they are in pain or fear or are overstimulated or poorly socialized.[6,11] However, ferrets are natural predators, so keep them away from rodents, birds, and other small animals.[7]

Domestic ferrets generally adapt to diurnal living and normally sleep 12 to 16 hours a day.[6,11] They often sleep quite soundly and require several minutes to awaken, particularly older ferrets and those with hypoglycemia associated with insulinoma.[6,11] Ferrets are usually quiet but can produce vocalizations such as the "dook," "buck-a-buck," or "chuckling," the most common sound.[6,7,11,44] The low- or high-pitched sound generally signifies excitement or pleasure. Other sounds include hissing (a sign of displeasure), screaming (a sign of fear or pain), and barking, or chirping.[6,7,11] The "weasel war dance," signifying pleasure and excitement, consists of a ferret jumping in the air and moving quickly from side to side or flipping or rolling, frequently "dooking."[6,7,11,44] Tail piloerection, or "bottle brush tail," can occur when a ferret is afraid, angry, or excited. It can also appear during vaccine-induced anaphylaxis.[11]

Ferrets are easily litter box trained and defecate frequently. They often prefer to eliminate in corners and may not use a litter box if it is not perfectly clean.[7,11,47] Ferrets also enjoy digging and caching objects and food in dark, enclosed spaces.[7,11]

HUSBANDRY

The following discussion of husbandry is a brief overview of the keeping of ferrets as pets. Details on the care of ferrets under research conditions are published elsewhere. [13,24,31,47]

Housing

Most domestic ferrets kept as pets are housed indoors, although some are allowed time outdoors, and some hunting ferrets are kept outdoors.[24] Although outdoor housing may allow enrichment opportunities and exposure to natural light, ferrets housed outdoors are at increased risk of escape, injury, predation, exposure to temperature extremes, and infectious diseases, such as rabies and heartworm disease. [13,17,24] Ferrets are adapted to temperate climates; therefore avoid temperatures above 86°F (30°C).[24] Provide a heated shelter in climates where temperatures drop below freezing. Detailed plans for outdoor enclosures for ferrets are published elsewhere.[24]

Wire cages provide good ventilation and are comparatively easy to clean, but bar spacing must be less than 1 inch (2.5 cm) to prevent escape. Wooden cages are challenging to keep clean but can be lined with waterproofing such as vinyl or linoleum. Do not house ferrets in glass aquariums, which do not allow for proper ventilation.[13,47]

Provide ferrets with dark areas for sleeping and retreat.[47] Access to a dark, enclosed area can reduce stress in a hospitalized ferret. Use cloth sacks and tubes, pillow cases, and towels for this purpose.[17] Slings, hammocks, and cage shelves are also popular.[17] If a ferret ingests fabric, use cardboard, plastic, or wooden boxes. Although many ferrets prefer sleeping together, provide at least one sleep area for each ferret in multi-ferret enclosures.[17]

Ferrets require access to litter boxes in the main enclosure and all play areas. Because ferrets often back into corners to eliminate, plastic corner litter boxes with tall rear sides are useful. Ferrets occasionally ingest litter, so use pelleted paper instead of clay or clumping litters.

Ferrets allowed to explore the home environment risk injury, escape, electrocution, foreign body ingestion, and poisoning, so monitor them closely and "ferret proof" all areas.[17] Ferrets can escape through small holes and ventilation ducts. They love to chew rubber and foam and enjoy burrowing in mattresses and furniture, so cover undersides of couches, chairs, and mattresses with wire mesh or a thin sheet of wood.[17] Remove plastic, foam, and rubber items—e.g., soft dog and cat toys, elastic bands, headphones, ear buds, erasers, and athletic shoes—from the environment. Also, avoid using reclining and rocking chairs around exploring ferrets.

Environmental Enrichment

Ferrets benefit from regular time out of the primary enclosure to play and explore. They enjoy burrowing and playing in tunnels, tubes, and dryer hoses.[31,47] Boxes filled with sterile soil or sand or other materials can stimulate natural digging behaviors.[31,46] Ferrets also enjoy climbing stairs and ramps, and some ferrets even enjoy playing in water.[47]

Popular enrichment objects include boxes, paper bags, crumpled paper balls, hard plastic or polyvinyl chloride pipes, fabric tubes, and rigid plastic toys. Boxes can be filled with biodegradable packing peanuts, rice, crumpled paper balls, or small solid plastic balls.[31] Ferrets especially like toys that move or make noise. Rotate enrichment items to avoid habituation.[47] Applying food scents or safe essential oil scents on toys can transform them into "new" items.

Wild mustelids spend a large percentage of their time exploring and foraging.[47] Provide a variety of foods and delivery methods as enrichment for domestic ferrets. Hide food items in objects and place them in different locations. Some ferret owners even feed whole prey diets, in part, to allow for natural feeding behavior.[47]

Positive-reinforcement training may strengthen the ferret–human bond and provide the ferret with mental stimulation.[17] Food can serve as a training reward if the ferret accepts treats.

NUTRITION

As obligate carnivores, ferrets naturally eat whole, small prey animals, including small to medium-sized mammals, birds,

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eggs, amphibians, reptiles, crustaceans, fish, worms, and insects.[14,17,31] Polecats cache their kill in the den, eating small frequent meals rather than gorging.[3] Ferrets have minimal gut flora, so they cannot digest fiber or efficiently metabolize carbohydrates. In general, they tolerate antibiotic administration without gastrointestinal upset.[3,17] Remember to expose juvenile ferrets to a variety of foods to promote dietary flexibility as adults.

The ferret's exact nutritional requirements are unknown, so most formulations rely on requirements for mink or cats.[12,31] A whole-prey or balanced fresh or freeze-dried carnivore diet is most appropriate. If an owner does not want to feed a 100% whole-prey diet, consider giving an occasional whole mouse or chick as environmental enrichment. Stools of ferrets on a whole-prey diets are firm and have a low volume and odor, whereas ferrets eating dry kibble produce formed stools that are soft and voluminous and may contain undigested grain.

Nevertheless, the most common diet fed to pet ferrets is dry kibble. Kibble is harder than natural food items, and ferret teeth wear down after long periods of consuming kibble. The wear pattern can even be exacerbated when ferrets selectively chew kibble in specific areas of the mouth.[9] However, commercial soft diets or diets based on lean meat can predispose ferrets to periodontitis.[1,22,34]

With any ferret diet, ensure that crude protein levels are 30% to 35% and fat content is 15% to 20%.[51] A diet of 35% protein and more than 20% fat is recommended for reproduction and growth.[3,12] Protein should consist of high-quality meat sources instead of grains or other vegetable matter such as pea protein. High levels of plant proteins can result in urolithiasis and do not meet a ferret's amino acid requirements.[3,14] Although it is not known whether taurine is an essential amino acid for ferrets, commercial diets are supplemented with taurine and vitamins to account for losses during processing.[14] A good-quality cat food that meets protein and fat requirements for ferrets can generally suffice for maintenance, but it may not be adequate for demanding life stages.[14]

Fat supplements containing omega-3 oils, fish oils, or meat fat should only be used in very small amounts or given as occasional treats or rewards. Foods to supplement kibble include fresh human-grade raw organ or muscle meat and raw egg. Although cooking meat or eggs may not be necessary if they are fresh and suitable for human consumption, raw or undercooked foods may carry *Salmonella* species, *Campylobacter jejuni,* or *Escherichia coli*. Adding a small amount of high-quality canned cat food can provide variety. Dairy products can be used as fat and protein supplements but may cause soft stools in some ferrets. Many ferrets like sweets, a fact that pet food companies may exploit by producing sugar-coated grain treats. Avoid these products, which may predispose to, or at least exacerbate, insulinoma. Similarly, although ferrets enjoy fruits, give them only occasionally and in very small amounts or not at all.

A good dietary strategy is to offer a variety of food items throughout a ferret's life, including a minimum of weekly whole-prey foods, daily high-quality ferret kibble, and small amounts of high-quality canned cat food or other meat-based treats fed two or more times a week. Offer dry kibble two or three times a day, and vary the times and locations of feeding. Provide water at all times in either sipper bottles or heavy crock-type bowls.[31] Adult domestic ferrets drink approximately 75 to 100 mL of water daily.[31] Many ferrets love to play in water, so use bowls that are not easily overturned.[31] Do not add supplements to a ferret's water supply.

Intact ferrets on a natural photoperiod normally increase their food intake by 30% in the winter and reduce their intake in the spring.[22] This pattern is less marked in neutered ferrets or ferrets on artificial photoperiods. Do not fast ferrets for more than 3 hours. Ferrets older than 3 years are prone to develop insulinoma, and a longer fast could result in a serious hypoglycemic episode.

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2

Basic Approach to Veterinary Care of Ferrets

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The approach to preventative medicine and basic veterinary care in ferrets is very similar to that used in dogs and cats. Special equipment needs are minimal, and pet ferrets can be easily incorporated into a general small animal practice. However, there are unique aspects of handling, restraint, and clinical and treatment techniques used in ferrets. For procedures not discussed here, modify techniques used in other small animals by using instrumentation appropriate for the ferret's small size and choosing appropriate sedation or anesthesia to facilitate the procedure while minimizing stress or discomfort in the ferret.

RESTRAINT AND PHYSICAL EXAMINATION

Restraint

Most ferrets are docile and can be easily examined without assistance. However, an assistant is usually needed when taking the rectal temperature, when administering injections or oral medications, or if an animal tends to bite. Young ferrets often nip, and nursing females and ferrets that are handled infrequently may bite. Ferrets often bite without warning. Therefore always ask the owner if the ferret bites before handling it and take precautions accordingly. Obtain the rabies vaccination history before physical examination. Be aware that rabies protocols for animal bites from vaccinated and unvaccinated ferrets differ by locale. Ferrets that are prone to biting and are not currently vaccinated for rabies may need to be sedated for procedures requiring restraint.

Depending on the ferret's disposition, several basic manual restraint methods can be used for examination. For tractable animals, lightly restrain the ferret on the examination table. Examine the mucous membranes, oral cavity, head, and skin. Then pick the ferret up and support its body with one hand while using the other hand to auscultate the thorax and palpate the abdomen. For an active animal or one that bites, scruff the ferret and suspend it with all four legs off the table (Fig. 2.1). Most ferrets become relaxed with this hold, and the veterinarian can examine the oral cavity, head, and body; palpate the abdomen; vaccinate; and clean the ears. However, even scruffing may not work for fractious animals. To restrain a ferret for a procedure, hold it firmly by the scruff of its neck and around the hips without pulling the legs back. Most ferrets struggle if their legs are extended by pulling on the feet. Some animals can be distracted during a procedure by feeding a meat-based canned food or a small amount of a supplement such as FerreTone (8-in-1 Pet Products, Islandia, NY) by syringe. For very fractious or anxious animals or for procedures requiring lengthy restraint, light sedation or anesthesia may be indicated (see Chapter 37).

Physical Examination

Most ferrets strenuously object to having their temperature taken with a rectal thermometer, and a temperature taken after a ferret struggles may be artificially high. Therefore measure the rectal temperature early in the physical examination with a

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Fig. 2.1 Restrain an active ferret by scruffing the loose skin on the back of the neck. The ferret will relax and allow you to palpate the abdomen or administer a vaccine.

flexible digital thermometer that is well lubricated. The normal rectal temperature of a ferret is 100.5°F to 102.5°F (38.0°C to 39.2°C); however, a mean of 102°F (38.8°C), with a wider range of 100°F to 104°F (37.8°C to 40.0°C), is also reported.[22]

Physical examination of a ferret can be performed quickly and efficiently if a few simple guidelines are followed. Observe the attitude of the animal. Ferrets may sleep in the carrier in the veterinary office; however, once awakened for the examination, a ferret should be alert and active. Assess hydration by observing the skin turgor of the eyelids, tenting of the skin at the back of the neck, and moistness of the oral mucous membranes. Note that skin turgor can be difficult to evaluate in a cachectic animal. Estimate the capillary refill time by digitally pressing on the gingiva.

Examine the eyes, nose, ears, and facial symmetry. Cataracts can develop in both juvenile and adult animals. Retinal degeneration occurs in ferrets and may be indicated by abnormal pupil dilation. Inspect for nasal discharge, and ask the owner about any history of sneezing or coughing. The ears may have a brown waxy discharge, but excessive brown exudate may indicate infestation with ear mites. Observe the facial symmetry. Although uncommon, salivary mucoceles occur in ferrets and present as a unilateral swelling on the side of the face, usually in the cheek or temporal area (see Chapter 3).

The teeth should be clean and the gingiva pink. Dental tartar is common in pet ferrets, possibly related to feeding kibble instead of natural prey.[13] Plaque buildup may be exacerbated by feeding a diet with a high mineral content.[26] Remove excess dental tartar by prophylactic techniques used in dogs and cats, and recommend measures to prevent tartar buildup. A pet toothpaste can be used to decrease the rate of calculus formation.[26,28,38] Gingivitis is a common sequela of excessive dental tartar. Ferrets often break off the tip of one or both canine teeth, and the broken tooth may appear dark. However, ferrets rarely exhibit sensitivity associated with a fractured canine. If the ferret exhibits sensitivity when the tip of the canine is probed, recommend a root canal or extraction, depending on the degree of tooth damage (see Chapter 36). Bruxism often indicates gastrointestinal discomfort.

Palpate the submandibular, axillary, popliteal, and inguinal lymph nodes. Nodes should be soft and may sometimes feel enlarged in overweight animals because of surrounding fat. Any firmness or asymmetry warrants fine-needle aspiration or biopsy. If two or more nodes are enlarged and firm, a diagnostic workup is indicated.

Auscultate the heart and lungs in a quiet room. Ferrets have a rapid heart rate (180 to 250 beats/min) and often a pronounced sinus arrhythmia. If a ferret is excited and has a very rapid heart rate, subtle murmurs may be missed. Valvular disease, cardiomyopathy, and congestive heart failure are seen in ferrets, and any murmur or abnormal heart rhythm should be investigated further (see Chapter 5). The ferret's normal respiratory rate is 33 to 36 breaths/min (see Chapter 6).

Palpate the abdomen while either scruffing the ferret or supporting it around the thorax with one hand. This allows the abdominal organs to displace downward, facilitating palpation. If the history is consistent with an intestinal foreign body or urinary blockage, palpate gently to avoid causing iatrogenic injury, such as a ruptured bladder. Palpate the cranial abdomen, paying attention to the presence of gas or any firm, irregularly shaped material in the stomach area, especially in ferrets with a history of vomiting, melena, or chronic weight loss. The spleen is often enlarged, which may or may not be significant, depending on other clinical findings (see Chapter 5). A very enlarged spleen may indicate systemic disease or, very rarely, idiopathic hypersplenism, and further diagnostic workup is warranted.

Examine the genital area, observing the size of the vulva in females. Vulvar enlargement in a spayed female is consistent with either adrenal disease or an ovarian remnant; the latter is rare. Examine the preputial area and size of the testicles of male ferrets; preputial and testicular tumors are sometimes seen.

Check the fur for evidence of alopecia. Tail tip alopecia is common and may be an early sign of adrenal disease. Symmetric, bilateral alopecia or thinning of the fur that begins at the tail base and progresses cranially is a common finding in ferrets with adrenal disease. Examine the skin on the back and neck for evidence of scratching. Pruritus is common with adrenal disease and also may indicate ectoparasites (e.g., fleas or *Sarcoptes scabiei*). Palpate and visually examine the skin thoroughly for masses. Mast cell tumors are common and are variable in size. Often, the fur around a mast cell tumor is matted with dried blood from the animal's scratching. Other types of skin tumors, such as sebaceous adenomas and basal cell tumors, are also common (see Chapter 9). Perform an excisional biopsy of any lump found on the skin.

PREVENTIVE MEDICINE

Young, recently purchased ferrets need serial canine distemper vaccinations until they are 14 weeks of age.[3] Rabies vaccines should be given annually beginning at 3 months of age.[14] Ferrets should be examined annually until they are 4 to 5 years

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of age; then, older animals may need examinations twice yearly because of the high incidence of metabolic disease and neoplasia. Annual blood tests are recommended for older animals. Measure the blood glucose concentration twice yearly in healthy middle-aged and older ferrets; more-frequent monitoring is needed in ferrets with insulinoma. Abdominal ultrasound scanning or an endocrine panel is indicated in ferrets with thinning fur on the tail or other clinical signs suggestive of adrenal disease (see Chapter 7). Testing for infectious diseases may be warranted, especially in new or young ferrets that will be introduced into a multi-ferret household or those that are taken to ferret shows. Ferrets can be tested for Aleutian disease virus and ferret enteric coronavirus by polymerase chain reaction testing (Michigan State University, Diagnostic Center for Population and Animal Health, www.animalhealth.msu.edu; Veterinary Molecular Diagnostics, www.vmdlabs.com; Zoologix, www.zoologix.com). Serologic tests for Aleutian disease by enzyme-linked immunosorbent assay (ELISA) and counterimmunoelectrophoresis are also available (see Chapter 5).

Vaccinations

Canine Distemper

Ferrets must be vaccinated against canine distemper virus (CDV). Currently, one vaccine is approved by the U.S. Department of Agriculture for use in ferrets: PureVax Ferret (Boehringer Ingelheim Animal Health, Duluth, GA). PureVax is a canarypox-vectored recombinant vaccine that does not contain complete CDV or adjuvants; thus, post-vaccination risks are reduced. This product has a wide safety margin and has proved effective in protecting ferrets against CDV.[69] Although supply from the manufacturer has been intermittently problematic in the United States, the vaccine is available.

Canine distemper vaccines that were previously used in ferrets but are now discontinued include Fervac-D (United Vaccines, Inc, Fitchberg, WI), a modified-live virus vaccine propagated in avian cell lines, and Galaxy D (Schering-Plough Animal Health/Merck), a modified-live virus vaccine derived from the Onderstepoort canine distemper strain and attenuated in a primate cell line. Galaxy vaccines are now marketed under the Nobivac (Merck Animal Health, Madison, NJ) trade name. In a safety and efficacy study, Galaxy D proved effective in preventing canine distemper in young ferrets challenged after serial vaccination.[74]

Other canine distemper vaccines have been used off-label in ferrets in countries other than the United States or when PureVax has been unavailable. Recombitek CDV (Boehringer Ingelheim Animal Health) is also a recombinant canarypox vaccine approved for use in dogs that has been used in ferrets. This CDV vaccine is marketed in several multivalent combinations including CDV with parvovirus: a monovalent product is not available in the United States. Nobivac Puppy-DPv (Merck Animal Health) is a modified live virus canine distemper vaccine combined with parvovirus vaccine, a virus that does not affect ferrets. Although these vaccines have been used clinically in ferrets, their safety and efficacy in ferrets have not been studied. A CDV vaccine approved for use in mink (Distemink; United Vaccines Inc, Fitchberg, WI) is available in 250-dose vials only. Because of the possibility of vaccine-induced disease, especially in immunosuppressed or sick ferrets, avoid using multivalent canine vaccines and do not use modified live CDV vaccines of ferret-cell or low-passage canine-cell origin.

Standard vaccination protocols for canine distemper in ferrets have been based on serial vaccinations of young ferrets at 6, 10, and 14 weeks,[3] with annual boosters. However, recent data suggest a modified vaccine schedule consisting of two initial vaccines with less-frequent boosters is effective. In an efficacy study of 150 ferrets, 90% of ferrets that were initially vaccinated at 9 weeks and given a booster vaccine between 14 and 16 weeks of age with one of three commercial vaccines (Purevax Ferret, Fervac-D, or Galaxy D) maintained protective antibody titers of >1:50 for at least 3 years.[72] The three commercial vaccines did not differ in efficacy of eliciting protective titers. Therefore an initial vaccination protocol of two vaccinations, starting at 8 to 9 weeks of age and separated by 4 weeks, followed by a booster every 3 years, should suffice in most cases (D. Perpiñan, personal communication, May 2018). For ferrets at high risk of contracting canine distemper or when highly pathogenic strains of CDV are circulating, consider more-intensive vaccination protocols. If the ferret is first vaccinated after 3 to 4 months of age, a series of two vaccinations separated by 4 weeks is sufficiently protective (D. Perpiñan, personal communication, May 2018).[29]

Rabies

All ferrets should be vaccinated against rabies.[14] Two inactivated (killed) rabies vaccines are approved for use in ferrets in the United States: Imrab-3 or Imrab-3 TF (Boehringer Ingelheim Animal Health) and Defensor 1 or Defensor 3 (Zoetis, Parsippany, NJ). Inactivated vaccines are effective at producing immunity for at least 1 year.[63] Current recommendations are to vaccinate healthy ferrets at 3 months of age at a dose of 1 mL administered subcutaneously (SC). Give booster vaccinations annually. Titers develop within 30 days of rabies vaccination.[63]

Clinical signs of rabies in ferrets can vary. In studies of experimentally induced rabies in ferrets, clinical signs range from restlessness, apathy, and paresis to ascending paralysis, ataxia, cachexia, bladder atony, fever, hyperactivity, tremors, and paresthesia.[8,48] Mean incubation period in experimental studies varies from 28 to 33 days.[48,49] Virus is present in the brain tissue and salivary glands of inoculated ferrets, and virus is shed in the saliva 2 to 6 days after onset of illness.[48,49] Ferrets are at least 25 times less susceptible than skunks to rabies infection when fed mice carcasses infected with rabies virus.[5] Survival and clearance of rabies virus infection was reported in one ferret experimentally infected with rabies virus of skunk origin. The ferret initially exhibited hindlimb paralysis that resolved to paraparesis. No virus antigen was found at necropsy 6 months after inoculation.[24]

Ferrets are considered currently immunized 28 days after the initial rabies vaccination and immediately after a booster vaccination.[14] If a healthy pet ferret bites a person, current recommendations of the Compendium of Animal Rabies Prevention and Control are to confine and observe the animal for 10 days, during which the ferret should not be vaccinated.[14] Any illness that develops during observation should be reported immediately to the local health department. If signs suggest rabies, the ferret must be euthanized, and protocols for rabies evaluation

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followed. For a ferret with a current vaccine status exposed to a possible rabid animal, recommendations are to revaccinate the ferret within 96 hours of exposure and then keep the ferret under the owner's observation and care for 45 days. Exposed ferrets that are overdue for a booster rabies vaccination should be evaluated on a case-by-case basis by the health department. An unvaccinated animal that is exposed to a rabid animal or a stray ferret that bites a person should be euthanized immediately and submitted for rabies testing. See the website of the Centers for Disease Control and Prevention (https://www.cdc.gov/rabies/specific_groups/veterinarians/) or the National Association of Public Health Veterinarians (http://www.nasphv.org/documentsCompendia.html) for specific guidelines.

Vaccine-Associated Adverse Events

In ferrets, adverse events associated with vaccination are primarily type I hypersensitivity reactions or anaphylaxis.[43] Ferrets with mild reactions may exhibit pruritus and skin erythema. More severe reactions are typified by vomiting, diarrhea, piloerection, hyperthermia, cardiovascular collapse, or death.

Vaccine reactions are most common after canine distemper vaccination but may also occur after rabies vaccination. In a study of vaccine-associated adverse events in 3857 ferrets in the United States, the incidence of adverse events associated with rabies vaccine alone, canine distemper vaccine alone, and rabies and canine distemper vaccines together were 0.51%, 1.0%, and 0.85%, respectively, with no significant difference among groups.[45] However, occurrence of a vaccine-associated adverse event was significantly associated with the cumulative number of canine distemper vaccinations, with an 80% increase in risk of an adverse event with each additional distemper vaccine. The canine distemper vaccines used in this cohort of ferrets were PureVax Ferret and Fervac-D; the two vaccines were grouped collectively in the analysis, and the incidence of adverse events associated with individual vaccines was not reported. All reactions occurred immediately after vaccination and most commonly consisted of vomiting and diarrhea. In another study of 143 ferrets, the incidence of adverse events after administering either canine distemper (5.9%) (Fervac D), rabies (5.6%) (Imrab-3), or both vaccines (5.6%) did not differ significantly between groups.[23] In a 2001 report of 83 vaccine reactions in ferrets reported to the U.S. Pharmacopeia Veterinary Practitioners' Reporting Program, 65% involved administration of FerVac D, 24% involved concomitant administration of FerVac D and Imrab 3, and 11% involved administration of Imrab alone (PureVax was not approved for use at the time these data were collected).[43] According to Merial's (now Boehringer Ingelheim) product information, the incidence of vaccine reactions with PureVax is 0.3%. No adverse events were reported in an efficacy study of vaccination of 150 ferrets with either PureVax Ferret, Fervac-D, or Galaxy D.[72] Surveillance of vaccine-associated adverse events relies on voluntary reporting by practitioners.[43] Vaccine-associated adverse events can be reported to the Center for Biologics, U.S. Department of Agriculture (https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/veterinary-biologics/adverse-event-reporting).

Always follow the manufacturer's instructions for vaccine administration, and inform the owner of the possibility of an adverse reaction before vaccinating. Because most reactions occur almost immediately after vaccination, have the owner monitor the ferret in the waiting area for 30 minutes or more after vaccination with any product.

If a ferret has an adverse reaction, administer an antihistamine (e.g., diphenhydramine hydrochloride, 0.5 to 2.0 mg/kg intravenously [IV] or intramuscularly [IM]), epinephrine (0.01 mg/kg IV, IM or intratracheally), or a short-acting corticosteroid (e.g., dexamethasone sodium phosphate, 1 to 2 mg/kg IV or IM), and give supportive care.

For any biologic product, veterinarians must assess risk versus benefit of vaccination. The treatment options for ferrets that have had a vaccine reaction are to administer diphenhydramine (2 mg/kg orally [PO] or SC) at least 15 minutes before vaccination or not to vaccinate if exposure risk is minimal.

Vaccine injection-site sarcomas have been described in ferrets.[46,47] In one report, 7 of 10 fibrosarcomas in ferrets were from locations used for vaccination.[46] Fibrosarcomas had similar histologic, immunohistochemical, and ultrastructural features as those reported for feline vaccine-associated sarcomas. In cats, adjuvanted vaccines are most likely to be involved in tumor development; however, no definitive association was made between the fibrosarcoma and the type of vaccine in ferrets. Ferrets appear less prone than cats to development of vaccine-induced tumors.

Parasites

Endoparasites

Gastrointestinal parasitism is most common in young or recently purchased pet ferrets and is relatively uncommon in mature ferrets in the United States. In a survey of ferrets that were either privately owned or in pet shops in Italy, 14 of 50 (28%) were positive for ancylostomids (hookworms) and one (2%) was positive for *Sarcocystis*.[17] Ferrets can be intermediate hosts or vectors of parasites from other natural hosts. Protozoan parasites are occasionally seen. Therefore perform routine fecal flotations and direct fecal smears for all young or recently acquired ferrets.

Coccidiosis (*Isospora* species) usually is seen in young ferrets, which shed oocysts between 6 and 16 weeks of age.[4] Infection is often subclinical, although ferrets occasionally may have loose stool or bloody diarrhea. Coccidiostats, such as sulfadimethoxine and amprolium, are effective and safe, and treatment should be continued for at least 2 weeks. Coccidia in ferrets may cross-infect dogs and cats; therefore check other pets in the household for coccidia and treat as needed.

Giardiasis is occasionally seen in ferrets. Results of studies on molecular characterization and host specificity of *Giardia duodenalis* isolates from pet ferrets vary. In one study, genetic sequences of giardia isolates from ferrets were similar to those of giardia associated with human infections.[55] Results of another study showed genetic sequences of giardia differed in ferrets and people and other mammals, suggesting that *Giardia* isolates from ferrets may be host specific.[2] *Giardia* can be detected by identifying cysts or trophozoites in a fresh fecal smear or zinc sulfate flotation, or by fecal ELISA. Treat ferrets with giardiasis with metronidazole (20 mg/kg PO every 12 hours for 5 to 10 days) or fenbendazole (50 mg/kg PO every 24 hours for 3 to 5 days).

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Cryptosporidiosis is described primarily in young ferrets.[60] Infection is associated with the ferret genotype of *Cryptosporidium parvum* and therefore is an unlikely source of human infection.[1] Infection is usually subclinical and, although most ferrets recover within 2 to 3 weeks, can persist for months in immunosuppressed animals. Oocysts of *Cryptosporidium* are small (3-5 μm) and difficult to detect but can be found in fresh fecal samples examined immediately after acid-fast staining.[4,60] Various drugs, including azithromycin, tylosin, and nitazoxanide, are used for treatment in dogs and cats, but efficacy in ferrets is not known.[64]

Heartworms *(Dirofilaria immitis)* can cause disease in ferrets. Ferrets that are housed outdoors in heartworm-endemic areas are most susceptible to infection; however, all ferrets in endemic areas should be treated with heartworm preventive (see Chapter 5 and Appendix).

Ectoparasites

Ear mites *(Otodectes cynotis)* are common in ferrets, but affected animals may not exhibit pruritus or irritation. This mite species also infects dogs and cats, and animals in households with multiple pets can transmit mites to other animals. A red-brown, thick, waxy discharge in the ear canal and pinna characterizes infection. A direct smear of the exudate reveals adult mites or eggs. Because ferrets normally have brown ear wax, the color or appearance of debris in the ear canal is not pathognomonic for mites. At the initial examination, check for ear mites and do follow-up checks at the annual examination in ferrets kept in multiple-pet households. Several products, including selamectin, are effective in treatment (see Chapter 9).

Flea infestation (*Ctenocephalides* species) is most common in ferrets kept in households with dogs or cats. Ferrets with chronic infestations can become severely anemic. Check ferrets during the physical examination for signs of fleas or flea dirt. Treat infested animals with products safe for use in cats, and institute flea control measures (see Chapter 9). Ticks are rarely seen on domestic ferrets, and Lyme disease in ferrets has not been reported.

HOSPITALIZATION

Ferrets can be hospitalized in standard hospital cages with some adaptations. Ferrets are agile escape artists and often can squeeze through vertical cage bar openings on standard hospital cages. For housing ferrets, use only commercial cages with small spacing between bars or use cages with attached Plexiglass fronts at least half the height of the cage door or higher to prevent escape. Small animal intensive care cages or incubators also can be used to house ferrets and are especially useful for animals that need supplemental heat or oxygen. Closely monitor the temperature in these cages when using supplemental heat to prevent hyperthermia or hypothermia. The cage should be large enough to accommodate a sleeping area and an area for defecation and urination. Ferrets typically do not soil their sleeping area, even when very sick.

All ferrets like to burrow and should be given opportunity to do so while hospitalized. Clean towels or a mound of shredded paper make excellent burrowing material. Take care with plastic-backed underpads, which ferrets may chew and ingest. Small padded pet beds and fleece pet "pockets" work well as sleeping areas.

Provide water in either water bottles or small weighted bowls. Before hospitalization, ask the owner which type of watering system the ferret is accustomed to. Ferrets can be finicky eaters and should be fed their regular diet while hospitalized, if possible. Otherwise, feed a very palatable ferret food or a premium high-protein cat/kitten kibble. For animals that are anorectic, force-feed a high-calorie semisolid food or supplement until the animal is eating on its own (see later discussion).

CLINICAL AND TREATMENT TECHNIQUES

Venipuncture

Most veterinary laboratories offer small mammal hematologic and biochemical panels that require 1.0 mL or less of blood. In-clinic, point-of-care analyzers require very small sample sizes (usually 100 μL). The blood volume of healthy ferrets is approximately 40 mL in average-sized females weighing 750 g and 60 mL in males weighing 1 kg.[22] Up to 10% of the blood volume can be safely withdrawn at one time in a normal ferret; however, collect only the minimum amount needed for analysis. Repeated blood drawing can contribute to anemia in sick animals hospitalized for long periods.

Obtaining a blood sample from a ferret is relatively easy. Venipuncture usually can be done with manual restraint, but some veterinarians prefer sedating or anesthetizing especially active animals. Several venipuncture sites are readily accessible; the technique and site chosen depend on how much blood is needed and the availability of assistants for restraint. Anesthesia or sedation can be used if assistants are unavailable. If needed, ferrets often can be distracted during restraint for venipuncture by offering semisolid food or a product such as FerreTone (8-in-1 Pet Products) by syringe. Avoid using supplements with corn syrup or other sugars, because this will affect blood glucose levels, and collect blood for glucose determination or other fasting samples before offering food.

The blood collection technique can affect hematologic test results. Isoflurane anesthesia can cause decreases in all hematologic values beginning at induction of anesthesia and reaching maximal effects at 15 minutes after induction.[41] Both isoflurane and sevoflurane can cause a decrease in packed cell volume.[32] Therefore hematologic results of blood samples collected while a ferret is anesthetized must be interpreted carefully (see Chapter 39).[41]

Two sites are commonly accessed to obtain large blood volumes in ferrets. Jugular venipuncture can be accomplished by extending the ferret's forelegs over the edge of a table and the neck up, or by restraining the ferret in lateral recumbency (Fig. 2.2). Have a second assistant restrain the ferret's hind end on the table to prevent twisting, or wrap the lower body in a towel. Use a 25-gauge needle bent slightly to a 20-degree angle with a 1- to 3-mL syringe for venipuncture in most ferrets; a 22-gauge needle can be used in large males. Shave the neck at the venipuncture site to enhance visibility of the jugular vein. The vein is relatively superficial and is located more laterally in the neck than it is in dogs or cats. Once the needle

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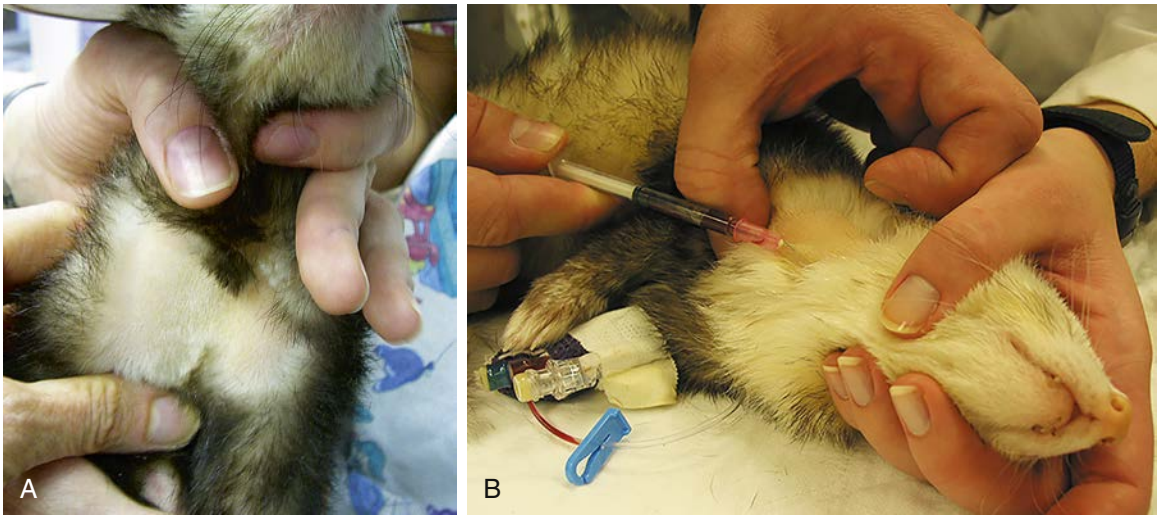


Fig. 2.2 Restraint for Jugular Venipuncture in a Ferret. (A) Shave the neck to improve visibility of the jugular vein in the lateral neck. The ferret can be restrained with the legs pulled down and the head back; after the vein is punctured, the head can be "pumped" up and down slowly to facilitate blood flow. (B) A sedated ferret placed in lateral recumbency for jugular venipuncture.



Fig. 2.3 (A) Dissection of the thoracic cavity of a ferret illustrating the site for blood collection by the anterior vena cava technique. The sternum and ventral ribs are removed. The site of venipuncture is either the right brachiocephalic trunk (RBT) or left brachiocephalic trunk (LBT) or the anterior vena cava (AVC), depending on the point of entry and depth of penetration (see marker). The jugular vein (JV) is usually lateral and cranial to the venipuncture site. The base of the first two ribs is shown by arrows. (B) A ferret is restrained for venipuncture of the anterior vena cava. Both forelegs are pulled back, hindlegs are restrained, and the neck is extended.

is inserted, the blood should flow easily into the syringe; if the neck is overextended and the head is arched back, the blood may not flow readily from the vein. Relax the hold on the head or gently "pump" the vein by moving the head slowly up and down to enhance blood flow into the syringe. With ferrets that resist limb extension, a towel-wrap technique can be used. Scruff the ferret with its front legs extended caudally against the ventral thorax and wrap the animal's body firmly with a towel from the base of the neck down. Have an assistant restrain the toweled ferret in dorsal recumbency while scruffing the neck or holding the head. However, with very fractious animals, even this technique may be difficult.

The second venipuncture site from which to obtain large blood samples is the cranial vena cava. The site of venipuncture is the anterior vena cava or the right or left brachiocephalic trunk, depending on the point of entry and the depth of needle penetration (Fig. 2.3, A). This technique is relatively safe in ferrets because of the long anterior vena cava and the caudal location of the heart in the thoracic cavity, which is approximately 3 cm from the thoracic inlet.

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TABLE 2.1 Reference Intervals for Hematologic Values in Ferrets

			ALBINO[70]		FITCH[33]	
Value	**Combined Sex[a]**	**Combined Sex[b]**	**Male[c]**	**Female**	**Male[d]**	**Female**
Hematocrit, %	36–48	—	44–61	42–55	46–57	47–51
Hemoglobin, g/dL	12.2–16.5	13.9–21.9	16.3–18.2	14.8–17.4	15.2–17.7	15.2–17.4
Red blood cells, $\times 10^6/\mu L$	7.01–9.65	7.4–13	7.30–12.18	6.77–9.76	—	—
Reticulocytes, %	—	—	1–12	2–14	—	—
White blood cells, $\times 10^3/\mu L$	4.3–10.7	3.0–16.7	4.4–19.1	4.0–18.2	5.6–10.8	2.5–8.6
Neutrophils, %	18–47	17–82	11–82	43–84	—	—
cells/μL	—	900–7400	—	—	616–7020	725–2409
Lymphocytes, %	41–73	13–81	12–54	12–50	—	—
(cells/μL)	—	600–10,500	—	—	1728–4704	1475–5590
Monocytes, %	0–4	0–6.5	0–9	2–8	—	—
(cells/μL)	—	0–500	—	—	0–432	100–372
Eosinophils, %	0–4	0–5.7	0–7	0–5	—	—
(cells/μL)	—	0–700	—	—	112–768	50–516
Basophils, %	0–2	0 –1.4	0–2	0–1	—	—
(cells/μL)	—	0–200	—	—	0–112	0–172
Bands, cells/μL	—	0–100	—	—	0–972	0–248
Platelets, $\times 10^3/\mu L$	200–459	172–1281	297–730	310–910	—	—
Mean corpuscular volume, fL	50–54	50–61	—	—	—	—
Mean corpuscular hemoglobin, g/dL	15–18	—	—	—	—	—
Mean corpuscular hemoglobin concentration, g/dL	32–35	29–34	—	—	—	—

[a]Combined male and female pet ferrets (*n* = 60). From Cray C, Avian and Wildlife Laboratory, Miller School of Medicine, University of Miami, Miami, FL.
[b]Data converted from SI units; modified from Hein, et al.[27] Blood was collected from the lateral saphenous vein of clinically healthy ferrets (n = 105 to n = 106) (age 11 weeks to 9 years; intact males and females, neutered males, spayed females, mixed haircoat) manually restrained.
[c]Intact males.
[d]Castrated males.

However, rare instances of hemorrhage into the anterior thoracic cavity can occur. For this technique, restrain the ferret on its back with the forelegs pulled caudally and the head and neck extended (Fig. 2.3, B). With manual restraint, two assistants are usually needed, one to restrain the forelegs and head and the other to restrain the rear just cranial to the pelvis. Use a 25-gauge needle with an attached 1-mL or 3-mL syringe; insert it into the thoracic cavity between the first rib and the manubrium at an angle 30 to 45 degrees to the body. Direct the needle toward the opposite rear leg or most caudal rib and insert it almost to the hub. Pull back on the plunger as the needle is slowly withdrawn until blood begins to fill the syringe. If the ferret struggles, quickly withdraw the needle and wait until the ferret is quiet before making a second attempt. In very fractious or active ferrets, jugular venipuncture or use of tranquilization are safer choices to avoid lacerating the vessels.

The lateral saphenous or cephalic vein can be used if only a small amount of blood is needed to measure a packed cell volume or blood glucose level. To prevent collapse of the vein during venipuncture, use an insulin syringe with an attached 27- or 28-gauge needle. The saphenous vein lies just proximal to the tarsus on the lateral surface of the leg; the cephalic vein is in the same anatomic location as in a dog. Before venipuncture, shave the fur from the area to enhance visibility of the vein.

Venipuncture of the tail artery is possible but rarely used in pet ferrets.[9] Venipuncture at this site is painful and requires anesthesia. Insert a syringe with a 21-gauge needle into the ventral midline of the tail directed toward the body. Once the artery is entered 2 to 3 mm deep into the skin, slowly withdraw the plunger until blood fills the syringe. Apply pressure to the venipuncture site for 2 to 3 minutes after withdrawing the needle.

Reference Intervals

Most commercial veterinary diagnostic laboratories provide laboratory-specific reference intervals for ferret hematologic and biochemical values (see Chapter 39). Published sources of reference intervals for both laboratory and pet ferrets are available.[22,27,33,67,70] Reference intervals for hematologic, biochemical, and plasma electrophoresis values in ferrets from select sources are listed in Tables 2.1, 2.2, and 2.3.

Coagulopathy is relatively rare in ferrets, and blood coagulation panels are done infrequently in clinical practice. Currently, reference values from commercial veterinary diagnostic laboratories for blood coagulation assays are not available. Results of several research studies investigating blood coagulation values in ferrets have been published.[7,16,37,68,70] Values determined by coagulation assays can vary significantly by methods used and by laboratory.[7,37] Table 2.4

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TABLE 2.2 Reference Intervals for Biochemical Values in Ferrets

		SERUM	
Analyte	**Plasma[a]**	**Albino[b]**	**Mixed Haircoat[c]**
Alanine aminotransferase, U/L	65–128	—	49–243
Albumin, g/dL	2.5–4.0	2.6–3.8	2.8–4.4
Alkaline phosphatase, U/L	25–60	9–84	13–142
Amylase, U/L	26–36	—	19–62
Aspartate aminotransferase, U/L	70–100	28–120	40–143
Bilirubin, total, mg/dL	0.2–0.5	<1.0	0.0–0.2
Blood urea nitrogen, mg/dL	18–32	10–45	13–47
Calcium, mg/dL	8.1–9.5	9.0–11.8	8.0–10.4
Carbon dioxide, mmol/L	22–29	16–25	—
Cholesterol, mg/dL	119–163	64–296	93–274
Chloride, mmol/L	—	106–125	108–120
Creatinine, mg/dL	0.2–0.5	0.4–0.9	0.3–0.9
Creatine phosphokinase, U/L	55–93	—	94–731
Glucose, mg/dL	80–117	94–207	54–153
Gamma glutamine transferase, U/L	8–34	—	0–14
Lactate dehydrogenase, U/L	200–1400	—	154–1781
Phosphorus, mg/dL	5.1–6.5	4.0–9.1	3.1–9.6
Potassium, mmol/L	4.5–6.1	4.5–7.7	3.9–5.9
Sodium, mmol/L	142–148	137–162	138–143
Total protein, g/dL	4.5–6.2	5.1–7.4	5.5–7.8
Triglycerides, mg/dL	30–140	—	44–248
Uric acid, mg/dL	1.3–1.9	—	—

[a]Combined male and female pet ferrets (n = 60). From Cray C, Avian and Wildlife Laboratory, Miller School of Medicine, University of Miami, Miami, FL.
[b]Combined values of male (n = 40) and female (n = 24) ferrets.[70]
[c]Data converted from SI units; modified from Hein et al.[27] Blood was collected from the lateral saphenous vein of clinically healthy ferrets (n = 94 to n = 109) (age 11 weeks to 9 years; mixed intact males and females, neutered males, spayed females; mixed haircoat type) that were manually restrained. Serum was assayed using the Hitachi 911 chemistry analyzer (Roche Diagnostics, Indianapolis, IN).

TABLE 2.3 Reference Intervals for Plasma Protein Electrophoresis in Ferrets

Analyte	Combined Sex[a]
Albumin, g/dL	2.50–3.31
α-1 globulin, g/dL	0.33–0.56
α-2 globulin, g/dL	0.36–0.60
β globulin, g/dL	0.83–1.20
γ globulin, g/dL	0.31–0.81
Albumin/globulin ratio	1.05–1.33

[a]Combined male and female ferrets (n = 60). From Cray C, Avian and Wildlife Laboratory, Miller School of Medicine, University of Miami, Miami, FL.

contains blood coagulation values determined in normal ferrets that can be used as guidelines in the absence of reference intervals specific to a laboratory or to coagulation analyzer equipment.

Intravenous Catheters

Indwelling intravenous catheters can be placed in the lateral saphenous or cephalic vein (Fig. 2.4). Jugular vein catheters are difficult to place and are rarely used. Except in very depressed animals, catheters are placed with the ferret sedated or anesthetized. Applying a topical anesthetic on the venipuncture site approximately 30 to 60 minutes before the procedure may facilitate catheter placement. To place the catheter, shave and aseptically prepare the area, then puncture the skin with a 20- or 22-gauge needle, taking care to avoid the vein. Introduce a short 22-, 24-, or 26-gauge over-the-needle catheter through the skin puncture into the vein, and secure the catheter routinely. Monitor ferrets with indwelling catheters to prevent the fluid line from tangling, and check the leg distal and proximal to the catheter frequently for soft tissue swelling. Most ferrets do not chew a catheter once it is placed and do not require an Elizabethan collar.

In ferrets that are collapsed with poor blood pressure or in young or very small ferrets, attempts to place an intravenous catheter may be unsuccessful. An intraosseous catheter can be placed in these animals. The proximal tibia is the most common site for intraosseous catheter placement in small mammals,[34] but the proximal femur can also be used and allows for a greater range of movement. Unless the ferret is very depressed, anesthesia is required to place the catheter. Sterilely prepare the insertion site

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TABLE 2.4 Blood coagulation values of normal ferrets

Analyte	Takahashi et al[68]	Benson et al[7]	Lewis[37]
Activated partial thromboplastin time, sec	17.0 ± 1.2 (15.3–18.7)	18.7 ± 0.9[a] (17.5–21.1) 18.1 ± 1.1[b] (16.5–20.5)	18.4 ± 1.4
Antithrombin activity, %	—	96 ± 12.7 (69.3-115.3)	—
Fibrinogen, mg/dL	486.7 ± 97.9 (382.5–658.3)	107.4 ± 19.8 (90.0–163.5)	—
Clotting time, min	—	—	2.0 ± 0.5[c] 3.0 ± 0.9[d]
Prothrombin time, sec	11.3 ± 0.4 (10.9–12.0)	12.3 ± 0.3[a] (11.6–12.7) 10.9 ± 0.3[b] (10.6–11.6)	10.3 ± 0.1
Thrombin time, sec	13.7 ± 2.7 (9.4–16.9)	—	28.8 ± 8.7

[a]Measured by fibrometer.
[b]Measured by automated system.
[c]Glass tubes.
[d]Silicone tubes.



Fig. 2.4 Placing an indwelling catheter in the cephalic vein of a ferret. The hair over the vein is shaved and the vein is held off. A 24-gauge, 0.75-inch intravenous catheter is introduced into the vein and taped in place.

and infiltrate the area with 1% to 2% lidocaine (maximum dose, 1 mg/kg).[34] Insert a 20- or 22-gauge, 1.5-inch spinal needle into the marrow cavity. Alternatively, use a 20- or 22-gauge hypodermic needle with a surgical steel wire inserted into the lumen to prevent a bone plug from occluding the needle during insertion.[52] The intraosseous catheter should occupy approximately 30% to 70% of the marrow cavity at the narrowest portion.[34] Administer drugs through intraosseous catheters in small volumes with minimal pressure to prevent leakage from the insertion site. If possible, change to an intravenous catheter as soon as the animal is rehydrated or blood pressure improves. Intraosseous catheters should not be left in place for more than 72 hours.[34]

Vascular access ports can be placed when repeated vascular access is required for any reason, such as for chemotherapy.[59] The technique used to place the catheter and port has been described and illustrated.[53]

Fluid Therapy

Hospitalized ferrets usually require fluid therapy to maintain hydration and correct dehydration. Daily fluid requirements of ferrets have not been determined; however, calculating fluid requirements at a rate of 60 to 70 mL/kg per day appears to be adequate for maintenance. One source estimates daily water consumption of adult ferrets as 75 to 100 mL/day.[44] Provide additional fluids to compensate for ongoing fluid loss and to correct dehydration calculated as a percentage of the body weight.

Intravenous fluids are preferred in ill animals. If possible, administer intravenous fluids by continuous-rate infusion. Alternatively, divide the calculated daily fluid volume into two or three doses and administer by a Buretrol (Baxter Healthcare, Glendale, CA) or syringe pump. Depending on the clinical condition of the ferret, supplements and drugs can be added to fluids by using the same criteria and calculations as for dogs and cats. Although subcutaneous fluids can be given, ferrets react painfully to subcutaneous administration, and adequate restraint is needed. Administer subcutaneous fluids in the loose skin along the back and dorsal cervical area, dividing the calculated daily fluid volume into doses given two or three times daily.

Colloids are effective in improving intravascular fluid volume and oncotic pressure in ferrets that are hypoproteinemic or in shock. Dosage and administration are like those used in other small animals (see Chapter 41).

Antibiotic and Drug Therapy

Antibiotics and other therapeutic agents are usually given at dosages like those in cats per kg of body weight (see Appendix). In hospitalized animals with an indwelling catheter, give medications intravenously if possible. However, monitor the leg where the catheter is placed carefully for phlebitis and cellulitis, particularly when caustic medications are administered. Antibiotics can be administered IM; however, if treatment continues over several days, subcutaneous administration is preferred in cachectic animals because of the limited muscle mass. Pills are very difficult to administer to ferrets; therefore oral medications are most easily given compounded into liquid form. Ferrets generally accept chicken and beef flavors of compounded medications but do not like the taste of fish flavors.

Pain Management

Pain management is important in the postoperative period, with diseases that create significant discomfort (such as gastrointestinal ulceration), and for traumatic injuries (see Chapter 37). Ferrets in pain may exhibit tachypnea, a stiff gait, a strained facial expression, teeth grinding, shivering, half-closed eyelids, aggression, focal muscle fasciculation, hiding, general malaise, bristling of tail fur, and appear "tucked" in the abdomen.[42,71] Many analgesic agents are used effectively in ferrets, including opioids, α-2 agonists, nonsteroidal antiinflammatory drugs (NSAIDs), and local anesthetics.[30] Clinically, buprenorphine,

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butorphanol, or meloxicam or combinations thereof are most commonly used for hospitalized animals and outpatients (see Chapter 37 and Appendix). Although no studies have evaluated efficacy of meloxicam for analgesia in ferrets, a meloxicam dose of 0.2 mg/kg in ferrets achieves plasma concentrations considered effective in other companion animals.[12]

Ferrets are sensitive to acetaminophen toxicity.[15] The activity of uridine 5′-diphospho (UDP)-glucuronosyltransferase in their livers compares with that of cats. Acetaminophen glucuronidation is slower in ferrets than in other nonfelid species. Unlike cats, however, no genetic mutations are associated with this slow metabolism, and the exact cause is unknown. Ibuprofen can be toxic in ferrets at high doses,[11] and accidental ibuprofen ingestion of 220 mg/kg can cause death.[62] Clinical signs of toxicosis are depression, coma, ataxia, recumbency, tremors, weakness, and death.[62] Therefore avoid acetaminophen in ferrets and use NSAIDs with caution. Do not use NSAIDs in ferrets being treated with a corticosteroid for insulinoma or other disease.

Epidural administration of analgesics before surgery appears to be effective in controlling postoperative pain in ferrets undergoing procedures involving the abdomen, spine, pelvis, hind legs, tail, and perineum (see Chapter 37).[18,66] The technique has been well described in ferrets and is similar to that used in other small animals.[18,25] Epidural injection is contraindicated in cases of coagulopathy, sepsis, hypovolemia, skin infection, and local fractures.[18]

Be careful in the immediate postoperative period when opioids, such as butorphanol or buprenorphine, are used. In cats, as well as in other species, opioids including hydromorphone, butorphanol, and buprenorphine are associated with an increase in body temperature.[58] Opioid analgesics also can cause pronounced sedation, and ferrets can remain very lethargic and immobile for long periods. Because of these two factors, immobile ferrets can overheat quickly if a heating lamp or other focused heat source is used during anesthetic recovery. Therefore closely monitor the body temperature of any immobile or lethargic ferret given opioids or sedatives to prevent overheating when using heat lamps or forced-air warming devices.

Nutritional Support

Many sick ferrets are either cachectic or hypoglycemic or have minimal body fat and require nutritional support. Products formulated as recovery diets for carnivores are available and readily accepted by most ferrets (Carnivore Care, Oxbow Animal Health, Murdock, NE; Emeraid Carnivore, EmerAid, Cornell, IL). Ferrets can be syringe-fed meat-based soft foods marketed for hospitalized dogs and cats (Maximum-Calorie Plus, The Iams Company, Mason, OH; Canine/Feline a/d, Hill's Pet Nutrition, Topeka, KS). Do not offer supplement gels that contain corn syrup because of the high sugar content. Force-feed anorectic ferrets as much as they will accept comfortably, usually 8 to 12 mL syringe fed three or four times daily. Ferrets that develop a taste for the food may eat it directly from a bowl.

Ferret owners often prepare homemade diets of "duck soup" or "chicken gravy" to nurse their pets at home. Many different recipe variations are available, and most are based on whole chicken with additives ranging from beef fat, dog kibble, nutritional supplement gels, or brewer's yeast to Echinacea capsules. The "duck soup" variations all provide a soft, porridge-consistency food that is usually readily eaten by sick and convalescing ferrets. Some recipes are very high in fat and carbohydrates. Unless the homemade diets are based on or used with a commercial ferret diet, they should not be used long term because of possible nutritional imbalances and deficiencies.

Although seldom used clinically, esophagostomy feeding tubes can be placed in ferrets to manage debilitated animals over the long term. The technique is like that used in cats.[21] Gastric feeding tubes have been placed in ferrets both experimentally and clinically.[6,10] In a study of 14 ferrets, gastrostomy tubes were placed percutaneously by a nonendoscopic technique. A gastrostomy tube was placed and maintained successfully in a ferret after surgical repair of an esophageal perforation caused by an esophageal foreign body.[10]

Total nutrient admixtures have been formulated to provide partial parenteral nutrition to ferrets.[52,61] Depending on the osmolarity of the solution, parenteral nutrition solutions can be delivered via a central, peripheral, intraosseous, or intraperitoneal catheter; however, the relatively high protein requirements of ferrets usually result in a solution of 600 to 800 mOsm/L, which should be administered into a large (central) vein.[61]

Urine Collection and Urinalysis

Urine samples can be collected by cystocentesis or by free catch after natural voiding or gentle manual expression of the bladder. The techniques for manually expressing the bladder and cystocentesis are the same as those used in dogs and cats. Anesthetize fractious ferrets to avoid trauma to the thin bladder wall. Use a 25-gauge needle for cystocentesis.

Reference values for urinalysis are listed in Table 2.5. In one study, the reference range for urine pH in ferrets was reported as 6.5 to 7.5; however, urine pH can vary according to the diet. The normal urine pH in ferrets fed a high-quality, meat-based diet is approximately 6.0.

Urinary Catheterization

Urinary catheterization is commonly indicated in male ferrets, but the procedure can be challenging. Although techniques have been described for both sexes,[40] clinical indications to place a urinary catheter in females are rare.

For females, tranquilize or anesthetize the ferret, then position it in ventral recumbency with the rear quarters elevated with a rolled towel. With a vaginal speculum, locate the urethral opening in the floor of the urethral vestibule, approximately 1 cm cranial to the clitoral fossa. Introduce a 3.5-French (Fr), red rubber urethral catheter fitted with a wire stylet into the urethral orifice.

In male ferrets, the urethral opening is very small and is located on the ventral surface of the penis, proximal to the J-hook in the end of the os penis. Use a 3.0- or 3.5-Fr polytetrafluoroethylene, silicone,[35] or polyurethane urinary catheter (Slippery Sam Tomcat Urethral Catheter, Surgivet, Smiths Medical, Dublin, OH; Tomcat Urethral Catheter, Surgivet; Tomcat/Small Animal Urinary Catheter, Mila International Inc., Florence, KY). Alternatively, use a 3.5-Fr rubber feeding catheter; estimate the length of the catheter that must be inserted to reach the bladder before placing (see also Chapter 4). If using a long rubber

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TABLE 2.5 Reference Values for Urinalysis in Ferrets

	MALES		FEMALES		COMBINED SEX
Parameter	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**	**Mean ± SD**
Volume, mL/24hr	26[70]	8–48[70]	28[70]	8–140[70]	24.9 ± 14.3[20]
pH	6.2 ± 0.1[22]	6.5–7.5[70] 6.0–6.5[22]	6.3 ± 0.3[22]	6.5–7.5[70] 6.0–6.5[22]	—
Protein, mg/dL	9.6 ± 1.4[22]	7–33[70]	7.6 ± 1.2[22]	0–32[70]	—
Specific gravity	1.051 ± 9[19]	1.034–1.070[19]	1.042 ± 8[19]	1.026–1.060[19]	—
Creatinine clearance, mL/min/kg					
Exogenous	—	—	—	—	3.3 ± 2.2[20]
Endogenous	—	—	—	—	2.5 ± 0.9[20]
Inulin clearance, mL/min/kg	—	—	—	—	3.0 ± 1.8[20]

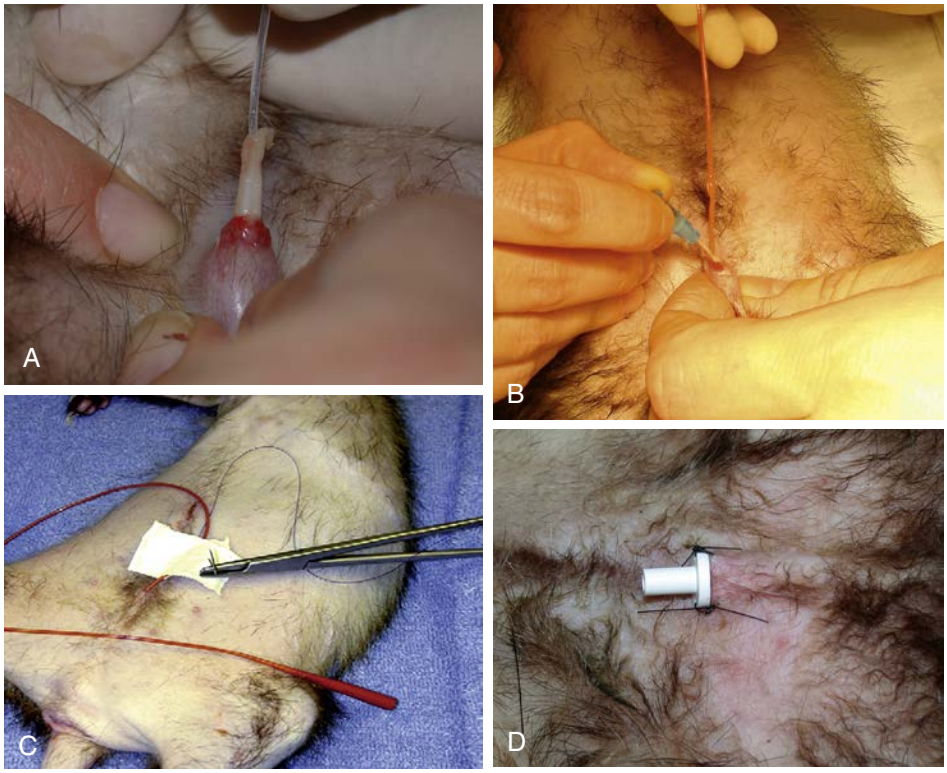


Fig. 2.5 (A) The urethral catheter is introduced into the urethral opening proximal to the J-shaped tip of the os penis. (B) The urethral opening has been dilated by placing the tip of an intravenous catheter just inside the opening and flushing gently with saline solution. The lubricated end of a 3.5-Fr red rubber or urinary catheter is then introduced into the opening and the intravenous catheter is removed. (C) A 3.5-Fr red rubber catheter is sutured in place using butterfly tape (photo courtesy Dr. Marla Lichtenberger). (D) The hub of a Slippery Sam urinary catheter is sutured in place to the prepuce.

catheter, use a stylet or flexible wire to stiffen the catheter if needed; the stylet can be retracted slightly while passing the catheter, but be very careful when rounding the pelvic flexure to avoid perforating the urethra. Another option is to use a 20-gauge or 22-gauge, 8-inch jugular catheter with the stylet removed.[52] To pass the urinary catheter, aseptically prepare the preputial area, locate the urethral opening, and introduce the catheter tip (Fig 2.5, A). If the urethral opening is difficult to see, dilate the opening by passing a 24-gauge intravenous catheter just inside the tip of the urethra and flushing gently with saline solution (Fig 2.5, B). Slip the tip of the lubricated urinary catheter gently into the dilated urethral opening alongside the intravenous catheter and, while gently flushing with saline solution, pass the catheter into the bladder. Often resistance is met at the pelvic flexure; if this occurs, try repeated gentle flushing and relubricating the catheter until it passes. Once in place, if using a red rubber catheter, place butterfly tape strips around the catheter just as it enters the urethra and at another point 3 to 5 cm distal, and suture these to the skin (Fig 2.5, C). If using a urethral catheter, suture the catheter hub to the prepuce (Fig 2.5, D). Attach a sterile urinary collection device and tape the tubing to the tail to further prevent tension. If needed, bandage the ferret's abdomen to minimize rotation of

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the catheter and to restrict the ferret from traumatizing it. Soft Elizabethan collars are needed in some ferrets to prevent chewing at the catheter. Maintain sterility of the collection system, and drain the bag by needle and syringe rather than opening the system (see also Chapter 4).

Temporary tube cystostomy has been used successfully to manage male ferrets with urinary obstruction caused by adrenal disease. In four ferrets treated surgically, a 5- or 8-Fr Foley catheter was placed in the bladder at the time of adrenalectomy and left in place for 5 to 14 days.[50] In these ferrets, immediate treatment of urinary blockage was by cystocentesis. A cystostomy catheter also can be placed by using interventional radiographic techniques. This is an option in obstructed ferrets in which a urethral catheter cannot be passed and surgery is considered high risk. A cystostomy catheter allows azotemic ferrets to be managed with diuresis before surgery; alternatively, in cases in which surgery is not an option, the catheter can remain in place pending response to medical management with leuprolide acetate.

Blood Pressure Monitoring

Indirect blood pressure monitoring techniques, using both Doppler ultrasonography and oscillometric methods, have been described in ferrets.[36,51,65,73] However, both methods poorly approximate direct arterial blood pressure measurements. Indirect blood pressure readings may be inaccurate because the neonatal blood pressure cuff does not fit securely on the short legs of ferrets (Doppler method), and pressure changes of the tail artery may not be sufficiently high to be detected by the oscillometric system.[51] In one study, the indirect systolic blood pressure values measured by Doppler on the tail of ferrets measured 28 mmHg less than the direct arterial systolic blood pressure values.[51] In a study using 14 male ferrets that compared indirect blood pressure measurements on the tail, forelimb, and hindlimb using an oscillometric sphygmomanometer and a high-definition oscillometric monitor with direct arterial blood pressure measurements, measurements using the tail were considered most reliable.[65] However, the oscillometric sphygmomanometer consistently overestimated the systolic arterial pressure. Indirect measurements of systolic, mean, and diastolic arterial pressures were consistently higher during hypotensive states but substantially lower in hypertensive states than corresponding direct blood pressure measurements. In a study of 63 healthy ferrets, sedation with butorphanol (0.2 mg/kg IM) and midazolam (0.2 mg/kg IM) was found optimal to allow indirect blood pressure measurement.[73] Reference values for indirect blood pressure measured with the cuff placed at the base of the tail were 94 to 155 mmHg systolic, 69 to109 mmHg mean, and 51 to 87 mmHg diastolic arterial pressure. Be aware of the above-described inconsistencies of indirect compared with direct blood pressure measurements and interpret clinical results carefully.

In clinical situations, indirect blood pressure is most useful for evaluating changes in blood pressure from a known baseline or for surgical monitoring of general trends rather than for exact blood pressure measurement. The Doppler method of indirect blood pressure measurement is most commonly used in ferrets. Shave the hair on the ventral tail and place a no. 1 (3 to 6 cm) cuff on the most proximal part of the tail and attach it to a sphygmomanometer. Place the Doppler transducer probe crystal with ultrasound gel on the shaved skin approximately 1 cm distal to the cuff and tape or hold in place. Alternatively, place the cuff just above the carpus or tarsus (overlying the radial artery on the front leg or the digital branch of the tibial artery on the rear leg, alternatively) or on the distal humerus.[36]



Fig. 2.6 Collection of a bone marrow sample from the femur of an anesthetized ferret. The femur is stabilized while inserting a 20-gauge, 1.5-inch spinal needle medial to the greater trochanter.

Bone Marrow Collection

Evaluating a bone marrow sample is a valuable diagnostic tool for many disease conditions, including anemia, thrombocytopenia, pancytopenia, proliferative abnormalities, and suspected hematopoietic malignancies. Although the proximal femur is usually the most readily accessible site (Fig. 2.6), the iliac crest, tibial crest, and humerus can also be used to collect bone marrow samples. Anesthesia is necessary to aspirate the bone marrow or perform a core biopsy. With the ferret in lateral recumbency, shave and aseptically prepare the area around the collection site. For the proximal femur,[54] make a small incision over the greater trochanter. Stabilize the femur with one hand while inserting a 20-gauge, 1.5-inch spinal needle into the bone, medial to the greater trochanter. Use steady pressure and an alternating rotating motion to advance the needle into the marrow cavity. Withdraw the stylet and attach a 6- to 12-mL syringe to the needle to aspirate the marrow, stopping suction as soon as the sample is visible (to prevent blood contamination). To collect a core biopsy sample, use the same technique, but use a 1.5-inch, 18-gauge needle in place of the spinal needle (see also Chapter 8). Collect samples from alternate sites by using the same basic technique.

Blood Transfusion

Blood transfusions may be needed in ferrets that are anemic from chronic disease, blood loss, or estrogen toxicosis, or in ferrets that are thrombocytopenic. As in other species, evaluate the need for a transfusion based on the packed cell volume or platelet count and clinical status of the ferret. Consider a transfusion if the packed cell volume is 25% or less in a ferret that exhibits clinical signs of anemia or requires surgery, or if a ferret is thrombocytopenic and exhibits ecchymosis, petechiation, or bleeding.

Ferrets lack detectable blood groups, and risk of transfusion reaction is minimal, even without cross-matching.[39] Because of a

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greater blood volume, large male ferrets are preferred over females as blood donors. Depending on the size of the donor ferret, 6 to 12 mL of blood can be safely collected for transfusion. Collect blood into an anticoagulant such as acid-citrate-dextrose or citrate-phosphate-dextrose-adenine (CPDA) at a ratio of 1 mL of anticoagulant to 6 to 9 mL of donor blood.[31] Ferret blood collected into CPDA at a 6:1 ratio has a shelf life of 7 days when stored at 4° C; after 7 days, deterioration of red blood cells (RBCs) causes a decrease in blood pH, glucose, and sodium and an increase in lactate and potassium.[56] Whenever possible, collect blood from donor ferrets shortly before transfusion. Always use a filter when transfusing whole blood, and use at least a 22-gauge catheter to prevent cell lysis during the transfusion. Intraosseous blood transfusions can be given to ferrets if an intravenous catheter cannot be placed.

Splenic Aspiration

Splenic aspiration is a common diagnostic technique in ferrets with enlarged spleens (see Chapter 5). The technique is simple and can be done in unanesthetized ferrets; however, if a ferret is fractious, use an injectable sedative. An ultrasound-guided aspirate is preferred, especially if a splenic mass is present. Alternatively, palpate the abdomen and immobilize the enlarged spleen next to the body wall and aspirate directly. A positive aspirate appears bloody. The most common findings on cytologic examination of a splenic aspirate are extramedullary hematopoiesis and lymphoma.

Cerebrospinal Fluid Tap

Analysis of cerebrospinal fluid (CSF) as a diagnostic tool is occasionally indicated in ferrets that present with neurologic signs. The volume of CSF fluid that can be removed safely is 0.26 mL/kg.[57] For a CSF tap, place the anesthetized ferret in lateral recumbency. Using a 25-gauge, 1.6-cm–long hypodermic needle, puncture the cerebromedullary cistern and allow free flow of the CSF fluid. In clinically normal ferrets, reference values for CSF tap are mean white blood cells (WBCs), 1.6 cells/μL (range 0–8 cells/μL); mean RBCs, 1041 cells/μL (range 0–11,560 cells/μL; and mean protein concentration, 31.4 mg/dL (range 28–68 mg/dL).[57] In a study of 42 ferrets in which a CSF tap was performed, RBCs of <100 cells/μL were obtained in 64% of cases, and the number of WBCs was significantly affected by blood contamination, but protein concentration was not.[57]

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3

Gastrointestinal Diseases of Ferrets

Heidi L. Hoefer, DVM, Diplomate ABVP (Avian)

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Disease of the gastrointestinal (GI) tract is quite common in ferrets. Clinicians should be familiar with the more prevalent GI disorders, be able to recognize clinical signs, and be prepared to differentiate among potential diagnoses.

DISORDERS OF THE ORAL CAVITY

Dental Disease

Dry kibble diets appear to result in significant wear to ferret premolars and molars.[12] Moist or semi-moist diets have been associated with the formation of dental calculi; however, most ferrets on a dry kibble diet also develop tartar and gingivitis that progress with age. Periodontal disease is pervasive in pet ferrets.[18,40,58]

Gnawing often results in discoloration, wearing, and blunting of the canine teeth. This does not usually result in obvious discomfort unless the dental pulp is exposed. Root canal restoration or surgical removal of affected teeth may be necessary. Extrusion and gingival recession of the canine teeth is common in ferrets; however, tooth root abscesses, periapical disease, caries, and tooth resorption are not.[18,58] Dental disease is often an incidental finding during physical examination.

Follow the basic principles for dental disease management that apply to dogs and cats. Daily at-home prophylaxis using an enzymatic pet toothpaste and finger brush is recommended.

Salivary Mucocele

Although uncommon, mucoceles have been described in ferrets. Salivary mucoceles can develop secondary to trauma to a salivary gland, and salivary microliths may contribute to adenitis and possible mucocele formation.[50] Salivary mucoceles may result in fluctuant facial swellings involving the commissures of the mouth, the top of the skull, or the orbital area.

Although mucoceles that bulge into the oral cavity can be marsupialized into the mouth, recurrence is possible (Fig. 3.1). Surgical excision of the affected salivary gland is preferred.[66] Injecting contrast medium into the mucocele may help trace the route of saliva.

Oral Ulceration and Fistulas

Oral ulcers may be associated with dental disease or concurrent diseases that cause nausea and pawing at the roof of the mouth (e.g., hypoglycemia from insulinoma, gastric reflux or pain from ulcers or foreign bodies, or *Helicobacter* gastritis). Perform serum chemistries, hematology, radiographs, and GI palpation under sedation. Address predisposing factors and treat oral

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Fig. 3.1 The medial aspect of this mucocele is marsupialized into the mouth.

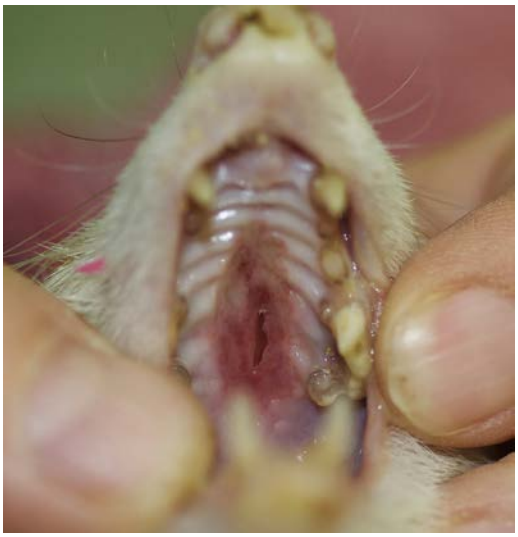


Fig. 3.2 Ulceration of the palate and oronasal fistula in a ferret.

ulcers with liquid sucralfate (100 mg/kg every 6 hours) and a gruel made of soaked kibble until the ulcer heals. In advanced cases, oronasal fistulas can form and can be difficult to repair surgically (Fig. 3.2).[80]

Oral Neoplasia

The oral cavity is an uncommon site of neoplasia in ferrets. Squamous cell carcinoma is the most commonly reported oral tumor in ferrets and typically manifests as a firm swelling of the upper or lower mandible.[5,29,43] Chapter 8 contains more information about oral neoplasia in ferrets.

DISORDERS OF THE ESOPHAGUS

Esophageal diseases are uncommon in ferrets. Megaesophagus, which describes an esophagus that is enlarged (dilated) on radiographic examination and that lacks normal motility, has been reported in ferrets and is associated with regurgitation,



Fig. 3.3 Lateral radiograph of a ferret with megaesophagus. Orally administered barium sulfate delineates the esophagus.

lethargy, inappetence or anorexia, dysphagia, and weight loss.[7,33] Some ferrets exhibit coughing or choking motions or labored breathing. The differential diagnosis includes an esophageal or gastrointestinal foreign body, gastritis, and respiratory disease.

On survey radiographs, the entire esophagus may be dilated and food may be seen in the lumen. Gastric gas is sometimes seen, and aspiration pneumonia may be evident. In suspect cases, always take abdominal radiographs to exclude lower GI disease. Administer barium sulfate or iohexol (8-10 mL/kg by mouth [PO]) to delineate the esophagus and evaluate for mural lesions, strictures, or obstructions (Fig. 3.3). Ferrets will take barium force-fed from a syringe; however, use iohexol instead of barium in cases of possible esophageal rupture. Use fluoroscopy, if available, to determine the motility of the esophagus after a barium swallow.

Palliative management of ferrets with megaesophagus is similar to that of dogs but is less successful. Promotility drugs such as metoclopramide and cisapride work on smooth muscle only, and the esophageal muscle in ferrets is striated along its entire length. These drugs act to increase lower esophageal sphincter pressure, potentially delaying esophageal emptying; therefore they are not useful for megaesophagus. Use ranitidine, famotidine, or omeprazole for reflux and esophagitis (see Table 3.1 for doses). Ferrets with megaesophagus may have malnutrition, hepatic lipidosis, and aspiration pneumonia. Most individuals die or are euthanized within days of being diagnosed with megaesophagus.

The cause of megaesophagus in ferrets is unknown. Autoimmune myasthenia gravis has been documented in two unrelated ferrets, but neither had signs of megaesophagus.[3,14] Diagnosis and treatment of myasthenia gravis is discussed in Chapter 10.

Esophageal foreign bodies have been successfully managed surgically or via endoscopic retrieval.[9,31] This author treated a ferret with a toy sponge foreign body lodged in its distal esophagus. The sponge was broken into smaller pieces by using a 2.7-mm rigid endoscope, and the foreign material passed through the GI tract without incident. Esophageal strictures have been reported and corrected with endoscopic balloon dilation and esophageal stenting.[31]

Ferrets with disseminated idiopathic myofasciitis—a musculoskeletal disease with generalized weakness, joint pain,

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TABLE 3.1 Summary of Suggested Treatment Regimens for *Helicobacter mustelae* Gastritis, Inflammatory Bowel Disease, Proliferative Bowel Disease, and Eosinophilic Gastroenteritis

Disease	Drug	Dosage
Helicobacter mustelae gastritis		
Original triple therapy[a]	Amoxicillin	10 mg/kg PO every 8 h[60]
	Metronidazole	20 mg/kg PO every 8 h
	Bismuth subsalicylate	17.5 mg/kg (1 mL/kg) PO every 8 h
Alternative therapy[a]	Clarithromycin	12.5 mg/kg PO every 8 h[48]
	Ranitidine bismuth citrate	24 mg/kg PO every 8 h[48]
	or	
	Enrofloxacin	5 mg/kg PO every 12 h[22]
	Colloidal bismuth subcitrate	6 mg/kg PO every 12 h
Acid suppressants	Famotidine	0.5-1 mg/kg PO, SC, IV every 12–24 h
	Omeprazole	1 mg/kg PO every 12 h
Inflammatory bowel disease	Azathioprine[b]	0.9 mg/kg PO every 24–72 h
	Prednisone	1 mg/kg PO every 12 h
	Sucralfate	100 mg/kg PO every 6 h
Proliferative bowel disease	Chloramphenicol	50 mg/kg PO, IM, SC every 12 h
Eosinophilic gastroenteritis	Prednisone	1.25-2.5 mg/kg PO every 24 h
	Ivermectin	0.4 mg/kg SC, PO once; repeat in 14 days

[a]Treat for a minimum of 21 days.
[b]Bone marrow suppression possible side effect. Monitor with complete blood count.
PO, by mouth; *SC,* subcutaneously; *IM,* intramuscularly; *IV,* intravenously.

fever, and anorexia—may have severe suppurative or pyogranulomatous inflammatory lesions of the esophagus, as well as other skeletal muscles and surrounding connective tissue (see Chapter 10).[68]

DISORDERS OF THE STOMACH AND GASTROINTESTINAL ULCERATION

General Gastritis and Ulceration

Gastric and duodenal ulcers are common in pet ferrets. Causes of GI ulceration include foreign body or toxin ingestion, *Helicobacter mustelae* infection, neoplasia of the intestinal tract, treatment with nonsteroidal antiinflammatory drugs (NSAIDs), and azotemia. Use NSAIDs cautiously, because overdose or prolonged use can cause ulceration. It is rare, however, for ferrets to have GI bleeding with corticosteroids, even at dosages as high as 2 to 3 mg/kg per day.

Signs of gastritis or duodenal ulceration include melena, anorexia, lethargy, and weight loss. Ferrets experiencing nausea or abdominal pain often hypersalivate, paw at the roof of the mouth, or display teeth-grinding. Vomiting is not common, but owners may describe coughing or gagging that could represent gastric reflux.

Diagnostic tests include whole-body radiography and blood tests. Fast the ferret for 4 to 6 hours to facilitate visualization of a gastric foreign body or hairball. The stomach should be empty; thus any ingesta may represent hair or other material. *Helicobacter mustelae* gastritis may be a diagnosis of exclusion of other common disorders, such as a GI foreign body.

Left untreated, ferrets with melena may die from blood loss or intestinal perforation. Hospitalize debilitated and anorexic ferrets for fluid therapy and parenteral treatment. Use an antiemetic, such as maropitant citrate (Cerenia; Zoetis, Kalamazoo, MI; 1 mg/kg every 24 hours), metaclopromide (0.5 mg/kg SQ, PO or [intravenously] IV every 8 hours), or ondansetron (0.5 mg/kg IM, IV, or PO every 8 hours). An antibiotic combination that targets *Helicobacter* is recommended for debilitated ferrets (see treatment for *Helicobacter* gastritis).

For ferrets that are not vomiting, offer multiple small feedings of a bland, moist diet (e.g., a/d Canine/Feline; Hill's Pet Nutrition, Inc., Topeka, KS) or a carnivore recovery diet (e.g., Carnivore Care, Oxbow Animal Health, Murdock, NE; or Emeraid Carnivore, EmerAid LLC, Cornell, IL). Calculate a minimum daily intake of 400 kcal/kg body weight and divide into four to six feedings per day. Avoid dry, high-fiber foods. For vomiting animals, withhold food for 4 to 6 hours and monitor for signs of hypoglycemia (older ferrets often have subclinical insulinomas). If vomiting resolves, introduce small frequent feedings. Antiemetics can also be used.

Bismuth compounds may inhibit development of peptic ulcers. Administer bismuth subsalicylate (17.5 mg/kg PO every 8 hours) or colloidal bismuth subcitrate (6 mg/kg PO every 8 hours). A suspension of sucralfate—a cytoprotective agent that binds to erosion sites—can be dosed at 100 mg/kg PO every 6 hours.

The H_2-receptor antagonists, such as ranitidine or famotidine, reduce gastric acid secretion. Ranitidine bismuth citrate has the added benefit of bismuth but is unavailable in the United States.[77] Famotidine is available for parenteral administration. Recent studies in dogs and cats have demonstrated superior acid suppression using proton pump inhibitors like omeprazole.[63,81] Use a compounding pharmacy or an omeprazole equine paste (GastroGard,

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Merial, Iselin, NJ). Dilute the paste to the desired concentration using cod liver oil or corn oil.[81] See Table 3.1 for doses.

Helicobacter Mustelae Gastritis

Helicobacter mustelae—a gram-negative bacterial rod—is related to *Helicobacter pylori*, a human pathogen associated with gastritis and ulcers.[20] In fact, ferrets are used as animal models for the study of *H. pylori* infection in people. Virtually all North American ferrets are likely to become persistently infected with *H. mustelae* at weaning unless they are treated or hand-reared in isolation.[78] Infection is lifelong in untreated ferrets. It may become clinically apparent in animals that are stressed by concurrent disease or recent surgery, and the severity of chronic *H. mustelae* gastritis increases with age.[22]

Helicobacter colonizes the antral area of the stomach and pyloric area of the duodenum. Chronic *H. pylori* gastritis in humans can lead to gastric adenocarcinoma or mucosa-associated lymphoid tissue (MALT) lymphoma.[17] Gastric MALT lymphoma associated with *H. mustelae* infection has also been reported in adult ferrets.[17] Spontaneously occurring gastric adenocarcinoma has been reported in pet ferrets,[70,76] and silver-stained (Warthin-Starry) organisms morphologically compatible with *H. mustelae* were seen in neoplastic tissues of one report.[21]

Whereas diagnosis is often based on history and clinical signs, definitive diagnosis of *Helicobacter* infection is confirmed by histopathologic examination of a gastric mucosal sample obtained by endoscopic or surgical biopsy. The organism can be seen in silver-stained sections of gastric mucosa. Gastric mucosa or fecal samples can be submitted for polymerase chain reaction (PCR)–based analysis (University of Georgia Veterinary Diagnostic Laboratory, Athens, GA; Veterinary Molecular Diagnostics, Milford, OH).

Treatment for *Helicobacter* includes antibiotic therapy, as well as the supportive treatment for ulcers outlined previously. Initial treatment is commonly a combination of amoxicillin, metronidazole, and bismuth subsalicylate (see Table 3.1 for dosing protocols).[60] Amoxicillin and metronidazole must be used in combination for at least 21 days with the goal of eradicating *Helicobacter*. Oral amoxicillin suspensions are palatable and well accepted by most ferrets. Metronidazole can be compounded into an oral suspension, but most ferrets find it unpalatable. Clarithromycin-based double therapy (used with either ranitidine bismuth citrate or omeprazole) was found to be more effective than amoxicillin-based triple therapy.[2,48] Either protocol is based on a three-times–daily dosing schedule, which is impractical for some owners. Enrofloxacin plus colloidal bismuth subcitrate is also effective.[22] Antacids can also decrease discomfort and reduce effects of acid reflux on esophageal mucosa (see treatment above for ulcers).

Gastrointestinal Polyps

Gastrointestinal polyps are rare in ferrets. One 6-year-old ferret had an adenomatous polyp of the descending colon that resulted in an intussception.[11] The ferret had chronic diarrhea and straining. Removal was uneventful, and the tumor was benign. Two ferrets with GI polyps have been seen by the author at the Animal Medical Center (New York, NY). Both ferrets exhibited lethargy, inappetence, melena, and weakness from anemia. Abdominal radiographs suggested GI abnormalities. On abdominal exploration, one ferret had a gastric polyp, and the other had a small intestinal polyp. Both ferrets recovered well after resection of the polyps, which were benign.

Gastrointestinal Foreign Bodies

GI foreign bodies are common in ferrets.[54,85] Foreign objects (particularly rubber or sponge products) are commonly ingested by ferrets younger than 2 years of age, whereas trichobezoars are more common in older ferrets. Linear foreign bodies are rare in ferrets.

The most common clinical signs of GI foreign bodies in ferrets are lethargy, inappetence, and diarrhea. Vomiting is uncommon but should always raise suspicion of a GI foreign body (Table 3.2). Some ferrets display bruxism, ptyalism, face-rubbing, and pawing at the mouth. Acutely obstructed ferrets may be recumbent. Chronic trichobezoars can be incidental findings during examination or surgery, but some can become acute outflow obstructions.

Palpate the abdomen carefully. Small intestinal foreign bodies are associated with localized discomfort or pain and can usually be palpated, especially with the animal under sedation. Gastric foreign bodies are more difficult to palpate. Hold the sedated ferret vertically to allow the spleen and stomach to drop down for easier palpation.

If a foreign body is suspected, obtain whole-body survey radiographs, including the thorax to evaluate the esophagus. Abnormal radiographic findings include segmental ileus, gas distention of the stomach, and, occasionally, a visible foreign object or trichobezoar. Contrast studies, using barium sulfate or iohexol (8–10 mL/kg PO), or a negative gastrogram with air can be helpful in determining the presence of hairballs (Fig. 3.4).[85]

Ferrets rarely pass GI foreign bodies unassisted. Occasionally, a small, partially obstructing object may pass after treatment with intestinal lubricants (i.e., hairball laxatives—e.g., Laxatone [Vetoquinol USA, Fort Worth, TX] at 1 mL every 8–12 hours) and replacement fluids. In some cases, small gastric foreign bodies can be removed endoscopically (see Chapter 35). However, most must be removed surgically. Stabilize debilitated ferrets, and then perform an exploratory laparotomy as soon as possible. Collect biopsy samples from the stomach, intestines, or other organs as indicated. Explore the abdomen carefully, because concurrent abdominal disease (e.g., involving the pancreas or adrenal glands) is common. Ferrets can often eat soft foods within 12 hours after GI foreign body removal, and most ferrets are discharged within 48 hours after surgery.

Prevention of foreign body obstructions includes regular use of a hairball laxative preparation during active shedding seasons and "ferret-proofing" the household. Ferrets should not be left uncaged or unsupervised. Advise owners to avoid small rubber "squeak" toys for pet ferrets and to remove rubber objects (e.g., rubber-soled shoes and earphones) from the ferret's environment.

Gastric Distention (Bloat)

Pet ferrets occasionally experience acute gastric or small intestinal foreign body blockage that results in a distended, fluid-filled stomach. These ferrets are acutely very weak.

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TABLE 3.2 Differentiation of Common Gastrointestinal Diseases That Cause Weight Loss and Diarrhea in Ferrets by Typical History, Clinical Findings, and Laboratory and Radiographic Results[a]

Disease	Typical Diarrhea	Vomiting/ Bruxism	Prolapsed Rectum/ Tenesmus	Physical Findings	Laboratory/ Radiographic Results	Comments
Eosinophilic gastroenteritis	Mucoid, green	Possible	No	± Thickened intestinal loops	Eosinophilia ± reactive hepatitis	Rare; multiple tissue involvement (visceral lymph nodes, spleen)
Ferret enteric coronavirus/ (epizootic catarrhal enteritis)	Acute: profuse, green Chronic: grainy ("bird seed")	Possible	No	Thickened or fluid-filled intestines	± Reactive hepatitis	Acute onset, can become chronic; exposure to new or young ferrets
Foreign body	Black, tarry or mucoid, green	Yes	No	Palpable gastric or intestinal gas; painful on abdominal palpation	± Reactive hepatitis Anemia (chronic) Gas in stomach or intestinal loops	Acute or chronic Young ferrets: rubber objects, toys Older ferrets: hairballs more common
Helicobacter mustelae gastritis	Black, tarry or mucoid, green	Yes	No	Enlarged mesenteric lymph nodes	± Reactive hepatitis ± Anemia Gas in stomach	Recent stress (i.e., surgery or concurrent disease); can increase in severity with age
Inflammatory bowel disease	Mucoid, tan or green	Possible	Possible	± Enlarged mesenteric lymph nodes	Reactive hepatitis ± Elevated globulins ± Elevated lipase	May develop secondary to other GI disease
Proliferative bowel disease	Mucoid, green	Rare	Yes	Palpably thickened large bowel; proliferative rectal mucosa	± Elevated globulins	Primarily affects young ferrets

[a]Although typical findings are listed, clinical signs and physical findings are variable in any of the described diseases.
GI, Gastrointestinal.

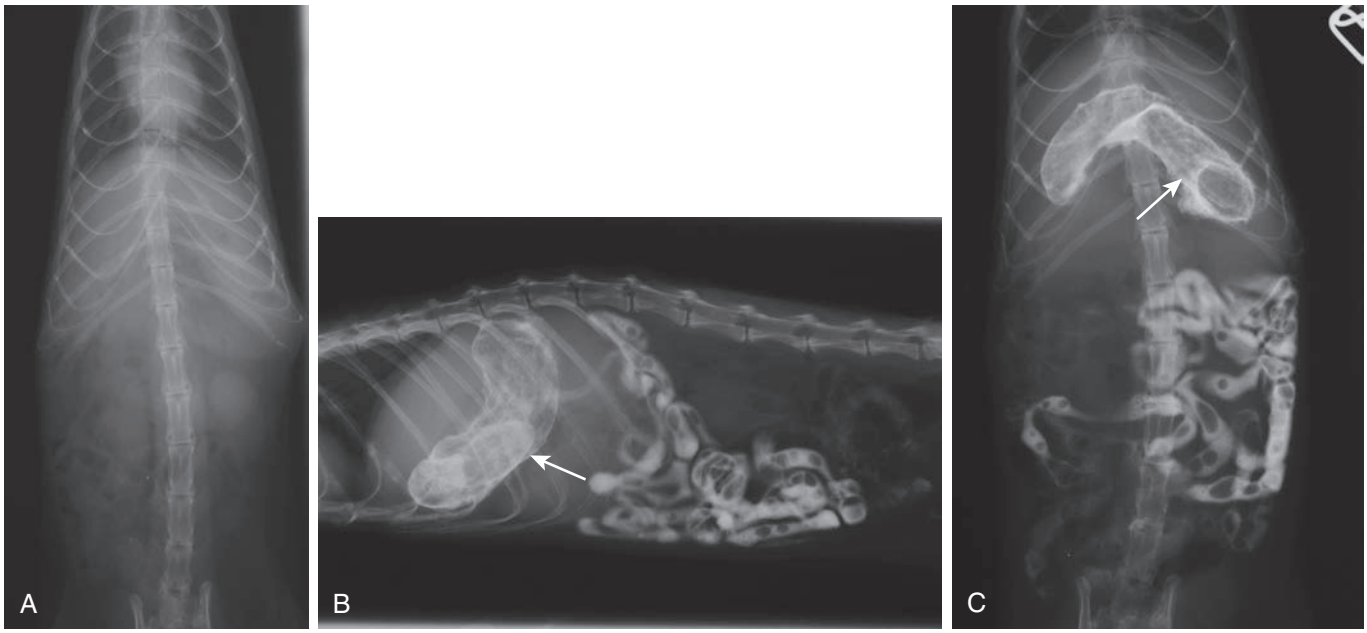


Fig. 3.4 (A) Ventrodorsal radiograph of a ferret with a gastric trichobezoar. The trichobezoar appears as a tubular soft tissue density poorly delineated in the stomach in upper left abdomen. Contrast studies were performed. (B) Lateral and (C) ventrodorsal radiographic view of the same ferret 30 minutes after administration of barium sulfate. Note the delineation of trichobezoars in the stomach (arrows).

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Full-body radiographs can confirm the diagnosis. Affected animals are in shock and need immediate aggressive therapy. Relieve gastric pressure by placing an orogastric tube (8- or 10-Fr red rubber feeding tube) with the ferret under sedation, treat the hypovolemic shock, and prepare for surgical exploratory when stable.

Pyloric stenosis and gastric outflow obstruction can manifest as acute bloat in ferrets. Pyloric adenocarcinoma has been associated with *H. mustelae* infection.[70,76] Pyloric stenosis caused by muscular hypertrophy of the pylorus has been seen clinically by the author, with one case occurring in a 4-month-old ferret. Pyloromyotomy and dilation of the pyloric outflow is the recommended treatment, especially where *Helicobacter* and neoplasia are not present.

Other than associated with obstructive disease, gastric bloat is rare in pet ferrets. However, gastric bloat has been reported on domestic ferret farms and in black-footed ferrets *(Mustela nigripes)*.[35,73] Clinical signs are usually seen in weanlings, but adult ferrets have also been affected. Signs can include acute gastric distention, dyspnea, cardiovascular compromise, and sudden death. The cause is unknown but is believed to be related to an abrupt dietary change and overgrowth of *Clostridium perfringens* type A (previously called *Clostridium welchii*).

ENTERITIS AND DIARRHEA

Normal ferrets nibble on food all day. Their GI transit time is only 3 hours, so defecation is frequent in the healthy state. Normal stool is slightly soft and formed. Anorexic ferrets may pass a very dark green (bile) stool that can resemble melena. Diarrhea in ferrets is difficult to classify by origin in the small intestine or colon. More important are the onset, duration, and severity of diarrhea, as well as concurrent clinical signs. Because the gut flora of ferrets is simple and plays no vital role in digestion, long-term administration of broad-spectrum antibiotics does not cause dysbiosis and diarrhea in ferrets.

Bacterial Disease

Salmonellosis

Salmonellosis is a contagious disease characterized by fever, bloody diarrhea, and lethargy. Conjunctivitis and anemia may also be present. Incidence is very low in pet ferrets, and infection may be associated with feeding raw or undercooked meat and meat by-products. Therapy consists of aggressive supportive care and antimicrobial therapy.

Mycobacteriosis

Mycobacterium bovis and *Mycobacterium avium* infections have been recognized in research, farm, and feral ferrets in England, Europe, and New Zealand. These infections have been associated with the feeding of raw meat and unpasteurized dairy products, or—in feral ferrets—feeding on carrion infected with *M. bovis*.[46] Infections with *M. avium, M. genavense, M. abscessus,* and *M. celatum* have also been reported in domestic ferrets.[45,47,52,65,72,74,83]

Ferrets with mycobacteriosis can have diarrhea, weight loss, lymph node enlargement, conjunctival lesions, splenomegaly, and pneumonia.[52,56] Diagnosis is confirmed by histopathologic examinination of tissue samples, acid-fast staining, PCR testing, and culture. Mycobacterial granulomas grossly resemble those seen with systemic coronavirus disease (see below) and must be differentiated histopathologically.[52] In several reported cases, treatment regimens for mycobacteriosis, including rifampicin monotherapy or in combination with enrofloxacin and azithromycin, have resulted in variable success. The zoonotic potential of mycobacteriosis in ferrets is unknown but should be discussed with owners before beginning treatment.

Campylobacteriosis

The importance of *Campylobacter jejuni* as a primary pathogen in pet ferrets is unknown. Ferrets experimentally infected with *C. jejuni* developed self-limiting diarrhea with mucous and blood, and the organism was recovered from the small and large intestine and from the liver.[59] In one report, two commercial vendors screened asymptomatic ferrets and found 8 of 10 and 43 of 73 cultured positive for *C. jejuni*.[6] Nonclinical shedding can cause infection in more susceptible species, including people. Diagnosis is through culture under microaerophilic conditions, or PCR testing of intestinal tissue. Treatment consists of supportive care, and antibiotics (e.g., erythromycin) are used to hasten the resolution of diarrhea in outbreaks.

Proliferative Bowel Disease

Proliferative bowel disease is a rare bacterial disease that causes intestinal thickening and diarrhea in ferrets 4 to 6 months of age.[23,79] The causative agent, *Lawsonia intracellularis*, primarily involves the colon and less commonly the small intestine.[13]

Ferrets with proliferative bowel disease have chronic diarrhea that varies from dark liquid feces streaked with bright red blood to scant stool, often with bright green mucus. Affected animals cry while straining to defecate, and rectal tissue may prolapse. Some ferrets lose weight rapidly in spite of eating. Affected intestines are palpable on physical examination.

Diagnosis is usually supported by clinical signs, gross or histopathologic lesions, and PCR performed on a rectal swab, feces, or intestinal biopsy sample. Severely affected animals will die if not treated appropriately. *Lawsonia intracellularis* is sensitive to chloramphenicol dosed at 50 mg/kg PO every 12 hours for at least 10 days.[42] Ferrets with rectal prolapse generally heal with medical treatment; therefore placement of a purse-string suture is rarely necessary (see below).

Viral Disease

Coronavirus

Ferret coronavirus is an important cause of enteric disease. The two closely related but genetically distinct forms of this ribonucleic acid (RNA) virus are an enteric coronavirus and a systemic coronavirus resembling feline infectious peritonitis (FIP). Ferret enteric coronavirus is the causative agent of epizootic catarrhal enteritis (ECE), a highly transmissible diarrheal disease of ferrets that was initially called "green slime diarrhea" disease.[88,89] Adult ferrets are most susceptible to ECE, and the typical history includes recent exposure to a new young ferret that is presumably an asymptomatic carrier. The incubation period is 48 to 72 hours, after which affected ferrets are anorexic and lethargic and

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develop profuse green diarrhea that can persist for several days and longer. The morbidity rate can be high, but the mortality rate is low in ferrets that are treated appropriately.

Coronavirus may be detected by PCR testing of fecal or small intestinal tissue samples (Diagnostic Center for Population and Animal Health, Michigan State University, Lansing, MI, or Veterinary Molecular Diagnostics, Milford, OH). Sample submission must be expedited because of the labile nature of RNA viruses. New research has established an enzyme-linked immunosorbent assay (ELISA)–based serologic test to detect serum antibodies against ferret coronavirus.[53]

Treat debilitated ferrets with aggressive fluid therapy, antibiotics, and supportive care and isolate them from asymptomatic or unexposed ferrets. After recovering from ECE, some adult ferrets develop a persistent, intermittent malabsorption syndrome with tan, seed-like diarrhea. The clinical course can last weeks to months. Recovery may be accelerated by treating with prednisone (1 mg/kg every 12 hours for 14 days) and feeding an easily absorbed diet. Tylosin powder (5 mg/kg mixed in soft food every 12 hours) may also be useful for long-term treatment of chronic diarrhea.

Ferret systemic coronavirus (FSCV) has been identified as the causative agent of a progressive systemic pyogranulomatous disease in young ferrets that resembles the dry form of FIP.[4,27,49,55,64] Affected ferrets average 11 months of age and exhibit chronic weight loss, a palpable abdominal mass or masses, diarrhea, hypergammaglobulinemia, leukocytosis, and anemia. Central nervous system (CNS) signs are also possible.[28]

Diagnosis of FSCV requires immunohistochemical staining of affected tissues with the anti-coronavirus antibody, FIPV3-70. The disease is progressive and carries a high mortality rate, with the duration of clinical illness averaging 67 days.[27] There is no treatment for this form of coronavirus in ferrets. Immunosuppressive therapy and supportive care—including nutritional supplementation, GI protectants, antiemetics, and empirical antibiotic therapy—were helpful in maintaining a favorable quality of life for 1 year after diagnosis in one ferret (see Table 3.3).[4,55]

Rotavirus

Farm outbreaks of diarrhea from infection with rotavirus are associated with high morbidity and mortality rates in neonatal kits from 2 to 6 weeks of age.[82,90] Morbidity is low in adult ferrets, but infection may result in a transient, green, mucoid diarrhea. Diagnosis is by PCR testing of fecal or tissue samples (jejunum or ileum) (Diagnostic Center for Population and Animal Health, Michigan State University). Treatment is supportive.

Canine Distemper

Canine distemper is caused by a highly contagious paramyxovirus that is usually fatal in unvaccinated ferrets. Clinical signs include diarrhea, nasal and ocular discharges, and a generalized orange-tinged dermatitis (see Chapter 6). Vaccination of ferrets against canine distemper virus has greatly limited its incidence. However, cold-like symptoms, dermatitis, and diarrhea in newly acquired, unvaccinated ferrets should arouse suspicion.

TABLE 3.3 Suggested Therapeutic Protocol for Systemic Coronavirus Disease

Drug	Dosage
Prednisolone	1–2 mg/kg PO every 12 h, initial dosing then taper
Doxycycline	10 mg/kg every 12 h
Pentoxifylline	20 mg/kg PO every 12 h
Polyprenyl immunostimulant	3 mg/kg PO 3 times weekly
Cimetidine	10 mg/kg PO every 8–12 h
Feline vitamin supplement	As directed on label and dosed by body weight

PO, By mouth.
Data from Murray J, Kiupel M, Maes RK. Ferret coronavirus–associated diseases. Vet Clin North Am Exot Anim Pract 2010;13:543–560.

Influenza

Ferrets infected with influenza, which is caused by an orthomyxovirus, sometimes have transient diarrhea. The virus also causes upper respiratory disease associated with coughing, sneezing, inappetence, and lethargy. Affected ferrets are often febrile (see Chapter 6).

Parasitic Disease

Although ferrets are susceptible to intestinal parasites, there are surprisingly few clinical reports. The most significant enteric parasitic disease appears to be coccidiosis. Severe morbidity and mortality associated with outbreaks of *Eimeria furonis* have been described in groups of densely populated ferrets.[75] Ferrets of all ages were affected and presented with acute diarrhea and dehydration. Fecal shedding was sporadic and inconsistent. Affected ferrets were treated with aggressive supportive care and sulfadimethoxine; however, some ferrets died despite treatment. Long-term therapy with sulfadimethoxine was ineffectual in completely eradicating the disease.

Giardia is rarely isolated in ferrets, and its clinical significance is unknown. In one report, 1180 fecal samples from small mammals in Europe were tested for *Giardia* by ELISA, and five ferrets tested positive for *G. duodenalis*.[62]

Cryptosporidiosis is described in ferrets but may not result in clinical disease.[1,69] Young ferrets can have subclinical infections of *Cryptosporidium parvum*, and coccidial oocysts can be shed by clinically normal ferrets. The zoonotic potential of the ferret genotype of *C. parvum* is unknown; however, if oocysts are detected, discuss the potential of transmission to immunocompromised owners.

Inflammatory Disease

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a relatively common cause of gastroenteritis in ferrets.[8,16] The pathogenesis is unknown. Inflammation, which occurs in the stomach and small intestine, is typically lymphoplasmacytic and can vary in severity. Although some eosinophilic infiltration can be seen, IBD should be distinguished from eosinophilic gastroenteritis, which often involves multiple tissues and eosinophilia (see below). Because it resembles ECE, dietary indiscretion, and lymphoma, IBD is

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easily overlooked in ferrets. Chronic GI inflammation has been associated with the development of MALT lymphoma (see above under *Helicobacter*).

Affected ferrets can have loose, seed-like stools, intermittent nausea, occasional vomiting, and weight loss. Clinical signs can be subtle and chronic, or some ferrets can have acute vomiting and lethargy. Ferrets with IBD are usually young or middle-aged adults and in multiple-ferret households; however, typically only one ferret in the household is affected. Results of blood tests may reveal an increase in liver enzymes and plasma globulins, and lymphocytosis is occasionally present. In some ferrets, laboratory results are unremarkable.

Diagnosis is based on clinical signs; a detailed clinical history that eliminates the possibility of exposure to ECE; and results of diagnostic tests. Intestinal lymphoma is the primary differential diagnosis (see Chapter 8). Definitive diagnosis can only be made by histologic examination of gastric and intestinal biopsy samples retrieved surgically or endoscopically.[16] Multiple full-thickness jejunal biopsy specimens may be necessary to distinguish IBD from lymphoma.[86]

Empirical treatment is common. Prednisone (1 mg/kg PO every 12–24 hours) is often used, but some ferrets with IBD respond poorly to long-term corticosteroid treatment. Azathioprine (Imuran, Prometheus Laboratories, San Diego, CA) (0.9 mg/kg PO every 24–72 hours) is another treatment option and seems to be well tolerated by ferrets.[8] Hypoallergenic diets made for cats (z/d feline; Hill's Pet Nutrition, Topeka, KS) can be tried, but ferrets are often reluctant to make dietary conversions. Avoid grain-free formulations, because some have been associated with the formation of cysteine uroliths (see Chapter 4).

Eosinophilic Gastroenteritis

Eosinophilic gastroenteritis is uncommon in ferrets. Affected animals typically have chronic diarrhea, with or without mucus and blood, and severe weight loss. Granulomas and a thickened bowel may be palpable. Signs may be clinically indistinguishable from persistent ECE. In all reported cases in ferrets, animals are older than 6 months; however, because of the small number of reports, the incidence of disease in young animals is unknown.[10,19,24,61]

Peripheral eosinophilia is common and highly suggestive of the disease. No pathogens have been observed in or isolated from lesions. A causative agent has not been found in ferrets, but food allergy is implicated in humans and some dogs. No reports of food elimination tests in affected ferrets could be found in the literature.

Remission has occurred in ferrets treated with prednisone (1.25–2.5 mg/kg PO every 24 hours for 7 days and every 48 hours thereafter). Immediate recovery also followed removal of an enlarged mesenteric lymph node in one ferret and treatment with ivermectin (0.4 mg/kg SC) in another.[61]

RECTAL DISEASE

Rectal prolapse can occur in ferrets. It is most often associated with diarrhea and is usually a disease of young ferrets. Possible causes include coccidiosis, proliferative bowel disease, colitis, and neoplasia.



Fig. 3.5 Rectal leiomyosarcoma in a ferret.

In some young ferrets, protrusion of rectal mucosa occurs subsequent to poor anal sacculectomy technique. Straining from prostatic disease, urinary outflow obstruction, or an enlarged sublumbar lymph node (e.g., with lymphoma) may result in rectal protrusion. Anal sac impactions or abscesses are rare in surgically descented ferrets; however, they can be seen in intact ferrets or ferrets that have been neutered but not descented. Sedate the ferret for a controlled removal of anal sac secretions. Anal sac removal is described in Chapter 31.

Neoplasia is rare in the rectal area, with one recent report of anal sac apocrine adenocarcinoma.[57] The author has seen a descented ferret with leiomyosarcoma that surrounded the rectal opening (Fig. 3.5). The ferret presented for rectal prolapse, and a tumor was detected on palpation.

In ferrets that present for straining, perform radiography and a fecal wet mount and flotation to check for parasites. Colonoscopy can be performed to obtain biopsy specimens (see Chapter 34).

Rectal prolapse often resolves with treatment of the underlying condition. Treat with antibiotics and parasiticides, as indicated. Control diarrhea with a kaolin/pectin oral preparation (1–2 mL/kg PO every 2–6 hours as required) and loperamide (0.2 mg/kg every 12 hours) if needed. Apply a topical corticosteroid ointment or hemorrhoid cream for palliation (Preparation H; Pfizer Inc, New York, NY). Although rarely necessary, rectal purse-string sutures can be placed if the prolapse is extensive. However, the owner must closely monitor the ferret for defecation, especially when the stool regains its normal consistency. Sutures should be removed in 2 to 3 days.

In young ferrets that have prolapse from poor anal sacculectomy technique, a surgical procedure to tighten the sphincter may be necessary.[39] Two or four wedge-shaped pieces of skin are removed from the perianal skin and closed with 5-0 suture to decrease the rectal opening. Treatment of rectal neoplasia

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involves surgical debulking, possible rectoplasty, and possible localized radiation therapy. Prognosis is poor.

GASTROINTESTINAL AND PANCREATIC NEOPLASIA

Pyloric adenocarcinoma and MALT lymphoma can occur in ferrets and may be related to chronic *Helicobacter*-induced gastritis (see above). Intestinal lymphoma tends to blend imperceptibly with surrounding tissue, whereas adenocarcinoma has more substantial tumor formation that can lead to intestinal blockage. Clinical signs with adenocarcinoma include nonresponsive diarrhea and weight loss, which is rapidly progressive and fatal. Differential diagnosis may include intestinal foreign body or systemic coronavirus with granulomas.

Intestinal lymphoma is common in ferrets but occurs less frequently than lymphoma in visceral and mesenteric lymph nodes, the liver, and the spleen (see Chapter 8). Intestinal lymphoma results in chronic weight loss and diarrhea and is often overlooked because it resembles other, more common causes of chronic diarrhea, such as ECE and IBD. Neoplasia affecting the gastrointestinal tract is described in more detail in Chapter 8.

Pancreatic endocrine neoplasia is much more common than exocrine neoplasia in ferrets, although both have been reported. Pancreatic islet cell tumor (beta cell carcinoma or insulinoma) is common and results in elevated insulin levels and hypoglycemia (see Chapter 7). Tumors of the exocrine pancreas often demonstrate aggressive behavior and can spread throughout the abdomen, resulting in carcinomatosis.[36,41,71,87] It is important to differentiate carcinomatosis from the gross lesions of ferret systemic coronavirus.

HEPATOBILIARY DISEASE

In most ferrets with liver disease, a high concentration of alanine aminotransferase (>275 IU/L) is present on plasma biochemical analysis. Alkaline phosphatase and γ-glutamyl transferase concentrations are sometimes increased. High total bilirubin levels can be seen, and affected ferrets are usually icteric with pigmented urine. Be cautious in diagnosing liver disease in ferrets based solely on high liver enzyme concentrations, because these findings are also common in ferrets with intestinal disease. Instead, base the diagnosis on persistently high liver enzyme concentrations, radiographic and ultrasound findings, and—for definitive diagnosis—analysis of liver biopsy samples. Although ultrasound-guided needle biopsy of the liver is possible, a full abdominal exploratory is often recommended because of the likelihood of concomitant disease in ferrets.

Inflammatory Hepatitis

Chronic lymphocytic-plasmacytic portal hepatitis is a common finding on histologic examination of hepatic biopsy samples in ferrets and is often subclinical. The cause is unknown but may be related to GI disease, such as IBD. In one ferret colony, chronic lymphocytic cholangiohepatitis with biliary hyperplasia was reported in 8 of 34 cohabitating ferrets.[26] Spiral-shaped bacteria were identified in the livers of three ferrets. The clustering of cases and pathologic findings suggested a possible infectious cause.

Recently, a novel hepatitis E virus (HEV) was identified in ferrets in the Netherlands, as well as in ferrets imported from the United States into Japan.[44,67] One study of 63 imported ferrets in Japan demonstrated subclinical infection, acute hepatitis, or persistent infection.[44] Hepatitis E virus is also known to cause acute hepatitis in people.[51]Although HEV is zoonotic, there are no reports to date of disease in humans resulting from exposure to infected ferrets.

Copper Toxicosis

Copper toxicosis was diagnosed in two sibling ferrets on the basis of high hepatic copper concentrations and histologic changes in hepatic tissue.[25] Clinical signs were mostly nonspecific and included severe CNS depression with hypothermia and hyperthermia, respectively. One ferret was icteric. Both ferrets died within a few days of clinical evaluation despite supportive care. A genetic predisposition to copper toxicosis was proposed, because the ferrets had the same phenotypic coat color and no environmental source of copper could be identified.

Copper toxicity was identified and treated in a 5-year-old pet ferret that presented with lethargy and high liver enzymes.[30] Liver biopsy revealed vacuolar changes, and 25% to 50% of hepatocytes stained positive for intracellular copper. Quantitative copper levels on a liver sample were 1720 ppm (normal in other species, 120–400 ppm). Treatment consisted of penicillamine (15 mg/kg PO every 12 hours), liver protectants (silybin, S-adenosylmethionine) and a low-copper diet. Dietary levels of copper are being evaluated in an ongoing study (Jennifer Graham, DVM, personal communication, December 2019).

Neoplasia

Several different types of hepatic neoplasms have been reported in ferrets (see Chapter 8).[15] Biliary cystadenomas are common and are often incidental findings. However, their multilocular cystic structures—although benign—can become quite large and invasive, resulting in significant morbidity.[38] When caught early, cystadenomas can be successfully treated with a partial liver lobectomy (see Chapter 31).

Pancreatic islet cell tumors, adrenal adenocarcinoma, exocrine pancreatic carcinomas, and hemangiosarcoma can metastasize to the liver. Prognosis is guarded regardless of tumor type.

Other Hepatopathies

Other than neoplastic diseases, primary hepatopathies are uncommon in ferrets. One 6-year-old ferret had an acute liver lobe torsion of the left lateral lobe.[84] The ferret presented with an acute abdomen and severe jaundice. Liver lobe torsion was diagnosed by radiology and ultrasonography. Hepatic lipidosis can be found in association with long-standing anorexia, which can result from chronic GI disease. Steroid hepatopathy is rare in ferrets, even with long-term steroid administration or hyperadrenocorticism.

Gall Bladder Disease

Cholelithiasis and cholestasis have been described in ferrets and may be underdiagnosed in clinical practice.[32,34,37] One ferret had

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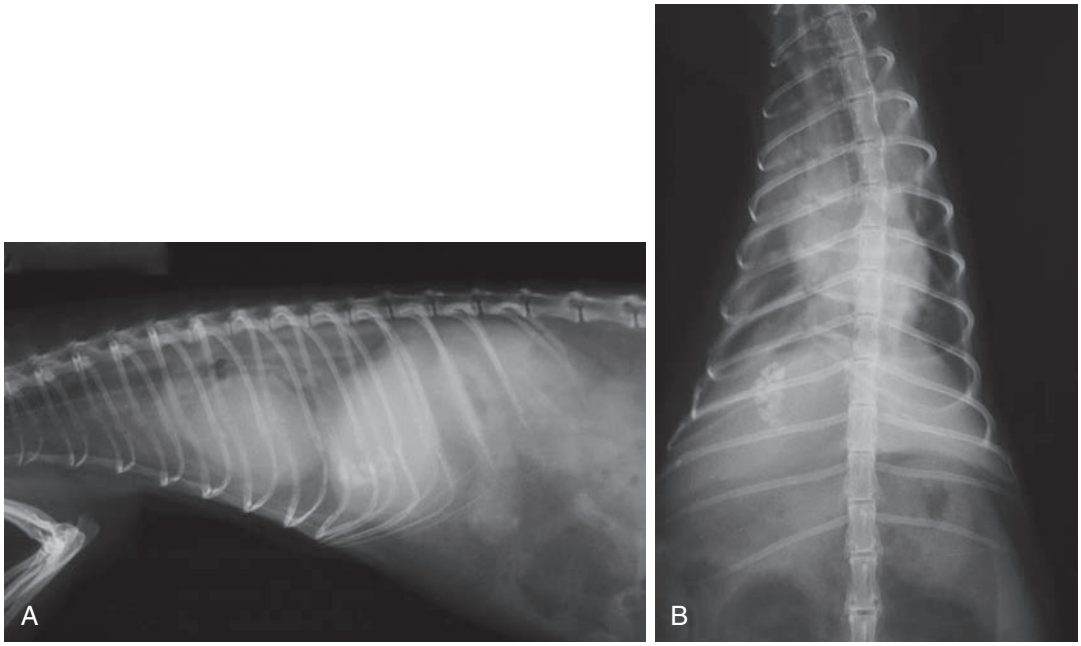


Fig. 3.6 (A) Lateral and (B) ventrodorsal radiographs in a ferret that presented with heart failure. There is cardiomegaly with edema and several choleliths in the gall bladder, which were considered an incidental finding.

cholecystitis with gallbladder rupture and subsequent bile peritonitis. Bacteriologic culture of the gallbladder revealed a pure growth of *Pseudomonas aeruginosa*.[37] In some other ferrets with extrahepatic biliary obstruction, no bacteria were cultured. This author treated a ferret with a foreign body in the proximal duodenum that obstructed the bile duct as it entered the small intestine. The ferret presented with jaundice and anorexia and had liver enzyme elevation and severe bilirubinemia. Enterotomy and foreign body removal were curative. Extrahepatic biliary obstruction can also be caused by pancreatic or other neoplasia.[71]

Diagnosis of gallbladder disease generally requires radiographs and ultrasound. Interestingly, one ferret with cholestasis, cholelithiasis, and very high liver enzymes had no clinical signs associated with liver disease.[32] This author has also found choleliths in several ferrets, which appeared to be incidental findings. Screening radiographs showed mineral densities in the right cranial abdomen, which were associated with the liver and confirmed on ultrasonography (Fig. 3.6).

Treatment for gallbladder disease is either medical or surgical. If possible, perform an ultrasound-guided cholecystocentesis to sample the bile for culture. Whereas some reports indicated no bacterial growth, *Pseudomonas* species, *E.coli*, and *Clostridium* species have been cultured.[37,38] Choose combination antibiotic therapy that targets both gram-negative bacteria and anaerobes. Surgical procedures include cholecystectomy or choledochoduodenostomy.

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4

Disorders of the Urinary and Reproductive Systems in Ferrets

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DISORDERS OF THE URINARY SYSTEM

The ferret has a classic bean-shaped kidney that sits in the retroperitoneal space; its dorsal surface lies in direct contact with the sublumbar musculature.[22] Paired ureters transport urine from renal calices to a pear-shaped urinary bladder. The urethra is compressed by the os penis in the male. Urinary pathologies—especially renal ones—are a common necropsy finding in ferrets.[26,38] Renal failure, urolithiasis, and ureteral disorders are seen with varying frequency in clinical practice.[15,62]

Renal Disease and Renal Failure

Variable degrees of chronic interstitial nephritis are commonly found at necropsy in geriatric ferrets.[41] Advanced interstitial nephritis, as well as pyelonephritis, glomerulonephritis, and immune complex–mediated glomerulonephropathy, can cause renal failure.[63] In one author's experience (N.D.), multiple cases of chronic kidney disease have been diagnosed in a group of young ferrets fed raw meat (e.g., as part of what is termed a biologically appropriate raw foods diet), which may suggest a dietary or familial cause. Although uncommon, renal tumors are another potential cause of chronic kidney disease in ferrets.[8] Chronic kidney disease may result in nephrotic syndrome, in which proteinuria and hypoalbuminemia lead to peripheral edema, ascites, or both.

Common causes of acute kidney injury (AKI) in the ferret are postrenal and intrinsic renal insults. In addition, postoperative renal failure can be seen in cases of severe anesthetic

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hypotension. Ureteral stenosis, prostatic enlargement, and urolithiasis may result in obstruction of urine flow. Infectious disease and toxin exposure may result in acute disruption of the renal parenchyma (Fig. 4.1). Toxin exposure is especially relevant because of the small size of ferrets and their inquisitive habits.[18] For example, the minimum lethal dose of ibuprofen is 220 mg/kg, which means that ingestion of one tablet could be fatal in a small ferret. Clinical signs appear within 48 hours and as rapidly as 4 hours after ibuprofen ingestion in 40% of ferrets. The most common clinical signs are neurologic, and more than half of ferrets also have gastrointestinal (GI) signs. In rare instances, acetaminophen ingestion can also cause AKI.[18] Renal failure has also been reported as a result of an epinephrine overdose administered to a ferret during a vaccine reaction.[17]

Clinical signs of renal failure may be nonspecific (e.g., anorexia, weight loss, and lethargy) but may also include ulcers, signs of GI abnormalities (including melena and, in rare instances, vomiting), ataxia, ascites, and peripheral edema. Physical examination findings can include dehydration, pallor, irregularities or asymmetry in the size and shape of the kidneys, and increased blood pressure. Polyuria and polydipsia may be seen with chronic kidney disease, whereas AKI is usually characterized by oliguria or anuria.

Abnormal serum biochemical results typically include increased blood urea nitrogen (BUN) and creatinine levels and may also include hyperphosphatemia, hyperkalemia, or hypokalemia and reduced total carbon dioxide levels. Azotemia must be interpreted with care, because gastric ulcerations and meat-based diet consumption may artificially increase BUN levels. Reference levels for creatinine in ferrets (0.2–0.8 mg/dL) are lower than those in dogs and cats,[34] and increases in creatinine levels with renal disease are usually moderate (generally <1.5 mg/dL). In two ferrets with severe renal disease confirmed by histologic examination, both ferrets had a creatinine level of 1.1 mg/dL in conjunction with BUN values of 140 and 320 mg/dL.[41]

Decreased urine specific gravity can suggest proteinuria, as well as the inability of the kidney to concentrate urine. Reference ranges for urinalysis in young healthy ferrets have been published.[20] Mean endogenous creatinine, exogenous creatinine, and inulin clearance rates have been established in ferrets to help evaluate glomerular filtration.[21] Although reference values for urine protein/creatinine ratios (UP:C) have not been established for ferrets, results of a systematic review of literature in humans indicate that a UP:C value of a random urine sample may help rule out the presence of proteinuria as judged by measurement of protein in a 24-hour urine sample.[66] Canine reference values for UP:C are generally <1.0 and cats are <0.6.[86] Symmetric dimethylarginine (SDMA), a novel marker of renal function in small animals,[32] could be an interesting tool for early diagnosis of renal disease in ferrets.[54] In a recent study performed in a clinical setting, SDMA was measured in healthy ferrets and ferrets with renal disease.[54] The SDMA values in control ferrets ranged from 1.2 to 18.8 µg/dL, whereas, in ferrets with confirmed renal disease values ranged from 15.2 to 80.8 µg/dL,[54] resulting in a cutoff value similar to that in dogs and cats (14 µg/dL).

If renal disease is suspected based on urinalysis and biochemical results, attempt to identify the underlying cause with ultrasound examination. Loss of corticomedullary distinction, focal and multifocal alterations in the parenchyma, renal pelvic dilation, and hydronephrosis are sonographic abnormalities that may be detected in ferrets with nephropathies. Ultimately, chronic renal disease may lead to renal atrophy. Sonographically, healthy ferret kidneys show a resistive index (RI) of 0.54 ± 0.04 and a pulsatility index (PI) of 0.83 ± 0.10.[31] Even with severe renal parenchymal changes, no significant alterations in blood flow parameters are seen; however, these indices do increase with age.[31] If necessary, ultrasound-guided renal aspiration or biopsy may be performed. At necropsy, kidneys with significant disease are often grossly pitted with large, focal depressions in the outer cortex secondary to scarring (Fig. 4.1).

Although treatment should be aimed at the underlying cause, nonspecific therapy of renal failure includes supportive care, such as fluid therapy, vitamin and iron supplementation, omega-3 fatty acid supplementation, and nutritional support. Additional therapy may include dietary phosphorus restriction, intestinal phosphate binders, antioxidant supplementation, antihypertensive drugs, angiotensin-converting enzyme inhibitors, and erythropoietin in case of anemia. Begin antibiotics if clinically indicated and use culture and sensitivity results when

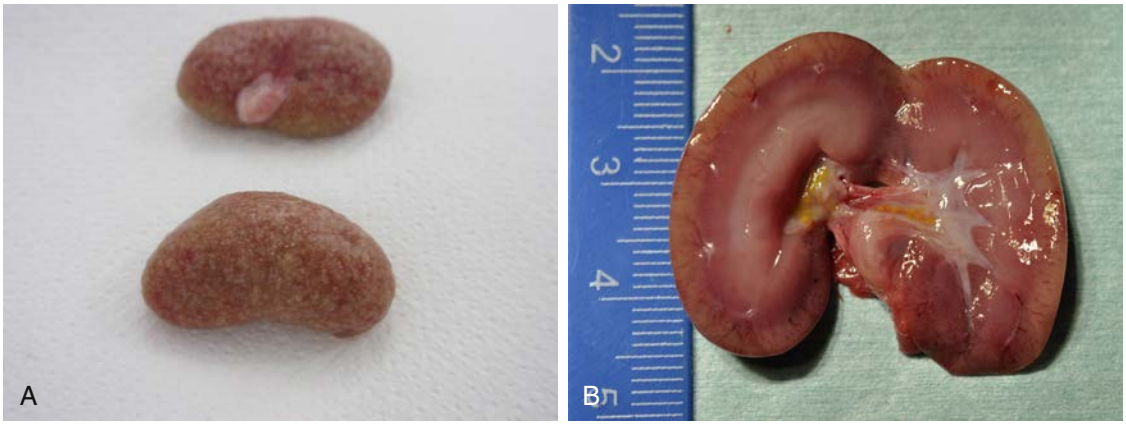


Fig. 4.1 (A) External surface of kidneys in a ferret with chronic kidney disease. (B) Hyperemia of the renal cortex in a ferret with canine distemper virus infection. (Courtesy Dr. Minh Huynh [A] and Dr. Nicola Di Girolamo [B].)

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available. Discontinue any potentially nephrotoxic drugs and administer diuretics as needed. The use of small animal renal diets is difficult because these products are not palatable to most ferrets. Furthermore, the effects of long-term protein restriction in ferrets requires study. The prognosis for ferrets with renal failure depends on the cause and severity of the primary disease and response to therapy.

Renal Cysts and Polycystic Kidney Disease

Renal cysts of various sizes are a common incidental finding in ferrets (Fig. 4.2). The incidence of renal cysts ranges greatly in different studies, from 32% to 63% of ferrets affected.[31,38,68,69] Cysts are usually present singly or in small numbers; they are unilateral in most cases but can be present in both kidneys.[78] Cysts are commonly found in the cortices, in close relationship to the pelvic recesses.[68] Rarely, multiple cysts are present in the form of polycystic kidney disease (Fig. 4.3).[69] The causes of renal cysts and polycystic kidney disease in ferrets are uncertain.[38]

Renal cysts may be detected during physical examination as one or more smooth masses on the renal surface. Polycystic kidneys are palpable as slightly irregular, enlarged, firm, oval masses.[38] Ultrasonographic examination is the ideal diagnostic tool for confirmation of renal cysts (Fig. 4.2). If extensive renal architecture is disrupted, cysts will lead to renal failure. Pyelography with an intravenous contrast medium or nuclear scintigraphy may be used to evaluate renal function in clinically affected ferrets.

There is no specific treatment for renal cysts. Ultrasound-guided paracentesis may be used as a palliative treatment, but fluid reaccumulates rapidly. In dogs and cats, renal cysts have been chemoablated by injection of ethanol after drainage.[88] Monitor affected ferrets with periodic ultrasound examination, biochemical analysis, and urinalysis. In people, simple cysts are usually clinically silent, although they occasionally hemorrhage and cause acute pain.[9]

Aleutian Disease

Many ferrets infected with the parvovirus that causes Aleutian disease are asymptomatic carriers. Clinical signs are usually consistent with chronic wasting and ataxia. Additional clinical signs may be attributed to immune complex deposition. Deposits in the kidney may cause membranous glomerulonephritis and tubular interstitial nephritis and possibly renal failure.[63] Aleutian disease virus may also cause liver failure,

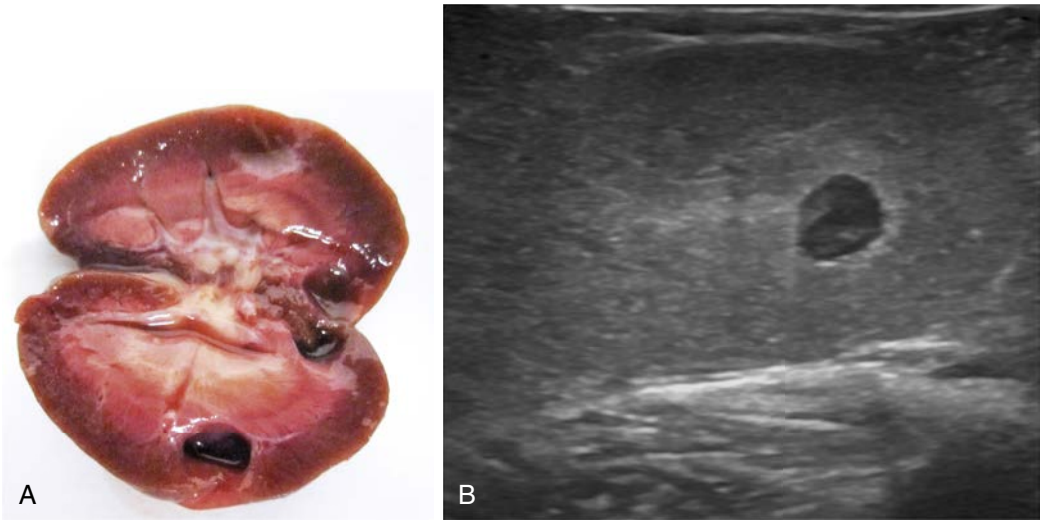


Fig. 4.2 (A) Cross-section of a kidney with two cortical cysts. (B) Sonogram showing a small renal parenchymal cyst of little clinical significance. (Courtesy Dr. Minh Huynh [A] and Dr. Nicola Di Girolamo [B].)

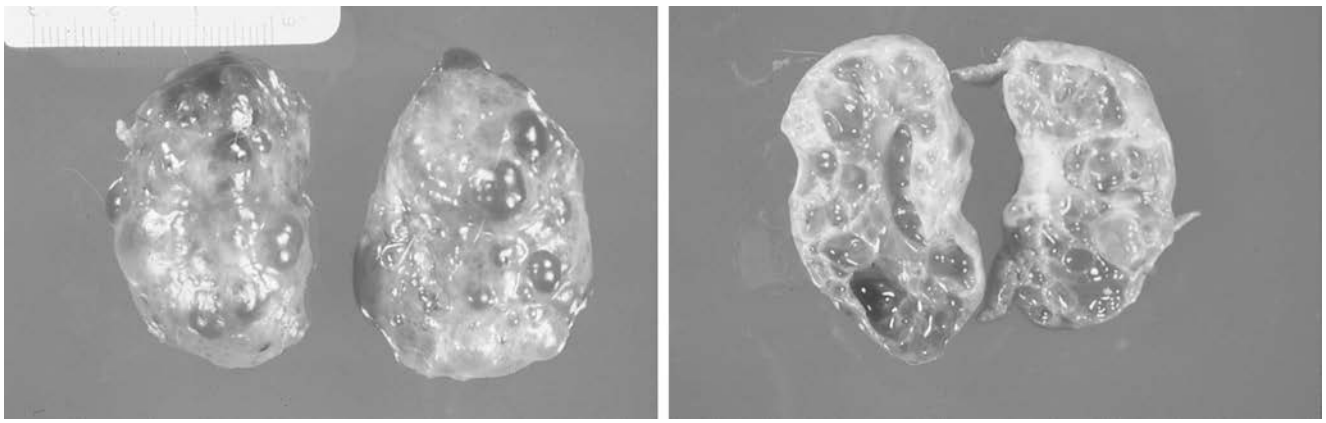


Fig. 4.3 Polycystic kidney in a 3-year-old female ferret in acute renal failure.

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intestinal disease (including melena), and central nervous system disease.[63] See Chapter 5 for diagnosis and treatment of Aleutian disease.

Coronavirus

Pyogranulomatous inflammation of the kidney and green-tinged urine have been seen in ferrets with ferret systemic coronavirus (FSCV).[28] One study of ultrasonographic changes in ferrets with FSCV identified nephromegaly and changes in renal cortex echogenicity in most ferrets.[16] Immune complex–mediated glomerulonephritis was seen in an 18-month-old male ferret diagnosed with feline coronavirus.[27] See Chapter 3 for further discussion of FSCV.

Nephrocalcinosis

In three separate sonographic surveys in Europe, hyperechogenicity of the renal medulla was seen in 40% to 58% of pet ferrets.[31,68,69] This sonographic finding was not identified in laboratory ferrets. Histologic evaluation revealed calcium deposits in the renal tubules consistent with renal calcification. Crystalline structures within the renal parenchyma that could not be found sonographically were believed to be urates. Dietary analyses suggested that the presumptive nephrocalcinosis was related to excess dietary calcium and phosphorus.[69]

Pyelonephritis

Pyelonephritis is an uncommon finding in ferrets, usually associated with an ascending bacterial urinary tract infection or sepsis. Hemolytic *Escherichia coli* and *Staphylococcus aureus* are the most common causative agents. Clinical signs are anorexia, lethargy, fever, and pain on palpation of the kidneys. Severe suppurative pyelonephritis progressing to end-stage chronic renal failure was reported in a ferret treated for lymphoma.[71] In that case, immunosuppression from long-term corticosteroid administration may have led to cystitis and secondary pyelonephritis.[71]

To differentiate pyelonephritis from lower urinary tract disease, perform urinalysis and abdominal ultrasound and consider pyelocentesis. In cases of pyelonephritis, urinalysis would be expected to show hematuria, pyuria, renal tubular cells, and cellular casts. Provide supportive care and administer antibiotics based on urine culture and sensitivity results for 3 to 6 weeks.

Renal Neoplasia

Renal tumors are uncommon in ferrets (see Chapter 8).[8,44]

Hydronephrosis

Hydronephrosis and hydroureter in ferrets may develop as a consequence of ureteral obstruction, neoplasia involving the renal pelvis, cystitis, herniation of the bladder, and ligation of the ureter during ovariohysterectomy.[8,15,57] In severe cases, hydronephrosis may lead to renomegaly, and the affected kidney may be palpable as an abdominal mass. On survey radiographs, the hydronephrotic kidney appears as a radiopaque, midabdominal mass with a large fluid density. Normal length of the kidneys, expressed as a ratio to the body length of lumbar vertebra 2 (L2), are between 2.21 to 2.31 vertebrae for the right kidney and 2.15 to 2.25 vertebrae for the left kidney.[19]

If hydronephrosis is suspected, obtain samples for a complete blood count (CBC), biochemical analysis, and urinalysis. Use ultrasonography to confirm the diagnosis. In certain instances, excretory urography or retrograde pyelography may be required to establish the exact location of the obstruction and to distinguish between the different causes (Fig. 4.4). Note that when retrograde pyelography is performed, a certain degree of calicectasis is expected (Fig. 4.5).

Treatment of hydronephrosis depends on the causes and severity of the disease. If diagnosed early, resolution of the obstruction is curative. If diagnosis is delayed, unilateral nephrectomy carries a good prognosis if function of the remaining kidney is normal.

Ureteral Disorders

Ureteral Rupture

Traumatic avulsion of the ureter was reported in a ferret with blunt trauma severe enough to also create a diaphragmatic hernia. No specific urinary tract signs or abnormal clinical pathologic findings were observed. Excretory urography was used to detect ureteral leakage, and treatment included ureteronephrectomy.[85]

Retrocaval Ureter

Retrocaval ureter (also known as circumcaval ureter) was diagnosed in a ferret that presented with clinical signs of AKI.[14] Depending on the degree of ureteral compression, retrocaval ureters may be incidental findings or may result in hydroureteronephrosis.[11] Ureteroneocystostomy (i.e., reimplantation of the ureter into the bladder) should be considered in symptomatic cases or in cases with evidence of hydronephrosis.

Congenital Ureteral Stenosis

A ferret with bilateral ureterovesical junction stenosis developed bilateral hydroureteronephrosis.[82] A subcutaneous ureteral bypass was placed in one of the kidneys and was removed after 3 months because of obstruction and persistent urinary tract infection. At that time, bilateral ureteroneocystostomy was successfully performed.

Congenital Hydroureter

Two ferrets with suspected congenital hydroureter have been described.[15] In both ferrets, hydroureter was an incidental finding. The ferrets were periodically monitored by ultrasound scanning and did not develop hydronephrosis. No treatment was deemed necessary in either ferret.

Urolithiasis

Urolithiasis is characterized by solitary or multiple calculi found anywhere throughout the urinary tract or by the presence of sandy material within the bladder and urethra.

The most common calculus composition reported in ferrets in both the United States and the United Kingdom used to be magnesium ammonium phosphate $6H_2O$, or struvite.[62,70] Dietary factors are believed to play an important role in struvite crystal formation. Urine pH is greatly influenced by diet,

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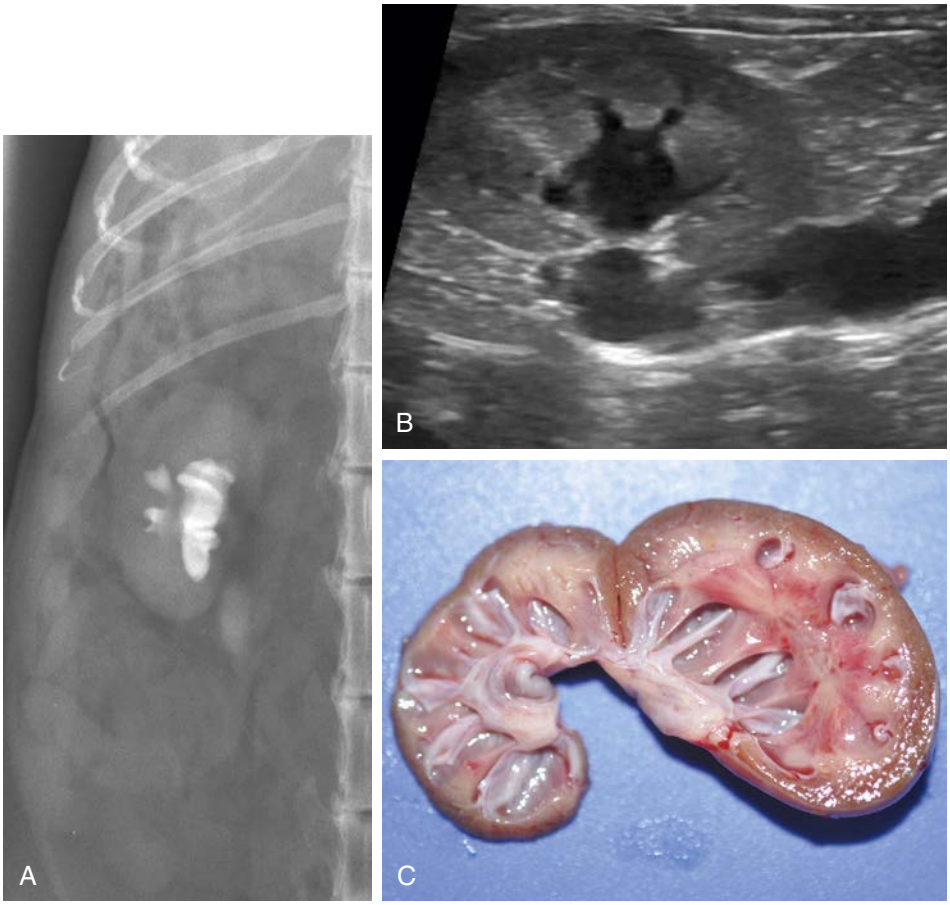


Fig. 4.4 Severe hydronephrosis and hydroureter in a ferret. (A) Excretory urogram shows accumulation of contrast material in the renal pelvis consistent with decreased renal outflow. (B) Sonogram shows distention of the renal pelvis and the proximal ureter. (C) Cross-section of the kidney after surgical removal. (Courtesy Dr. Nicola Di Girolamo.)

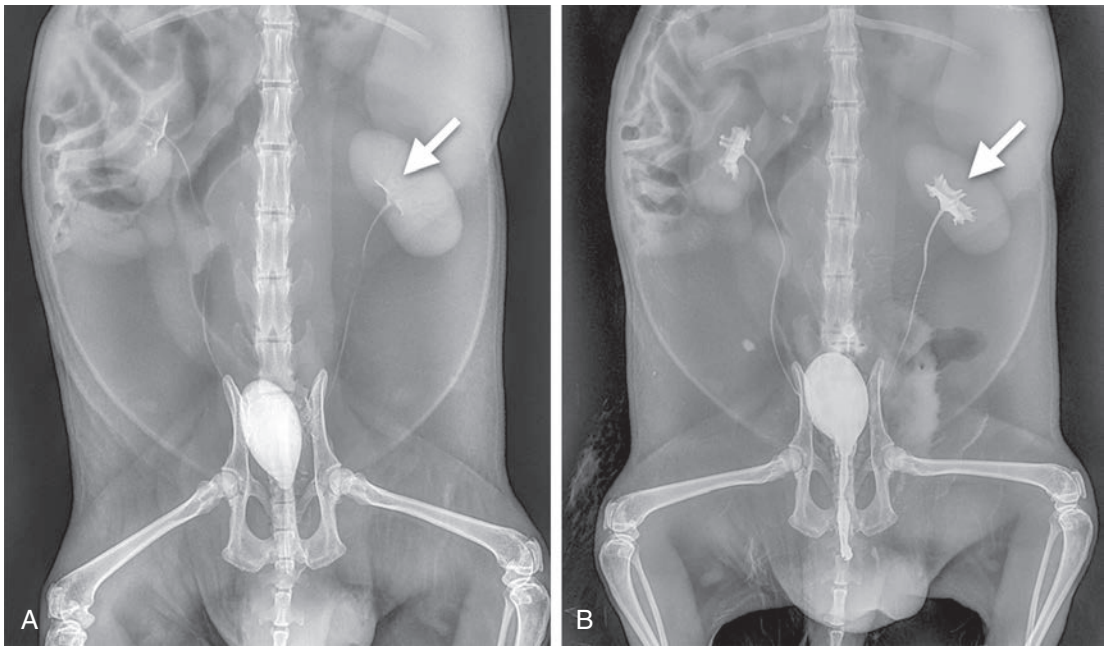


Fig. 4.5 Representative comparison of excretory urogram (A) and retrograde pyelogram (B) in the same renal-healthy ferret. Notice the increased dilation of the calix in the retrograde pyelography image, caused by the pressure required to make the contrast media reach the kidneys. (Courtesy Dr. Nicola Di Girolamo.)

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specifically by the source of dietary protein. Metabolism of animal protein tends to produce acidic urine, whereas plant-based protein diets, such as dog food or inexpensive cat foods, produce alkaline urine. Struvite crystals commonly form at a urine pH exceeding 6.6. Significant crystalluria leads to the development of calculi or sandy material in the bladder and urethra. In one report, 6 of 43 ferrets (14%) fed dog food had renal or cystic calculi at necropsy.[59] In ferrets, struvite uroliths appear to be uncommonly associated with urease-producing microbial urinary tract infections.[62]

However, in the last decade, cystine has become the most prevalent ferret calculus component in the United States.[53] Based on data from the Minnesota Urolith Center, which included 1108 ferret uroliths, cystine uroliths shifted from 15% of the total uroliths in 1981–2007 to 89% in 2010–2017.[53,62] In the same time frame, in Europe only 27% of the uroliths submitted to commercial laboratories were cystine.[53] A familial pattern due to inbreeding, similar to what is described in other carnivores, may explain such a dramatic increase in cystine prevalence in North America.[53,62].

Urolithiasis is seen most commonly in adult neutered males.[61] A small percentage of uroliths are voided.[62] However, most struvite uroliths are retrieved in the urinary bladder, whereas most cystine uroliths are retrieved from the urethra.[61,62]

Clinical signs of urolithiasis are stranguria, dysuria, pollakiuria, hematuria, urine dribbling, and frequent licking of the prepuce. If not corrected, urinary obstruction can result in severe metabolic disturbances, coma, and death. Affected jills may be asymptomatic or show intermittent straining for days or weeks. Although urethral obstruction is most common in male ferrets, females can also become obstructed, sometimes straining hard enough to cause rectal or vaginal prolapse and potentially fatal hemorrhage.[7]

Cystic calculi or sand is often palpable in ferrets without obstruction, and a distended bladder is readily palpable in obstructed ferrets. Abdominal radiographs allow evaluation of the entire urinary tract for radiodense uroliths and other abnormalities. Calculi lodged at the os penis can be difficult to detect. Abdominal ultrasound scanning provides additional information regarding the urinary tract, including visualization of radiotransparent uroliths, and can be used to concurrently screen the adrenal glands and prostate. In affected ferrets, submit samples for a CBC, biochemical analysis, urinalysis, and, ideally, urine bacterial culture and sensitivity testing.

If the ferret is not obstructed, provide supportive care, including parenteral fluids, and then schedule cystotomy to remove cystic calculi and flush the bladder. Submit calculi for mineral analysis and send crushed calculi and a sample of the bladder mucosa for bacterial culture and sensitivity testing. However, most calculi in ferrets are sterile.[61] Renal calculi may be managed by medical and dietary therapy unless clinical signs warrant immediate surgical removal.

Begin antibiotics before surgery if you suspect infection. Select a broad-spectrum antibiotic that reaches high levels in the urinary tract until culture and sensitivity results are available. Administer antibiotics for a minimum of 10 to 14 days, but use urinalysis and urine culture results to guide the duration of therapy. Continue antimicrobials several days past resolution of clinical signs. In male ferrets with urethral calculi, retrograde urohydropulsion can be attempted by placing a urinary catheter (see Chapter 2) and then flushing the urolith into the urinary bladder for future removal via cystotomy. If this procedure is unsuccessful, a perineal urethrostomy should be performed. As a part of the long-term management of urolithiasis, convert the ferret to an animal protein–based diet.

The prognosis is good for urethral or cystic calculi with aggressive treatment. As in other species, the prognosis for bilateral renal calculi is guarded.

Urethral Obstruction

Urethral obstruction is an important reason for emergency treatment of male ferrets. In the United States, urethral obstruction is most frequently caused by adrenal-associated prostatic disease or, less commonly, urolithiasis. Neoplasia and iatrogenic trauma are also considered. On physical examination, the urinary bladder is distended and painful. Results of biochemical analysis may include azotemia, hyperkalemia, hyperphosphatemia, and metabolic acidosis.

Urethral catheter placement is described in Chapter 2. Relief of obstruction and forced diuresis are usually sufficient to manage hyperkalemia. Medical treatment is indicated if an arrhythmia is present in addition to poor perfusion or altered mentation. To provide additional relief for acute urethral obstruction, some clinicians use smooth muscle relaxants, such as diazepam or midazolam.

Monitor urine production in catheterized ferrets by using a closed line attached to a 150- to 250-mL intravenous bag. Urinary output should be at least 1 to 2 mL/kg per hour, and with diuresis, urine production may be as high as 140 mL per ferret per day. Maintain the urinary catheter for 1 to 3 days while providing aggressive supportive care: correct metabolic and acid–base disturbances and administer fluids to correct perfusion abnormalities and rehydrate the patient. Monitor the ferret carefully for signs of overhydration.

If attempts at urinary catheterization are unsuccessful, consider cystocentesis to help stabilize the patient before surgery,[6] although there is some risk of urinary bladder rupture and subsequent uroabdomen. Temporary tube cystostomy has been described in cases of prostatic or paraurethral cysts (Fig. 4.6).[60] A 5- or 8-Fr Foley catheter is placed through the abdominal wall into the bladder during laparotomy. The catheter is left in place for 1 to 5 days.[60] Particular care must be taken to avoid self-removal by the ferret.[60]

In case of permanent damage (penile amputation or bladder atony), a long-term cystostomy tube can be placed. Two case reports describe using a silicon low-profile gastrotomy tube as a cystostomy tube.[36,77] Before tube placement, a Foley catheter must be in place for 1 to 2 weeks to create a continuous ostium between the abdominal wall and the bladder. The low-profile tube is inserted in the ostium and secured with a purse string suture (Fig. 4.6). Daily care of the tube is required to maintain a clean environment, and regular urinary culture must be performed to screen for urinary tract infection. One ferret reportedly tolerated the tube for more than 1 year.[36] Complications include removal and leakage of the device, mechanical cystitis, urinary tract infection, and septicemia. A urethrostomy may be needed in male ferrets with preputial neoplasia or recurrent urethral obstruction.[24,80]

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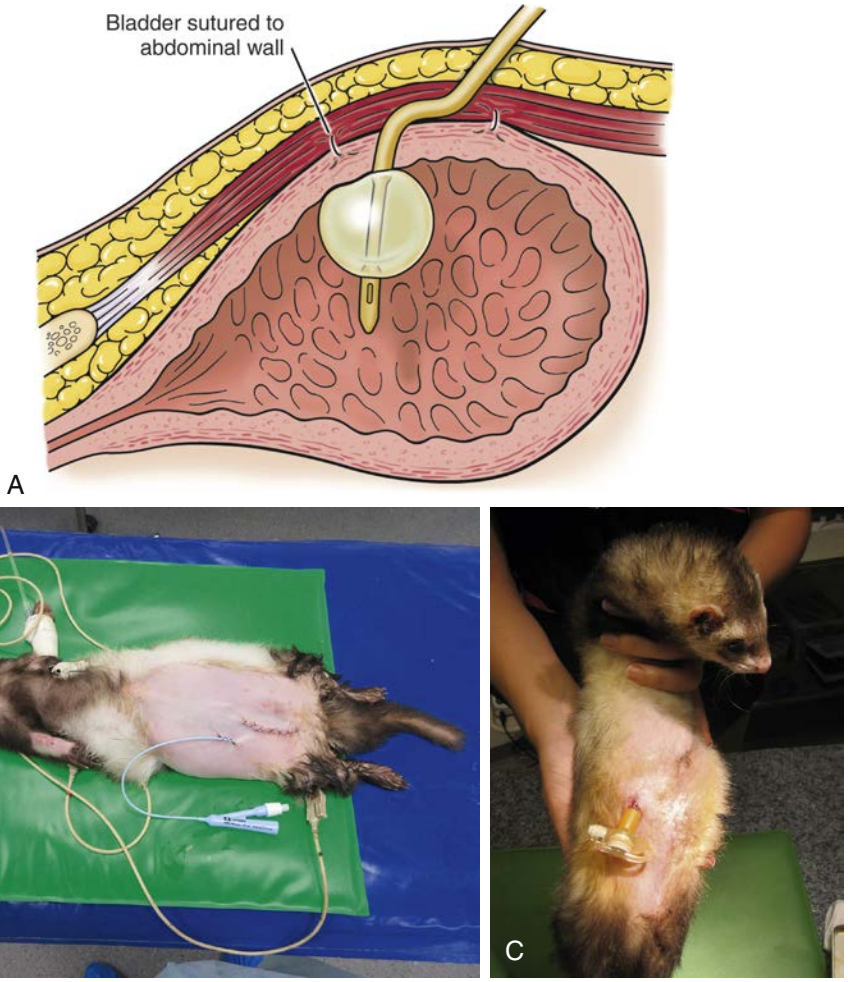


Fig. 4.6 Percutaneous cystostomy in ferrets. (A) A Foley catheter is placed within the bladder, and the bladder wall is sutured to the abdominal wall. (B) Ferret with a temporary cystostomy tube (Foley catheter) in place. (C) Ferret with a low-profile cystostomy tube in place. (Courtesy Dr. Marla Lichtenberger [A] and Dr. Minh Huynh [B, C].)

Cystitis

Spontaneous bacterial cystitis is rare in ferrets. If cystitis is identified, screen the ferret for underlying disease, such as adrenal-associated prostatomegaly or urolithiasis. Long-term corticosteroid use for concurrent disease (e.g., insulinoma, lymphoma) may predispose to urinary tract infection. A possible adverse effect of cyclophosphamide chemotherapy is hemorrhagic cystitis induced by the metabolite of the drug.

Infection may initially be asymptomatic; however, by the time of treatment, most ferrets demonstrate pollakiuria, dysuria, hematuria, and urine staining of the perineum. Ferrets with severe cystitis may have anorexia, lethargy, weakness, or even collapse. The abdomen may be painful, and the bladder wall may feel thickened.

Obtain a urine sample, ideally via cystocentesis, for urinalysis and bacterial culture and sensitivity testing. Urinalysis may reveal hematuria, pyuria, bacteriuria, and tubular casts. The CBC and biochemical results are often unremarkable, although an inflammatory leukogram may be observed with an ascending bacterial infection. Because primary cystitis is rare, consider survey abdominal radiography and abdominal ultrasound scanning to help identify the underlying cause of infection.

Administer a broad-spectrum antibiotic until culture results are available, and then adjust antibiotic therapy accordingly. Continue treatment for a minimum of 10 days and for at least 4 weeks in complicated cases. Provide fluids and supportive care as needed and ensure that the ferret is fed a high-quality diet with a meat-based protein source.

Bladder Neoplasia

There are rare reports of transitional cell carcinoma of the urinary bladder in ferrets (see Chapter 8).[87]

Urinary Incontinence

True urinary incontinence is rare in ferrets. More commonly, ferrets are treated for dribbling due to overfill of the urinary bladder as a result of partial urethral obstruction secondary to urolithiasis or prostatomegaly. True incontinence may be associated with bladder neoplasia, severe cystitis, or Aleutian disease virus. Additionally, although rabies virus is extremely rare in domestic ferrets, bladder atony and incontinence were reported in 65% of experimentally infected ferrets.[58] Bladder atony can also be seen with long-term paresis in ferrets with lumbar trauma or neoplasia.[36,37]

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Paraurethral Cysts or Paraurethral Disease

Paraurethral cysts rarely affect both female and male adult ferrets.[43] Cysts may be single or multiple and of various sizes, with variable communication between the cysts and the bladder, urethra, or both. Paraurethral cysts appear to be most common on the dorsal aspect of the urinary bladder trigone and the proximal urethra. Clinical signs may include dysuria, hematuria, and alopecia, as well as vulvar swelling in females. On physical examination, cysts may be palpable as fluctuant masses caudodorsal to the bladder. In a study of six ferrets (four males and two females) with paraurethral cysts, adrenal hyperplasia or neoplasia was detected in five ferrets, and the adrenal gland was not evaluated in the sixth animal.[43] Initial therapy involves relief of the urethral obstruction, hydration, and treatment of secondary bacterial infection. Definitive therapy is surgical.

DISORDERS OF THE REPRODUCTIVE SYSTEM

Primary reproductive tract disease is uncommon in ferrets in the United States, where animals historically have been routinely spayed and neutered at 6 weeks of age. Outside the United States, most ferrets are either not gonadectomized or are gonadectomized at 5 to 6 months of age. A recent randomized trial has confirmed the association between surgical gonadectomy and adrenocortical disease.[73] Therefore other preventive measures, such as chemical sterilization, may be considered in favor of surgical neutering.[30,72,81]

Refer to Chapter 1 for normal reproductive parameters in ferrets. The ferret's breeding season occurs from September to December in the Southern Hemisphere and from March to August in the Northern Hemisphere.[1] Ferrets are "long-day" breeders, and providing more than 12 hours of light promotes reproductive activity.[1]

The Male Ferret

Plasma testosterone levels increase at the end of January in the Northern Hemisphere, and a peak plateau is maintained from the end of February until late July. Increases in testicular size begin in late January and peak in April. The stages and cycle duration of ferret spermatogenesis are similar to those reported in other carnivores.[56]

Cryptorchidism

Ferret testes usually descend into the scrotum during fetal development, but complete descent may take several months after birth. Cryptorchidism is uncommon and was reported in less than 1% of 1597 male ferrets.[10] Cryptorchid testes may become neoplastic and should be surgically removed or closely monitored.

Tumors of the Male Reproductive Tract

Testicular tumors are not uncommon in middle-aged to older ferrets and are considered more common in cryptorchid testes.[40,87]

Prostatic Cysts

Prostatic disease is the leading cause of urinary tract disease and urethral obstruction in middle-aged and older male castrated ferrets in the United States, where it is associated with adrenal disease.[12] Adrenocortical disease in the ferret has been correlated with gonadectomy,[73,76] which is routinely performed at 6 weeks of age in the United States. Outside of the United States, most ferrets are not gonadectomized but are instead chemically neutered with long-term 4.7-mg deslorelin acetate implants (Suprelorin, Virbac, https://virbac.com). In these cases, adrenal disease and prostatic cysts are relatively uncommon.

Adrenocortical disease in the male ferret is associated with the development of sterile prostatic cysts. Although the exact pathogenesis is unclear, high levels of circulating sex steroid hormones appear to stimulate proliferation of prostatic tissue (see Chapter 7).[12] Prostatic cysts can become very large and compress the urethra, leading to urethral obstruction.[12]

Although prostatic disease may be seen at any age, it is most common in neutered ferrets at least 3 years of age. Signs of lower urinary tract disease caused by prostatomegaly are pollakiuria, hematuria, stranguria, dysuria, or anuria. Ferrets may lick excessively, creating an inflamed prepuce. Because of straining, some ferrets may be presented with diarrhea or, in rare instances, rectal prolapse. Signs of adrenal disease, such as alopecia, pruritus, or behavioral changes, may be present.[2,60] Ferrets with urethral obstruction may have a history of anorexia, lethargy, weakness, or collapse.

The enlarged prostate may be palpable as a variably-sized fluctuant mass dorsal to and near the base of the urinary bladder (Fig. 4.7), although not all ferrets with prostatic disease demonstrate prostatomegaly. Perform a full medical workup in affected ferrets. On radiographs, prostatomegaly may appear as a mass lesion caudodorsal to the urinary bladder, displacing the bladder cranioventrally. Use ultrasound scanning to evaluate the adrenal glands, kidneys, urinary bladder, and prostate. Computed tomography allows identification of contact of the prostate with the surrounding structures. Prostatic cysts

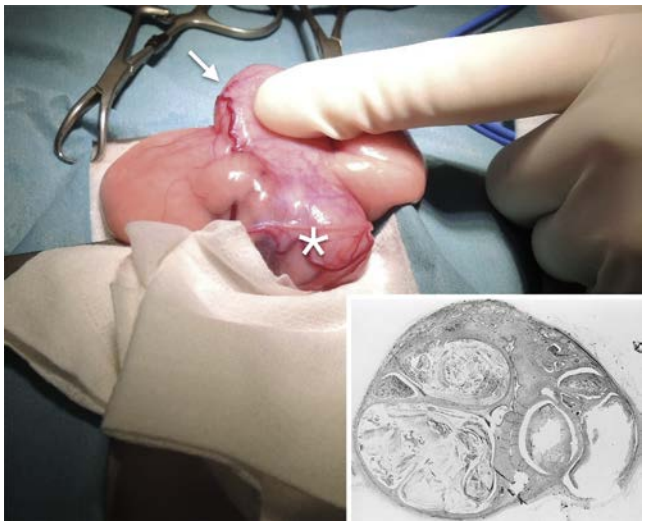


Fig. 4.7 Gross aspect of paraprostatic cyst (asterisk) in a ferret. The urinary bladder is manually retracted (arrow). (Inset) The prostate is expanded by cysts of various sizes filled with keratin and proteinaceous debris. (Courtesy Dr. Minh Huynh; [Inset] From Coleman GD, Chavez MA, Williams BH. Cystic prostatic disease associated with adrenocortical lesions in the ferret. Vet Pathol 1998;35:547-549.)

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contain hypoechoic to anechoic fluid. Collect cyst fluid via ultrasound-guided fine-needle aspiration for cytologic examination and aerobic and anaerobic culture. Contrast cystography may show an irregular blockage around the bladder neck (Fig. 4.8). Submit blood samples for a ferret adrenal panel available through the University of Tennessee College of Veterinary Medicine Endocrinology Lab (www.vet.utk.edu/diagnostic/endocrinology/index.php) to confirm the presence of adrenocortical disease, particularly if ultrasound results are equivocal.

Medical therapy is generally attempted as first-line treatment. This involves managing urethral obstruction, if present, and adrenocortical disease (see Chapter 7). Medical therapy includes placing a 4.7-mg deslorelin acetate implant (Suprelorin, Virbac,).[42,84] Another alternative is to administer the depot formulation of the synthetic gonadotropin-releasing hormone (GnRH) agonist, leuprolide acetate (100 to 250 µg/kg/month intramuscularly [IM]).[83] Administration of high-dose leuprolide acetate can cause prostatic tissue to shrink within 12 to 48 hours, and the ferret may even begin to urinate around the urethral catheter. Oral melatonin (0.5 by mouth every 24 hours) may also be administered.[67] Surgical therapy involves adrenalectomy, and large prostatic cysts may require surgical debulking. Cystic prostatic hypertrophy usually begins to resolve within 2 to 3 days after surgery.[2]

In addition to standard treatment for adrenal disease, the use of antiandrogen agents, such as flutamide, bicalutamide, and finasteride, has been suggested. Effects may be seen within days in some ferrets; however, use caution in patients with liver disease. Because research findings on the use of these drugs are lacking, their effectiveness and safety are still unclear.

If left untreated, prostatic disease can lead to urethral blockage, acute renal failure, and death. Fortunately, the prognosis for prostatic cysts is generally good in ferrets that undergo aggressive therapy for underlying adrenocortical disease. Ensure that prostatic cysts resolve completely by monitoring their sonographic appearance. Long-term persistence of cysts may promote the development of bacterial prostatitis and abscessation.

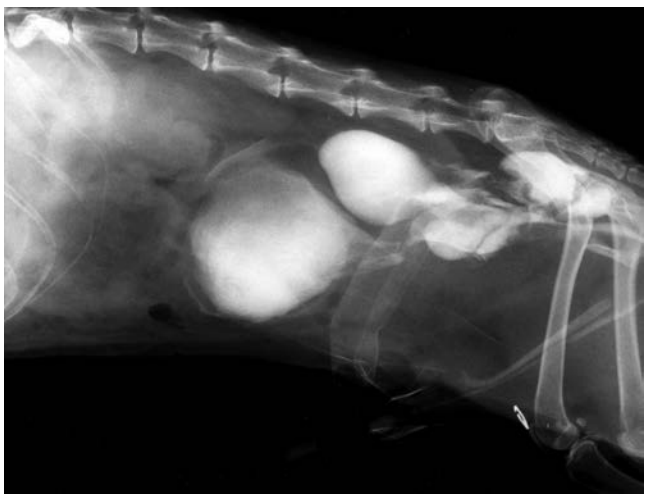


Fig. 4.8 Contrast cystography illustrating irregular mass lesions near the bladder neck caused by prostatitis. Note the caudal extension of the inflamed prostate gland.

Also, monitor patient progress by following sex steroid hormone levels and size of the adrenal glands.

Prostatitis and Prostatic Abscesses

The pathogenesis of bacterial prostatitis and prostatic abscessation in ferrets is poorly understood. Urine stasis secondary to adrenal-associated prostatomegaly may promote bacteriuria and regional migration of bacteria into prostatic tissue. Bacteria may also enter the prostate hematogenously. Prostatitis has been described in a ferret with a Sertoli cell tumor associated with a retained testicle, and there are rare reports of prostatic abscesses associated with transitional cell tumors of the bladder.[87] Prostatitis has been associated with heavy growth of *E. coli*, as well as *Staphylococcus*, nonhemolytic *Streptococcus*, *Proteus*, and *Pseudomonas* species.

A thick, white to yellow, opaque penile discharge may be seen with prostatitis, and a purulent discharge may be associated with urination. Round structures may be palpable near the urinary bladder, and the abdomen may be swollen, tense, and painful.[65]

An inflammatory leukogram may be observed, although results of biochemical analysis are frequently unremarkable.[65] Urinalysis and urine culture results are variable. Abdominal ultrasound of the prostate shows hypoechoic to anechoic fluid-filled cysts with hyperechoic sediment. Perform ultrasound-guided fine-needle aspiration of prostatic cysts with the ferret sedated. Aspirated fluid may be turbid or flocculent and appear yellow to green,[65] and results of cytologic examination will reveal suppurative exudate. Submit the sample for aerobic and anaerobic bacterial culture and sensitivity.

Select a lipid-soluble antibiotic known to penetrate the prostatic capsule, such as a potentiated sulfa or fluoroquinolone. Use culture and sensitivity results to adjust therapy, and administer antibiotics for at least 4 to 6 weeks.[2,3,6] Although antimicrobials are an important ancillary treatment, antibiotics generally fail to achieve effective tissue levels throughout the prostate. Therefore, surgical management of prostatitis or prostatic abscess is recommended.

If prostatitis is secondary to adrenal gland disease, treatment is the same as for prostatic cysts. In cases of primary prostatitis, ultrasound-guided chemoablation or surgical treatment, including marsupialization and omentalization, can be considered (see Chapter 11).[2,3,6] In marsupialization, the infected prostate is flushed and marsupialized to the abdominal wall. Marsupialization allows for repeated lavage. Because drainage is external to the abdominal cavity, the risk of peritonitis may be reduced.[2] Omentalization of prostatic abscess can be performed in ferrets by using a technique similar to that described in dogs.[2,3,6,65] The prostatic abscess is opened and flushed, and as much of the cranial capsule is excised as possible. The caudal aspect of the abscess may extend deep into the pelvic canal.[65] The remaining abscess cavity is irrigated, then a portion of greater omentum is inserted into the abscess and sutured into place. Omentum is believed to promote tissue adhesion, angiogenesis, hemostasis, peritoneal lymphatic drainage, fibrinolysis, and immune system function.[35]

Regardless of the surgical technique selected, potential complications are recurrent cystitis and peritonitis.[3] Prostatic cysts

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may extend into bladder or urethral tissue, increasing the risk of urinary incontinence, uroabdomen, or urethrocutaneous fistula formation.[3]

Culture prostatic fluid and urine 2 to 4 weeks after completing antibiotic therapy, and use serial abdominal ultrasound scanning to monitor the prostatic abscess. Follow underlying adrenal disease by measuring serial sex steroid hormone levels.

Penile Lesions

Penile lesions are occasionally seen in male ferrets kept on hay bedding when grass awns catch in the prepuce. Breeding males may also incur injury as they move along the ground pressing their groin down to mark their territory. Anesthetize ferrets to remove foreign bodies in the prepuce, then apply a topical antibiotic-corticosteroid ointment.

Preputial gland neoplasia is relatively common in ferrets. Lesions are frequently malignant and require aggressive treatment. Surgical resection, including penile amputation, with margins of at least 1 cm is indicated.[80]

The Female Ferret

Proestrus usually occurs in January or February and is signaled by increasing vulvar tumescence.[45] The advent of estrus is variable and can be seen from late January to early August. The jill may eat and sleep less, and she may become irritable. Superficial epithelial cells make up 90% or more of epithelial cells in vaginal cytology, and, after several days, cells are fully keratinized. Neutrophils are common during all stages of the estrous cycle. Until mated, jills may exhibit constant estrus for up to 5 months, and hyperestrogenism may occur.[45]

Ferrets are induced ovulators, and coital stimulation is required to trigger ovulation.[1,49] Once ovulation is induced, either pregnancy or pseudopregnancy occurs. Several days after induced ovulation, numbers of superficial vaginal cells decline to anestrus levels and the vulva decreases in size and turgidity.[45] Transfer of embryos has been described in mustelids and could be potentially feasible in ferrets.[46] See Chapter 1 for additional information on reproductive parameters in ferrets.

Hyperestrogenism

Hyperestrogenism is extremely common in female ferrets that are not bred or artificially stimulated to ovulate.[45] Estrus lasting more than 1 month is associated with hyperestrogenism, which leads to bone marrow depression and hypoplasia of all cell lines.[33] Other potential causes of estrogen toxicosis are cystic ovaries, an estrogen-secreting ovarian remnant, and ovarian neoplasia.[50,64] Untreated adrenocortical disease may also lead to hyperestrogenism.

Clinical signs may include bilaterally symmetric dorsal alopecia, vulvar swelling, vulvar discharge, pallor, and a systolic murmur. Extended hyperestrogenism may cause melena and petechial or ecchymotic hemorrhages. Metritis, pyometra, or vaginitis may also be involved.

Results of a CBC generally reveal nonregenerative anemia with a hematocrit less than 25%, nucleated red blood cells, neutropenia, and thrombocytopenia.[33,75] Hemorrhage may occur when platelet counts fall below 20,000 cells/μL.[75] Confirm nonregenerative anemia with a reticulocyte count. In intact female ferrets, recent estrus and consistent clinical signs are usually sufficient for a preliminary diagnosis. In spayed ferrets, abdominal ultrasound scanning may help to discriminate between an ovarian remnant and adrenal disease.

Treatment of hyperestrogenism includes stabilizing the ferret and reducing estrogen levels. Ferrets do not have blood groups; therefore, if necessary, multiple transfusions from multiple donor ferrets are possible.[48] Less commonly, bone marrow transfusions have also been described. Additional supportive care measures may include anabolic steroids, corticosteroids, and iron dextran.

In the United States, the widespread practice of routinely spaying female ferrets not intended for breeding by 6 months of age has drastically reduced the prevalence of hyperestrogenism. However, early gonadectomy in ferrets is currently discouraged, given its proven association with later development of adrenal disease.[73,76] As an alternative to surgical sterilization, hyperestrogenism is prevented by injecting a long-term GnRH-agonist (4.7 mg deslorelin acetate [Suprelorin, Virbac]) implant, every 1 or 2 years.[81] If the ferret is presented after the onset of estrus, a long-term GnRH-agonist, a short-acting GnRH agonist (e.g., buserelin [0.25 mg IM per ferret, repeated in 14 days] or leuprolide acetate [100 to 250 ug/kg IM]), human chorionic gonadotropin (hCG, 100 IU IM per ferret), or a second-generation progestogen (proligestone, 40-50 mg SC per ferret) can be used to induce ovulation.[26] Give hCG at least 10 days after the onset of estrus and repeat in 7 days if vulvar swelling has not resolved.[52] Monitor the reproductive tract with serial ultrasound scans to identify changes in the uterine structure or content (e.g., development of pyometra).

Tumors of the Female Reproductive Tract and Mammary Glands

Both neoplasia of the ovaries and uterus occur in ferrets.[44] Mammary gland tumors are a rare differential diagnosis for severely swollen, firm glands in domestic ferrets (see Chapter 8).[26,87]

Pyometra and Mucometra

Pyometra is often documented in intact females, particularly jills with estrogen toxicosis or in older, pseudopregnant jills. Stump pyometra is occasionally seen in spayed females because of elevated sex steroid hormone levels secondary to adrenocortical disease.[23] Bacteria that have been cultured from pyometras include *E. coli*, as well as *Staphylococcus*, *Streptococcus*, and *Corynebacterium* species.[26]

Clinical signs of pyometra are similar to those in dogs and cats. In a case seen by one author (N.D.), pyometra developed approximately 1 week after administration of 4.7-mg deslorelin acetate (Suprelorin, Virbac) to a ferret in estrus. This was presumed to be a consequence of a reversed estrogen/progesterone ratio after a long period of estrogenic stimulation. Therefore, when administering a GnRH agonist to suppress estrus, perform serial abdominal ultrasound scans to monitor the status of the uterus.

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Determine whether the ferret with pyometra is suffering from estrogen-induced bone marrow suppression.[75] Definitive treatment of pyometra or mucometra involves ovariohysterectomy or surgical excision of the infected stump and adrenalectomy. Provide systemic antibiotics and supportive care such as fluids, analgesia, and nonsteroidal antiinflammatory drugs. Medical management of pyometra has also been described, but it should be reserved for cases where surgery is not an option. In these cases, administer prostaglandin F2-α (dinoprost tromethamine) (0.1 to 0.5 mg IM; Lutalyse, Zooetis, Parsippany, NJ), followed in 1 hour by oxytocin (0.2–3 IU SC, IM) to stimulate myometrial contraction and expulsion of exudate.[55]

Hydrometra

Hydrometra is the accumulation of aseptic fluid within the uterus in the presence of persistent corpora lutea and is typically associated with ovarian disease (Fig. 4.9).[39,64] Segmental atresia of the uterus associated with hydrometra has also been reported in a 2-year-old ferret.[5] Definitive treatment relies on ovariohysterectomy.

Vaginitis/Vulvar Swelling

Primary vaginitis is uncommon in ferrets. More frequently, vaginitis is associated with chronic vulvar swelling subsequent to hyperestrogenism caused by persistent estrus, an ovarian remnant, adrenal disease, or estrogen-secreting neoplasia. Less commonly, vulvar swelling develops with cystitis, crystalluria, or even aggressive hob mating behavior. Poor husbandry and inadequate sanitation may also promote vaginitis in breeding jills kept on particulate bedding when hay, straw, or shavings adhere to the swollen vulva during estrus. Vaginitis is associated with overgrowth of bacteria such as *E. coli, Staphylococcus, Streptococcus, Proteus,* or *Klebsiella* species.[26] Vaginitis may be differentiated from the swelling associated with estrus by history, results of vaginal cytology, presence of mucopurulent vaginal discharge, and ultrasound of the reproductive tract. Administer systemic antibiotics and treat the underlying problem, including reducing estrogen levels as necessary.

PERIPARTURIENT DISEASE

Normal Parturition

Parturition normally lasts approximately 2 to 3 hours. Approximately five kits are born per hour, although some jills take longer. Progress should be steady, and no signs of distress should be seen. Domestic ferrets average 8 or 9 kits (range 7–15) per litter.[1,45] Newborn kits are altricial and weigh 6 to 12 g at birth.[7]

Females will return to estrus within 2 weeks after weaning if exposed to the appropriate photoperiod. If kits are removed at birth, the jill will return to estrus 8 weeks after mating, as will pseudopregnant females and females with resorbed fetuses. If a jill gives birth to a small number of kits (five or fewer), she may return to estrus while nursing.[25]

Management of Breeding Ferrets

Successful breeding requires constant supervision during gestation, parturition, and lactation. Breeders should monitor jills closely for any change in appetite or body condition, particularly late in gestation.[4,7]

Place the pregnant jill's cage in a quiet area well before parturition. Minimizing stress is particularly important in young primiparous jills. Avoid environmental stressors such as excessive heat. Room temperature should not exceed 70°F (21°C). Place a heat lamp over only part of the nesting box so that the jill and kits can select warmth as necessary. The risk of poor mothering also increases with crowding or unusual noise and nearby activity. Jills become excited and may bury the kits in bedding or place them in a pile in a corner or in food or water containers. Some jills will cannibalize the first few or all of their kits as they are born. Handling kits does not appear to cause rejection of the litter.[7]

The jill must also be able to easily enter and exit the nesting box without traumatizing her mammary glands. Shredded aspen shavings, recycled paper bedding, or small cloth towels are practical choices for whelping nest substrate. Do not use large towels because kits can get lost in them.[7]

Feed jills proper nutrition containing 36% to 40% animal-based protein and 18% to 20% fat.[26] Make food and fresh water available at all times.

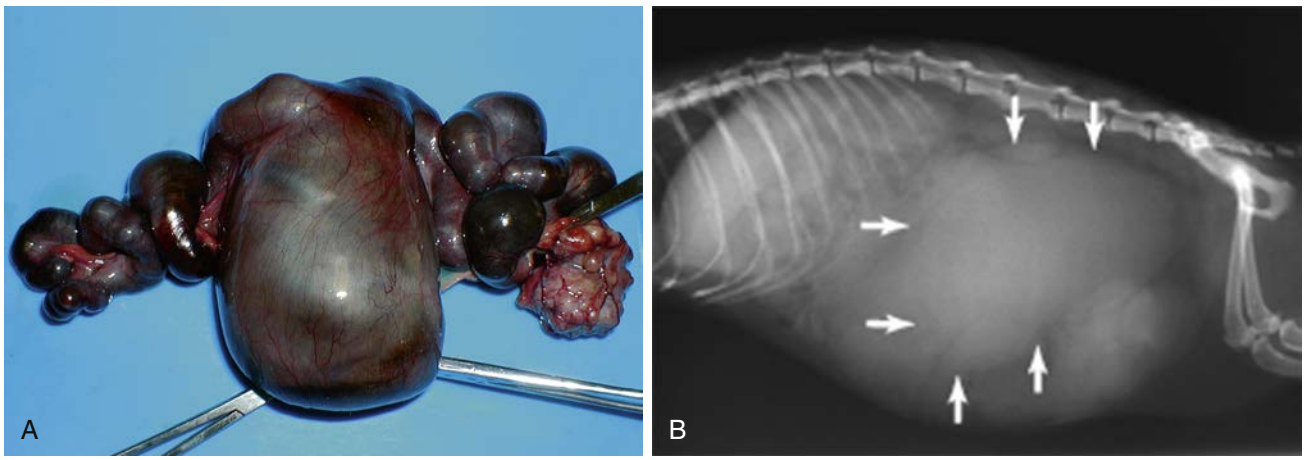


Fig. 4.9 Hydrometra in a ferret. (A) Gross image of hydrometra in association with an ovarian tumor (far right). (B) Lateral radiograph shows a soft tissue opacity (arrows), creating a mass effect in the ventrocaudal aspect of the abdomen. (Courtesy Dr. Vladimir Jekl.)

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Diseases of the Jill

Pregnancy Toxemia

Pregnancy toxemia is a life-threatening disease seen sporadically in jills, especially young primiparous females, during late gestation.[4] Negative energy balance promotes abnormal energy metabolism and subsequent hyperlipidemia, hypoglycemia, ketosis, and hepatic lipidosis during the 10 days before parturition. This energy deficiency is caused by either inadequate dietary intake or excess demand for nutrients due to an exceptionally large litter (e.g., 15 or even 20 kits).[4,7]

Common clinical signs include acute onset of severe lethargy, anorexia, dehydration, weight loss, and excess shedding.[4,13,26] There may also be diarrhea with or without melena. In some cases, sudden death occurs.[4,7,26]

Hematologic and biochemical abnormalities may include anemia, hypoproteinemia, azotemia, hypocalcemia, hyperbilirubinemia, increased liver enzyme activities, and hypoglycemia.[4,26] Urinalysis may reveal ketonuria. In a survey of 10 jills with pregnancy toxemia, hepatic lipidosis was observed grossly in the 7 jills that died.[4]

Provide aggressive treatment in the form of cesarean section and intensive supportive care. Correct fluid and electrolyte imbalances and provide nutritional support. Gastroprotectants are commonly indicated because of the high incidence of concurrent gastrointestinal ulcers. After surgery, surviving jills frequently produce no milk for at least several days, and cross-fostering of kits is often required.[7]

Because of the guarded prognosis, prevention through client education is much more effective than treatment. Advise breeders to provide consistent proper nutrition, avoid stressors, and be vigilant for any changes in the jill's appetite or body condition.[4] Make palatable food available at all times and provide several small food dishes so that accidental spillage or contamination does not restrict the jill's intake. During the last week of gestation, even one overnight fast can induce toxemia in a jill with a large litter. Provide plenty of fresh water because jills will also stop eating without adequate water.

Dystocia

Dystocia is defined as labor exceeding 12 to 24 hours or whenever there are signs of difficulty. Potential causes of dystocia are pregnancy in an older jill or an elevated environmental temperature (above 70°F [21°C]). Kits of very large size (more likely with small litter size), posterior or sideways presentation, and deformed or anasarcous fetuses may also increase the risk of dystocia.[7] In one case of dystocia, a "single ferret kitten" syndrome was suspected,[29] where a young jill with only one kit may not exhibit expulsive efforts because of lack of cortisol stimulation from the fetus. Depending on the underlying cause of dystocia, jills may be managed medically with oxytocin (5–10 IU IM) or surgically via cesarean section. Follow current standards for management of dystocia in other domestic carnivores.

Pseudopregnancy

False pregnancy is caused by failure of implantation, which is associated with reduced light intensity 1 month before the start of breeding, or failure to conceive.[26] For instance, jills may be bred with infertile hobs, particularly males less than 6 months of age. Pseudopregnancy has also been associated with termination of estrus through hCG use or mating with vasectomized hobs. In pseudopregnancy, the physical and behavioral changes normally associated with pregnancy may be seen, such as weight gain, mammary gland enlargement, and nesting behavior. Jills may also mother inanimate objects. One important difference is that pseudopregnant jills develop a full hair coat approximately 1.5 weeks before "whelping," whereas pregnant jills lose their coat and develop hairless rings around their teats. After "whelping," pseudopregnant jills return to estrus if it is early in the breeding season, or they become quiescent if it is late in the breeding season.[7] Minimize the risk of pseudopregnancy by ensuring that jills are exposed to maximum light intensity during the spring, and artificially extend light hours in late summer.

Agalactia

Agalactia is defined as failure of the jill to lactate enough milk for a normal litter of eight or nine kits. Agalactia may be seen when the jill is stressed because of environmental factors such as overcrowding, noise, visits from strangers, or overheating (temperature exceeding 70°F [21°C]). Agalactia may be inherited, and some ferret breeds (e.g., Angoras) are known to have little to no production of milk. Agalactia is also more common in litters with fewer than five kits and in jills on a poor diet or suffering from systemic disease or chronic mastitis.[7] Agalactia leads to thin kits that cry and move around restlessly. Determine the underlying cause while offering the best-quality diet available to lactating jills.[7]

Mastitis

Mastitis is occasionally seen in pet ferrets and frequently in laboratory ferrets.[26] Acute mastitis develops soon after whelping or after the third week of nursing when milk production peaks and kits become more aggressive feeders. Because kits demand greater quantities of milk, this may stress the jill, or the kits' teeth can damage the nipples. Potential etiologic agents may include *Staphylococcus* species and coliforms such as hemolytic *E. coli*.[7,26]

A firm, painful swelling in one or more glands and red or purple discoloration of the overlying skin may be evident. Milk may be discolored and clotted. If not recognized and treated early, infection will spread rapidly to nearby glands.[26] In severe cases, abscesses may form. The affected jill may present with signs of systemic illness such as depression, fever, anorexia, and dehydration.[26] Chronic mastitis may develop as a result of acute mastitis.

Begin systemic antibiotics, such as clavulanic acid–amoxicillin, for both acute and chronic mastitis.[7] For acute mastitis, culture a milk sample before starting antibiotics, and apply warm compresses to affected glands. More aggressive treatment is indicated for gangrenous mastitis. Perform wide surgical resection of the involved gland and adjacent tissue in combination with analgesia, fluid therapy, nutritional support, and systemic antibiotics.[7]

The kits will require nutritional support. One option is to remove and hand-feed kits, although neonates are very difficult

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to hand-raise. If kits must be left with the dam, provide supplemental feedings at least three or four times daily. Kits may also spread bacteria to unaffected glands.[7] Kits may also be fostered, but there is significant risk of infecting the foster dam. Some clinicians also routinely treat the kits and foster mother with oral antibiotics.[7]

Postparturient Hypocalcemia

Postparturient hypocalcemia, or "milk fever," was reported in primiparous jills that exhibited posterior paresis, hyperesthesia, and seizure activity 3 to 4 weeks postpartum. Jills responded to treatment with parenteral calcium borogluconate injections.[26] Prevent hypocalcemia by providing a balanced diet and calcium supplementation if needed.

Metritis

Metritis develops in the immediate postpartum period and occasionally after abortion or breeding. Metritis may also be associated with retained fetuses or placenta. On physical examination, the uterus is distended, and a red vaginal discharge may be seen. Definitive treatment is ovariohysterectomy. Medical management of metritis includes analgesics, systemic antibiotics, and prostaglandin F_2-α (Lutalyse, 0.5 mg IM) to evacuate the uterus. Select an antimicrobial that reaches high urinary levels to reduce the risk of ascending cystitis and secondary urolithiasis.[7]

Diseases of the Kit

The Normal Kit

Ferret kits have little ability to maintain a normal body temperature for the first 2 weeks of life. A healthy litter normally lies quietly close to the jill, nursing and sleeping except when the jill leaves the nest. When kits reach 3 weeks of age, they begin to explore and nibble on soft food, even though their eyes are still closed. Eyes usually open by day 30 to 35 and as early as day 25. Kits generally weigh 8 to 10 g at birth, 30 g at 1 week, 60 to 70 g at 2 weeks, and 100 g at 3 weeks. Kits are weaned at 6 to 8 weeks.[7]

Caring for Ill Kits

Provide supplemental heat, offering kits a temperature gradient of 85°F to 104°F (30°C–40°C).[47] Hypothermic kits do not nurse, so it is prudent to also administer a few drops of 50% dextrose solution by mouth or to rub sugar syrup on the gums.[7] Then administer warmed fluids (50–100 mL/kg) subcutaneously. Feed kits only once they are normothermic and hydrated.

Neonatal ferrets have voracious appetites and are difficult to hand-rear. Kits require ferret milk for the first 7 to 10 days of life.[7,47] The composition of ferret milk varies over the course of lactation (Table 4.1).[74] Some success has been described feeding neonates with pipettes every 1 to 1.5 hours. By day 10 to 21, kits may be offered puppy or kitten milk replacer 4 to 6 times daily.[25] Some authors recommend enriching milk replacer with cream until the fat content is 20%, and additional hand-feeding recipes are available.[7,47] At week 4 to 5, offer a slurry of milk replacer and kibble mixed with solid food.[7]

Because hand-rearing is so challenging, consider supplemental hand-feedings when the jill's milk production is reduced because of illness. The stimulus of nursing may promote lactation as the jill improves. Cross-fostering is an alternative. In fact, it is best to breed jills in pairs so one may serve as a foster mother if problems arise. Most jills accept kits of any size or age at any stage of lactation. Merely remove kits from both litters for a short time, mix the two litters together, and then replace all kits with the foster mother.[7]

TABLE 4.1 Composition of Ferret Milk

Postpartum (Days)	Mean % Fat	Mean % Protein	Mean % Lactose
5	7.8–8.5	7.2–8.8	2.7–4.2
11	9.3–10.5	6.3–7.9	2.8–4.4
19	8.9–10.8	6.0–8.3	3.8–4.2
25	8.8–9.5	5.0–7.9	3.3–4.2
33	9.2–10.3	8.6–9.8	3.0–4.1
39	9.0–13.0	8.4–10.6	1.5–3.2

Data from Schoknecht PA, Cranford JA, Akers RM. Variability in milk composition of the domestic ferret *(Mustela putorius). Comp Biochem Physiol A Comp Physiol* 1985;81:589-591.

Entangled Umbilical Cords

Kits in large litters are occasionally born so rapidly the dam is unable to chew the placenta off each individual, creating a mass of kits bound together by their umbilical cords. The entanglement may be exacerbated if kits are born on coarse, sharp-edged shavings. The mass of entangled kits cannot nurse, so they quickly become hypoglycemic. In addition, the jill cannot curl around them and they also become hypothermic. If this occurs, carefully dissect placentas from each kit's umbilicus with blunt scissors as far as possible from the kit's abdomen.[25] If the placenta has become dry, soften tissue with water. Minimize the risk of entangled cords by closely supervising whelping. If necessary, pick up kits as they are born and separate the placenta.[7,25,51]

Diarrhea

Diarrhea in kits may be caused by ferret rotavirus alone, concurrent rotaviral and bacterial infections (e.g., *Campylobacter jejuni, E. coli, Proteus* species, *S. aureus,* and *Enterobacter cloacae*), or bacterial infection alone. Ferret rotavirus is carried by adults and may cause diarrhea in stressed kits or even unstressed kits if they have no passive immunity.[7,79] The jill typically grooms away all evidence of diarrhea, but the kits will appear wet and dehydrated. Disease may be mild and self-limiting in older kits but is potentially life-threatening during the first week of life. The prognosis is good if kits receive aggressive supportive care. Provide fluids and oral broad-spectrum antibiotics for 5 to 7 days. Monitor the jill closely because anorexia in the kits may promote mastitis, agalactia, or both.[7,25]

Neonatal Conjunctivitis

In neonatal conjunctivitis, or ophthalmia neonatorum, purulent discharge collects in the conjunctival sac behind the unopened eyelids of the kit. A variety of pathogens have been cultured. Unilateral or bilateral conjunctivitis is typically seen

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in kits between a few days to 3 weeks of age. Kits typically stop nursing because of the pain associated with pressing their eyes against the dam. Open the eyelids by cutting along the natural suture line with a small scalpel blade or 25-gauge needle bevel. Flush debris and apply a broad-spectrum ophthalmic ointment. Littermates are often affected; therefore carefully examine the entire litter regularly. The prognosis is good in 3-week-old kits because the eyelids will stay open. In younger kits, the eyelids may reseal, and infection may recur.[7]

Splay-Legged Kits

Splay-legged kits, or "swimmers," are tetraparetic. Affected kits must lie on their sternum leading to rib compression and death secondary to anoxia by 8 weeks of age. Although the cause is unknown, "splay leg" has been theorized to be either hereditary or husbandry-related when a rapidly growing kit housed on smooth flooring places excessive weight on its immature limbs.

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5

Cardiovascular and Other Diseases of Ferrets

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CARDIAC DISEASE

Cardiac disease is relatively common in pet ferrets and is suspected based on the presence of radiographic cardiomegaly, a heart murmur on auscultation, or clinical signs consistent with congestive heart failure (CHF). In addition, a thorough cardiac evaluation should be considered for any ferret undergoing anesthesia. For these reasons, practitioners working with ferrets should be familiar with the clinical signs and diagnosis of heart disease, as well as the treatment options available. Reference data for common testing modalities, including echocardiography, electrocardiography (ECG), and radiography, have been published for ferrets. This section provides readers with this information, as well as our own accumulated clinical experience to facilitate the diagnosis and treatment of cardiovascular diseases in ferrets. In ferrets, acquired heart disease is most commonly reported and described, whereas congenital disease has been rarely described, with case reports of ferrets with tetralogy of Fallot and ventricular septal defect recently published.[14,41,88]

General Principles of Cardiac Disease and Congestive Heart Failure

History and Clinical Signs

Most ferrets presenting because of cardiac disease are middle-aged (i.e., approximately 3 years of age) or older. Typical presenting clinical signs may be confused with those of other diseases; therefore a thorough history is important. Question the owner about changes in the animal's appetite, activity level, sleep patterns, exposure to other ferrets, and exposure to the human influenza virus.

Ferrets with cardiac disease show a variety of clinical signs similar to those observed in other species, including lethargy, exercise intolerance, weight loss, anorexia, ascites, coughing, and dyspnea.[18,43,66] In addition, ferrets with cardiac disease may present with hind limb weakness. It is unclear why the hind limbs are preferentially affected compared with the front, but thromboembolic disease does not appear to be a cause. The diagnosis of cardiac disease may be an incidental finding in some ferrets; either these ferrets have compensated for mild cardiac disease, or the owner has not noticed the often insidious signs.

Physical Examination

Perform a thorough and systematic physical examination in ferrets with suspected cardiac disease. Examine the oral mucous membranes for color and refill time (<2 seconds is normal). Pale or cyanotic mucous membranes with a prolonged capillary refill time may be related to CHF or reduced cardiac output. Jugular pulses may be visible in ferrets with right-sided CHF. Palpate femoral pulses for quality, character, and the presence of any deficits. Pulses may be weak, irregular, or normal with cardiac disease. Bounding pulses are uncommon but could potentially be seen with a severe aortic insufficiency or a patent ductus arteriosus. Abdominal palpation of ferrets with heart disease may reveal ascites, hepatomegaly, or splenomegaly. Other findings on physical examination may include hypothermia, lethargy, generalized weakness, and dehydration.

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The ferret heart is auscultated between the sixth and eight ribs, much more caudally than in the dog or cat. The normal heart rate is between 180 and 250 beats/min. Ferrets may normally have a pronounced sinus arrhythmia that causes a dramatic decrease in heart rate or sinus pauses during auscultation. This normal variation will resolve with stimulation, such as a toe pinch. Relevant findings on auscultation are bradycardia, tachycardia, murmurs, gallop rhythms, and muffled heart sounds. Murmurs are usually associated with valvular insufficiency and increased outflow tract velocities. An S_3 gallop occurs secondary to dilation of the left ventricle, and an S_4 gallop occurs secondary to an accentuated atrial contraction filling a hypertrophied and noncompliant ventricle. Ferrets with cardiac disease may show signs of dyspnea and tachypnea. Auscultation of the lungs may reveal crackles, muffled lung sounds, or increased bronchovesicular sounds.

Diagnosis

A suspected diagnosis of heart disease can be made on the basis of the history and physical examination findings discussed previously. A definitive diagnosis of cardiac disease requires an echocardiogram, thoracic radiographs, and possibly an ECG. These testing modalities are discussed in detail later. For all patients with documented or suspected heart disease, complete a minimum database, including a complete blood count (CBC), biochemical profile, and urinalysis, before instituting therapy. Heartworm testing is indicated in ferrets with clinical signs suggestive of infection and for those from heartworm-endemic areas. If thoracocentesis or abdominocentesis is performed, cytologic and fluid analysis of the aspirated sample may provide insight into the cause of the effusion.

Radiography. Standard two-view thoracic radiographs provide a general impression of cardiac size and are required to diagnose CHF definitively. Pulmonary edema is seen as a mixed patchy alveolar and interstitial pattern more prominent in the caudodorsal lung regions. Because lesions in the anterior mediastinum are common, the entire thorax should be included in the radiographs. Physical restraint is usually adequate to obtain radiographs, although a short dose of inhalant anesthesia or midazolam (0.3–0.5 mg/kg intramuscularly [IM]) may be used safely. The typical landmarks used for dogs and cats are inaccurate in ferrets because of the shape of the ferret's thorax, which is elongated and flattened dorsoventrally.[75] The normal ferret heart is more globoid in appearance than a dog or cat heart and is located approximately between the sixth and eighth intercostal spaces. The right ventricle may have slight contact with the sternum (Fig. 5.1). If heart disease is present, the cardiac silhouette may appear enlarged, resulting in tracheal elevation, rounding of the cardiac silhouette, and increased sternal contact on the lateral view. On the ventrodorsal view, the heart may be elongated and widened, filling up a larger portion of the thorax.

The size of the cardiac silhouette can be quantified by the use of a modified vertebral heart score (VHS).[75] The technique involves measuring the length and width of the heart on the right lateral radiograph and expressing this measurement in units of vertebral length (Fig. 5.2). This method corrects for differences in size between ferrets. Because the presence of pericardial fat on the ventrodorsal view makes the edges of the cardiac silhouette more difficult to discern, the lateral view is more accurate. On the lateral view, the long axis of the heart is the length from the ventral border of the bifurcation of the trachea to the apex of the heart, and the short axis is the maximum length from the cranial to the caudal edges. On the ventrodorsal view, the long axis is the length of the heart along midline from the cranial border of the heart to the apex. The short axis is the maximum width of the heart measured perpendicular to the long axis. These measurements are compared with the length of the thoracic vertebrae (v), beginning with the cranial edge of the fifth thoracic vertebra (T5) to the caudal aspect of the eighth thoracic vertebra (T8) and estimated to the nearest 0.25 vertebra. The heart length and width measurements in vertebral lengths from a single projection are then added to obtain a total score. The median VHS on the right lateral projection is 5.33 v, with a range of 5.23 to 5.47 v. The heart length plus width is 5.35 cm, with a range of 5.02 to 5.48 cm. The median VHS on the ventrodorsal view is 6.0 v, with a range of 5.73 to 6.15 v. The thoracic vertebrae in ferrets are generally 1 cm long between T5 and T8. Therefore you can measure length plus width, and the sum of these approximates the VHS.

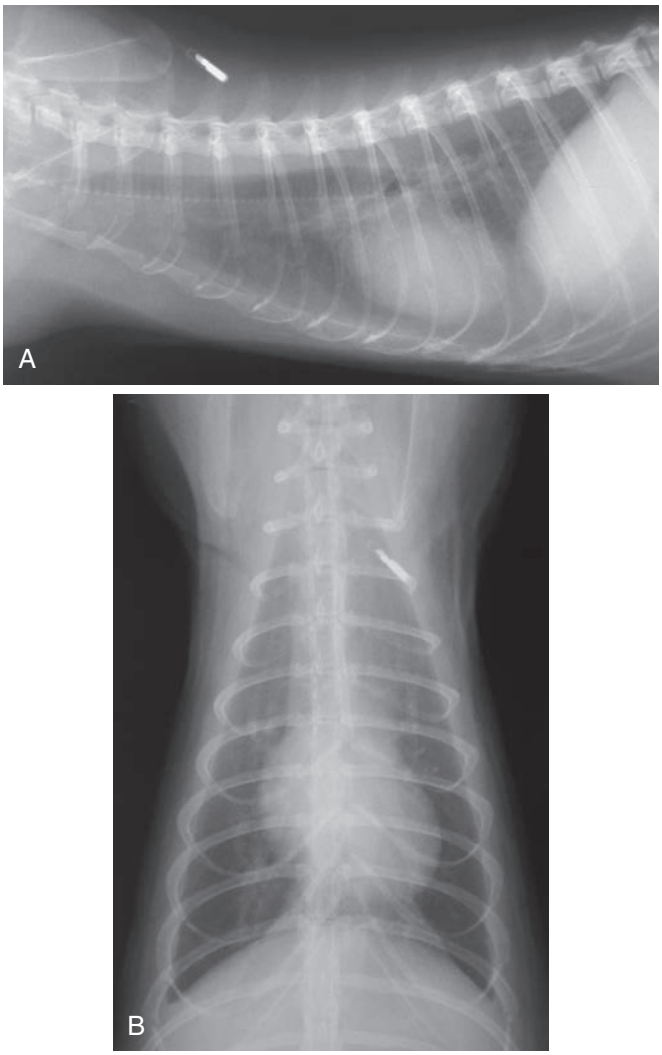


Fig. 5.1 Normal lateral (A) and ventrodorsal (B) thoracic radiographs of a 3-year-old, clinically normal ferret.

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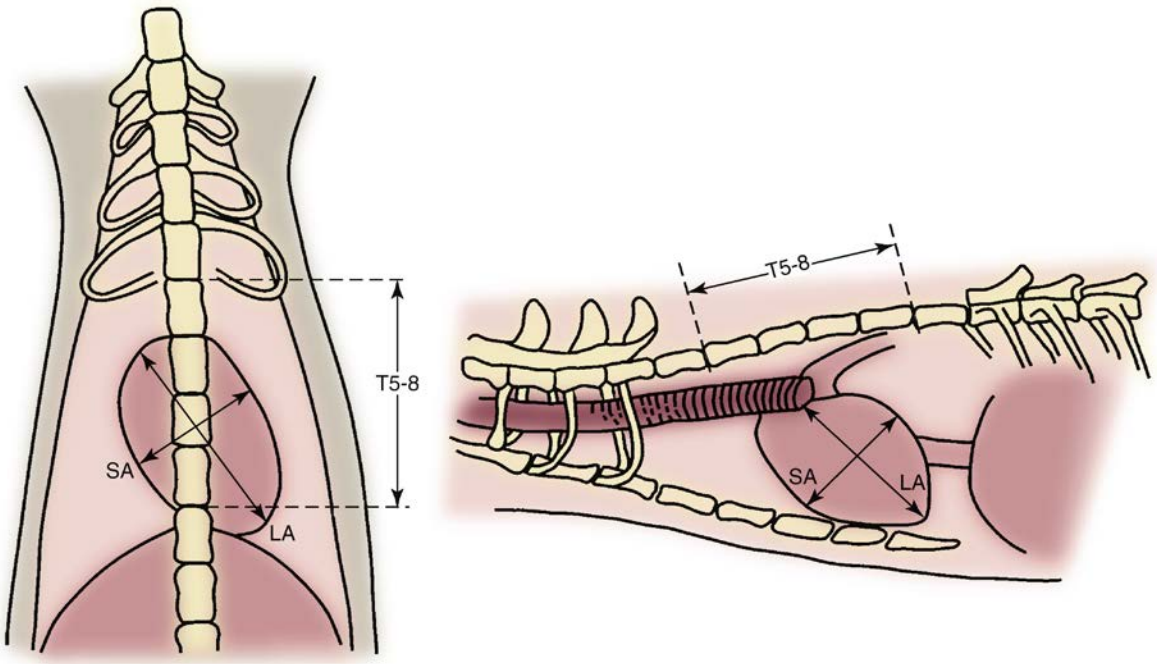


Fig. 5.2 Drawings of lateral (right) and ventrodorsal (left) views of the thorax indicating measurements of the cardiac silhouette in both long axis (LA) and short axis (SA). The sum of the LA and SA measurements is expressed in terms of vertebral length, beginning at the cranial edge of the fifth thoracic vertebra (T5) and estimated to the nearest 0.25 vertebra. The vertebral length and width measurements are then added to obtain a vertebral heart score. (Adapted from Stepien RL, Benson KG, Forrest LJ. Radiographic measurement of cardiac size in normal ferrets. *Vet Radiol Ultrasound* 1999;40:606-610.)

Radiographically, CHF may be seen as pleural effusion, pulmonary edema, or pulmonary venous congestion. Pulmonary edema typically appears as a patchy interstitial and alveolar pattern. Abdominal radiographs may reveal hepatomegaly, splenomegaly, and ascites.

Electrocardiography. In ferrets, ECGs are used primarily to determine the presence of abnormal rhythms and conduction disturbances. Reference values for ECGs in ferrets have been published[6,8,15,22,73]; values from select studies are summarized in Table 5.1. A variety of common arrhythmias have been recorded in ferrets (Fig. 5.3). Sinus rhythm and sinus tachycardia are the most common rhythms seen on presentation with cardiac disease. Sinus bradycardia can be associated with hypoglycemia, commonly seen in ferrets with insulinoma. Second-degree atrioventricular (AV) block can occur as a normal finding in healthy ferrets. High-grade second-degree AV block and complete (third-degree) AV block are uncommon. Clinical signs of weakness, syncope, and dyspnea associated with CHF often accompany complete AV block.[45] Epicardial transdiaphragmatic pacemakers have been used to successfully treat complete AV block (Fig. 5.4). Atrial and ventricular premature contractions may be recorded on some ferret ECGs. Although atrial fibrillation can occur in the presence of significant atrial enlargement, this diagnosis appears to be rare in ferrets.[45] There is one case report of atrial fibrillation occurring in a ferret, believed to be mediated by increased vagal tone due to butorphanol administration.[65]

Electrocardiography is ideally performed without sedation with the animal in right lateral recumbency (Fig. 5.5). The ECG clips can be flattened to produce a smooth surface that does not result in pinching; alternatively, atraumatic clips can be purchased. Because most ferrets object to the use of alcohol, ECG coupling gel (or ultrasound gel) is recommended. The ferret can be distracted by offering a nonsugary treat such as FerreTone (8 in 1, Islandia, NY) from a syringe while the ECG is being recorded.

Echocardiography. Echocardiography remains the test of choice for diagnosing structural and functional cardiac abnormalities. This modality is used in conjunction with good-quality thoracic radiographs to properly identify the severity of underlying cardiac disease and the presence of CHF. In addition, echocardiography can be useful in identifying mediastinal masses and as an aid in detecting heartworm disease.[70] It can often be obtained without the use of sedation. If sedation is required, use either a short-acting injectable anesthetic or an inhalant anesthetic. Echocardiography is performed with the animal in both right and left lateral recumbency. Imaging planes similar to those obtained in other species are recorded.[81] Two-dimensional echocardiography provides an assessment of cardiac size and function. Standard M-mode measurements are obtained, including chamber dimensions, wall thickness, and indexes of systolic function. Spectral Doppler imaging is used to quantitate the velocity of normal and abnormal blood flow. Color-flow Doppler echocardiography provides a visual inspection of blood flow direction and detection of turbulent flow, including valvular regurgitation. Echocardiographic reference values in the sedated and awake ferret have been published and are summarized in Table 5.2.[15,76]

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TABLE 5.1 Electrocardiographic Values (Lead II) in Clinically Normal Ferrets[a]

Parameter	Conscious[b] (n = 43)[15]	Sedated with Ketamine-Diazepam[c] (n = 80)[8]	Sedated with Ketamine-Xylazine[c] (n = 27)[22]
Age, months	18 (10–84)	12 (2–72)	5.2[d]
Male/female	0.59	0.95	1.25
Body weight, kg		—	—
Males	1.47 ± 0.36		
Females	0.79 ± 0.14		
Heart rate, beats/min		333 (136–429)	233 ± 22
Males	255 (210–315)		
Females	285 (210–405)		
P wave amplitude, mV	0.175 (0.1–0.3)	0.1 (0–0.25)	0.122 ± 0.007
P wave duration, s	0.03 (0.02–0.04)	0.02 (0.005–0.02)	0.024 ± 0.004
P-R interval, s	0.08 (0.06–0.1)	0.04 (0.03–0.07)	0.047 ± 0.003
R wave amplitude, mV	1.8 (1.4–3.2)	1.8 (0.9–3.1)	1.46 ± 0.84
QRS duration, s	0.04 (0.02–0.04)	0.04 (0.02–0.05)	0.043 ± 0.003
Q-T interval, s	0.09 (0.06–0.16)	0.1 (0.06–0.18)	0.12 ± 0.04
T wave amplitude, mV	0.2 (0.1–0.4)	0.05 (–0.4 to +0.4)	0.22 ± 0.12
Mean electrical axis	80 (43–99)	90 (70–100)	77.22 ± 12

[a]Values are expressed either as median (range) or mean ± standard deviation.
[b]Ferrets restrained in so-called "hanging position."
[c]Ferrets in right lateral recumbency.
[d]Mean without SD data.

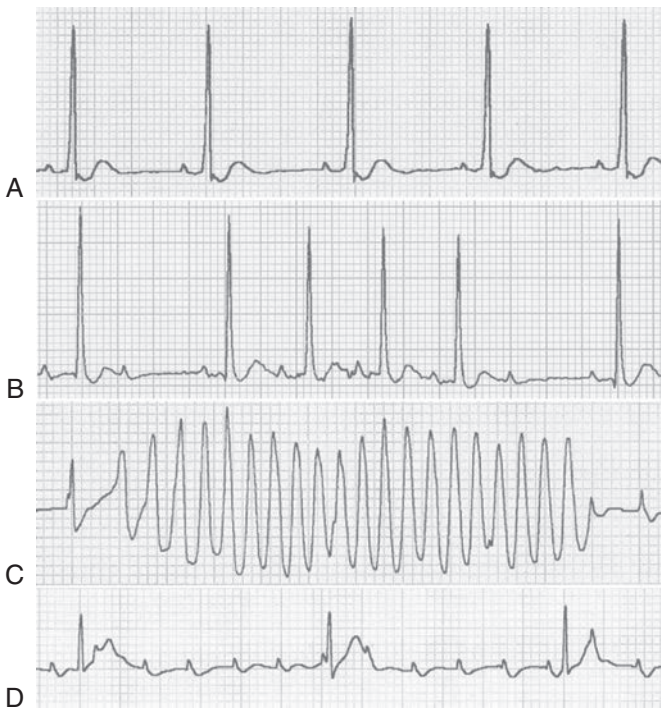


Fig. 5.3 Electrocardiograms recorded from four ferrets, showing normal rhythm (A), second-degree atrioventricular (AV) block in an asymptomatic ferret (B), paroxysmal ventricular tachycardia (C), and complete AV block (D).

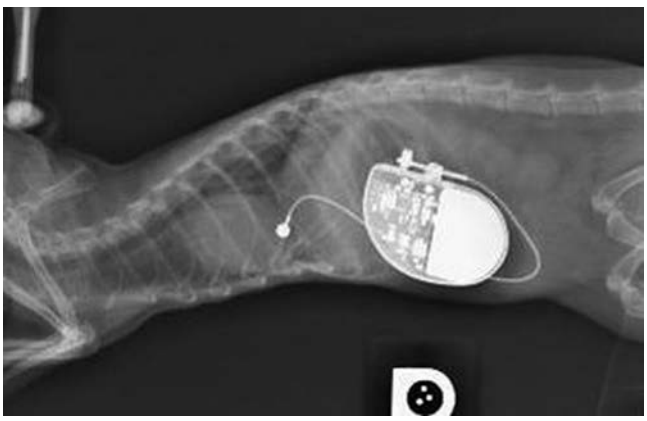


Fig. 5.4 Radiograph of a ferret with an implanted cardiac pacemaker. The ferret exhibited signs of collapse and weakness with profound bradycardia due to complete AV block.

Treatment

Basic therapeutic principles for CHF and cardiac disease are applied to ferrets. If a published ferret dose is not available, feline doses are often used as a starting point. Therapy for acute CHF (Table 5.3) focuses on improving oxygenation and reducing preload and afterload. Oxygen is provided by placing the animal in a closed cage or incubator with supplemental oxygen. Diuretics reduce preload by reducing blood volume.[55] Furosemide is the most commonly used diuretic; it is most effective when given either IV or IM in the acute setting. Ferrets tolerate doses of 1 to 4 mg/kg every 8 to 12 hours. Nitroglycerin 2% ointment is a venous dilator that can be applied on a hairless body surface, such as inside the pinna or on the skin in the axilla or inguinal area. Ferrets are sensitive to the hypotensive effects of nitroglycerin. Angiotensin-converting enzyme (ACE) inhibitors are given to reduce afterload by causing arterial vasodilation and to reduce preload by decreasing salt and water retention.[38] The

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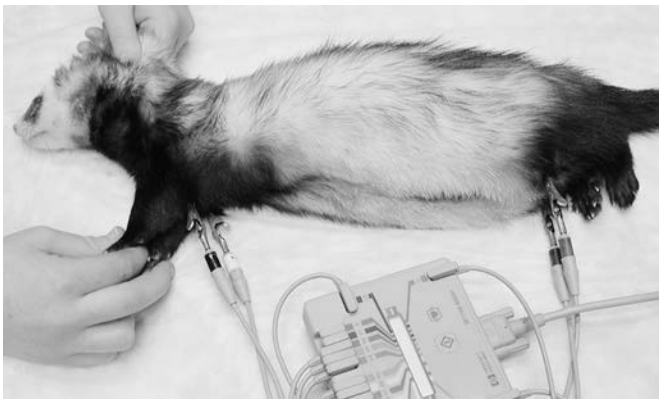


Fig. 5.5 Ferret restrained in right lateral recumbency for recording an ECG.

dose is usually started at 0.5 mg/kg by mouth (PO) given every 48 hours and then titrated up to every 24 hours if tolerated. In the first 24 to 48 hours of therapy, treatment with ACE inhibitors may result in hypotension or lethargy. The use of ACE inhibitors and concurrent diuretic therapy in ferrets with CHF can result in severe azotemia, and initiation of therapy with ACE inhibitors may be delayed until the patient is stable and on oral diuretics. Renal perfusion is reduced in CHF secondary to use of diuretics, decreased cardiac output, dehydration, and hypotension.[29] If significant pleural effusion is present, resulting in an increased inspiratory effort, perform pleurocentesis, and submit the fluid for fluid analysis and cytologic examination. In acute disease, monitor ferrets closely for respiratory rate and effort, mucous membrane color, heart rate and rhythm, body weight, and hydration as well as electrolyte, blood urea nitrogen (BUN), and creatinine values. Obtain serial radiographs to assess the response to therapy. Adjust medication dosages on the basis of the listed monitoring parameters.

Long-term therapy typically includes furosemide, ACE inhibitors, and the positive inotrope pimobendan (Vetmedin; Boehringer Ingelheim Vetmedica, St. Joseph, MO), if systolic dysfunction is present (Table 5.4). Furosemide is given orally at a dosage of 1 to 4 mg/kg every 8 to 12 hours; ACE inhibitors (eg, enalapril or benazepril) are given at a dosage of 0.25 to 0.5 mg/kg every 24 to 48 hours, depending on the drug. Pimobendan is used at a dosage of 0.625 to 1.25 mg per ferret every 12 hours. In addition to its positive inotropic effect, pimobendan has neurohormonal effects, which include decreasing levels of inflammatory cytokines and plasma epinephrine. Clinical studies in dogs with CHF secondary to dilated cardiomyopathy or chronic valvular disease reveal improved quality of life and survival with pimobendan therapy.[26] Whether this beneficial effect exists in ferrets is unknown. However, some experimental studies with pimobendan in ferrets have been performed.[40,42,44]

Long-term management includes periodic monitoring for recurrence of CHF and changes in body weight, renal values, and heart rate and rhythm. If CHF recurs with standard therapy protocols, additional diuretics may be used, including thiazide diuretics or potassium-sparing diuretics, such as spironolactone. Published feline dosages are used, and the dose is titrated on the basis of clinical response. Closely monitor electrolyte levels after beginning more aggressive and mixed diuretic therapy. In ferrets with CHF receiving steroid therapy for lymphoma, spironolactone should be considered early in the disease process because of its effects on the aldosterone receptor in the distal renal tubule.[55]

The use of antiarrhythmic drugs is not well documented in ferrets. Digoxin therapy is used to depress AV nodal conduction with supraventricular arrhythmias, especially if it is desirable to avoid negative inotropic effects of drugs such as calcium channel blockers.[38] Digoxin elixir (0.05 mg/mL) is recommended because of the small doses required in ferrets. The recommended starting dosage is 0.005 mg/kg PO every 12 to 24 hours (start low and titrate upward), based on lean body weight, usually 70% of body weight.[66] Begin therapy once daily and then titrate up to twice daily depending on the clinical response and serum digoxin levels. To measure digoxin levels, serum samples are taken after 5 to days of therapy and approximately 6 to 8 hours after drug administration.[74] Reference values for dogs and cats (0.8–2.0 ng/mL) are extrapolated to interpret values in ferrets. Adverse effects of digoxin are inappetence, lethargy, vomiting, diarrhea, and arrhythmias.[74] Contraindications for the use of digoxin are significant azotemia, hypokalemia, bradyarrhythmias (including AV block), and severe ventricular arrhythmias.[38]

Atenolol, dosed at 3.125 to 6.25 mg/kg every 24 hours and titrated to effect, can be given for many supraventricular and ventricular arrhythmias. Diltiazem can be used for many supraventricular arrhythmias either to reduce spontaneous occurrence or to slow AV nodal conduction.[37] Intravenous lidocaine can be used in ferrets with ventricular tachycardia; however, the dose should be reduced from that used in cats and then titrated to effect. With this class of antiarrhythmic drugs, close observation for the development of neurologic and gastrointestinal signs is essential.[37]

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) has been described in ferrets and has clinical characteristics similar to those observed in dogs and cats.[18,23,43] Although DCM appears to be diagnosed infrequently, it is often associated with CHF, based on results of a retrospective study of ferret echocardiographic studies in a clinical practice.[45] The disease results in a dilated left ventricle, right ventricle, or both, with global systolic dysfunction. The cause of the disease in ferrets is not known; in one ferret, it was reported in association with a cryptococcal infection.[23] To date, no cases of taurine-responsive DCM have been documented in ferrets. Lethargy, dyspnea, anorexia, and weight loss are common complaints in the history. Physical examination findings can include hypothermia, heart murmur, tachycardia, pallor, weakness, or ascites. Pleural effusion manifests as an increased inspiratory effort with muffled heart sounds. Pulmonary edema is heard as moist rales and increased respiratory sounds. In many cases, both pulmonary edema and pleural effusion are present simultaneously, resulting in a combination of the clinical signs mentioned.

Echocardiography is used to make a definitive diagnosis of DCM. Typical echocardiographic changes are similar to those

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TABLE 5.2 M-mode and Doppler Echocardiographic Values for Normal Ferrets[a,b]

Parameter	Sedated With Ketamine and Midazolam (n = 30)[76]	Awake (n = 19, Males)[15]	Awake (n = 27, Females)[15]
Body weight, kg	1.17 ± 0.36	1.47 ± 0.36	0.79 ± 0.14
Age, years	2.3 ± 1.0	Median 1.5 (range 0.8–7)	Median 1.5 (range 0.8–7)
Sex			
Male	16	19	
Female	14		27
Heart rate, beats/min	273 ± 31 (n = 29)	—	—
IVSd, mm	3.6 ± 0.7	3.1 ± 0.3	2.6 (2.4–2.9)[c]
IVSs, mm	4.8 ± 1.1	4.1 ± 0.4	3.4 ± 0.4
LVIDd, mm	8.8 ± 1.5	13 ± 1.2	10.4 ± 1.6
LVIDs, mm	5.9 ± 1.5	8.9 ± 1.2	7.1 ± 1.5
LVFWd, mm	4.2 ± 1.1	3.3 ± 0.3	2.8 ± 0.4
LVFWs, mm	5.8 ± 9.9	4.4 ± 0.5	3.6 ± 0.4
FS %	33 ± 14	32 ± 7	34 ± 6
EF %	69 ± 19 (n = 27)	—	—
LA, mm	7.1 ± 1.8 (n = 26)	10 (9.1–10.9)[c] (2D)	8.9 (8.0–9.4)[c] (2D)
Ao, mm	5.3 ± 1.0 (n = 25)	5.5 ± 0.6 (2D)	4.6 ± 0.4 (2D)
LA/Ao	1.33 ± 0.27 (n = 26)	—	—
PA, mm	4.8 ± 9.0 (n = 27)	5.2 ± 0.5	4.5 ± 0.4
RVFWd, mm	1.2 ± 0.3 (n = 27)	—	—
RVIDd, mm	3.8 ± 1.0 (n = 28)	—	—
Ao_{max}, m/s	0.89 ± 0.20 (n = 25)	—	—
PA_{max}, m/s	1.10 ± 0.14 (n = 29)	—	—
Mitral E, m/s	0.70 ± 0.10 (n = 15)	—	—
Mitral A, m/s	0.52 ± 0.11 (n = 15)	—	—
Mitral E/A	1.38 ± 0.32 (n = 15)	—	—

[a]Values are mean ± standard deviation unless indicated otherwise.
[b]Values are M-mode derived unless marked 2D (two-dimensional).
[c]Median (first–third quartile).
Ao, aorta diameter; *Ao_{max},* maximal aortic outflow velocity; *EF,* ejection fraction; *FS,* fractional shortening; *IVSd,* interventricular septum in diastole; *IVSs,* interventricular septum in systole; *LA,* left atrial diameter; *LVIDd,* left ventricular internal diameter in diastole; *LVIDs,* left ventricular internal diameter in systole; *LVFWd,* left ventricular free wall in diastole; *LVFWs,* left ventricular free wall in systole; *Mitral A,* peak transmitral late diastolic (atrial contraction) velocity; *Mitral E,* peak transmitral early diastolic velocity; *PA,* pulmonary artery diameter; *PA_{max},* maximal pulmonary artery outflow velocity; *RVFWd,* right ventricular free wall in diastole; *RVIDd,* right ventricular internal diameter in diastole.

TABLE 5.3 Dosages and Treatment Goals of Drugs Commonly Used to Treat Acute Congestive Heart Failure in Ferrets

Drug	Indication	Dose	Frequency
ACE inhibitors	Overt CHF	0.5 mg/kg PO	Every 48 h; increase to every 24 h if tolerated
Dobutamine	Inotropic support, acute CHF	5–10 μg/kg per minute IV	CRI
Furosemide	Overt CHF	1.0–4.0 mg/kg IV (preferably by IV bolus, then CRI at 0.7-1 mg/kg per hour); can also be administered IM or SC	Every 8–12 h
Nitroglycerin 2% ointment	Overt CHF, preload reduction	Topical 1/16- to 1/8- inch inside the pinna or on skin in the axilla or inguinal region	Every 12–24 h

CHF, congestive heart failure; *CRI,* constant rate infusion; *IM,* intramuscularly; *PO,* orally; *SC,* subcutaneously; *IV,* intravenously.

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TABLE 5.4 Maintenance Dosages of Drugs Commonly Used to Treat Congestive Heart Failure in Ferrets

Drug	Indication	Maintenance Dose (mg/kg)	Frequency
ACE Inhibitor	Overt or impending CHF[a]		
Benazepril[b]		0.25–0.5	Every 24 h
Enalapril[b]		0.25–0.5	Every 24–48 h
Atenolol	Arrthymias	3.125–6.25	Every 24 h
Digoxin (pediatric elixir, 0.05 mg/mL)	Atrial fibrillation or SVT	0.005–0.01[c]	Every 12 h
Diltiazem	Atrial fibrillation	1.5–7.5	Every 12 h
	SVT (rare)	2–6	Every 12 h
Furosemide	Overt CHF	1.0–4 .0	Every 8–12 h
Pimobendan	Systolic dysfunction	0.25 mg/kg or 0.625 to 1.25 mg/ferret	Every 12 h
Spironolactone[d]	Aldosterone escape Electrolyte control	1–2	Every 12 h

[a]When to initiate ACE inhibitor therapy for impending CHF is controversial.
[b]Initiate at 0.25 mg/kg and increase to 0.5 mg/kg after ensuring that renal function is normal.
[c]Start at the low end of the dose range and titrate upward as needed and based on digoxin level monitoring.
[d]Preserves magnesium and potassium while antagonizing aldosterone action.
ACE, angiotensin-converting enzyme; *CHF,* congestive heart failure; *SVT,* supraventricular tachycardia.

observed in other species.[50,83] The left ventricle appears dilated, with increased end-systolic dimensions, and the left atrium is typically dilated (Fig. 5.6). Fractional shortening, a commonly used index of systolic function, is reduced. If the right side of the heart is involved, the right ventricle is dilated, right ventricular systolic motion is reduced, and the right atrium is enlarged. In advanced disease, mitral and tricuspid regurgitation secondary to dilation of the valve annulus is seen. Left ventricular outflow tract velocities can be normal or reduced.

Radiographically, the cardiac silhouette appears enlarged. Congestive heart failure manifests as pleural effusion or pulmonary edema. If the abdomen is included in the radiograph, hepatomegaly, ascites, or splenomegaly may be present. A variety of ECG abnormalities may be evident, including ventricular premature contractions, atrial premature contractions, atrial tachycardia, and ventricular tachycardia.[50,83]

Therapy for acute clinical CHF was described above and includes oxygen, diuretics, nitroglycerin, and pleurocentesis, if necessary. After the ferret's condition is initially stabilized, therapy for chronic disease begins with diuretics, ACE inhibitors, and pimobendan (for severe systolic dysfunction, the combination may be beneficial). Diuretics should be reduced to the lowest dosage that prevents reaccumulation of pleural effusion and pulmonary congestion. A low-salt diet and exercise restriction are theoretically beneficial in the management of CHF but in practice can be difficult to accomplish in ferrets.

Long-term therapy includes periodic monitoring of thoracic radiographs, ECG findings, and plasma BUN, creatinine, and electrolyte concentrations. The clinical response to therapy is often good, and ferrets tend to respond better to treatment than do dogs or cats with similar echocardiographic findings.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) occurs in ferrets, but the clinical characteristics have not been well described and no reports of HCM have been published. Physiologically, the presence of left ventricular hypertrophy results in impaired filling of the left ventricle (diastolic function). Left ventricular diastolic pressure progressively increases, and the subsequent increase in left atrial pressure results in the development of left-sided CHF.[2] Left ventricular hypertrophy has not been documented secondary to hypertension or hyperthyroidism in ferrets. The course of disease is likely to be similar to that in cats, remaining silent until the onset of CHF, thromboembolic events, or sudden death.[2,67]

Hypertrophic cardiomyopathy should be a differential diagnosis in ferrets with suspected cardiac disease based on auscultation, radiographic findings, or clinical signs of CHF. Echocardiography is used to definitively diagnosis this disease. The entire left ventricle or isolated segments of the left ventricle

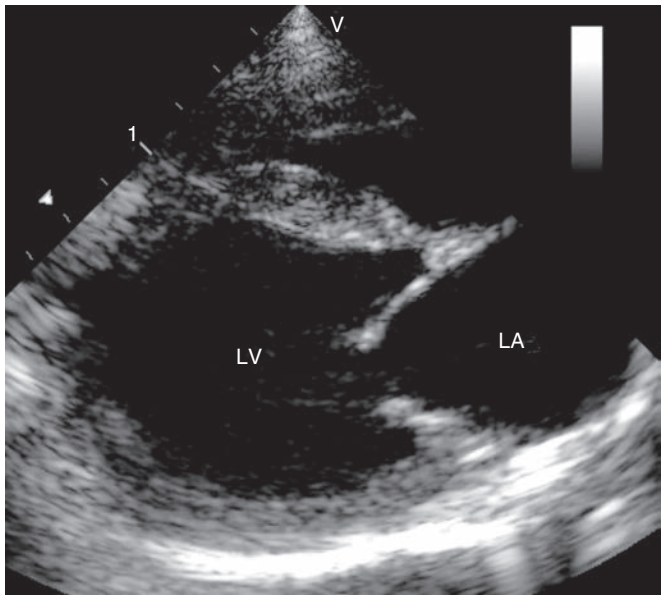


Fig. 5.6 Two-dimensional echocardiogram of a ferret with dilated cardiomyopathy. The left ventricle *(LV)* is dilated, with rounding of the left ventricular apex, and the left atrium *(LA)* is enlarged.

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can be hypertrophied. The left ventricular diastolic and systolic dimensions are reduced, and the fractional shortening is normal or increased. Left atrial enlargement may be present. Systolic anterior mitral valve motion may be seen and is often associated with interventricular septal hypertrophy. Doppler echocardiographic abnormalities can include turbulence in the left ventricular outflow tract secondary to dynamic obstruction and mitral regurgitation.

Treatment is aimed at improving the diastolic efficiency of the left ventricle and relieving signs of CHF. The most commonly used drugs for treating ferrets with HCM include β-adrenergic blocking drugs (e.g., atenolol at 3.13–6.25 mg/ferret PO every 24 hours) or calcium channel blockers (e.g., diltiazem at 1.5–7.5 mg/kg PO every 12 hours).[52] These drugs reduce heart rate and contractility, resulting in better filling of the left ventricle. Therapy is titrated to achieve an effective reduction in heart rate and clinical improvement. With both medications, adverse effects include lethargy, inappetence, bradycardia, and hypotension. If clinical signs of CHF are present, treatment with diuretics is recommended (see earlier discussion). Therapeutic monitoring includes periodic echocardiography to determine the extent of progressive cardiac hypertrophy and atrial enlargement. In those ferrets with CHF, results of thoracic radiographs, ECGs, and plasma biochemical profiles should be monitored. Thromboembolic disease secondary to cardiac disease in ferrets has not been reported, but one case of atrial thrombosis has been seen by one of the authors (J.K.M., unpublished data, 1997).

Valvular Heart Disease

Valvular heart disease most commonly occurs in middle-aged to older ferrets and is being recognized with increasing frequency. Valvular regurgitation was the most common abnormal echocardiographic finding in a retrospective study of echocardiographic findings in client-owned ferrets, with the aortic valve being the most commonly affected valve.[45] Clinical signs vary depending on the severity of the underlying disease. Trivial to mild aortic insufficiency is a common incidental finding on echocardiographic examination of ferrets. However, CHF develops more commonly with mitral and aortic valve disease, especially when both valves are affected (aortic insufficiency alone being rarely associated with CHF).[45] Mitral regurgitation is auscultated as a systolic murmur over the left apical region, and tricuspid regurgitation is auscultated in the right parasternal location. A diastolic murmur of aortic or pulmonic insufficiency is rarely heard on physical examination. Femoral pulses can be hyperdynamic with significant aortic regurgitation, but they most often remain normal or reduced with CHF.

The ECG signs vary but may indicate atrial arrhythmias associated with atrial enlargement. Echocardiography shows thickening of the affected valves and atrial enlargement (Fig. 5.7). The left ventricular diastolic dimension is increased, with a normal systolic dimension and preserved fractional shortening. The left ventricular wall thickness is normal. Regurgitation can be identified and quantified with the use of Doppler echocardiography.

If radiographic evidence of CHF is present, administer furosemide and titrate the dose to effect while monitoring renal values at periodic intervals. Pimobendan can be beneficial in the acute treatment setting (if receiving an oral medication is not too stressful for the patient) because of its rapid hemodynamic effects. Treatment with ACE inhibitors blunts the neurohormonal activation that occurs with advanced cardiac disease and CHF[38]; however, only administer an ACE inhibitor once the ferret is stabilized and after ensuring there is no current hypotension or significant azotemia. Pimobendan may be used for stabilization of heart rate, positive inotropic effects, and control of supraventricular arrhythmias. The management of CHF is described above.

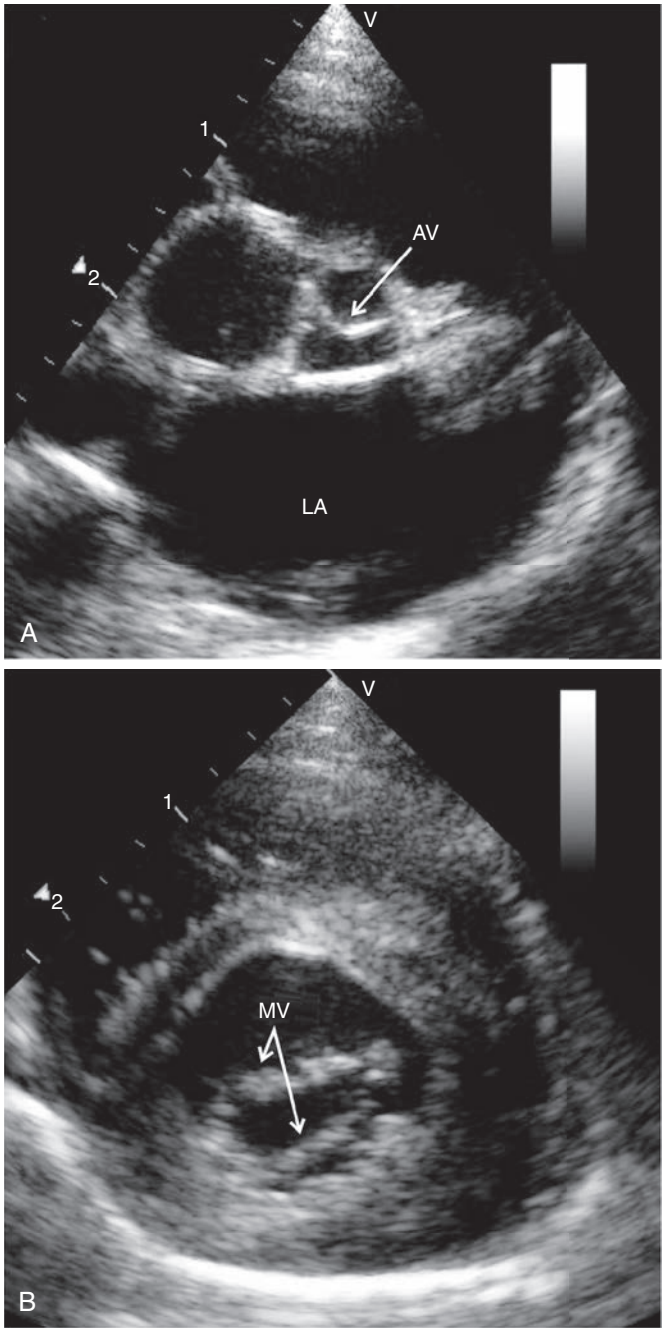


Fig. 5.7 Two-dimensional short-axis echocardiograms from a ferret with mitral and aortic regurgitation. (A) The aortic valve *(AV)* is thickened and the left atrium *(LA)* is severely dilated. (B) The mitral valve *(MV)* is thickened.

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Several factors influence the prognosis of ferrets with chronic valvular disease, including renal function, coexisting disease, and cardiac rhythm. Insufficient data are available to predict the prognosis in ferrets with CHF caused by chronic degenerative valvular disease.

Myocarditis

Myocarditis typically manifests as infiltration of the myocardium with inflammatory cells that results in reduced myocardial function, arrhythmias, and fibrous tissue replacement of normal myocardium.[24] Causes of myocardial inflammation are systemic vasculitis and parasitic, autoimmune, bacterial, and viral disorders. A *Toxoplasma*-like organism has been described as causing multifocal myocardial necrosis.[82] Aleutian disease virus can cause fibrinoid necrosis and mononuclear cell infiltration in arterioles of the heart.[13] Because of the presence of cytokines and other inflammatory factors, systemic inflammatory diseases, including sepsis, can result in reduced myocardial function.

The gold standard for the diagnosis of myocarditis is histologic evaluation of the myocardium, making antemortem verification difficult. Because a cardiac biopsy specimen is clinically difficult to obtain, the use of the cardiac biomarker troponin is the best alternative. Cardiac troponin I (cTnI) is a highly sensitive and specific biomarker of myocardial injury in human medicine, which is used to diagnose and provide prognostic information in patients with myocardial infarction, sepsis, and traumatic myocardial injury.[31,69,87] Blood cTnI levels have been reported in clinically normal cats and dogs, as well as in disease states (e.g., gastric dilation and volvulus, CHF, chemotherapy, heat stroke, cardiomyopathy, and pericardial disease).[3,28,47,58,71,72] A point-of-care analyzer (i-STAT 1; Abaxis Union City, CA) is available and validated for measurement of cTnI in people.[87] The company has published reference values for cats, dogs, and horses. However, the accuracy of this instrument in detecting ferret troponin is unknown. The amino acid sequence of cTnI is highly conserved and more than 90% identical to that from human, canine, and feline cTnI proteins, and the epitopes detected by commercial analyzers are highly conserved across species.[87] These findings substantiate the measurement of cTnI in ferrets and the use of commercial analyzers. To date, we are unaware of published data on cTnI in ferrets; however, based on other species, the "normal" value seen in one author's clinic (J.K.M.) should be less than 0.1 ng/mL.

Myocarditis should be suspected if arrhythmias and acute myocardial dysfunction are found in the presence of a multisystemic illness and in conjunction with an increased cTnI. The primary therapeutic goal is directed at the underlying cause of the systemic disorder. Cardiovascular support, including diuretics or antiarrhythmic agents and corticosteroids, may be necessary.

Neoplasia

Neoplasia involving the myocardium or pericardium has not been reported in ferrets. Lymphoma, a common tumor found in ferrets, can involve the cranial mediastinum. Ferrets with a cranial mediastinal mass are often presented because of dyspnea associated with the presence of pleural effusion.[19]

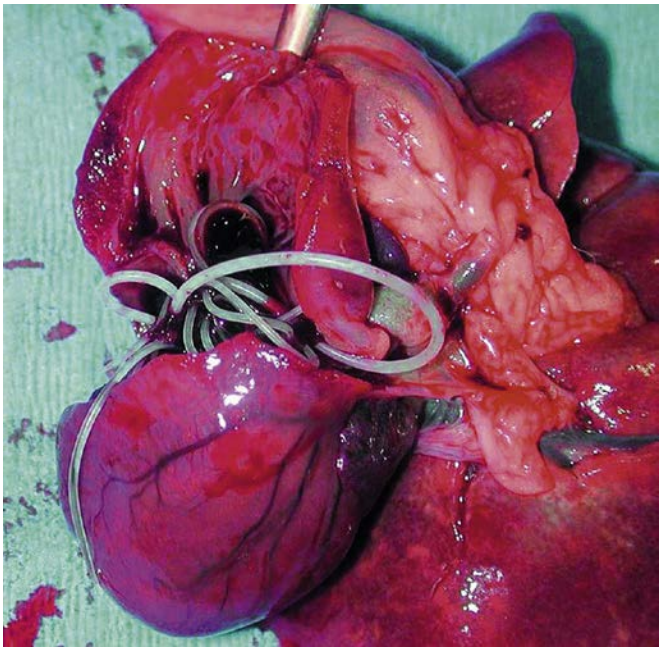


Fig. 5.8 The heart of a ferret that presented for moderate dyspnea and coughing. Necropsy demonstrated three female and seven male *Dirofilaria immitis* worms in the heart.

Ultrasonography is useful to rule out the presence of cardiac disease and to visualize any mass that may be present. Fine-needle aspiration of the tumor, or in some cases cytologic examination of the fluid, can be used to make a diagnosis.

Heartworm Disease

Natural and experimental infections with the canine heartworm *Dirofilaria immitis* have been reported in ferrets.[4,7,9,49,51,60] Ferrets living in or originating from a heartworm-endemic area are most susceptible to infection. The susceptibility and life cycle of this parasite have been studied in ferrets and are similar to those of heartworm in dogs; however, because of the small size of ferrets, the clinical presentation more closely resembles that of infected cats.[80] Microfilaria have been reported in ferrets in both natural and experimental infections and are present in 50% to 60% of infected animals.[80]

Ferrets can be severely affected by the presence of only a single worm. With natural infections, worm burdens ranging from 1 to 21 worms have been reported (Fig. 5.8).[7,49,51,60] The worms can be found within the pulmonary arteries, right side of the heart, and vena cava. Because of the ferret's small size, infection with a small number of worms can cause mechanical obstruction to blood flow, resulting in clinical signs of right-sided heart failure. Right ventricular and right atrial enlargement develop as a result of pulmonary hypertension and mechanical obstruction. Thickening of the tricuspid valve may result from chronic damage caused by the presence of worms. Pleural effusion, ascites, and congestion of abdominal organs may also be present. Aberrant larval migration has not been reported in ferrets. Clinical signs in affected ferrets include coughing, lethargy, weakness, dyspnea, and hypothermia. Sudden cardiac death occurs, most likely from pulmonary artery obstruction.[49,60] Thoracic radiographs should be obtained and may show pleural effusion and cardiomegaly (Fig. 5.9). Enlargement of

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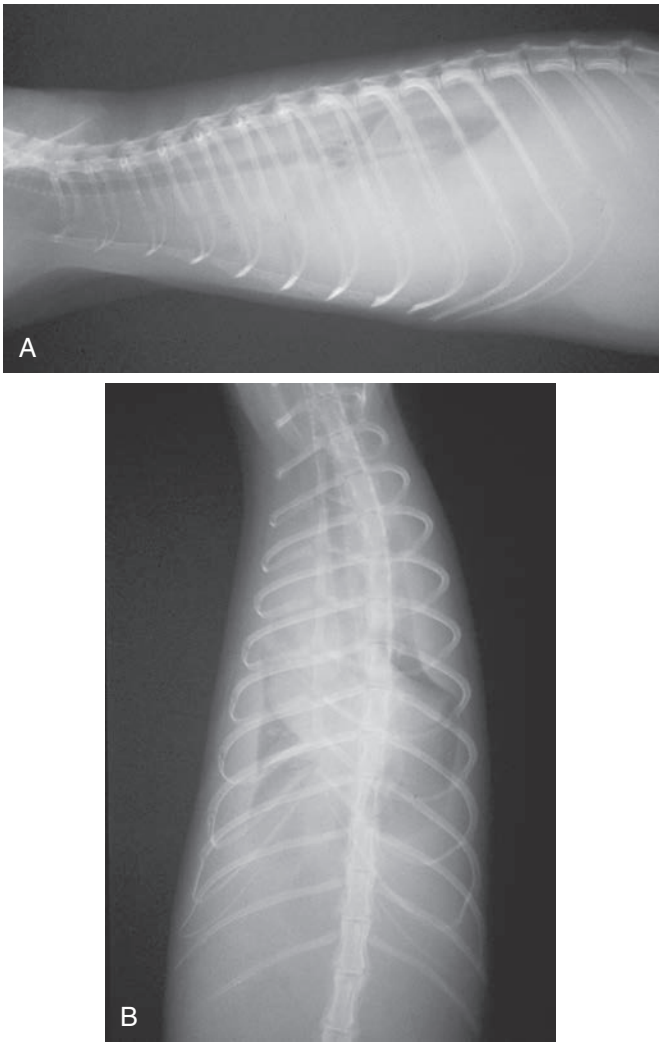


Fig. 5.9 Lateral (A) and ventrodorsal (B) radiographs of a ferret with pleural effusion caused by heartworm disease.

the right atrium, caudal vena cava, and right ventricle are commonly seen. Unlike in dogs, radiographic signs of peripheral pulmonary artery changes are not severe in ferrets, probably because the worms reside primarily in the right heart and in the main pulmonary artery.[49,60,79] Echocardiographic examination may identify the presence of parasites in the pulmonary artery, right ventricle, or right atrium. Right ventricular and right atrial dilation may be seen.[70] The presence of pulmonary hypertension should also be suspected and can be diagnosed with the use of Doppler echocardiography.[32]

Diagnosis of heartworm disease is based on clinical signs, radiographic and echocardiographic findings, and results of heartworm blood testing. Microfilaria are seen in only about 50% of infected ferrets. The antigen test used most commonly to diagnose heartworm infection is an enzyme-linked immunosorbent assay (ELISA).[52] Antigen is shed into the circulation by adult female heartworms. Because antigen testing detects only female worms, there is less likelihood of positively identifying ferrets with low worm burdens. Studies are needed to further evaluate the sensitivity and specificity of heartworm testing in ferrets.

Successful therapy for heartworm disease depends on early, accurate detection. The recommended treatment protocol for ferrets is ivermectin (50 µg/kg SC every 30 days), given until clinical signs resolve and microfilaremia is absent. Management of pleural effusion with diuretics or pleurocentesis may be necessary. Prednisone (0.5 mg/kg PO every 12–24 hours) is recommended throughout this period and until clinical signs resolve. Whether pretreatment with doxycycline for *Wolbachia* (a bacteria present within *D. immitis* that contributes to renal and pulmonary pathology) will enhance the efficacy of heartworm therapy in ferrets is unknown (www.heartwormsociety.org). Perform a follow-up ELISA for heartworm antigen approximately 3 months after starting therapy and repeat testing at monthly intervals until the results are negative. If results remain positive, further diagnostic imaging may be necessary to determine whether heartworm infection persists. Most ferrets become seronegative within 4 months after successful adulticide therapy. Transvenous heartworm extraction has been reported in a ferret with caval syndrome.[7]

Preventive therapy is recommended for ferrets previously infected with heartworm disease and for all ferrets in heartworm-endemic areas. Ivermectin (0.05 mg/kg) can be given orally or SC once a month. One-quarter of the smallest-size canine or feline ivermectin oral tablet (yield, approximately 14–17 µg) (Heartgard-30 and Heartgard-Feline; Merck & Co. Inc., Whitehouse Station, NJ) is adequate for ferrets. Because the drug deteriorates once the pill is broken, the remainder of the pill must be discarded. Selamectin (Revolution; Zoetis, Parsippany, NJ) and imidacloprid/moxidectin (Advantage Multi; Bayer, Shawnee, MO) topically, as well as milbemycin oxime (Interceptor, Novartis, Morris Plains, NJ) orally, can also be used effectively in ferrets (see Appendix for recommended dosages).

OTHER DISEASES

Aleutian Disease

Aleutian disease is caused by a parvovirus and was first reported as a disease of mink in the 1940s.[39] Mink homozygous for the Aleutian (blue) gene are most severely affected, thus giving the disease its name. The disease is an immune complex-mediated disorder that causes hypergammaglobulinemia and immune complex deposition in a variety of tissues, giving it the alternative name mink plasmacytosis. Aleutian disease virus (ADV) can affect raccoons and bobcats as well as skunks and other mustelids. It also may be associated with vascular disease in people. The disease was first seen in ferrets in the late 1960s, and it has been seen in ferrets in the United States, United Kingdom, Sweden, New Zealand, Japan, and Canada.[21,35,48]

There are several strains of ADV in mink, the most common being ADV-Utah. These strains vary in the immune response elicited and therefore in virulence. Although the mink virus can infect ferrets, at least three separate viral strains that are distinct from the mink ADV have been documented in ferrets.[53,62] The most common strain is called *ADV-F*.[68] Mink can be infected with ferret ADV, but the virulence is lower.[13,54,62]

Aleutian disease is transmitted by aerosol or direct contact with infected saliva, urine, blood, or feces. Fomites, including people, may be a source of infection, because parvoviruses are typically stable in the environment. Vertical transmission has not been reported in ferrets but is known to occur in mink.

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Asymptomatic animals have been shown to have persistent viral shedding for more than a year without clinical signs.[61] The seroprevalance for infection ranges from 6% to 60%, depending on the study, and seems to be higher in the United States than in other countries.

Clinical Signs

Overt signs of Aleutian disease are uncommon in ferret. Ferrets experimentally infected with mink or ferret strains of ADV developed infections that persisted for up to 180 days; however, the clinical signs that are seen in naturally infected ferrets did not develop.[34] Those signs relate to deposition of immune complexes and can vary significantly. Some ADV-infected ferrets die in good body condition without any clinical signs.[13] Most ferrets show signs of a chronic wasting disease, with varying degrees of progressive weight loss, weakness, ataxia, and posterior paresis. Central nervous system (CNS) signs can include tremors, convulsions, and paralysis.[77,86,89] Hepatomegaly, splenomegaly, pallor, and melena are also consistent findings. In a clinical report, respiratory signs, including acute dyspnea, were described.[84] Ferrets infected at older ages usually show fewer clinical signs; however, ferrets can be infected for years before clinical signs become apparent. Most reported cases have been in ferrets between 2 and 4 years of age.

Clinical pathologic findings in infected ferrets can also vary. The most consistent findings are hypoalbuminemia and hypergammaglobulinemia. Protein electrophoresis of plasma samples from these animals usually demonstrates gamma-globulins amounting to 20% to 60% of the total protein concentration (Fig. 5.10). Rare cases with normal protein fractions have been recorded.[84] Because the immune complexes damage internal organs, other biochemical abnormalities, such as azotemia and high liver enzyme concentrations, may be present. Anemia of chronic inflammation can also develop.

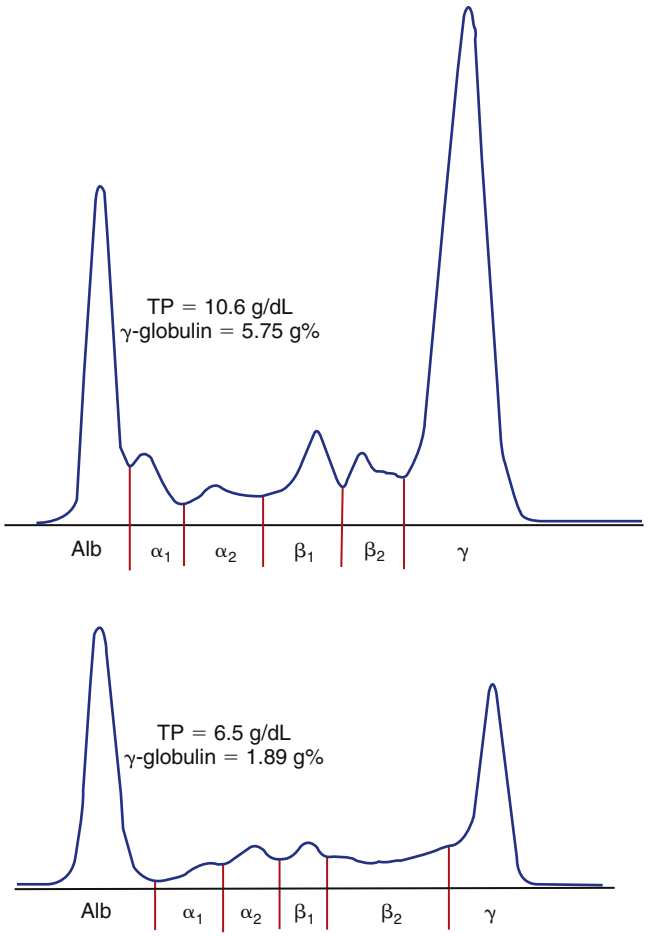


Fig. 5.10 Serum protein electrophoretograms from two ferrets with syndromes associated with Aleutian disease. Top, Ferret 1: Notice the pronounced hypergammaglobulinemia. The gamma-globulin fraction *(γ)* equals 54% of the total protein concentration. Bottom, Ferret 2: The gamma-globulin fraction equals 29% of the total protein concentration. Hypergammaglobulinemia is the hallmark of Aleutian disease virus infection. Alb, Albumin; TP, total protein. (From Palley LS, Corning BF, Fox JG, et al. Parvovirus-associated syndrome [Aleutian disease] in two ferrets. *J Am Vet Med Assoc* 1992;201:100-106.)

Diagnosis

A presumptive diagnosis is based on the history, clinical signs, and a high gamma-globulin concentration. Antemortem diagnosis can be made on the basis of clinical signs and a positive serum titer coupled with hypergammaglobulinemia, positive results of polymerase chain reaction (PCR) testing, or histologic evidence of associated lymphoplasmacytic inflammation in tissue biopsy samples. Counterimmunoelectrophoresis (referred to as CIEP or CEP) historically was the standard for antibody testing in mink and in ferrets and is still used a screening tool on most mink farms. At present, ferret ADV CIEP testing is available through Blue Cross Animal Hospital (Burley, Idaho; FerretADV.com). This is the standard screening test in mink for all ADV strains. It is used routinely in ferrets and has been shown to be an effective method of serologically identifying ferrets with ADV antibodies.[77,86,89] Diagnostic testing for ADV by PCR and serology is offered by several laboratories, including PCR testing of fecal swabs or intestinal or splenic tissue samples (Diagnostic Center for Population and Animal Health, Michigan State University, Lansing, MI, www.animalhealth.msu.edu), PCR testing of tissue and blood (Veterinary Molecular Diagnostics, Milford, OH, www.vmdlabs.com), and PCR testing of urine and oral swab samples and ELISA testing of serum samples (Infectious Disease Laboratory, University of Georgia, Athens, GA; https://vet.uga.edu/diagnostic-service-labs/infectious-diseases-lab/). The ELISA developed by the University of Georgia detects two major capsid proteins of the ADV that are present during replication and latency. False negatives with this test can occur if the host only produces antibodies to the nonstructural viral proteins. For this reason, both ELISAs may be used concurrently to detect structural and nonstructural ADV antigens. The PCR method can be added to detect viremia in an active ADV infection and may be especially useful in detecting asymptomatic animals.

The presence of ADV antibody in a ferret is not necessarily diagnostic of disease. In serologic surveys of large pet ferret populations, 8.5% and 10% of ferrets surveyed were antibody-positive without clinical signs of disease.[86] Also, immunocompetent adult ferrets experimentally infected with ferret ADV can develop persistent infection (with viral shedding) without clinical disease. As in mink, ferrets probably develop persistent,

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nonprogressive infection as well as nonpersistent, nonprogressive infection with ADV.[5,59] Ferrets infected with these forms of ADV could be seropositive without clinical disease. Judicious use of the ELISA tests, PCR, and DNA in situ hybridization may be best to characterize infection status in ferrets.

At necropsy, gross changes in ferrets with Aleutian disease include hepatomegaly, splenomegaly, lymphadenopathy, and thymic enlargement. A positive diagnosis is made by demonstrating lesions consistent with ADV infection on histopathologic examination, such as periportal hepatitis with aggregates of lymphocytes, plasmacytes, and neutrophils. Bile duct hyperplasia and periportal fibrosis are common findings, and mild membranous glomerulonephrosis may also be seen. In the CNS form of the disease, perivascular cuffing in the brain and spinal cord and lymphoplasmacytic meningitis may be present. The DNA of ADV can be detected by in situ hybridization, confirming infection and identifying infected cells.[25] This test can also be used on formalin-fixed, paraffin-embedded biopsy samples as an antemortem screening method to aid in the diagnosis and prognosis of the disease.

Treatment and Prevention

No definitive treatment exists for ADV infection in ferrets. In mink, immunosuppressive therapy with cyclophosphamide (10 mg/kg intraperitoneally 3 times per week for 13 weeks) has been used to control infection and prevent immune complex deposition in the kidneys; however, viral titers did not change in treated animals.[11,39] Treatment of infected mink kits with gamma-globulin–containing ADV antibody has decreased mortality rates.[1] In ferrets with clinical disease, supportive care, use of antiinflammatory agents, and immunosuppressive therapy with prednisone or cyclophosphamide could be considered. Use of melatonin implants has had some protective action against Aleutian disease, probably due to melatonin's ability to scavenge free radicals; however, it could also be due to the induction of antioxidant enzymes or to the modulation of immunity.[16] No vaccine exists for Aleutian disease, and vaccination is probably contraindicated given the immune-mediated nature of the disease. In mink farms, testing by CIEP and removal of animals that test positive has been effective in eradicating the disease[12]; therefore testing and removal or isolation should be considered as a control method in ferret colonies and shelters as well. Excellent hygiene is imperative in light of the ability of people to act as vectors.[30] Because asymptomatically infected animals can shed virus in bodily secretions, follow strict quarantine protocols.

Splenomegaly

Splenomegaly is a very common clinical finding in ferrets older than 1 year of age. A variety of conditions can cause splenomegaly, including extramedullary hematopoiesis (EMH), neoplasia, and heart disease. Hypersplenism, splenic torsion, abscess, and rupture are rare in ferrets. Splenomegaly is usually a normal finding, unrelated to any disease state. Often, splenomegaly is present concurrently, as an incidental finding, with diseases such as adrenal disease and insulinoma.

The normal ferret spleen is quite large for the size of the animal, measuring approximately 5 cm in length, 2 cm in width, and 1 cm in thickness. The spleen may enlarge slightly with age in ferrets, for reasons that are poorly understood. Long-term immune stimulation or compensation for erythroid bone marrow insufficiency may play a role. More research is needed to determine whether splenomegaly is indicative of other disease problems.

The most common cause of splenomegaly in ferrets is EMH. This appears grossly as a smooth dark-red spleen. The cause of this syndrome is unknown, although compensation for myeloid insufficiency has been suggested.[20] Most ferrets with EMH do not show evidence of anemia or other hematologic deficiencies. Splenic lymphoproliferation and resultant splenomegaly in response to chronic immune stimulation has also been suggested as a cause. In mice, evidence exists that chronic infection with *Helicobacter felis* induces this change[17]; a similar situation may exist in ferrets infected with *Helicobacter mustelae*.

Although hemangioma, hemangiosarcoma, and other tumors can occur, lymphoma is the most common neoplasia of the ferret spleen. On gross examination, a spleen with lymphoma often has irregular borders and texture, as well as white to tan nodules on the surface and within the parenchyma. Splenic neoplasia often involves other organs, such as the liver and intestinal lymph nodes.

Hypersplenism involves destruction of one or more blood cell lines by the reticuloendothelial system within the spleen. Affected ferrets have blood dyscrasias such as anemia, leukopenia, thrombocytopenia, or pancytopenia. The bone marrow may be normal or hypercellular. Clinical signs are associated with the predominantly decreased blood cell count; they include weakness, pallor, petechiae, and secondary infections. Diagnosis is made on the basis of abnormal CBC findings coupled with cytologic results indicating a normal to hypercellular bone marrow and no other sign of blood loss, infection, or neoplasia. Results of radiographs and plasma biochemical analyses are usually normal but help to rule out other possible causes of disease. The relationship of EMH to hypersplenism is unclear. In one report, ferrets with anemia of undetermined cause responded to splenectomy, but the histologic appearance of the spleen was found to be that of EMH.[20] Two of these ferrets developed systemic disease (lymphoma and multifocal granulomatous disease) within 4 months after splenectomy.

As part of the diagnostic approach to an enlarged spleen in a ferret, perform a thorough examination with particular attention to palpation of the spleen. With EMH, the spleen is usually of normal shape and consistency with regular borders; neoplasia of the spleen may cause irregular borders and palpable lumps within the spleen. Palpation is best done with care, because some diseases cause the spleen to be more friable and at risk of splenic rupture. Radiographs may be helpful to define the borders of the spleen and to evaluate for other abnormalities that may be associated with splenomegaly, such as hepatomegaly, cardiomegaly, and other systemic problems.

Aspiration or biopsy can best determine the cause of splenomegaly. Splenic aspiration with a 22- or 25-gauge needle and a 3-mL syringe can usually be performed with manual restraint.

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On cytologic examination of an aspirate, EMH typically shows a mixed population of mature and immature red cells, whereas lymphoma or other lymphoproliferative diseases show a predominant or homogenous population of lymphocytes. Biopsy of the spleen is best performed surgically or endoscopically; however, surgery for the sole purpose of obtaining a splenic biopsy is rarely indicated unless other tests are nondiagnostic and primary splenic disease is suspected. Obtaining biopsy samples is the best method to maintain cellular architecture for an accurate diagnosis. Percutaneous biopsy equipment should not be used because it is too large and too long for use in ferrets.

Ultrasonography of the spleen is used to evaluate for areas of altered echogenicity. Typically, the spleen is of uniform echogenicity with EMH, whereas with neoplasia, the splenic parenchyma appears mottled. If the splenic parenchyma is irregular, obtain a diagnostic sample by ultrasound-guided aspiration.

Treatment of splenomegaly depends on the cause. No treatment is known or required for EMH; however, if the spleen has become so large that movement is hampered, splenectomy may be warranted. Do this cautiously, because anemia can result. Splenectomy is recommended for hypersplenism, rupture, torsion, infection, or neoplasia of the spleen. Ferrets with peripheral lymphomas do not necessarily benefit from splenectomy.

Anemia

As in other species, anemia in ferrets is caused by decreased production of erythrocytes, destruction of existing erythrocytes, or blood loss. The normal hematocrit of ferrets (46%–61%) is higher than that of other species; therefore mild anemia may go unrecognized unless clinicians keep this fact in mind. Erythrocyte numbers are also higher; cell numbers can be as high as 17.4 × 106 cells/μL (see also Chapter 39).[63] As in other species, hemoglobin concentration and mean cell volume, respectively, can be used to characterize the anemia as normochromic or hypochromic and as normocytic, macrocytic, or microcytic. Normal reticulocyte counts in ferrets can be as high as 10%. Counts higher than 12% indicate a regenerative response. Examination of the bone marrow is indicated in any ferret with a nonregenerative anemia that does not respond to treatment within 3 to 6 days.

Decreased production of erythrocytes can be caused by chronic disease or inflammation, bone marrow suppression, or neoplasia. Anemia of chronic disease, also called anemia of chronic inflammation, can develop with any long-term illness. It results from decreased iron availability, decreased erythrocyte survival, or decreased response to the anemia.[85] Cytokines secreted during inflammation mediate the response and cause a nonregenerative, normocytic, normochromic anemia. In animals with this type of anemia, results of bone marrow examination are usually normal. In pet ferrets, hyperestrogenemia resulting from an ovarian remnant or adrenal disease is the most common cause of bone marrow suppression. Chronic estrus as a cause of hyperestrogenemia is rare in the United States because pet ferrets are typically spayed before purchase. Neoplasia that affects the bone marrow (e.g., leukemia, myeloma) can suppress erythroid series production because the marrow is replaced by tumor or fibrosis.[36] This typically results in a normocytic, normochromic anemia with a low reticulocyte count. Systemic neoplasia can also cause anemia of chronic disease.

Erythrocytes can be destroyed by immune-mediated disease, toxins, parasites, or septicemia. Pure red cell aplasia (PRCA) is a nonregenerative anemia characterized by a marked deficiency of erythroid precursors despite normal numbers of granulocytes and megakaryocytes in the bone marrow. Primary PRCA has been reported in several ferrets.[46,90] These ferrets ranged in age from 8 months to over 4 years old. Clinical signs were related to the anemia. No underlying cause of inflammation was seen in these cases; therefore this syndrome is believed to be immune-mediated. This is further corroborated by the favorable response to immunosuppressive agents. Treatment with multiple blood transfusions, prednisolone (2 mg/kg PO every 12 hours), and cyclosporine (4–6 mg/kg PO every 12 hours) have been beneficial in normalizing the packed cell volume (PCV).[90] Cyclosporin levels should be monitored to prevent serious adverse effects.

No viral diseases or blood parasites that elicit immune-mediated hemolysis of red blood cells are known to exist in ferrets. Heavy-metal toxicosis and certain drugs are possible causes of hemolytic anemia. Zinc toxicosis as a cause of hemolytic anemia in a ferret has been documented.[78] This type of anemia is uncommon in ferrets, but it may be underdiagnosed because of the inherent difficulties in identifying the toxic agents.

Anemia resulting from blood loss can be caused by trauma, bleeding lesions, parasites, or hemostatic disorders. Trauma is common in ferrets because of their inquisitive nature, and hemorrhage can be internal or external. Bleeding ulcers develop commonly with gastritis caused by *H. mustelae* infection, gastrointestinal foreign bodies or trichobezoars, or other causes (e.g., chronic use of nonsteroidal antiinflammatory drugs [NSAIDs]). Parasitism is a less common cause of anemia in ferrets, although coccidiosis in young ferrets or flea infestation can be severe enough to cause anemia. Hemostatic disorders such as thrombocytopenia can develop from estrogen toxicosis. Other coagulopathies, such as rodenticide poisoning and disseminated intravascular coagulation, can also occur. An acute hemorrhagic syndrome of ferrets was reported in young ferrets between 8 and 24 weeks of age.[33] These ferrets had been recently shipped to distributors or pet stores. Clinical signs started with epistaxis and oral ulceration and included hemorrhage that progressed to petechiae, ecchymoses, internal hemorrhage, and death. Treatment with vitamin K and supportive care was successful in early cases. The cause of this syndrome was unknown, but exposure to toxins (including NSAIDs) or viral agents was considered.

To diagnose anemia in ferrets, obtain a complete history, perform a thorough physical examination, and submit samples for a CBC, reticulocyte count, and, if indicated, bone marrow examination. A plasma biochemical analysis, radiographs, and an abdominal ultrasound examination may be helpful, depending on the differential diagnoses.

The treatment of the anemia is tailored to the specific cause. Supportive care can include one or more transfusions of fresh whole blood, iron dextran therapy, and erythropoietin or darbepoietin. Ferrets lack blood types, and transfusion reactions

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are difficult to induce, even with repeated transfusions between the same animals. Indications for transfusion in a ferret are a low PCV, worsening clinical signs, and the possibility of continued blood loss. The decision to transfuse a ferret is based on its clinical status and the PCV. Transfusion in a ferret with acute blood loss may be considered if the PCV falls to less than 25%. If the anemia has developed gradually, the ferret may tolerate a lower PCV, although its clinical status may benefit from a transfusion if the PCV is less than 25%. In determining the need for transfusion, take into account the volume of blood that has been extracted for diagnostic tests.

The blood volume required for transfusion can be estimated by the following formula:

$$BV_{donor} = BV_{recipient} \times [(PCV_{post} - PCV_{pre}) / PCV_{donor}]$$

where BV is blood volume in mL, calculated as 8% of the body weight in kg, and PCV_{post} is the desired PCV after transfusion. The value of PCV_{post} is ideally within the reference range, but it is more often 5% to 10% higher than the pretransfusion PCV (PCV_{pre}). A simpler method is to administer 10% to 20% of the recipient's blood volume in a single transfusion given over at least 4 hours. Use of a filter is advised to prevent clots from being administered. Donor blood is collected in sodium citrate or acid-citrate-dextran (ACD). If citrate is used, 1 mL is used for each 9 mL of blood collected; for ACD, 1 mL per 6 mL of blood is used. Long-term storage of ferret blood is possible with the use of typical mammalian storage media, but it is not currently practiced.

Because they are inexpensive and generally safe, oral iron supplements are preferred for treatment in small animals. Ferrous salts are absorbed better than ferric salts. A total daily dose of 15 mg/kg divided two or three times is recommended in small animals.[27] Continue treatment for several weeks after the anemia resolves to replenish whole-body iron stores. The hemoglobin substitute hemoglobin glutamer-200 (bovine) solution (Oxyglobin, Biopure Corporation, Cambridge, MA) has been shown to be safe and effective in ferrets[56]; however, this product is no longer being produced. Although erythropoietin is rarely indicated, it can be used in ferrets with chronic renal failure at a dosage of 100 U/kg up to three times weekly until the PCV is stabilized and then up to twice weekly. Darbepoietin has replaced erythropoietin in dogs and cats, but its use in ferrets has not been reported.

Ibuprofen Toxicosis

Ibuprofen toxicosis has been documented in many ferrets[10,64] and is seen clinically, often as an emergency presentation. Prostaglandin inhibition by ibuprofen and other NSAIDs can cause altered renal blood flow, ulceration of the gastrointestinal tract, and platelet dysfunction. Clinical signs include vomiting, CNS depression, anorexia, diarrhea, and melena. Severe overdose can cause renal failure, resulting in azotemia and oliguria or anuria. Gastrointestinal signs develop as early as 2 to 6 hours after ingestion; renal signs may develop within 12 hours after ingestion or as long as 5 days later.[57] Seizures can occur with a massive overdose.

Treatment depends on the clinical signs, time elapsed since ingestion, electrolyte imbalances, and azotemia. Treatment is directed at preventing absorption (if possible), managing bleeding ulcers, and maintaining renal perfusion and electrolyte balance. Induction of emesis is effective only within the first 30 to 60 minutes after ingestion, although activated charcoal may be beneficial if given within the first few hours. Intravenous fluids (0.45% NaCl and 2.5% dextrose) should be administered, even if no signs of renal compromise are apparent. To control hemorrhage and hypotension, electrolyte solutions, colloids, and transfusions may be needed. Gastrointestinal protectants, such as ranitidine (24 mg/kg PO every 8 hours), cimetidine (5–10 mg/kg PO every 8–12 hours), omeprazole (0.7 mg/kg PO every 24 hours), or sucralfate (25 mg/kg PO every 8 hours), are helpful in controlling ulceration.

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6

Respiratory Diseases of Ferrets

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Primary respiratory disease is uncommon in ferrets. The most common causes are canine distemper virus (CDV) and influenza virus, although several other diseases may manifest with respiratory signs.

CANINE DISTEMPER

Canine distemper virus (CDV) is an RNA virus of the genus Morbillivirus in the family Paramyxoviridae. Different viral strains vary in virulence, but CDV is typically fatal in ferrets. Because it is ubiquitous among dogs, ferrets risk being exposed through canine contacts. Reservoirs of CDV are members of the families Canidae, Mustelidae, and Procyonidae, although bears, marine mammals, pangolins, hyenas, and certain other mammals are susceptible to CDV.[23]

Canine distemper virus is most commonly transmitted by aerosol exposure but can also be spread by direct contact with conjunctival and nasal exudates, urine, feces, and skin.[1,23] Ferrets shed virus within approximately 7 days after exposure.[1] Fomites are also implicated in transmission; CDV is viable for up to 20 minutes on gloves.[23] Once in a ferret's body, CDV appears to spread hematogenously.[23] The incubation period is typically 7 to 10 days, although incubation periods of up to 56 days have been reported.[23,35]

History and Physical Examination

Characteristics of infection vary greatly depending on the strain of CDV, route of infection, infective dose, and immune status of the ferret. Infection with CDV should be suspected in any unvaccinated and exposed ferret showing compatible clinical signs, particularly in animals with exposure to wildlife or feral dogs or those subjected to stressful conditions.[23]

Initial clinical signs are lethargy, photophobia, and loss of appetite, which are quickly followed by systemic disease affecting the dermatologic, respiratory, and neurologic systems. Erythematous and pruritic rashes can appear on the footpads and chin, around the mouth and eyes, and in the interscapular and perineal areas. Rashes develop into hyperkeratosis and crusts (Fig. 6.1). Respiratory signs include dyspnea, tachypnea, oculonasal discharge, and, more rarely, coughing and sneezing. Fever is sporadic. Neurologic signs (e.g., paresis, muscle tremors, incoordination, convulsions, and coma) can be seen during advanced stages of the disease. Immunosuppression can result in secondary bacterial infections, particularly in the lungs.[1,23,35]

Diagnosis

History of exposure and consistent clinical signs are highly suggestive of infection. Although clinical signs initially can resemble those of influenza, clinical signs of CDV are much more severe and manifest as a combination of respiratory, neurologic, and dermatologic signs not seen with influenza.

Antemortem diagnostic testing consists primarily of antigen detection by fluorescent antibody labeling or polymerase chain reaction (PCR) on conjunctival, tonsillar, or respiratory samples. A mild nonregenerative anemia and an increase in alpha and beta globulins may be evident on blood tests, and radiographic changes may be suggestive of pneumonia.[23,35]

On postmortem examination, CDV inclusion bodies may be seen in the respiratory system, skin, brain, and urinary bladder. Inclusion bodies are usually intracytoplasmic but can be intranuclear.[23,35] Antigen detection can be performed with fresh, frozen, or formalin-fixed tissue samples.[1,23]

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Fig. 6.1 Severe crusting dermatitis on the face in a ferret with advanced canine distemper.

Treatment

There is no specific treatment for canine distemper in ferrets, and the mortality rate may be as high as 100%. Depending on the strain, death can occur within 5 to 35 days after clinical signs first appear and may or may not be preceded by neurologic disease.[23] With advanced disease, euthanasia is usually the most humane option. However, treatment may be successful in some cases, particularly in infections with strains of low pathogenicity and when affected ferrets are treated very early in the course of disease. Treat with broad-spectrum antibiotics (e.g., amoxicillin/clavulanate 12.5 mg/kg orally [PO] every 12 hours), vitamin A (50,000 IU [15 mg] of retinol palmitate intramuscularly [IM] every 24 hours for 2 days), vitamin C (250 mg intravenously [IV] every 24 hours for 3 days), and hyperimmune serum against CDV (1 mL IV; if not commercially available, use serum from a healthy, vaccinated ferret). Vaccination may be effective when performed very soon after infection, especially in the face of an outbreak. Supportive and symptomatic therapies include meloxicam, famotidine, diphenhydramine (to help reduce pruritus), buprenorphine, bronchodilators, fluid therapy, and nutritional support. Even with treatment, inform owners that recovery is uncommon.[23,35]

Prevention

Vaccination has greatly reduced the incidence of canine distemper in ferrets. Immunity against CDV is long-lasting after recovery from natural infection or booster vaccination. However, immunity may become compromised on exposure to a highly virulent strain or to a large quantity of virus, or if the ferret becomes immunocompromised or stressed. In the face of an outbreak of canine distemper, remove/isolate all affected animals, and vaccinate healthy ferrets immediately. See Chapter 2 for an in-depth discussion of CDV vaccines, vaccination protocols, and vaccine-associated adverse reactions.

Canine distemper virus is relatively labile and is destroyed by heat, ultraviolet light, drying, detergents, and disinfectants.[23] Routine cleaning and disinfection procedures effectively destroy CDV on hard surfaces.

INFLUENZA

Ferrets are susceptible to influenza virus types A and B of the class Orthomyxoviridae. Natural outbreaks or clinical cases of influenza have occurred in ferrets with common human influenza type A viruses, the human strain of pandemic H1N1 virus, and swine-origin H1N1 influenza virus.[8,33,41,44] The pathogenicity of type B influenza virus in ferrets appears to be low. In a recent report documenting natural cases of pandemic H1N1 influenza in ferrets, transmission was most likely from infected humans.[44] Ferrets have long been important animal models for the transmission, pathogenicity, and treatment of influenza A virus in humans.[49]

Ferrets contract influenza from infected people or other infected ferrets. Although all ferrets are susceptible to influenza, the disease is typically more severe in neonates than in older ferrets. Although the virus can be transmitted from ferrets to humans,[30] there is only one report of this, from the 1930s. In that report, an animal-passage influenza strain was inoculated into a laboratory ferret, and a laboratory investigator was infected after close contact with the animal.[40] Influenza virus is transmitted primarily by aerosol droplets, and the risk of transmission is greatest from the height of pyrexia through the next 3 to 4 days.[42] In ferrets, as in people, influenza primarily causes upper respiratory disease. Influenza A subtypes vary in virulence and their association with secondary bacterial infections, both of which account for the difference in severity of clinical signs.[3,36] Infection with highly pathogenic human influenza viruses also produces severe disease in ferrets.[46]

History and Physical Examination

Clinical signs appear within 48 hours of exposure to influenza virus and include sporadic pyrexia, mild respiratory signs (e.g., sneezing, serous oculonasal discharge), lethargy, anorexia, photophobia, and conjunctivitis.[4,23,30,42] Hearing loss, limited enteritis, and hepatic and renal dysfunction have also been reported.[21,23,37] Influenza in neonates and severe cases in older ferrets may evolve to bronchitis, pneumonia, otitis, periocular and perinasal dermatitis, and neurologic signs such as ataxia, torticollis, and hind limb paresis.[6,39] Death can occur from lower airway obstruction, secondary pulmonary infections, or from neurologic disease.[30]

Diagnosis

A presumptive diagnosis is based on compatible clinical signs and history, antigen detection in oculonasal secretions, and recovery within 4 to 5 days.[23] Antigen detection tests can be performed using fresh or frozen tissues, nasal swabs, or bronchoalveolar washes.[23] Antigen detection tests commonly available in diagnostic laboratories include immunofluorescence, rapid immunoassay, and real-time reverse transcription PCR. In-clinic antigen detection tests (e.g., Directigen Flu; Becton Dickinson, Franklin Lakes, NJ) are also available in many countries. Hematologic and biochemical values in affected ferrets are generally within reference intervals, although a transient leukopenia can be seen in some cases.[21]

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TABLE 6.1 Clinical Distinctions Between Canine Distemper Virus and Influenza Virus Infection in Ferrets

Clinical Findings	Canine Distemper Virus	Influenza Virus
Nasal and ocular discharge	+++ (Mucopurulent)	++ (Mucoserous)
Sneezing	+	+++
Coughing	+	+++
Pyrexia	+++ (> 104°F [40°C])	++[b]
Dermatitis (chin, lips, inguinal)	+++	—
Footpad hyperkeratosis	++	—
Central nervous system signs	+[a]	—
Outcome	Approaches 100% fatality	Self-limiting[c]

[a]May be seen in advanced stages of disease (rarely the only signs).
[b]Occurs early in the disease course and may be resolved by the time of presentation.
[c]Can be fatal in neonates.

An important differential diagnosis is canine distemper, but influenza is generally less severe. Table 6.1 highlights important distinctions between influenza and canine distemper.

Treatment

Influenza has an approximately 5 to 7 day course in adult ferrets and is associated with low mortality rates. The disease is generally mild, and treatment, when necessary, consists of supportive care. Instruct owners to offer favorite foods, chicken or beef broth, or specialized carnivore diets (e.g., Carnivore Care; Oxbow Animal Health, Murdock, NE). Force-feed and offer water by syringe as needed. If clinical signs progress, consider using palliative agents such as cough suppressants, bronchodilators, or decongestants. Antibiotics and parenteral fluids are rarely required but may be indicated in severe cases and in neonates.[19] Use of antipyretics to control fever is debatable, because fever is an important host defense mechanism. In a recent meta-analysis of the use of antipyretics in animal models of influenza virus, risk of death increased with the use of certain antipyretics (aspirin, paracetamol, and diclofenac).[13]

Experimental studies have shown that antiviral treatment in ferrets can prevent disease, reduce clinical signs, and reduce virus-induced lesions. Human antiviral drugs used in experimental studies to treat ferrets with influenza include oseltamivir (2.5 to 5 mg/kg PO every 12 hours for 10 days; increase to 12.5 mg/kg PO every 12 hours in severe cases) (Tamiflu; Genentech, San Francisco, CA) and zanamivir (0.3 to 1 mg/kg every 12 hours, or up to 12.5 mg/kg one-time intranasal dose) (Relenza; GlaxoSmith Kline, Research Triangle Park, NC) alone or in combination with amantidine.[3,11,15,20] Other agents used experimentally to treat or prevent influenza in ferrets include cyanovirin-N, human monoclonal antibodies, and interferon α.[17,24,38] However, because of antiviral resistance, potential adverse effects, and minimal efficacy, these drugs have limited to no practical use in clinical situations. Because many antiviral drugs developed for use in people are tested in ferrets, new drugs that potentially can be used for treating ferrets with influenza are likely to become available in the future.[23]

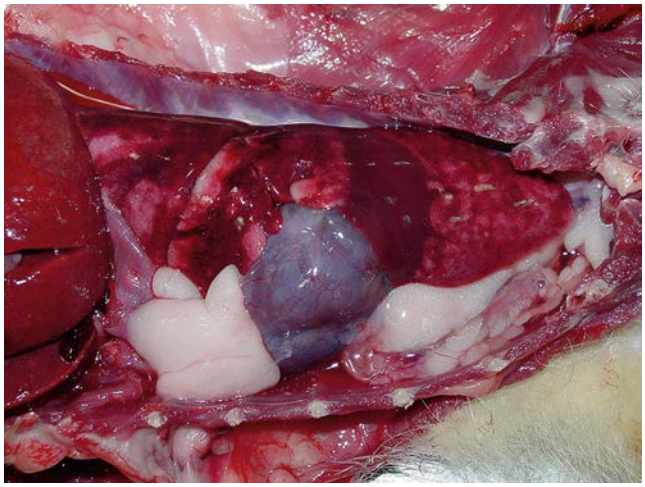


Fig. 6.2 Bacterial pneumonia in a ferret. The lungs are diffusely congested with dark areas of consolidation.

Prevention

Preventing influenza relies primarily on avoiding exposure to infected individuals. Newborn ferrets are protected by maternal antibodies in the jill's milk. Experimentally, ferrets remain resistant to infection from the same influenza viral strain by 5 weeks after primary infection.[23]

Vaccinating ferrets against influenza virus is not generally recommended. Influenza is a relatively benign disease in ferrets, and the wide antigenic variation of the virus results in low vaccination efficacy. However, if vaccination is deemed advisable, use a live or recombinant rather than an inactivated vaccine to induce a more robust immune response.[14,27] Currently, no influenza vaccines are licensed for ferrets; however, most vaccines licensed for people have been tested in ferrets.

PNEUMONIA

Pneumonia is not commonly diagnosed in ferrets. Viral causes of pneumonia include CDV and influenza virus, and these conditions often involve secondary bacterial infections. Pneumonia may appear rarely as part of systemic infections, such as with Aleutian disease virus and ferret systemic coronavirus.[18,23,32,47]

Bacterial pneumonia without an underlying pathology is rare in ferrets (Fig. 6.2). Primary or secondary bacterial pathogens reported to cause pneumonia in ferrets include *Streptococcus zooepidemicus,* other streptococcal species, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Pseudomonas luteola, Bordetella bronchiseptica, Listeria monocytogenes,* and numerous mycobacterial species.[10,23,26,31,43,48] Infection with *P. luteola* is associated with pyothorax, mediastinal lymphadenopathy, and multiple white nodules in the lung.[31] A novel *Mycoplasma* species was identified as a cause of respiratory disease in young ferrets aged 6 to 8 weeks in a large breeding facility. Ferrets exhibited nonproductive coughing; less common clinical signs included hemoptysis, labored breathing, sneezing, and conjunctivitis. The disease was characterized by high morbidity (95%) and very low mortality rates.[22]

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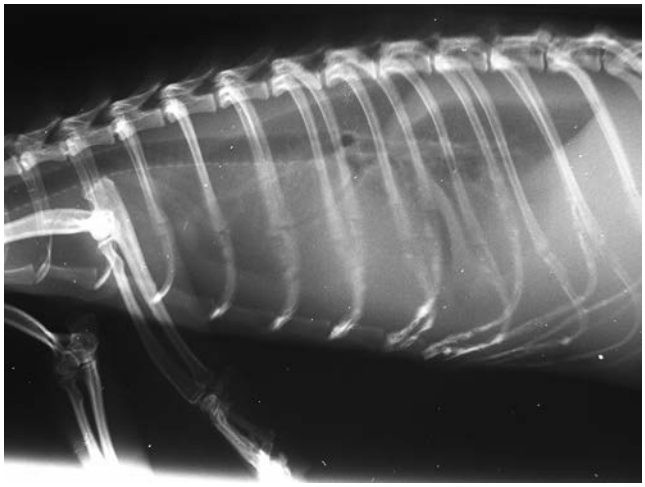


Fig. 6.3 Lateral radiograph of a ferret showing pleural effusion, as can be seen with endogenous lipid pneumonia or *Pseudomonas luteola* infection.

Endogenous lipid pneumonia is a disease characterized by the accumulation of foamy macrophages in the pulmonary parenchyma. It is an idiopathic condition that is identified incidentally at necropsy and is believed to be secondary to other conditions such as systemic coronavirus in ferrets.[34] In rare cases, endogenous lipid pneumonia alone has been associated with severe respiratory signs and death.[34]

History and Physical Examination

Ferrets with pneumonia can exhibit labored breathing, dyspnea, cyanotic mucous membranes, increased lung sounds, nasal discharge, fever, lethargy, and anorexia. Fulminant pneumonia leading to sepsis and death has been reported.[43]

Diagnosis

The diagnosis of pneumonia is based on clinical signs, radiographic findings, and results of supportive diagnostic tests. Pneumonias caused by viruses have been described previously in this chapter. Results of a complete blood cell count may reveal leukocytosis caused by a neutrophilia with a left shift in cases of bacterial infection. Very rarely, pneumonia in young ferrets may be caused by Aleutian disease virus, with hypergammaglobulinemia and positive serologic results.

Early in the disease, radiographs may show an interstitial pattern that progresses to an alveolar pattern with worsening pneumonia. In cases of aspiration pneumonia, dependent lung lobes are primarily involved. Marked bronchial patterns suggest primary airway disease. Pleural effusion may be evident radiographically in some conditions, such as endogenous lipid pneumonia and *P. luteola* infection (Fig. 6.3).

Microbial cultures of samples from bronchoalveolar lavages (BAL) are invaluable for definitive diagnosis and treatment. Submit samples for culture (bacterial, fungal, mycobacterial, or other) based on cytologic analysis of the collected fluid and debris. Cytologic assessment of tracheal wash samples from a ferret with pneumonia typically reveals septic inflammation and degenerative neutrophils. Results may also suggest the severity, cause, and chronicity of disease. The bronchointerstitial pneumonia caused by *Mycoplasma* species may produce few inflammatory cells on cytologic examination of BAL samples; however, those samples can be submitted for PCR. Foamy macrophages can be seen on BAL cytology in cases of endogenous lipid pneumonia.[5]

Treatment

Treat affected ferrets with supportive care, including fluid therapy, force-feeding, and oxygen therapy, as well as antimicrobials tailored to test results. First-line empirical antibiotic choices include amoxicillin/clavulanate, a fluoroquinolone, trimethoprim-sulfamethoxazole, or a cephalosporin. Treatment for mycoplasmosis should include doxycycline, enrofloxacin, or azythromycin.[22] In a report of two ferrets with mycobacterial pneumonia, both responded successfully to clarithromycin,[26] but combination antibiotic therapy may be preferable. Corticosteroid therapy is used to treat endogenous lipid pneumonia in people.[5,34]

The prognosis depends on the cause of pneumonia and response to treatment. Most ferrets with bacterial pneumonia respond to antibiotic therapy and supportive care. In some cases that recover from *Mycoplasma* infection, ferrets become chronic carriers and may have recurring episodes of coughing.

Prevention

Help prevent pneumonia by avoiding stress and overcrowding.

PULMONARY MYCOSES

Pulmonary mycoses are uncommon in pet ferrets because most pet ferrets live indoors and are rarely exposed to mycotic spores. However, cases have been described involving fungal organisms such as *Pneumocystis carinii, Blastomyces dermatitidis, Coccidioides immitis,* and *Cryptococcus bacillisporus* (formerly *Cryptococcus neoformans* var. *gattii*). Ferrets treated with steroids (e.g., for insulinoma, endogenous lipid pneumonia, lymphoma, Aleutian disease, and some cases of enteritis) may be at increased risk of mycoses. Although particular mycotic infections are endemic in certain areas of the United States, they are rare in Europe.

History and Physical Examination

Not all animals with mycoses exhibit signs consistent with pulmonary disease. If lesions develop in the lungs, animals usually cough. Other signs consistent with mycotic infections include anorexia, wasting, lethargy, lymphadenopathy, lameness, ocular and nasal discharge, and draining tracts unresponsive to antibiotic therapy.[12,45] The prognosis for ferrets with pulmonary mycoses is poor.

Cryptococcosis

Cryptococcosis, caused by *C. bacillisporus* (which is part of the *C. gatti* complex) and *C. neoformans var grubii,* has been diagnosed in a small number of ferrets.[28,29] *Cryptococcus* species grow in soil and bird droppings.[16] Infection can cause rhinitis, pneumonia, and pleuritis. Regional lymph node involvement is also common and may cause dyspnea if the retropharyngeal or

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mediastinal lymph nodes are involved.[28] Additionally, infection of any other organ of the body is possible. Invasive cryptococcal rhinitis has been successfully treated with itraconazole and surgical debulking.[29] Other cases of systemic cryptococcosis have been treated with itraconazole, with better results in early stages of the disease.[16,28]

Blastomycosis

Blastomycosis, caused by *B. dermatitidis,* is endemic in the southeastern United States, the Mississippi River Valley, and the Ohio River Valley.[45] Two cases of chronic granulomatous mycosis, primarily affecting the lungs, were reported in ferrets from the United States, one of which occurred in a ferret housed indoors.[7,25] Both presented with respiratory signs, and neither survived.

Coccidioidomycosis

Coccidioides immitis is endemic in the southwestern United States and parts of Latin America. Among the few cases of coccidioidomycosis reported in ferrets, clinical signs included cough, nasal discharge, anorexia, lethargy, and wasting. A diffuse interstitial pattern is generally observed on thoracic radiographs, and complement fixation or detection of spores in cytologic samples may yield positive results. The reported animals did not survive, in part to due to the chronicity of the condition. Recommended treatment is based on that for cats with coccidioidomycosis and includes the use of amphotericin B and ketoconazole or itraconazole.[12,16,45]

Infection by *Pneumocystis carinii*

Originally considered a protozoan, *P. carinii* is known to involve the lungs and cause infection in immunocompromised ferrets. Latent infections can become active with immunosuppression, and organisms can also be transmitted via aerosol exposure.[2,9,16] Diagnosis is based on identifying the organism in a tracheal or lung wash, using culture or PCR testing. Treatment recommendations for *P. carinii* pneumonia, based on those for dogs, include pentamidine isethionate or trimethoprim-sulfamethoxazole.[16]

OTHER CAUSES OF RESPIRATORY SIGNS

Differential diagnoses for tachypnea, dyspnea, and respiratory distress are similar to those for other small animals. After the history and physical examination, diagnostic imaging (i.e., radiography or computed tomography) is the most important tool to differentiate the causes of lower respiratory tract symptoms. Ferrets that have severe traumatic injuries, such as from a high fall, can develop pneumothorax or diaphragmatic hernia. These animals should be managed as one would a dog or cat with the same injuries. Ferrets with heartworm disease often present with coughing and tachypnea as the only clinical signs, even with moderate worm burdens (see Chapter 5). Congestive heart failure, heatstroke, anemia, anaphylactic reactions, and other systemic conditions such as lymphoma, Aleutian disease, and systemic coronavirus can also produce respiratory clinical signs.

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7

Endocrine Diseases of Ferrets

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Endocrine diseases, especially insulinomas and adrenocortical neoplasia, are commonly seen in ferrets. Another well-known endocrine disorder in ferrets is persistent estrus in nonneutered female ferrets (jills). Jills come into and remain in estrus when daylight lasts for a period longer than 12 hours per day. Estrogen-induced bone marrow suppression, and thus pancytopenia, may develop during this prolonged estrus.[6] Therefore neutering is recommended in any ferret that is not bred. However, evidence suggests that surgical neutering plays a role in the development of adrenal neoplasia, thereby explaining the high incidence of hyperadrenocorticism in pet ferrets. Less common endocrine diseases in ferrets are (spontaneous) diabetes mellitus and hypothyroidism. Endocrine diseases that have, thus far, not been described in ferrets are growth hormone deficiency or growth hormone excess, diabetes insipidus, hyperthyroidism, hyperparathyroidism, and spontaneous hypoadrenocorticism (Addison's disease). Excluding these diseases from a differential diagnosis list, however, is not recommended because novel cases are reported regularly. Examples include reports of C-cell carcinoma[24] and pseudohypothyroidism[88] in ferrets. Therefore, when the clinical signs seen in a ferret correspond with those seen in a dog or cat with the aforementioned endocrine diseases, performing the diagnostic workup for suspect type of endocrine disease is recommended.

DISEASES OF THE ADRENAL GLAND

Hyperadrenocorticism/Hyperandrogenism

Hyperadrenocorticism is defined as an increased production of hormones in the adrenal cortex, which comprises three layers (Fig. 7.1). In each of these layers, different types of hormones are produced (Fig. 7.2); increased production of any of these hormones is associated with specific syndromes. An increased production of mineralocorticoids by the zona glomerulosa results in hyperaldosteronism or Conn's syndrome; an increased production of glucocorticoids by the zona fasciculata results in hypercortisolism or Cushing's syndrome; and an increased production of androgens by the zona reticularis results in hyperandrogenism. In pet ferrets, hyperandrogenism is the most common form of hyperadrenocorticism.[68] Since its first description in the late 1980s, hyperadrenocorticism in ferrets has been recognized as a highly common disease affecting pet

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ferrets around the world.[7,13,18,25,27,35,36,39,47,51,61,63,65,84] Typically it is seen in middle-aged to older ferrets. Clinical signs of adrenocortical disease in ferrets differ from those of classic Cushing's disease in dogs. Disease in ferrets is most commonly characterized by alopecia in both sexes and by vulvar enlargement in jills.[25,39,65] Rather than leading to increased plasma cortisol concentrations, adrenocortical hyperplasia, adenomas, or adenocarcinomas in ferrets result in increased plasma concentrations of androstenedione, estradiol, 17α-hydroxyprogesterone, or other androgens.[66]

Etiopathogenesis

Early neutering (i.e., at an age of 6 weeks) has long been postulated as the cause for the high prevalence of adrenal tumors in ferrets. This was based on observations in some strains of mice whereby gonadectomy at an early age led to unilateral or bilateral adrenocortical nodular hyperplasia or neoplasia with associated hypersecretion of estrogens or androgens.[21,50,76] Because most commercially raised ferrets in the United States are spayed or castrated before they are 6 weeks of age, early spay/castration was postulated as leading to adrenal tumors in this species as well.[63] However, the incidence of adrenal tumors in the Netherlands, where ferrets are spayed or castrated just before the start of the breeding season (when ferrets are approximately 8 to 11 months of age), is comparable to that in the United States.[70] Therefore early neutering is an unlikely explanation for the high incidence of hyperadrenocorticism. An alternate hypothesis suggests that increased concentrations of gonadotropins, which occur after neutering due to the loss of negative feedback, persistently stimulate the adrenal cortex, eventually resulting in adrenocortical growth. Support for this hypothesis can be found in the fact that luteinizing hormone (LH) receptors have been detected in the adrenal glands of ferrets with hyperadrenocorticism.[71] These receptors are considered functional because plasma concentrations of adrenal androgens increase 30 minutes after intravenous injection of 10 μg of a synthetic GnRH analogue (gonadorelin).[71] In addition, the depot GnRH agonist deslorelin is currently used successfully in managing the clinical signs of hyperadrenocorticism in ferrets.[37,81,83]

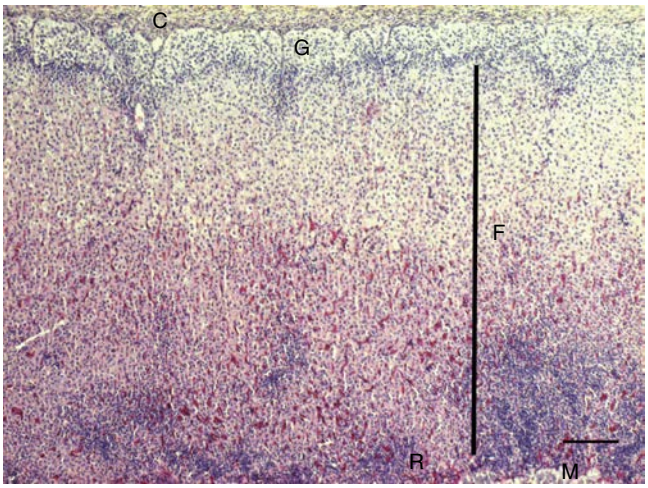


Fig. 7.1 Histologic section of an adrenal gland of a healthy ferret: *C,* Capsule; *G,* zona glomerulosa; *F,* zona fasciculata; *R,* zona raticularis; *M,* medulla. Hematoxylin & eosin stain; bar = 100 μm.

Keeping ferrets indoors has also been proposed as a possible risk factor for the development of adrenal tumors in this species.[33,49,59] In indoor housing, the hours per day of artificial light received is likely longer than with natural light in outdoor housing. Because gonadotropins are secreted with the light period exceeding 12 hours per day, plasma concentrations of these hormones will be increased for longer periods of time in indoor ferrets, thereby rendering them at higher risk for developing hyperadrenocorticism than ferrets that are housed outdoors.[82,83]

A genetic background has been suggested as an underlying factor in the development of hyperadrenocorticism in ferrets. Although

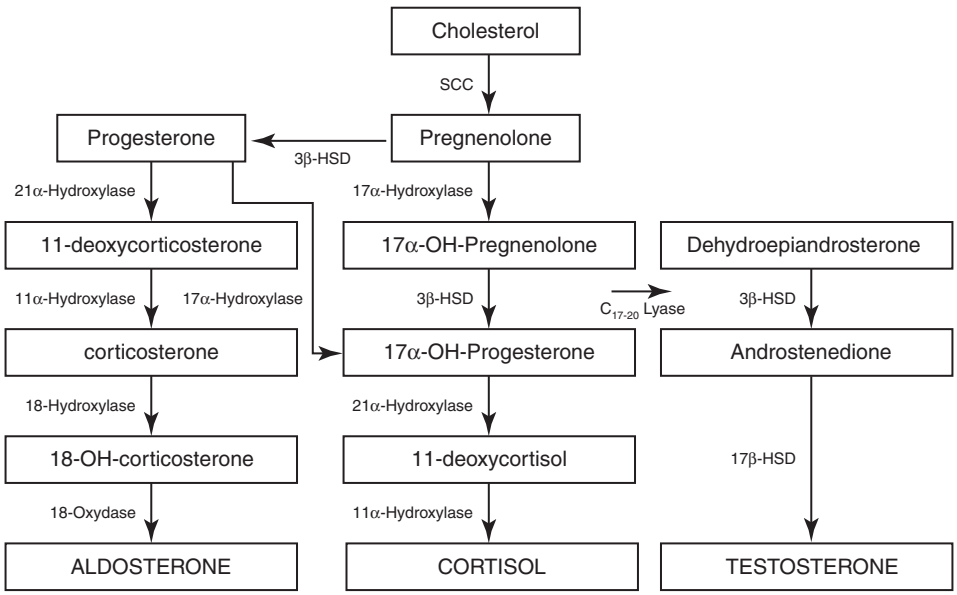


Fig. 7.2 Major biosynthetic pathways of adrenocortical steroid synthesis. 3β-HSD, 3β-hydroxysteroid dehydrogenase; 17 β-HSD = 17β-hydroxysteroid dehydrogenase; *SCC,* side chain cleavage.

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alterations of specific genes (i.e, sfrp1 and Foxl2) have been found in adrenocortical tumors,[14,67] further studies are needed to elucidate the etiopathogenesis for the development of these tumors in ferrets.

History and Physical Examination

Signs of hyperadrenocorticism may be seen in ferrets as young as 2 years of age but are most common in animals older than 3 years. There is no sex-related predilection. Progressive alopecia is seen in more than 90% of ferrets with adrenal gland disease (Fig. 7.3). Usually, the alopecia is symmetrical, beginning on the rump, the tail, or the flanks and progressing to the lateral trunk, dorsum, and ventrum. In more than 33% of ferrets with adrenal gland disease, owners report the ferret as pruritic. In some ferrets, this may actually be the only clinical sign that is observed. Most frequently, the pruritus is located on the dorsum between the shoulder blades. Excoriations and erythema will often be visible as a result of scratching (Fig. 7.3).[58,61,65,84]

Spayed jills with adrenocortical disease frequently have a history of vulvar enlargement. A seromucoid discharge may be present, and results of cytologic examination may show localized vaginitis. The perivulvar skin can appear dark and bruised. Occasionally, mammary gland enlargement may be seen in jills. In male ferrets (hobs), return of sexual behavior is a common finding, often accompanied by an increased skin odor produced by the sebaceous glands. The ferret may also exhibit increased aggression. Hobs can also be presented with partial or complete urinary blockage, caused by urethral narrowing as a result of prostatic enlargement and the development of periurethral cysts in the region of the prostate (Fig. 7.4).[13,61] Affected ferrets will display signs of dysuria or stranguria. Because of the urethral narrowing, passing a urinary catheter into the bladder of these ferrets can prove difficult (see Chapter 2). Urethral blockage can result in life-threatening metabolic derangements (i.e., hyperkaliemia, azotemia). On physical examination, enlarged adrenal glands are sometimes palpable as small, firm, round masses craniomedial to the kidneys. The left adrenal gland is usually more easily identified than the right because the latter is partially covered by the caudate liver lobe.

Differential Diagnoses

The most important differential diagnoses for jills with signs of hyperadrenocorticism are an ovarian remnant, an ovarian neoplasm (granulosa cell tumor), or a nonneutered animal with intact ovary.[66] Ferrets with an ovarian remnant are usually younger than 3 years, whereas ferrets with hyperadrenocorticism or an ovarian neoplasm are usually older than 3 years. The physical examination often will allow distinction between ovarian disease and hyperadrenocorticism because an enlarged ovary (neoplasm) is palpable as a mass caudal to the kidneys, whereas the mass will be palpable cranial to the kidneys in cases of an adrenal tumor.

In hobs, the differential diagnoses include a Sertoli cell tumor (in cryptorchid, intact hobs) and hypothyroidism, although both are considered rare.[73] In addition, pruritus has not been reported in either of these conditions.

If the ferret is showing signs of severe alopecia and pruritus, then food intolerance, atopy, and infectious skin diseases (e.g., dermatophytosis, demodicosis, sarcoptic mange, and bacterial dermatitis) should be considered in the differential diagnoses.[73] Infectious diseases, however, will often result in presence of skin lesions. Seasonal alopecia, characterized by a seasonal occurrence of alopecia at the base of the tail, is also commonly mentioned as a differential diagnosis. The actual cause for this condition is currently not known, but the authors suspect that it may be an early sign of hyperadrenocorticism.

Clinical Pathology and Diagnostic Testing

A presumptive diagnosis of adrenal gland disease is usually based on the history, clinical signs, and exclusion of other differential diagnoses. Imaging techniques can help to localize the affected adrenal gland(s). Results of the complete blood count are usually unremarkable, although in rare instances pancytopenia (anemia, thrombocytopenia, leukopenia) may develop secondary to hyperestrogenism.[66]

In most cases, adrenal gland enlargement is slight to moderate, thereby limiting the ability to detect the altered gland



Fig. 7.3 A 7-year-old male castrated ferret displaying severe alopecia and severe signs of pruritus as a result of hyperandrogenism. (Photo previously published by Schoemaker NJ, van Zeeland YRA. Disorders of the endocrine system. In: Johnson-Delaney CA, ed. *Ferret Medicine and Surgery*. Boca Raton, FL: CRC Press; 2016:191-218.)

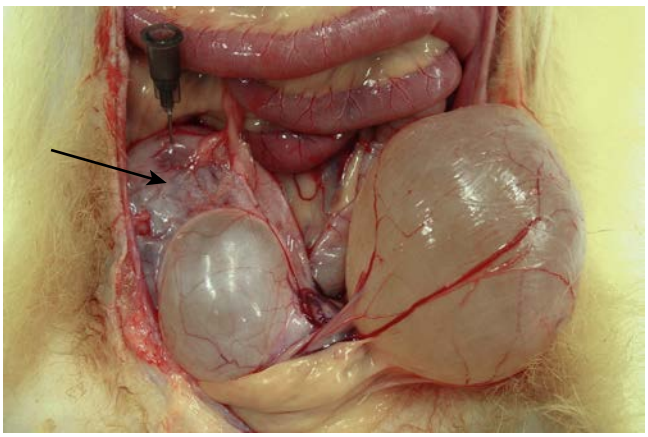


Fig. 7.4 Postmortem image of a urine-filled bladder in a 5-year-old male castrated ferret with confirmed adrenal gland disease and a peri-prostatic cyst *(arrow)* that was drained with a hypodermic needle.

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on a radiograph. Only in rare cases where the adrenal gland is greatly enlarged will the mass itself or the resulting displacement of other organs be visible. Mineralization of the adrenal gland usually is not visible on radiographs.[66]

Abdominal ultrasound scanning is the single most useful tool to determine whether one or both adrenal glands are affected or whether an ovarian remnant is present. Similarly, ultrasound scanning allows for confirmation of the presence of hyperadrenocorticism-related prostatic enlargement or uterine disease.[7] The adrenal glands can be identified easily by using specific landmarks. The left adrenal gland is located ventrolateral to the aorta, at the level of the origin of the cranial mesenteric artery. The right adrenal gland is located more cranial than the left and is attached to the dorsolateral surface of the caudal vena cava, at the level of origin of the cranial mesenteric artery, lying adjacent to the caudomedial aspect of the caudate process of the caudate liver lobe. Ultrasonographic findings in ferrets with hyperadrenocorticism can include increased width (>3.9 mm), rounded appearance, heterogeneous structure, increased echogenicity, or mineralization of the affected adrenal gland(s).[35] However, ultrasound scanning only allows for evaluation of the size and structure of the adrenal glands; it does not provide any information on the functionality of the tumor or hyperplasia. Thus only one adrenal gland may be enlarged on ultrasound scanning, even while both adrenal glands contribute to androgen release; or, alternatively, neither gland may be enlarged in a ferret with clinical signs resulting from an adrenal tumor.

In addition to ultrasound scanning, computed tomography can be useful for evaluating ferret adrenal glands. The use of an intravenous contrast medium helps to better delineate the adrenal gland from the caudal vena cava, thereby enabling its visualization (Fig. 7.5).[73]

Ancillary Diagnostic Tests

The most widely reported diagnostic technique is measurement of serum or plasma hormone concentrations (i.e., androstenedione, estradiol, and 17α-hydroxyprogesterone). However, increased levels of one or more of these hormones can also be seen in intact jills during estrus (Table 7.1).[66] As a result, these analyses will not allow differentiation between a ferret with hyperadrenocorticism and one with an active ovarian remnant.[68] Nevertheless, hormone analysis can be useful to monitor the effect of treatment, as well as the progression, of the disease.

A stimulation test with human chorionic gonadotropin (hCG), an LH-receptor agonist, can be done in those ferrets in which it is certain that their gonads have been completely removed. For this test, collect blood samples immediately before and 60 minutes after an intramuscular injection of 100 IU hCG. In ferrets with hyperadrenocorticism, stimulation with hCG results in increased androstenedione concentrations, even if baseline androstenedione concentrations are below the detection limit. In healthy, neutered ferrets, androstenedione concentrations should remain below the detection limit of the assay.[68]

In dogs, the urinary corticoid-creatinine ratio (UCCR) is a commonly used test to diagnose adrenocortical disease. Research findings have indicated that the UCCR in ferrets with adrenocortical disease is elevated compared with the reference value of 2.1×10^{-6}.[75] However, similar to hormone analyses, this

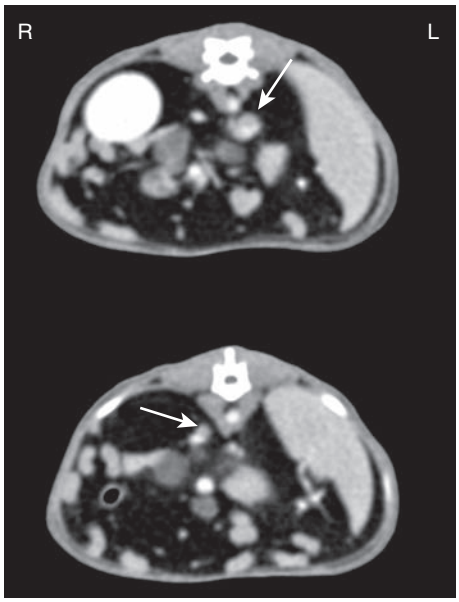


Fig. 7.5 Computed tomographic images of the left (A) and right (B) adrenal gland of a 6-year-old ferret with an adrenal adenoma of the left adrenal gland. The *arrows* point out the adrenal glands in each image.

TABLE 7.1 Mean Serum Concentrations and Reference Intervals of Steroid Hormones in Neutered Adrenal Disease and Healthy Ferrets Compared With Intact Female Ferrets[66]

	NEUTERED		INTACT
Hormone	**Adrenal Disease**	**Healthy (n = 26) (13 male, 13 female)**	**Female (n = 11)**
Androstenedione, nmol/L	67 (n = 25)	6.6 (< 0.1–15)	58 (20–96)
Dehydroepiandrosterone sulfate, mmol/L	0.03 (n = 27)	0.01	—
Estradiol, pmol/L	167 (n = 28)	106 (30–108)	166 (122–210)
17α-Hydroxyprogesterone, nmol/L	3.2 (n = 20)	0.4 (< 0.1–0.8)	7.7 (2.3–13.1)

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ratio will not help to differentiate between a ferret with hyperadrenocorticism and one with an active ovary, as the UCCR is also increased in intact ferrets during the breeding season (N. Schoemaker; unpublished data, 1999).

Unlike in dogs, the adrenocorticotropic hormone (ACTH) stimulation test and the dexamethasone suppression test are not considered useful to diagnose adrenal disease in ferrets. Both healthy ferrets and those with adrenal disease respond equally well to an ACTH stimulation test, probably because most ferrets with this disease do not produce abnormally high concentrations of cortisol.[64] Moreover, plasma concentrations of ACTH and α-melanocyte-stimulating hormone (α-MSH) in ferrets with adrenal disease are similar to those of healthy ferrets, suggesting that adrenal disease in ferrets is independent of ACTH and α-MSH.[69]

Similar to dogs with Sertoli cell tumors, an increase in cornified preputial epithelial cells can be found in hobs with hyperadrenocorticism.[58] Although preputial cytology has been suggested as a screening test for diagnosing hyperadrenocorticism in hobs, the added value of this test in clinical practice is questionable.

Histologic evaluation of surgically resected adrenal glands may reveal hyperplasia, adenoma, carcinoma, or a combination of these changes.[65] Clinically, histologic findings seldom result in a change in the treatment protocol.

Surgical and Medical Management

The most commonly used treatment modalities for ferrets with hyperadrenocorticism are surgical removal of the gland(s), the use of a long-acting GnRH analogue, or both. The choice of treatment is influenced by many factors. Factors such as the age of the ferret, presence of concurrent disease (e.g., renal failure, lymphoma, or cardiomyopathy), risk of surgery (higher risk when the right or both adrenal glands are involved), or financial limitations may lead to the owner declining surgery. In a comparison study of treatment modalities in ferrets, average disease-free period after treatment with a deslorelin implant was 16.5 months (range 3–30 months) compared with 13.6 months (range 0–38 months) for surgical intervention.[37] On the basis of these results, the recommended treatment for an adrenal tumor has changed from surgical treatment to administering a deslorelin implant, which is registered for this purpose in the United States.

Surgical treatment. The left adrenal gland can be fairly easily removed, whereby the adrenal gland is dissected out of the retroperitoneal fat and removed after ligating the adrenolumbar vein (See Chapter 31). Resection of the right adrenal gland, however, is more difficult and carries more risk because of its attachment to the caudal vena cava and close proximity to the liver (Fig. 7.6). Complete or partial resection of the right adrenal gland combined with cryosurgery has a less favorable outcome than partial resection alone.[77] Moreover, survival times in ferrets after debulking (partial resection) of the right adrenal gland were comparable to those in ferrets after complete resection of the left adrenal gland.[77] To allow for complete removal of the right adrenal gland, some surgeons have ligated the caudal vena cava. However, this is only feasible if this vein is already occluded for a major portion of its diameter and collateral vein circulation has been established. If this is not the case, risk of hypertension distal to the ligation is high, which may lead to acute and potentially fatal kidney failure.[74]

In cases where both adrenal glands are affected, some surgeons remove the entire left adrenal gland and part of the right adrenal gland. In one study, this treatment modality led to an Addisonian crisis in 5% of patients.[85] In these instances, drug therapy, consisting of either the parenteral administration of desoxycorticosterone pivalate at 2 mg/kg intramuscularly every 21 days, or oral supplementation with fludrocortisone acetate at a dosage of 0.05 to 0.1 mg/kg orally (PO) every 24 hours or divided every 12 hours,[66] may be needed for an unspecified time to compensate for the lack of corticosteroid and mineralocorticoid production. Survival rates 1 and 2 years after surgical intervention of 98% and 88%, respectively, have been reported.[77] After surgical removal of a unilateral adrenal tumor, the disease commonly recurs because of development of alterations in the contralateral adrenal gland.[84]

Adrenal disease can recur in approximately 15% of ferrets due to development of disease in remaining adrenal gland tissue.[85] In addition, up to 6% of ferrets may die during surgery because of surgical complications (e.g, hemorrhage).[37,85]

Medical Treatment. Medical management is aimed at moderating the clinical signs rather than curing the disease.[66] The depot GnRH-agonist deslorelin (Suprelorin F; Virbac, Fort Worth, TX) is the only drug licensed in the United States for use in the treatment of hyperadrenocorticism in ferrets. The drug suppresses the release of gonadotropins by continuously releasing deslorelin into the circulation, thereby overriding the pulsatile release of GnRH that is needed for the release of gonadotropins.[83] Because of the initial (short-lived) release of gonadotropins, this effect is delayed by approximately 2 weeks after placement of the implant, during which time the clinical signs may worsen. During this period, the androgen receptor

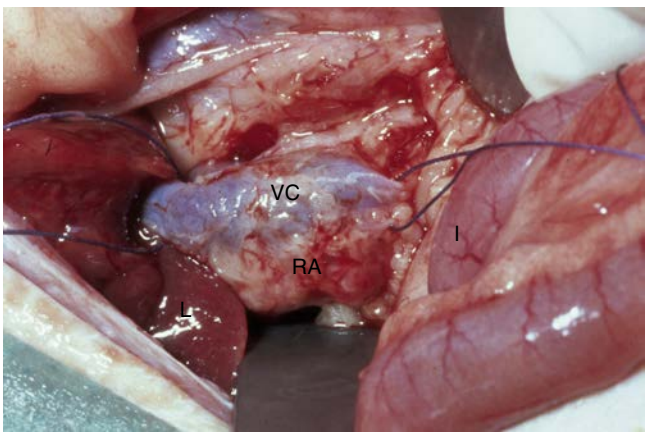


Fig. 7.6 The right adrenal gland tumor (RA) of this 5-year-old male castrated ferret is attached to the caudal vena cava (VC). Complete surgical resection without damaging the vena cava is next to impossible. Preventive ligatures are therefore placed cranial and caudal to the adrenal gland so that these may be tightened when the wall of the vena cava is cut. Vascular surgeons can suture the wall of the vena cava, which will allow full functionality of the vein after resection of the tumor. L = liver, I = intestine.

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blocker flutamide (10 mg/kg PO every 12–24 hours) may be used to inhibit the androgen secretion until the implant gains effectiveness.[74] In the experience of the authors, the tumor does not decrease in size after placement of the implant. Autonomous production of steroids by the adrenal gland may occur over time, resulting in a loss of efficacy of the implant and recurrence of clinical signs.

In a recent study, administration of a GnRH vaccine resulted in relief of clinical signs of hyperadrenocorticism.[46] However, at this time, the vaccine is only available for research purposes and therefore currently not a viable option in practice.

Other drugs such as ketoconazole, mitotane, and melatonin are not recommended in the treatment of hyperadrenocorticism in ferrets because they are deemed ineffective or are associated with (severe) adverse effects, or both. Although melatonin has been found to alleviate the clinical signs, hormone concentrations do not decrease, thereby enabling the tumors to continue to grow.[59] The 3β-hydroxysteroid dehydrogenase (3β-HSD) blocker trilostane has been used anecdotally in ferrets. Although 3β-HSD is necessary for the synthesis of androstenedione and 17α-hydroxyprogesterone, and a blocking agent would likely be effective in the treatment of hyperadrenocorticism in ferrets, progression of clinical signs was seen in ferrets with hyperadrenocorticism that received 5 mg trilostane PO once daily. The decrease in 3β-HSD is hypothesized to lead to activation of 17–20-lyase and thus activation (instead of deactivation) of the androgen pathway. This drug therefore is not recommended before understanding the mode of action in ferrets.[73]

Prognosis

Ferrets with an adrenal neoplasm may live for several years with this condition. The prognosis is highly variable and depends on factors such as age, type of tumor, presence of concurrent disease, and clinical signs. Pruritus, for instance, may be unbearable for the ferret, and some of these animals appear to be more lethargic as well. In one case seen by the authors, a ferret with a right adrenal gland tumor was found dead due to a rupture of the caudal vena cava that had been invaded by this tumor. In hobs, prostate involvement may result in a life-threatening urinary blockage, thereby influencing chances of survival if not treated promptly. In some ferrets, removing the diseased adrenal tissue and draining the cysts resolves the urinary blockage within 1 or 2 days; during this period, the bladder should be emptied regularly. If no urine can be expelled by applying pressure to the bladder, a prepubic catheter can be placed to facilitate emptying of the bladder. Although metastases are rarely seen, prognosis is guarded to poor when present.

Prevention

Surgical neutering has been implicated as a causative factor in the development of hyperandrogenism in ferrets.[70,71,82,83] However, neutering is considered necessary to prevent hyperestrogenism-related pancytopenia resulting from persistent estrus in jills, as well as to reduce intraspecies aggression (enabling ferrets to be kept in groups) and decrease the intensity of the musky odor in hobs.[6,72] In recent years, chemical neutering using a depot-deslorelin implant (Suprelorin, Virbac) has been investigated as an alternative for surgical neutering in ferrets in Europe. In hobs, the implants were found to suppress plasma follicle-stimulating hormone and testosterone concentrations, decrease testis size, and inhibit spermatogenesis. In addition, the musky odor, sexual behavior, as well as aggressive behavior could be effectively reduced.[72] In jills, deslorelin implants were also effective in preventing estrus. The duration of effectiveness of a 4.7-mg deslorelin implant varies between 1 to 3 years in both jills and hobs.[79] After placement of the implant, minor local adverse effects (e.g, scab formation, pruritus) have been observed in less than 20% of ferrets. Placement of the implant may induce a temporary estrus, which lasts up to 2 weeks and only incidentally results in development of pseudopregnancy that requires medical intervention.[79] Based on the results of the aforementioned studies, deslorelin implants are considered a suitable alternative for surgical neutering in ferrets. Support for the hypothesis that the use of a deslorelin implant reduces the incidence of hyperandrogenism in ferrets can be found in a recent study on the use of a GnRH vaccine (GonaCon, United States Department of Agriculture) in ferrets as an alternative for surgical neutering. The probability of ferrets developing hyperadrenocorticism was significantly reduced in young (1–3 years of age) ferrets after vaccination when compared with untreated, neutered control animals.[45]

Preliminary results from a study, performed by the authors, comparing the increase in size of adrenal glands of surgically neutered jills and those receiving a yearly implant containing 4.7-mg deslorelin indicate that, over a period of 6 years, adrenal glands increased in size significantly more in surgically neutered jills than in jills that received implants. This finding suggests that it is indeed likely that the GnRH-containing implants have a preventive effect on the development of adrenal gland disease in ferrets.

Other Conditions Affecting the Adrenal Gland

Abnormalities of the adrenal glands other than hyperadrenocorticism have been reported in ferrets but should be considered rare. These include teratoma, aldosterone-secreting adenoma, neuroblastoma, and pheochromocytoma.[46] In addition, cases of LH-dependent hypercortisolism[68] and adrenohepatic fushion[56] have been reported.

Hyperaldosteronism/Conn's Syndrome

Conn's syndrome has been described in a 6-year-old ferret with an aldosterone-secreting adrenocortical adenoma. The ferret presented with alopecia, pruritus, lethargy, and chronic cough. Ancillary tests revealed hypertension, hypokalemia, and increased plasma concentrations of aldosterone.[16] In addition to hyperaldosteronism, this ferret also had increased plasma concentrations of estradiol, 17α-hydroxyprogesterone, and androstenedione. Despite initial improvement with treatment of leuprolide acetate, potassium gluconate, spironolactone, amlodipine, and benazepril, the ferret deteriorated and was euthanized two months after diagnosis. Postmortem examination revealed an 8-cm mass in the left adrenal gland, with immunohistochemical results revealing the neoplastic cells staining positive for aldosterone.[16]

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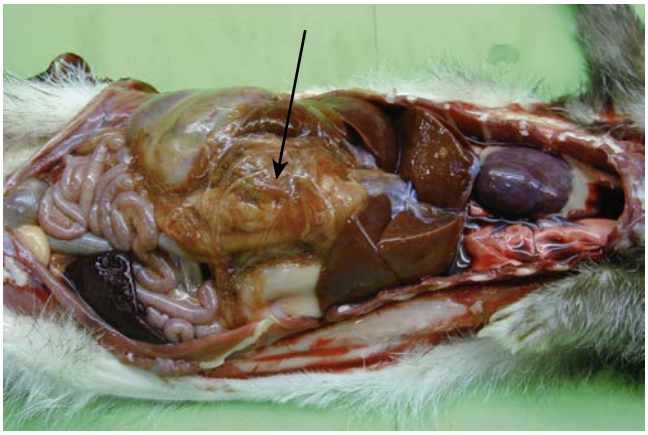


Fig. 7.7 A large right adrenal gland tumor was found in this ferret. Histologic evaluation of the tumor was suggestive of a pheochromocytoma *(arrow)*. Confirmation of this diagnosis was unsuccessful with immunostaining.

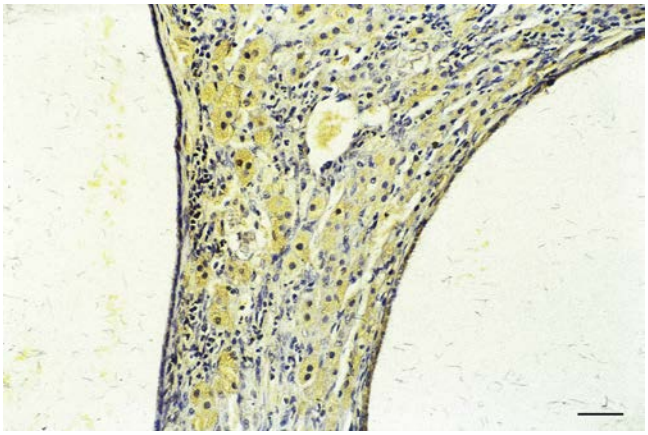


Fig. 7.8 Histologic section of a right adrenal gland tumor, immunohistochemically stained with the P1B4 LH-receptor antibody, which was tightly associated with the liver. The brown cells are LH-receptor-positive adrenal cells, whereas the nonstained cells are hepatocytes. The areas adjacent to the stained tissue are part of the cysts. This area is referred to as *adrenohepatic fusion* and is frequently seen in right adrenal tumors that show cystic alterations. Bar = 60 μm.

Hypercortisolism/Cushing's Syndrome

Iatrogenic hypercortisolism has been diagnosed by the authors in ferrets that have been treated for long periods of time with prednisone for the management of insulinomas. After these ferrets were put on a treatment with diazoxide and the administration of prednisone was gradually decreased, the signs of hypercortisolism disappeared and the ferrets returned to normal.

A case of LH-dependent hypercortisolism has also been described in a 5-year-old castrated hob that was presented with polyuria and polyphagia.[68] Abdominal ultrasonography revealed an enlarged right adrenal gland and atrophy of the left adrenal gland. An hCG stimulation test demonstrated increases in plasma cortisol and androstenedione concentrations. Based on these findings, LH/hCG-dependent hypercortisolism and hyperandrogenism was suspected, and treatment was started with a deslorelin-containing implant. Within 3 weeks after placing the implant, all clinical signs had disappeared. Three months later, the endocrine parameters had normalized, whereas abdominal ultrasonography revealed that the right adrenal gland had diminished in size, and size of the left adrenal gland returned to normal. No recurrences of clinical signs were seen in the 2 years after placement of the deslorelin implant.[68]

Pheochromocytoma

Pheochromocytomas, which are tumors originating from the adrenal medulla that produce excessive amounts of catecholamines, have been reported in ferrets.[24,77] Although these tumors (Fig. 7.7) are usually much larger than tumors of the adrenal cortex, they can go unnoticed for a long period of time. Clinical signs that have been described are tachycardia, dyspnea, and cardiovascular collapse.[66] Based on signs seen in other species, other clinical signs that may be observed include hypertension, arrhythmia, or retinal pathology.[74] Diagnosis thus far is made during postmortem examination. To confirm the diagnosis antemortem, measurement of urinary metanephrine would be necessary, which, to the authors' knowledge, has not yet been reported in ferrets. Because ferrets with pheochromocytomas reportedly respond poorly to chemotherapy, surgical excision is the only treatment option.[66] However, when the tumor is manipulated during surgery, a potential surge of catecholamines may occur, which can lead to life-threatening arrhythmias or hypertension. As a result, a ferret with a pheochromocytoma has a very poor prognosis for survival.

Adrenohepatic Fusion

An anomaly of the right adrenal gland resulting from a union of the adrenal gland with hepatic tissue—adrenohepatic fusion—has been described in two ferrets, neither of which had clinical or microscopic evidence of adrenal gland disease.[56] Histologically, a close fusion of the respective parenchymal cells was found, with partial absence of an intervening connective tissue septum. Although this is the only report of this adrenal alteration, the authors have seen similar alterations in multiple ferrets with right adrenal tumors (Fig. 7.8). The cystic changes seen in these cases are most likely dilated bile ducts. This anatomic anomaly does not appear clinically relevant.

DISEASES OF THE THYROID AND PARATHYROID

The thyroid gland produces the thyroid hormones L-thyroxine (T_4) and, to a lesser extent, tri-iodothyronine (T_3) and calcitonin. Thyroid hormones play an important role in stimulating the basal metabolic rate. Especially in young animals, thyroid hormones also act as a tissue growth factor. Iodine is the main building block of the thyroid hormones.[60] Diseases of the thyroid gland may result in hypofunctioning or hyperfunctioning of the gland, but unaltered production of thyroid hormone may also be seen. Hypofunction of the thyroid gland in dogs may be the result of an immune-mediated inflammation or idiopathic. A hereditary component may also play a role.[52] Thyroiditis has been found in ferrets with Aleutian disease but was not associated with hypothyroidism.[46] Although rare, several cases of ferrets with

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Fig. 7.9 Severe obesity seen in a 5-year-old female neutered ferret with confirmed hypothyroidism by lack of response to the administration of 100 µg of human recombinant thyroid-stimulating hormone. (Courtesy Angela Lennox.)

hypothyroidism have been described. In some herbivorous and granivorous species, consumption of goitrogenic nutrients may result in a decreased production of thyroid hormone. The latter is usually compensated by hyperplasia of the gland (goiter), which can be corrected easily by providing a well-balanced diet containing sufficient amounts of iodine. To the authors' knowledge, neither goiter nor hyperthyroidism or alterations in the production of calcitonin have been reported in ferrets.

The parathyroid gland secretes parathyroid hormone (PTH), which, together with vitamin D_3, plays an important role in regulating plasma calcium concentrations.[78] Conditions affecting the parathyroid gland of ferrets are considered extremely rare.

Hypothyroidism

Hypothyroidism is a seemingly rare disease in ferrets. Clinical signs described in ferrets with hypothyroidism include obesity, lethargy, and hindleg weakness (Fig. 7.9).[80] Hair loss, hypoglycemia, and hypercholesterolemia, which are all common signs described in hypothyroid dogs, have thus far not been reported in the ferrets diagnosed with hypothyroidism.

Similar to dogs, the diagnosis of hypothyroidism is based on the finding of low thyroid hormone levels (<10 ng/mL [13 nmol/L]) and lack of response to a thyroid-stimulating hormone (TSH) stimulation test, which is performed to eliminate the possibility of sick euthyroid syndrome. The TSH stimulation test can be performed by giving an intramuscular injection of 100 µg of human recombinant TSH (Thyrogen; Sanofi Genzyme, Cambridge, MA) and measuring T4 and T3 before and 4 hours after injection. In euthyroid ferrets, post-stimulation levels will increase to 1.4 times the pre-stimulatory levels, whereas ferrets with hypothyroidism have maximally shown an increase of 1.2 times baseline levels (Table 7.2).[43,80] In ferrets with confirmed hypothyroidism, oral treatment with levothyroxine (50–100 µg PO every 12 hours) was found to be effective in resolving clinical signs and normalizing serum T_4 concentrations.[80]

Hyperthyroidism and Thyroid Neopalsia

Clinical hyperthyroidism has not been reported in ferrets. A medullary thyroid carcinoma (also referred to as *C-cell carcinoma*) was diagnosed at necropsy in an adult neutered male ferret. Antemortem, this ferret had a reduced appetite and displayed weight loss, lethargy, decreased activity, and thinning of the hair coat. On physical examination, a firm, infiltrative soft tissue mass was palpated in the region of the thyroid gland. The tentative diagnosis of a thyroid neoplasia was made based on radiographs, serum biochemical results, and results of a fine-needle aspirate of the mass. Hyperthyroidism, however, could not be confirmed antemortem. Because surgical excision was unsuccessful, the ferret was euthanized.[24] Follicular adenocarcinoma of the thyroid gland has been reported in ferrets. These rapidly growing malignant tumors can be found upon palpation of the ventral cervical region. In one case, thyroid hormone levels were measured and considered within the normal range.[46]

TABLE 7.2 Published Reference Values of Cortisol and Thyroid Levels in Ferrets

Hormone	Sex	Values
Cortisol		
	—	0.94–8.52 µg/dL (26–235 nmol/L) Mean 2.67 µg/dL (74 nmol/L) [a]
Thyroxine (T_4)		
	M	1.01–8.29 µg/dL (13–107 nmol/L) Mean 3.24 µg/dL (42 nmol/L) [b]
	F	0.71–3.43 µg/dL (9–44 nmol/L) Mean1.87 µg/dL (24 nmol/L) [b]
	M	2.69 ng/mL (35 nmol/L) at 0 h; 3.37 ng/mL (43 nmol/L) at 2 h; 3.97 ng/mL (51 nmol/L) at 4 h; 3.45 ng/mL (44 nmol/L) at 6 h [c]
	M/F	1.66 µg/dL (21 nmol/L) at 0 h; 2.32 µg/dL (30 nmol/L) at 4 h [d]
Tri-iodothyronine (T_3)		
	M	45–78 ng/dL (0.69–1.2 nmol/L) Mean, 58 ng/dL (0.89 nmol/L) [b]
	F	29–73 ng/mL (0.45–1.12 nmol/L) Mean 53 ng/dL (0.82 nmol/L) [b]

[a]Intramuscular administration of cosyntropin at 1 µg/kg caused a three- to fourfold increase in plasma cortisol concentration.[63]
[b]Data from Garibaldi et al.[26]
[c]Mean thyroxine at baseline (0 hours) and at 2, 4, and 6 hours after 1 U bovine thyroid stimulating hormone IV. [29]
[d]Mean thyroxine at baseline (0 hours) and at 4 hours after 100 µg/kg intramuscularly of recombinant human thyroid-stimulating hormone.[43]

Hypoparathyroidism

Hypoparathyroidism is considered rare in ferrets. [15,42] In one reported case, diagnosis was based on the inability to identify the parathyroid glands at necropsy.[42] Clinically, this ferret exhibited intermittent seizures and depression. Hypocalcemia and hyperphosphatemia were found on plasma biochemical analysis, while serum PTH concentrations were low to low-normal. Life-long administration of calcium and vitamin D resulted in resolution of the clinical signs for at least 21 months.[42]

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Pseudohypoparathyroidism

Pseudohypoparathyroidism is a condition in which normal levels of circulating parathyroid hormone are present, but the animal is unable to maintain functional plasma concentrations of calcium and phosphorus. One case of suspected pseudohypoparathyroidism has been described in ferrets.[88] This animal, a 1.5-year-old neutered hob, was presented with intermittent seizures, muscle fasciculations, disorientation, and lethargy. Serum biochemical results revealed low calcium, high phosphorus, and high PTH concentrations. Unfortunately, no PTH (Ellsworth-Howard) challenge test or diagnostic imaging were performed to confirm the diagnosis. Clinical improvement was seen after treatment with calcium carbonate (100 mg PO every 12 hours) and dihydrotachysterol (0.01 mg/kg PO twice per week). The ferret lived for at least another 3.5 years in good health, although it remained obese.[88]

DISEASES OF THE PANCREAS

Diabetes Mellitus

Etiopathogenesis

Spontaneous diabetes mellitus is uncommon in ferrets.[5,8] No sex, age, or breed predispositions have been reported. Although ferrets may develop iatrogenic diabetes from aggressive insulinoma surgery, it is uncommon.

History and Physical Examination

Clinical signs are identical to those seen in most species and include polyuria/polydipsia, lethargy, and weight loss despite good appetite. In advanced stages of the disease, anorexia, depression, ataxia, vomiting, or hepatomegaly may develop secondary to hepatic lipidosis and ketoacidosis. Physical examination findings are often unremarkable.

Clinical Pathology and Diagnostic Testing

Plasma glucose concentrations greater than 400 mg/dL (21 mmol/L) are suggestive of the diagnosis, although repeated measurements are advised. Glucosuria is present as well but should not be considered diagnostic. A reference interval for fructosamine levels has been determined in ferrets (101–202 µmol/L).[30] However, to date, measurement of plasma fructosamine concentrations in ferrets with confirmed diabetes mellitus has not been reported. Measurement of plasma insulin concentrations is also possible (reference range 4.6–43.3 µU/L; 33–311 pmol/L).[66] However, the value of this measurement is questionable in diabetic ferrets because little is known about regulation of insulin release in ferrets. Moreover, some laboratories may not offer tests that have been validated for use in ferrets.[81,83]

Aside from glucosuria, urinalysis can reveal secondary bacterial cystitis, ketonuria, or both, particularly in late stages of the disease. Concurrent diabetic ketoacidosis may be evident by findings of hypokalemia, hyponatremia, ketonemia, hypochloremia, and hypobicarbonemia. A complete blood cell count and plasma or serum biochemical analysis, radiographs, and ultrasound may be performed to rule out concurrent disease (e.g, hepatic lipidosis, atherosclerosis).[74]

Management

Hyperglycemia seen as a consequence of pancreatectomy is often transient and frequently resolves within 1 to 2 weeks without further therapeutic intervention.[66] Institute insulin treatment in ferrets with blood glucose concentrations greater than 300 mg/dL (16.7 mmol/L) on repeated measurements.[66] Treatment of spontaneous diabetes mellitus in ferrets, often associated with concurrent diabetic ketoacidosis, frequently requires hospitalization and intensive care (including aggressive fluid therapy) to correct water and electrolyte imbalances and reverse the ketonemia and acidosis. Administration of NPH insulin (0.1–1.0 units/ferret subcutaneously [SC] every 12 hours), which has an intermediate duration of action, or the longer-acting ultralente insulin (1.0 units/ferret SC every 24 hours) have been recommended for the treatment of diabetes mellitus in ferrets. Unfortunately, the latter drug is no longer available in most countries.[74] Alternatively, the long-acting glargine insulin—which is the first drug of choice in cats—has been reported to be effective in treating spontaneous diabetes mellitus in an elderly ferret (0.5 units SC every 12 hours).[31] Because ferrets with spontaneous diabetes mellitus have a tendency to respond unpredictably to the administration of insulin, closely monitor patients at the start of insulin therapy, which can best be achieved during hospitalization. In this period, gradually increase the insulin dose until blood glucose concentrations stabilize between 125 to 200 mg/dL (6.9–11.1 mmol/L). For at-home monitoring, instruct the owners to monitor their ferret's urine closely for glucosuria and ketonuria. If no or trace amounts of glucose are found in the urine, the insulin dose can be kept unaltered. However, if large amounts of glucose are found in the urine, increase the insulin dose in small, incremental steps.[66] In addition, instruct owners to offer a low-carbohydrate, protein-rich diet in multiple (>4) portions per day. The portions are offered concurrently with each insulin injection and 4 to 6 hours after the injection. In other animal species, glipizide, an oral hypoglycemic drug, is used in patients with (type II) diabetes mellitus. However, in ferrets, information regarding use of this drug or its efficacy in treating hyperglycemia is currently lacking.

Prognosis

Prognosis of ferrets with diabetes mellitus after partial pancreatectomy is usually good. In ferrets with spontaneous diabetes mellitus that develop ketoacidosis or continue to be hyperglycemic for more than 2 weeks after surgery, prognosis is often considered guarded to poor.

Pancreatic Islet Cell Tumor

Insulinomas (pancreatic islet cell tumors) are tumors that originate from the beta cells of the pancreas. These tumors are usually small (i.e., 0.5–2 mm in diameter) (Fig. 7.10). Most tumors are well circumscribed, but infiltration in surrounding tissues may occur. In contrast to other species (e.g., dogs), insulinomas rarely metastasize in ferrets.

With a reported prevalence of 20% to 25% of all diagnosed neoplasms in ferrets, insulinomas are one of the most commonly diagnosed tumors in ferrets from 2 to 8 years of age (median 5 years).[38,87] No sex predilection has been reported.

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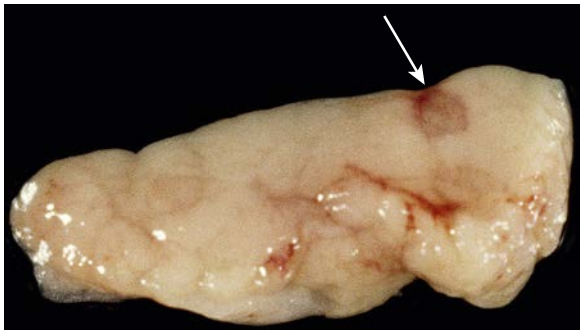


Fig. 7.10 Part of the pancreas that was removed during surgery in a ferret with hypoglycemia. On palpation of the pancreas, a small firm nodule could be palpated *(arrow)*. Histologic evaluation confirmed this to be an islet cell adenoma. (Photo previously published by Schoemaker NJ, van Zeeland YRA. Disorders of the endocrine system. In: Johnson-Delaney CA, ed. *Ferret Medicine and Surgery*. Boca Raton: CRC Press; 2016:191–218.)

Etiopathogenesis

The islets of Langerhans contain four cell types that each secrete a different peptide: alpha cells secrete glucagon, beta cells secrete insulin, delta cells secrete somatostatin, and P (F) cells secrete pancreatic polypeptide.[28] In healthy individuals, the ratio between the blood insulin and glucose concentrations remains constant because of control by the beta cells of the pancreatic islets.[22] Insulin secretion increases when blood glucose concentration are high, while insulin secretion is inhibited when blood glucose is low.[22] When neoplastic beta cells are present, they synthesize and release insulin autonomously despite hypoglycemia.[22]

Although a genetic component has been suggested in the development of insulinoma in ferrets, the exact cause is unknown.[11] Based on the natural carnivorous diet of mustelids, a diet high in carbohydrates has been suggested as a contributing factor to the development of these tumors.[23] On a dry-matter basis, a diet high in protein (42%–55%) and fat (18%–30%) and low in carbohydrates (8%–15%) and fiber (1% to 3%) has been advised, because this may help to reduce the incidence of the disease.[23] A proposed alternative is feeding entire prey animals or a canned food diet with no carbohydrates. However, currently no studies have been done to support these suggestions.

History and Physical Examination

Clinical signs of insulinoma are secondary to the hypoglycemia resulting from the excess production of insulin by these tumors. Signs vary from lethargy, slight incoordination (ataxia), stargazing ("staring off into space"), disorientation, and weakness in the hind limbs, to complete collapse, generalized seizures, and coma. Progression of clinical signs can extend over a period of days to weeks or months. In people, overdose of insulin may result in stimulation of the autonomic nervous system, resulting in nausea.[3,32] Evidence of nausea is also commonly seen in ferrets with an insulinoma and manifests in the form of ptyalism and pawing at the mouth. In addition, owners may notice a glazed look in the eyes of their ferrets. Clinical signs are most evident when the ferret has not eaten for some time and may last from several minutes (most common) to several hours.

TABLE 7.3 Reference Ranges for Insulin Values in Ferrets

INSULIN VALUE			
µIU/mL	pmol/L	N	Fasted
6.4–17.6[41]	44–122	15	4 h
4.6–43.3[40]	32–300	30	Overnight
5–35[a]	35–243	—	—

[a]Clinical Endocrinology Laboratory, College of Veterinary Medicine, University of Tennessee. No longer commercially available.[66]

The signs usually disappear after providing food or oral glucose supplementation.[19,22,57] The most important question to ask the owner is whether the signs wax and wane with the provision of food. If the latter is not the case, other diseases affecting the hind limbs should be considered.

During the physical examination, usually no remarkable abnormalities will be found, unless the ferret is in a hypoglycemic crisis. In those instances, instability of the hind legs (paresis) may be seen, as well as lethargy. Sinus bradycardia is also a common finding in ferrets with an insulinoma.[48]

Clinical Pathology and Diagnostic Testing

Blood glucose concentrations lower than 60 mg/dL (<3.3 mmol/L; reference range 90–125 mg/dL [5.0–7.0 mmol/L]), after withholding food for 4 hours, are highly suggestive of an insulinoma.[66] In ferrets with blood glucose concentrations between 60 to 90 mg/dL (3.3–5.0 mmol/L), the fasting period can be prolonged another 2 hours. In many cases, the blood glucose will then drop below 60 mg/dL (3.3 mmol/L), thereby confirming the tentative diagnosis.[74] Portable blood glucose meters (PBGM) can be used as a quick diagnostic test. An additional benefit is that these glucometers only require one drop of blood. Because of the method of analysis, heparinized blood should not be used. In a comparison study, the veterinary PBGM used in the canine setting produced the most agreeable results, whereas human PBGMs severely underestimated actual glucose concentrations.[54] Therefore use caution when interpreting PBGM results. Instead, hypoglycemia is best confirmed by using a laboratory analyzer that is able to accurately assess glucose values.[74]

Aside from blood glucose, plasma insulin concentrations can be measured. Reference ranges are reported (Table 7.3). In ferrets with hypoglycemia due to insulinoma, insulin concentrations will usually be increased above the reference range and, in some cases, values can be very high. However, insulin concentrations within the reference range also may be seen because of the presumed pulsatile insulin secretion by some insulinomas.[34,66] The concurrent finding of hypoglycemia and insulin concentrations within the reference range should be considered abnormal, as insulin plasma concentrations should be low during a hypoglycemic event.[62] When analyzing plasma insulin concentrations, samples should be submitted to clinical laboratories that have validated the assay for ferrets, as different values can be obtained depending on the method used.[81,83]

Low concentrations of fructosamine have been found in dogs with insulinomas.[55] Analogous to dogs, fructosamine levels in

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ferrets with insulinomas would be expected to be low as well. However, in a recent report, fructosamine concentrations did not differ significantly between healthy and hypoglycemic ferrets. Fructosamine measurements are therefore unlikely to be useful in determining chronic, insulinoma-associated hypoglycemia in ferrets.[17]

Abdominal ultrasound scanning can be useful in confirming the presence of a nodule before exploratory surgery in ferrets with clinical signs of insulinoma. In a recent study describing ultrasonographic features of 28 pancreatic nodules confirmed as insulinoma in six ferrets, nodules were hypoechoic (89%) and homogenous (46%), with smooth margins (79%).[89] Size of the nodules varied from 1.5 × 1.5 to 4.1 × 5.6 mm, and 46.4% were in the left lobe, 50% in the right lobe, and 3.6% in the body of the pancreas. Ultrasonography can also be helpful to identify pancreatic adenocarcinomas and associated metastases.[10] Benign pancreatic nodular hyperplasia sometimes can be confused with insulinoma.[53] In dogs, insulinomas frequently metastasize to the liver. These metastases can be visualized on ultrasound scanning, thereby aiding in the diagnosis and serving as a prognostic indicator. However, in ferrets, most insulinomas are benign and infrequently metastasize.

Advanced imaging techniques, such as MRI and nuclear scintigraphy with octreotide or indium-111, have, to the authors' knowledge, not been used successfully in ferrets to diagnose insulinomas. Contrast-enhanced computed tomography has a high success rate in detecting insulinomas in dogs, although location accuracy in the pancreas is low.[9] Computed tomography has been used in a limited number of clinical cases to confirm the presence of pancreatic nodules in ferrets (K. Quesenberry, personal communication, 2019). Newer advanced imaging techniques, such as positron emission tomography/computed tomography, may prove useful in insulinoma cases in the future.

Differential Diagnoses

The differential diagnoses for hind limb weakness are neurologic disease (e.g., trauma, intervertebral disk disease, Aleutian disease), cardiac disease, generalized weakness, and metabolic disorders, such as hypoglycemia.[1] In ferrets, hypoglycemia is the most common cause of hind limb weakness. Within the differential diagnosis of hypoglycemia, excessive glucose-consuming conditions such as rapidly multiplying neoplastic cells, severe hepatic disease, severe malnutrition or starvation, sepsis, or iatrogenic insulin overdose should be considered.[22] These conditions can usually be ruled out based on the results of the history, physical examination findings, and additional diagnostic test results.[66]

Surgical and Medical Management

Both surgical and medical treatment options exist for the management of insulinomas. Many factors, including the age of the ferret, concurrent medical conditions, prognosis for resolution of hypoglycemia, and financial restrictions, play a role in the decision-making process. When advising owners, always discuss all of the facts of the disease to allow the owner to make an informed decision based on the pros and cons of each method.[74]

TABLE 7.4 Survival Times or Disease-Free Intervals of Ferrets Diagnosed With Pancreatic Beta Cell Tumors (Insulinoma) and Treated With Medical or Surgical Therapy or Both

Treatment	Survival Time, (days)	Mean Disease-Free Interval, Days	Ferrets (n)
Medical therapy only			
	180–267[10]	—	3
	0–504[20]	—	3
	186 (36–273)[84]	22	10
Surgery ± medical therapy			
	46–503[41]	—	6
	—	240[20]	17
	510 (14–1207)[10]	—	20
Nodulectomy only[84]	456 (93–826)	234	27
Nodulectomy + partial pancreatectomy[84]	668 (219–1002)	365	29

Whichever treatment option is chosen, advise owners to monitor for occurrence of hypoglycemia-associated signs. Feeding a high-protein meal may be all that is needed if a ferret is only showing mild clinical signs. Any ferret with an insulinoma should be fed free choice, and owners must ensure that it is eating throughout the day.[66] Recommend that owners discontinue feeding treats high in simple sugars to prevent insulin surges from occurring.[11]

Surgical therapy. Surgical removal of the insulinoma(s) is seemingly the best option to eliminate the source of excess insulin production. Nodulectomy, partial pancreatectomy, or both are done depending on the number and location of the pancreatic nodules (see Chapter 31). Recovery from insulinoma surgery in ferrets is usually rapid and uneventful, with postoperative pancreatitis being rarely reported despite the pancreas being manipulated.[10,66,86] One or two pancreatic nodules are usually found at surgery, but as many as seven to nine nodules have been reported.[10,86] Because preoperative visualization of (all) the tumors can be limited, depending on diagnostic imaging results, the possibility to excise the insulinoma(s) can only be evaluated during surgery. Because very small insulinomas may be missed during exploratory surgery, clinical signs may not always be alleviated after surgical intervention. In ferrets with multiple nodules, partial pancreatectomy may be preferable to pancreatic nodulectomy alone to allow for removal of undetected islet cell tumors.[86] If a partial pancreatectomy is done, take care not to remove too much of the pancreas, as this can result in transient or permanent diabetes mellitus that will require medical management (see above diabetes mellitus). The mean disease-free state after partial pancreatectomy is approximately 1 year, although survival times of over 3 years have been reported (Table 7.4).[66,86] Clinical signs usually recur because of growth of new tumors rather than metastases of the removed tumor.

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Medical management during an acute hypoglycemic crisis. Emergency treatment of a ferret with a hypoglycemic crisis consists of administering an intravenous (IV) bolus of 50% dextrose diluted 1:1 with saline solution or lactated Ringer's solution (0.25–2 mL over 1 to 3 minutes, titrated to effect).[57] In some cases, diazepam can be added to the treatment of patients that continue to seizure despite the intravenous administration of dextrose.[57] To prevent rebound hypoglycemia, maintenance IV fluids can be supplemented with 5% dextrose. Once the clinical signs have subsided, feed the ferret frequent high-protein meals to maintain a constant plasma glucose level.

Administering glucagon has been suggested over the use of dextrose for short-term management of hypoglycemic crises in dogs and cats because of the diminished risk for rebound hypoglycemia and consequent fluctuations in blood glucose concentrations. A case report in which glucagon was provided through constant rate infusion as emergency treatment in a geriatric, severely hypoglycemic ferret suggested a similar effect in this species. Although other types of therapy did not yield a response, a dose extrapolated from dogs and cats (15–40 ng/kg/min) was effective in increasing blood glucose levels and alleviating the clinical signs.[4]

Medical management of chronic hypoglycemia. The goals of medical management of chronic hypoglycemia are to reduce the frequency and severity of clinical signs and to avoid acute hypoglycemic crises.[22] Because clinical signs may progress over time, incremental doses of implemented drugs and combinations of drugs will often be needed.[19]

Prednisone and diazoxide are the most commonly used drugs for treating insulinomas. Octreotide acetate, a synthetic long-acting analog of somatostatin that inhibits the synthesis and secretion of insulin by normal and neoplastic beta cells, has been used in ferrets at a dosage of 1 to 2 µg/kg SC every 8–12 hours. However, no clear beneficial effects were seen when this medication was compared with the two other modes of treatment.[10,44,57]

Prednisone and other glucocorticoids, which stimulate gluconeogenesis,[12] are frequently considered the drugs of first choice in treatment of insulinoma in ferrets. Although glucocorticoids are known to have various adverse effects in other species, ferrets will generally respond well to treatment with these drugs and rarely develop adverse effects.[66] However, weight gain and impaired hair growth (suggestive of iatrogenic Cushing's disease) may develop in ferrets that have received glucocorticoids for long periods of time, as the authors have witnessed.[11] Moreover, the gluconeogenic mode of action of glucocorticoids results in an increase in plasma glucose concentration, which may increase the risk of stimulating the secretion of insulin, which is preferably prevented.

To allow for accurate dosing and facilitating intake of the medication, prednisone is best given in an oral solution.[2] Although ferrets enjoy the taste of sweet flavors, owners and compounding pharmacies are advised not to add flavors or additives that contain sugar to the medications.[66] Chicken flavoring as an alternative is preferred by most ferrets. Although dosages of up to 2 mg/kg PO every 12 hours have been used in ferrets without any immunosuppressive or other adverse effects,[2,57] a starting dose of 0.25 to 0.5 mg/kg PO every 12 hours may suffice to control hypoglycemic episodes in the initial stages of the disease, while limiting the risk of adverse effects. However, the dose may need to be increased if clinical signs recur or are unresolved. Preferably, the dose is increased in incremental steps until signs of hypoglycemia are no longer present to ensure using the lowest dose possible.[22]

Diazoxide, which is registered for treating people diagnosed with an insulinoma, is a benzothiadiazide diuretic that increases the glucose concentration in the bloodstream by inhibiting insulin release from the beta cells, stimulating hepatic gluconeogenesis and glycogenolysis, and inhibiting cellular uptake of glucose.[22] Diazoxide is commonly added to the treatment protocol at the same time as prednisone or after sole use of prednisone is no longer effective in controlling signs of hypoglycemia. However, the authors prefer the initial use of this drug rather than glucocorticoids. Diazoxide is more expensive than prednisone, which may be a factor in choosing initial treatment with prednisone. However, the ferret's low body weight limits the daily quantities that are needed, thereby rendering diazoxide an affordable alternative in many countries.[74] Compounding the drug is necessary to allow for accurate dosing. The compounded mixture has been found to be stable for at least 6 months at the veterinary pharmacy at Utrecht University; however, stability guidelines vary by the compounding pharmacy used. To prevent adverse effects, start treatment with diazoxide at the lower end of the dose range (5 mg/kg PO every 12 hours) and then gradually increase the dose, based on the response to treatment (as evidenced by disappearance or continuation of clinical signs). When using plasma glucose concentrations to monitor the effect of treatment, collect blood samples at least 4 hours after giving the diazoxide. During this period, withhold food from the ferret. Once the dose of diazoxide has been increased to 15 to 20 mg/kg PO every 12 hours without resolution of clinical signs, or if adverse effects occur (e.g, anorexia, vomiting), add prednisone (0.2–1 mg/kg PO every 12–24 hours) to the treatment regimen.[74] For both drugs, doses may be increased further, if necessary. There are no real upper limits of the drug doses; in fact, the authors consider the development of adverse effects as the only limiting factor of further increase of the drug doses.[22] Using the aforementioned medical protocol, hypoglycemia may be controlled for a period up to 18 months, with some ferrets in the authors' clinic surviving for more than 2 years.[57,74]

Prognosis

In ferrets with insulinomas, metastases are rare (<4%).[66] As a result, the prognosis is better than in dogs, in which metastases are very common. Nevertheless, clinical signs frequently recur, often because of the development of new tumors rather than metastases of the initial tumor. If clinical signs recur after surgery, medical management may be attempted. In cases that are poorly manageable with medication, prognosis is usually poor.[66]

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8

Neoplasia in Ferrets

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Neoplasia has long been studied as a common cause of disease in ferrets in the United States,[52,95] but it is now the most common disease in ferrets presenting to hospitals in Asia and Europe,[22,41,57] showing the ubiquitous nature of neoplasia in domestic ferrets on a worldwide scale. The probability is good that most ferrets will develop a neoplasm of the endocrine system during the "golden age" for tumors (4–6 years) and high that some type of neoplasm will become evident over the course of a lifetime.

One tenet should be considered by all veterinarians treating ferrets with neoplasms: a ferret is not a cat or a dog. The clinical behavior, prognosis, and paraneoplastic syndromes in ferrets are often far different from what is seen with similar neoplasms in dogs or cats. For example, insulinoma in ferrets is a neoplasm that rarely metastasizes, as opposed to the same neoplasm in dogs and cats, which metastasizes widely and rapidly and results in short survival times. Adrenocortical carcinoma, a neoplasm prone to metastasize widely in dogs in most cases, warrants a good prognosis with early removal or treatment in ferrets. Mast cell tumors, often malignant (and fatal) in dogs, are invariably benign and associated with a good prognosis in ferrets. Thus extrapolating diagnostic and therapeutic options from comparable syndromes in more traditional pet species can be problematic.

ETIOLOGY

Little information is definitive on the causes of many common neoplasms in ferrets. Many theories abound but only rarely with supportive evidence, and some neoplasms may be multifactorial in origin. Three main schools of thought are the following:

1. Husbandry issues. The "domestication" of the ferret as a pet species involves varying degrees of environmental and surgical manipulation of the animal itself. Several factors relating to this have been postulated as causative for common neoplasms in this species—early neutering, as well as indoor housing and artificial lighting (adrenocortical neoplasia)[8,76,77] or feeding high-carbohydrate diets and treats (islet cell tumors).[76]
2. Genetic (familial) predisposition. Although genetic or chromosomal aberrations are yet to be studied in domestic ferrets, the high incidence of neoplasia in American bloodlines of ferrets compared with their European counterparts, as well as the documentation of multiple endocrine neoplastic syndromes[31] (resulting from genetic point mutations in people), lends credence to this belief.
3. Infectious agents. Infectious causes have been proposed for neoplasms in ferrets, including retroviruses (lymphoma)[5,26] and *Helicobacter mustelae* (gastric adenocarcinoma[30,31,49] and gastric B-cell [mucosal-associated lymphoid tissue] lymphomas[25]).

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DIAGNOSIS

Initial diagnostic testing for suspected neoplasia in ferrets includes the judicial use of blood tests and diagnostic imaging. A complete blood count (CBC) and serum/plasma biochemical analysis is mandatory to evaluate the patient's overall health status and may lead directly to a definitive diagnosis (e.g., hypoglycemia associated with islet cell tumors or hyperproteinemia resulting from myeloma).

Radiography and ultrasonography are used not only to diagnose tumors but also to help stage neoplastic disease, plan therapy, and monitor response to therapy. More advanced diagnostic imaging modalities, such as computed tomography, magnetic resonance imaging, and contrast studies, are useful in a wide variety of neoplastic diseases and are becoming more widely available.

In most cases of neoplasia, definitive diagnosis requires sampling of the neoplasm and microscopic analysis. Although examination of cytologic preparations helps to develop a diagnostic plan and in some cases yields a definitive diagnosis, biopsy usually results in a definitive diagnosis and often yields additional information about tumor phenotype (important in lymphoma), staging, and prognosis.

TREATMENT

Before initiating treatment, practitioners should always discuss therapeutic goals, potential outcomes, prognosis for cure, and adverse effects of treatment options versus the effects of palliative care in cases of life-threatening disease.

Potential therapies in oncology include the following:

- *Surgery.* Surgery is the treatment of choice for curing solitary tumors with limited metastatic potential. Surgery is used to obtain biopsy samples, debulk tumors as an adjunct to radiation or chemotherapy, or simply for palliation of symptoms. Cryosurgery or hyperthermia can be used with small solitary solid tumors.
- *Chemotherapy.* Several chemotherapeutic protocols for ferrets have been reported. In addition to primary treatment, chemotherapy may be used before surgery or radiation therapy to decrease tumor size or after surgery to eliminate small foci of metastasis, to prevent recurrence after incomplete surgical excision, or as palliative treatment when a definitive cure is not an option. Reported chemotherapeutic agents used in ferrets are listed in Tables 8.1, 8.2, and 8.3. When calculating chemotherapeutic doses, a ferret-specific formula for body surface area can be used (Table 8.4); however, there are only minor differences between this formula and the feline-derived formula.
- *Radiation.* Use of radiation therapy in ferrets has been reported with variable success. It is used for control of local solid tumors, either alone or in combination with surgery, or as a palliative treatment when surgery is not an option.
- *Supportive care.* As with any oncologic patient, supportive care and management of paraneoplastic symptoms is paramount. Appropriate nutrition and hydration, proper analgesia, maintenance of hydration, antiemetic therapy, and control of secondary infections is paramount in ferrets undergoing treatment.

TABLE 8.1 Modified COP Protocol (IV, PO, SC drugs) for 52 Weeks' Duration, Gulf Coast Veterinary Specialists[3]

Week	Drug	Dosage
0, Day 3	L-asparaginase	400 U/kg SC (pretreat with diphenhydramine @ 1 mg/kg IM)
1	Cyclophosphamide	10 mg/kg PO or SC
	Prednisone (throughout therapy)	1 mg/kg PO every 24 h until week 13, then 1 mg/kg PO every 48 h
	Vincristine	0.12 mg/kg IV
2	Vincristine	0.12 mg/kg IV
3	Vincristine	0.12 mg/kg IV
4	Cyclophosphamide	10 mg/kg PO or SC
	Vincristine	0.12 mg/kg IV
7 - Repeat every 3 wk (i.e., week 10, 13, 16, etc.) until week 52, then restage	Cyclophosphamide	10 mg/kg PO or SC
	Vincristine	0.12 mg/kg IV
Rescue	Doxorubicin	1-2 mg/kg IV over 20 min

Weekly CBCs are also performed to ensure the neutrophil count is remaining ≥ 1000 cells/μL. If the neutrophil count is <1000 cells/μL, delay treatment by 1 week and repeat another neutrophil count.
CBC, Complete blood count; *COP,* cyclophosphamide, vincristine (Oncovin), and prednisone; *IV,* intravenously; *PO,* orally; *SC,* subcutaneously.

TABLE 8.2 Tufts University "No-IV" Chemotherapy Protocol

Week	Drug	Dosage
1	L-asparaginase	10,000 IU/m^2 SC
	Cyclophosphamide	250 mg/ m^2 PO, give with 50 mL/kg of LRS
	Prednisone (throughout therapy)	2 mg/kg PO every 24 h × 7 days, then 2 mg/kg PO every 48 h
2	L-asparaginase	10,000 IU/m^2 SC
	CBC	
3	L-asparaginase	10,000 IU/m^2 SC
	Cytarabine	300 mg/m^2 SC every 24 h × 2 days (dilute 100 mg with 1 mL sterile water for injection)
4	CBC	
5	Cyclophosphamide	250 mg/m^2, give with 50 mL/kg of LRS
7	Methotrexate	0.8 mg/kg IM
8	CBC	
9	Cyclophosphamide	250 mg/m^2 PO, give with 50 mL/kg of LRS
11	Cytarabine	300 mg/m^2 SC every 24 h × 2 days (dilute 100 mg with 1 mL sterile water for injection)

Continued

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TABLE 8.2 Tufts University "No-IV" Chemotherapy Protocol—cont'd

Week	Drug	Dosage
	Chlorambucil	2 mg tablet PO once or 1 mg (1/2 tablet) PO every 24 h × 2 days
12	CBC	
13	Cyclophosphamide	250 mg/m^2 PO, give with 50 mL/kg of LRS
15	Procarbazine	50 mg/m^2 PO q24h × 14 days
16	CBC	
17	CBC	
18	Cyclophosphamide	250 mg/m^2 PO, give with 50 mL/kg of LRS
20	Cytarabine	300 mg/m^2 SC every 24 h × 2 days (dilute 100 mg with 1 mL sterile water for injection)
	Chlorambucil	2 mg tablet PO once or 1 mg (1/2 tablet) PO every 24 h × 2 days
23	Cyclophosphamide	250 mg/m^2 PO, give with 50 mL/kg of LRS
26	Procarbazine	50 mg/m^2 PO every 24 h × 14 days
27	CBC, biochemistry	
*If not in remission, continue weeks 20–27 for three cycles		

CBC, Complete blood count; *IM,* intramuscularly; *IV,* intravenously; *LRS,* lactated Ringer's solution; *PO,* orally; *SC,* subcutaneously. Courtesy Dr. Joerg Mayer, University of Georgia.[56,95] Non invasive chemotherapy protocol (PO, SC drugs) for 26-week duration. If the CBC results show myelosuppression, reduce the dose by 25% the next treatment.

TUMORS OF THE ENDOCRINE SYSTEM

Most neoplasms in domestic ferrets arise in the endocrine system, with tumors of the pancreatic islets and the adrenal cortex being the two most common neoplasms in these species. Detailed descriptions of these disease syndromes and treatment options are discussed in Chapter 7.

Islet Cell Tumors (Insulinoma)

Although multiple studies have pointed to insulinomas (also known as *islet cell tumors*, arising from the β cells of the pancreatic islets) as the most common neoplasm of ferrets, these tumors may be slightly overrepresented because of their relatively obvious symptomatology, response to surgical excision, and tendency to recur over time.[2,4,9,10,23,52,57,89,95] This neoplasm is most commonly seen in middle-aged ferrets, with the incidence slightly higher in males than in females; however, this may reflect a bias of ferrets that present to hospitals with clinical signs rather than a true sex predilection.[9,23,89]

Insulinoma in the ferret exhibits a far different behavior than in the dog or cat.[9,89] In the dog and cat, these are highly malignant neoplasms with marked metastatic potential, leading to a short survival time. In ferrets, these same neoplasms have low metastatic potential and respond well to surgical excision, resulting in a symptom-free or medication-free interval,[89] and nonsurgical patients may be medically managed for long periods of time. Recurrence is relatively common with surgical management of insulinoma in ferrets; however, true metastasis, the translocation of malignant cells to a distant organ or lymph node, is uncommon.

Adrenocortical Neoplasms

The second most common neoplasm in domestic ferrets is also of endocrine origin and originates in the adrenal cortex.[2,4,9,10,23,52,57,73,89,95] In the intact ferret, seasonal stimulus of the hypothalamus results in the release of a variety of hormones, including luteinizing hormone, which stimulates sex steroid production from the ovaries or testes. In neutered animals, the absence of gonads results in a lack of negative feedback for the hypothalamus, and, under the constant stimulation of luteinizing hormone, pluripotential cells of the zona reticularis differentiate into cells capable of producing estrogen and other intermediate sex steroid metabolites, including androstenedione and hydroxyprogesterone.[75] Multiple studies have reported the average age of ferrets with adrenal disease at approximately 4.5 years,[9,88,95] but the disease has also been reported in ferrets under 12 months of age,[52] with no sex predilection.

The relatively obvious clinical signs exhibited by most ferrets with adrenal disease contribute significantly to the frequency of their presentation for treatment. Affected ferrets exhibit a constellation of cutaneous, behavioral, and reproductive signs that make them easily identifiable. Characteristic bilateral truncal alopecia develops in about half of affected animals, and patchy hair loss in others. Vulvar swelling may be seen in up to 90% of affected neutered jills.[73,82] The effects of estrogen on the prostatic glandular epithelium in male ferrets may result in dysuria due to prostatic cysts or abscesses; if not treated promptly, azotemia, obstruction, and ultimately uremia are probable sequelae. Finally, the presence of increased levels of testosterone in the male or estrogen in the female may result in a return to intact sexual behavior such as mounting, urine marking, and aggression.

Proliferative lesions of the adrenal cortex are distributed equally between the left and right adrenal glands, and approximately 20% are bilateral.[95] From a clinical (and prognostic) standpoint, proliferative lesions in the adrenal cortex fall into a spectrum ranging from hyperplastic lesions to benign or malignant neoplasms (Fig. 8.1). A good prognosis appears warranted in the case of most extirpated lesions, regardless of location, histologic grade, or completeness of excision.[82,95] It is important to inform owners that lesions in the contralateral adrenal gland occasionally develop, resulting in recurrent disease at a later date, and metastatic disease may be seen in a low percentage of highly anaplastic carcinomas.[66]

Other neoplasms may arise in the ferret adrenal gland. Leiomyosarcomas of the adrenal capsule are common.[36]

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TABLE 8.3 Published Dosages of Drugs Used to Treat Tumors in Ferrets

Drug	Dosage	Mechanism of Action	Use	Adverse Effects
Bleomycin	10 U/m^2 SC[38]	DNA cleavage	Metastatic squamous cell carcinoma in a ferret[38]	• Pulmonary fibrosis in humans
Chlorambucil	• 1 mg/kg PO every 7 d[44] • 20 mg/m^2 PO[68]	Nitrogen mustard derivative, alkylating agent	Lymphoma	• Myelosuppression, (neutropenia and thrombocytopenia)
Cyclophosphamide	• 200 mg/m^2 PO, SC × 4 consecutive days weekly[31] • 10 mg/kg PO[2,9,92] • 80 mg/m^2 PO every 24 h × 3 days every 2 wk[68]	Nitrogen mustard derivative, alkylating agent	Lymphoma	• Myelosuppression, (neutropenia) seen in one ferret at 150 and 200 mg/m^2 SC necessitating discontinuation of medication[44] • GI (nausea, vomiting, diarrhea) • Hemorrhagic cystitis (therefore usually given with SC fluids)
Cytarabine (cytosine arabinoside)	300 mg/m^2 SC every 24 h × 2 days[56]	Competitive inhibitor of DNA polymerase α, incorporated into DNA	Leukemia, lymphoma (especially with CNS involvement)	• Myelosuppression • Mild GI disturbances
Doxorubicin	• 20 mg/m^2 IV[44] • 2 mg/kg[44] • 2.8 mg/kg IV every 3 wk × 3 doses[68] • 30 mg/m^2 IV[68] • 1 mg/kg IV every 3 wk × 4 treatments[2]	Multimodal mechanism of cellular toxicity	Lymphoma, osteosarcoma, and most mesenchymal and epithelial neoplasms	• Hypersensitivity (infusion rate–dependent) • Myelosuppression • GI toxicity • Cardiotoxicity (cumulative dose-related) • Renal tubular damage (cats—repeated dosing) • Tissue necrosis with extravasation
Isotretinoin	2 mg/kg every 24 h PO[72]	Exact mechanism unknown but suspect induction of apoptosis	Cutaneous epitheliotropic lymphoma in a ferret,[72] rarely to prevent squamous cell carcinoma in humans	• Teratogen when taken PO in humans • Myelosuppression in humans • Dry skin, chelitis in humans
L-Asparaginase	• 400 IU/kg SC, IM[44,95] • 5000 IU[68] • 10,000 IU/m^2 SC[56]	Inhibition of protein synthesis in tumor cells lacking L-asparagine synthetase	Lymphoma (in dogs and cats used for cases of relapsed lymphoma to prevent resistance)	• Hypersensitivity reactions (higher risk after repeated exposures); therefore pretreat with diphenhydramine (1 mg/kg IM) or dexamethasone (0.5 mg/kg SC, IM, IV)
Methotrexate	0.5 mg/kg IV[9,68]	Folate analog—depletes the usable folate that is required for purine and thymidylate biosynthesis	Lymphoma (currently it is rarely used in cats and dogs)	• GI toxicity • Myelosuppression at high doses
Prednisone/Prednisolone	• 2 mg/kg every 24 h[40,92] • 1 mg/kg every 48 h[26] • 20 mg/m^2 every 24 h × 2 mo then every 48 h[44] • 2 mg/kg PO every 24 h × 7 days then every 48 h[56] • 1 mg/kg PO every 24 h × 13 weeks then every 48 h[3] • 40 mg/m^2 PO every 24 h[29]	Induction of apoptosis of hematopoietic cancer cells through the glucocorticoid receptor	Lymphoma, brain tumors, can be used to manage hemorrhagic cystitis and hypersensitivities	• Eventually tumor cells of hematopoietic origin resist steroid-induced killing • Polydipsia and hyperglycemia seen at 40 mg/m^2 PO every 24 h that resolved when dose decreased to 30 mg/m^2 PO every 24 h[44]
Procarbazine	50 mg/m^2 PO every 24 h × 14 day[56]	Inhibition of DNA and RNA synthesis	Lymphoma	• Neurotoxicity if given IV in humans
Vincristine	• 0.75 mg/m^2 IV every 7 d[44] • 2 mg/m^2 IV[44] • 0.12 mg/kg IV[2,9] • 0.2 mg/kg IV[95] • 0.5 mg/kg IV every 7 d[26]	Vinca alkaloids, inhibits microtubule assembly	Lymphoma	• Myelosuppression • Peripheral neurotoxicity • Ileus • Tissue necrosis with extravasation (not as severe as doxorubicin)

CNS, Central nervous system; *GI,* gastrointestinal; *IM,* intramuscularly; *IV,* intravenously; *PO,* orally; *SC,* subcutaneously.

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TABLE 8.4 Weight-to-BSA Conversion Chart for Ferrets

Weight (kg)	BSA (m^2)
0.2	0.034
0.3	0.045
0.4	0.054
0.5	0.063
0.6	0.071
0.7	0.078
0.8	0.086
0.9	0.093
1.0	0.099
1.1	0.106
1.2	0.112
1.3	0.118
1.4	0.124
1.5	0.130
1.6	0.136
1.7	0.141
1.8	0.147
1.9	0.152
2.0	0.158
2.1	0.163
2.2	0.168
2.3	0.173
2.4	0.178
2.5	0.183
2.6	0.188
2.7	0.193
2.8	0.197
2.9	0.202
3.0	0.207

Calculations based on ferret-specific formula BSA (m^2) = 9.94 × (body weight in grams)$^{2/3}$ × 10^{-4}.
BSA, Body surface area.
Modified from Jones KL et al. Evaluation of a ferret-specific formula for determining body surface area to improve chemotherapeutic dosing. *Am J Veter Res.* 76.2 (2015):142–148.

These firm neoplasms resemble tumors of the adrenal cortex and cannot be differentiated at surgery. The presence of these tumors may also mask the presence of proliferative adrenocortical lesions on histologic examination unless multiple sections at 1 mm or more are examined. Estrogen receptors have been demonstrated on the smooth muscle cells in several of these tumors, suggesting a possible cause for their development.[61]

Thyroid Neoplasms

Thyroid neoplasms are rare in ferrets. A nonfunctional thyroid follicular adenocarcinoma was reported in one ferret with infiltration into the surrounding tissue,[96] and in another ferret a tumor was identified that had metastasized to the cervical lymph nodes and liver.[11] One case of a C-cell carcinoma (seen along with concurrent adrenocortical adenoma and insulinoma) has been reported.[31] Clinical signs were not observed in any ferret with a thyroid tumor.

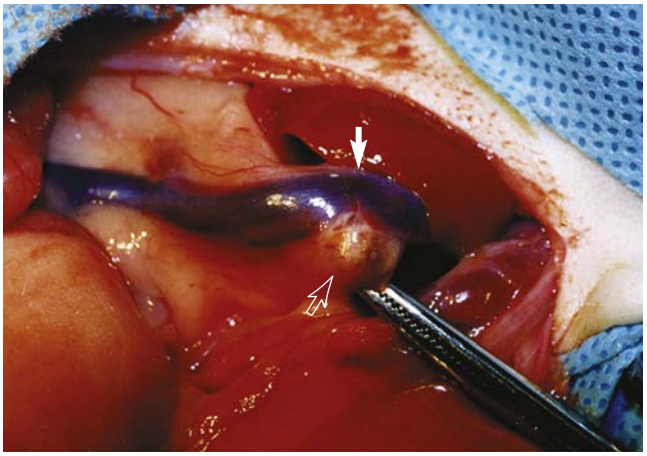


Fig. 8.1 Carcinoma of the right adrenal gland in a ferret *(open arrow),* demonstrating the proximity between these neoplasms and the caudal vena cava *(closed arrow).* Note that degree of malignancy cannot be determined by size or degree of invasiveness as visualized at surgery.

TUMORS OF THE HEMOLYMPHATIC SYSTEM

Lymphoma (malignant lymphoma, lymphosarcoma) is the most common hemolymphatic malignancy in domestic ferrets and the third most common neoplasm overall,[4,9,10,23,52,57,89,95] accounting for 10% to 15% of ferret neoplasms in the United States[52] and Europe.[4,22]

Although causative genetic mutations are well documented in people and in some domestic animal species with lymphoma, these aberrations have not been elucidated in the ferret, and environmental and infectious triggers have yet to be identified. Horizontal transmission of lymphoma in ferrets by using cell or cell-free inoculum in clustered outbreaks has prompted speculation that some variants of lymphoma in ferrets may be the result of a retroviral infection.[26–28]

Classification of Lymphoma

Appropriate classification of lymphoma is paramount to achieve the best therapeutic outcome and requires surgical biopsy in all cases. Clinicians should obtain as much descriptive information as possible for all cases, following the guidelines below, to ensure the most appropriate diagnosis and treatment for each individual. This may also improve prognostic ability in the future.

All diagnostic workups should include both *grading* (histologic description in as much detail as possible), *staging* (classification of disease based on spread of the neoplasm), and *phenotyping* (identifying T- vs B-cell origin).[39] The most commonly accepted grading system in companion animal medicine is the National Cancer Institute Working Formulation, which differentiates cells based on morphology.[59,63] The most commonly accepted staging system in veterinary medicine is the World Health Organization staging system, which is also generally accepted by the American College of Veterinary Pathologists (ACVP).[59] The importance of phenotypic information is illustrated by one study of ferrets with lymphoma treated with chemotherapy, in which those with B-cell lymphoma lived almost twice as long as those with T-cell lymphoma, (8.8 vs 4.3 months, respectively).[1]

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Fig. 8.2 Cutaneous lymphoma in a ferret. Surgical excision of this ulcerated neoplasm *(arrow)* was accomplished and, despite several recurrences, the ferret was still alive 3 years later.

Two other types of lymphoma seen in ferrets are cutaneous lymphoma and gastric lymphoma. Cutaneous epitheliotropic lymphoma is of T-cell origin and possesses a mature lymphocytic phenotype and a profound affinity to infiltrate epithelial structures, such as the epidermis and hair follicles (Fig. 8.2). It alone among the ferret lymphomas does not warrant a poor prognosis at onset, because prolonged survival times (possibly up to 3–4 years) are often seen, especially in cases in which skin lesions are rapidly excised. Unlike epitheliotropic lymphoma (mycosis fungoides) in dogs and people, epitheliotropic lymphoma in ferrets does not necessarily progress to systemic involvement (Sézary's syndrome). It is commonly seen in the feet and extremities of ferrets, resulting in grossly swollen, hyperemic, alopecic feet. Untreated, these lesions grow in size, and multiple lesions will develop. Complete surgical excision of cutaneous lesions can result in prolonged disease-free intervals; chemotherapeutic attempts, both topical and systemic, have generally proved unsatisfactory.[50,72]

Gastric lymphomas, or mucosal-associated lymphoid tissue lymphomas, have also been reported in four ferrets.[25] Considered akin to lymphomas associated with *Helicobacter pylori* infection in people, these neoplasms arise in the stomach of ferrets infected with *Helicobacter mustelae*. Although neoplastic cells varied in phenotype (two lymphocytic and two lymphoblastic forms), all four cases were composed of monoclonal B lymphocytes.[25]

Signalment and Clinical Signs

There is no universal signalment or clinical presentation for lymphoma in ferrets. It may develop at any age and has been reported in ferrets as young as 2 months, and no sex predilection is apparent. Although early reports linked more aggressive, lymphoblastic lymphomas with younger animals,[24,27] more recent studies have demonstrated this not to be the case.[1,63]

The clinical presentation of ferrets with lymphoma is nonspecific and likely reflects the organ systems affected. Ferrets may present with varying degrees of lethargy, inappetence, weakness, diarrhea, dyspnea, or respiratory signs, or they may be completely symptom free. Although splenomegaly and lymphadenopathy may be seen in ferrets with lymphoma, they are not pathognomonic for these conditions and are seen in several other common diseases. Splenomegaly is a common finding in ferrets with various inflammatory conditions, especially of the gastrointestinal tract; enlargement of the mesenteric lymph nodes can also be seen in these conditions. Fat deposits, seen in older ferrets and often seasonally during the winter, may be deposited around peripheral nodes, mimicking lymphadenomegaly.

Laboratory Evaluation

Anemia is the most consistent laboratory abnormality in ferrets with lymphoma and is consistently nonregenerative.[1,81] Lymphocytosis and thrombocytopenia are rare, and neutropenia is only occasionally identified.[1] These findings suggest that results of CBCs and peripheral blood smears may yield valuable information in some cases but are rarely diagnostic for lymphoma. Persistently high lymphocyte counts cannot be used as evidence of lymphoma; as in other species, chronic smoldering infection is a far more common cause of lymphocytosis in ferrets. The ubiquitous nature of *Helicobacter* and coronavirus infection in the U.S. ferret population has tremendous potential for inciting this nonspecific change.

Serum/plasma biochemical results are also inconsistent in patients with lymphoma, with abnormalities more relevant to the location of the disease or organ involvement than to any specific cause.[81] Hyperproteinemia and hyperglobulinemia are rare in ferrets with T-cell lymphoma,[81] and hypoalbuminemia has been documented in animals with intestinal forms. Hypercalcemia was present in 2 of 28 ferrets (both with T-cell lymphoma).[1]

Diagnostic Imaging

Radiography is necessary in ferrets suspected of having lymphoma, although results are not considered diagnostic. Radiographs should be examined for the presence of mediastinal masses, thoracic lymphadenopathy, and pleural effusion, as well as enlargement of the liver, spleen, or kidneys. The absence of radiographic abnormalities, however, does not rule out the possibility of lymphoma.

Ultrasonography is perhaps the most valuable clinical tool available to most practitioners in evaluating ferrets for lymphoma. In addition to evaluating the abdominal and mesenteric lymph nodes, ultrasound also enables the clinician to assess the liver, spleen, kidneys, mediastinum, and sometimes even the gastrointestinal (GI) tract for infiltrative disease. Figs. 8.3 and 8.4 show the gross and ultrasound images of ferrets with lymphoma infiltrating the liver and spleen. Fig. 8.5 demonstrates radiographic findings in a ferret with lymphoma affecting the abdominal lymph nodes. Note that abdominal nodes are often enlarged in older ferrets as a result of chronic bowel inflammation; the finding of severely enlarged abdominal nodes should never be considered evidence of lymphoma without biopsy. Normal radiographic and ultrasound findings for the abdominal lymph nodes and the spleen are published.[65,81a]

In one study, abdominal lymphadenopathy (12 of 14), peritoneal effusion (11 of 14), and splenomegaly (8 of 14) were reported as the most common findings in ferrets with lymphoma.[81] Pleural effusion and osteolytic lesions were less commonly identified in ferrets in this series.[81]

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Cytologic and Histologic Description

Histologic or cytologic examination is the only reliable tool with which to diagnose lymphoma. The definitive diagnosis of lymphoma is best accomplished by a pathologist experienced in evaluating ferret lymph nodes, as often the histologic picture of lymphoma overlaps considerably with that of other non-neoplastic causes of lymphadenomegaly. Avoid biopsy (either needle or excisional) of abdominal lymph nodes whenever possible, because chronic GI inflammation, a common problem in older ferrets, may yield reactive changes almost indistinguishable from lymphoma. Peripheral nodes, such as popliteal and scapular nodes, are less likely to be affected by local inflammation; excisional biopsy of these nodes is easily accomplished, and complications of this procedure are extremely rare (Fig. 8.6).

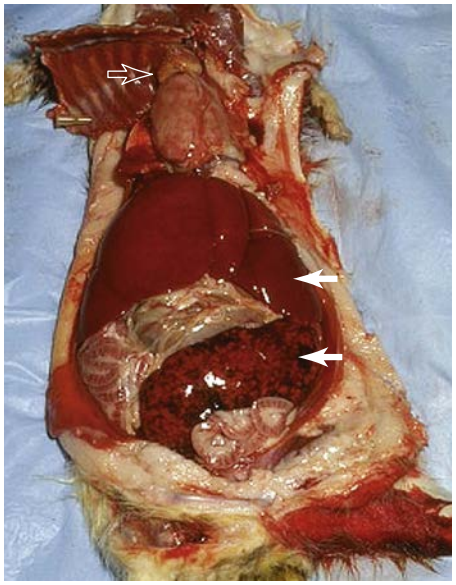


Fig. 8.3 Multicentric lymphoma in a 1-year-old ferret. Note the thymic mass *(open arrow)* and marked hepatosplenomegaly *(closed arrows)* as a result of massive infiltration by this neoplasm.

In many cases, fine-needle aspirates are performed as part of an initial examination, especially when clinical signs strongly suggest lymphoma. Aspirates of enlarged nodes may result in a diagnosis in the hands of a trained pathologist or experienced practitioner, but erroneous diagnoses may result from sample preparation, reactive changes, and neoplasms composed of well-differentiated lymphocytes. The possibility of erroneous diagnosis is increased when aspirates of abdominal nodes are performed. Reference results for cytologic populations of mesenteric lymph node aspirates in ferrets are available.[65]

In cases of suspected leukemia, a bone marrow aspiration via the proximal femur using an 18- to 20-gauge collection needle may yield good results. An alternate technique for obtaining a sample is a core bone biopsy, which may provide a better diagnostic yield. In most cases of leukemia, the bone marrow is hypercellular and often monomorphic. Microscopic examination reveals a significant decrease or total absence of normal marrow elements such as fat.

Pathologists are commonly asked to evaluate splenic aspirates from animals with enlarged spleens. More than 95% of these cases are the result of extramedullary hematopoiesis (EMH), a stereotypical response to chronic (GI) inflammatory disease. Evidence of erythrocyte precursors, megakaryocytes, and abundant peripheral blood on splenic aspirates suggests a diagnosis of EMH. Alternatively, cases of splenic lymphosarcoma are identified by the presence of a monomorphic population of neoplastic lymphocytes with large nuclei, prominent nucleoli, and minimal cytoplasm as well as an absence of erythrocyte precursors and minimal peripheral blood elements. Mitotic figures should be present within the monomorphic cell population.

Treatment

The goal in treating any patient with cancer is to achieve improvement in their clinical signs and quality of life. Comparative data on the various published protocols and chemotherapeutic agents used in ferrets do not exist as they do for human and canine patients; therefore any protocol followed should be based on the

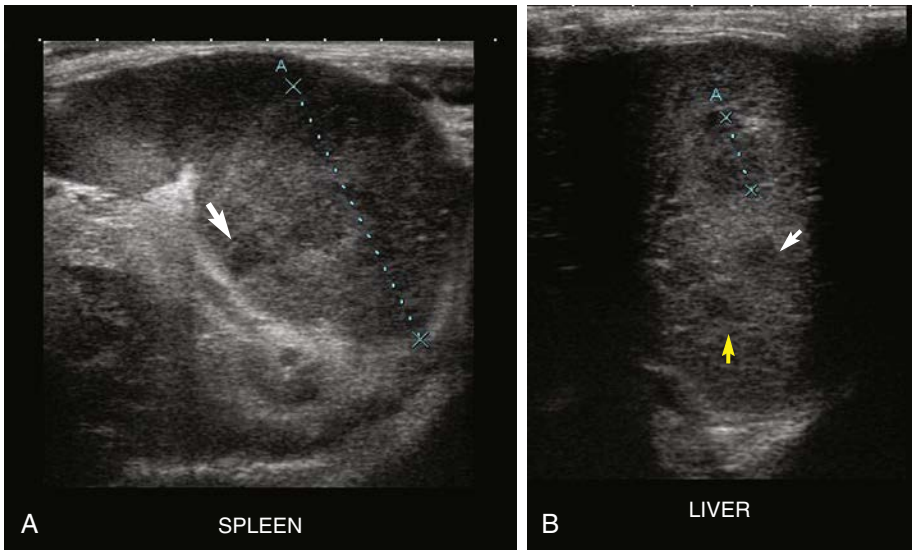


Fig. 8.4 Ultrasound images from a ferret with lymphoma demonstrating infiltrative disease in the spleen (A) and liver (B). Note the mottled appearance and hypoechoic regions *(arrows)* in both tissues. (Courtesy of Dr. Jantra Suran.)

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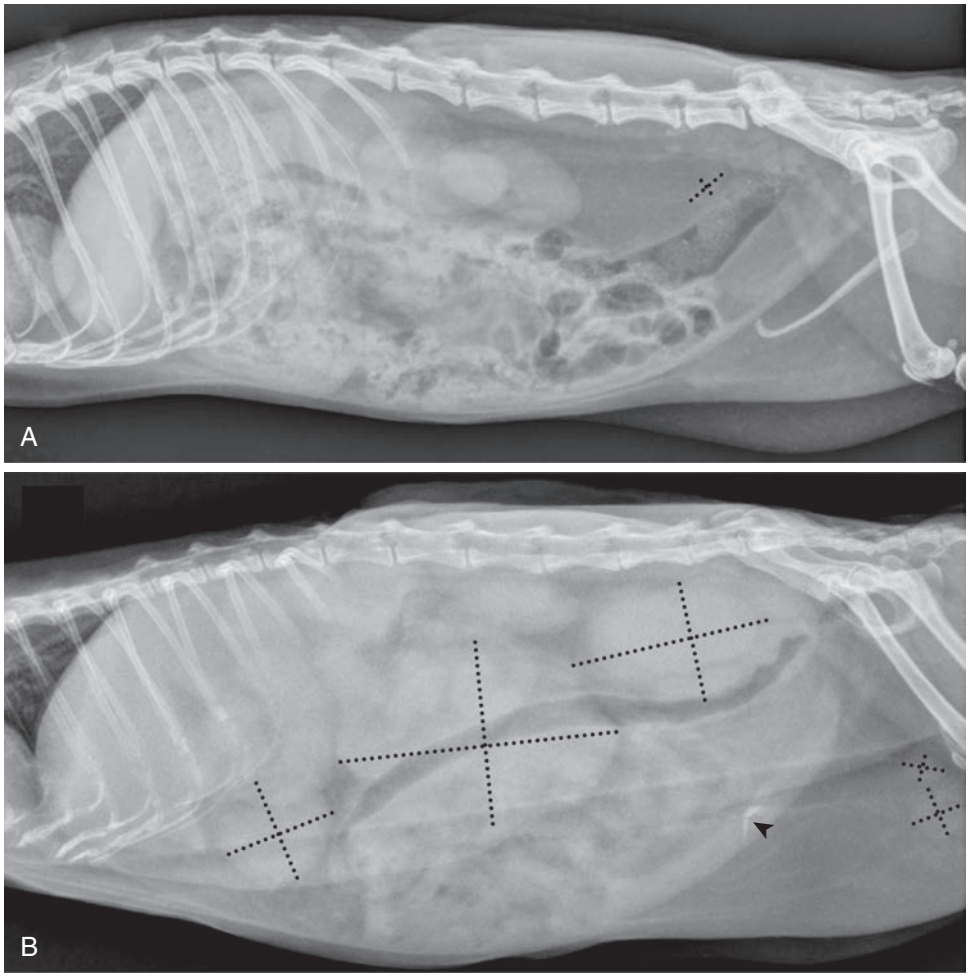


Fig. 8.5 (A) Lateral abdominal radiograph of a clinical healthy ferret demonstrating the size of a normal caudal mesenteric lymph node *(dotted lines)*; Lateral abdominal radiograph of a ferret with lymphoma (B). Enlarged lymph nodes *(dotted lines)* displace viscera. Enlarged inguinal node are visible *(dotted lines* at right.) Wet hair artifact (arrowhead) is superimposed on the caudoventral abdominal body wall. (Courtesy of Dr. Jantra Suran.)



Fig. 8.6 Presentation of submandibular lymph node enlargement *(arrow)* in a ferret with lymphoma.

ease of administration, client and veterinary preference, level of comfort for the patient, and the owner's goals (i.e., achievement of complete remission vs palliation).

In most cases, lymphoma is a systemic disease requiring chemotherapy. In rare cases where a single organ is affected (usually extranodal lymphoma), surgery or radiation therapy can lead to a successful cure, but the patient must be closely monitored to look for signs of recurrent disease or spread. Combination therapy may be useful in ferrets as in other domestic species.

Chemotherapy

Chemotherapy may be used for induction, maintenance, reinduction, or as a rescue for patients with lymphoma. Most lymphoma protocols published for ferrets use some modification of the CHOP (cyclophosphamide, hydroxydaunorubicin [doxorubicin], vincristine [Oncovin], and prednisone) protocol that was adapted from human oncology; cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine (Oncovin), and prednisone. In two published ferret protocols using modified COP (cyclophosphamide, vincristine/oncovin, prednisone) or CHOP, both incorporated L-asparaginase, and one also incorporated methotrexate. Several

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case reports using a modified COP protocol have resulted in long-term clinical improvement.[9,20,22,24,44,74] Based on the evidence in canine[43,69] and feline patients, the CHOP protocol (or its variants) should be reserved for those ferrets with intermediate- to high-grade lymphoma. For ferrets with small cell or indolent lymphoma, a protocol using chlorambucil and prednisone similar to that used in cats may be more appropriate. The recommended dosage for cats with small cell, mucosal alimentary lymphoma is chlorambucil (20 mg/m^2 by mouth [PO] every 2 weeks or 2 mg PO every other day) and prednisone or prednisolone (initially 1–2 mg/kg PO daily, reduced to 0.5–1.0 mg/kg every other day over several weeks).[85] In addition to multimodal chemotherapy, single-agent therapy with doxorubicin has been described in ferrets with lymphoma with variable success.[56] The indolent nature of small cell lymphoma in some ferrets is supported by the fact that some ferrets can survive up to 2 years with no treatment at all.[56]

In cases where multiple intravenous drugs will be administered, placing a subcutaneous venous access port (VAP) may be helpful to prevent repeated sedation for intravenous (IV) drug administration. Specific VAPs are made for ferrets; VAPs designed for rats are also available and may be more useful, especially in small ferrets. If a VAP is not placed, the ferret must be sedated because chemotherapeutic agents should never be administered into a vessel that has had multiple attempts at IV placement.

Because intravenous access may be difficult in ferrets, a novel chemotherapy protocol has been established that uses only oral or subcutaneous chemotherapeutic agents. This 27-week protocol uses prednisone (PO), L-asparaginase (subcutaneously [SC]), cyclophosphamide (PO), cytarabine (SC), methotrexate (intramuscularly [IM]), chlorambucil (PO), and procarbazine (PO). The only drawback to this protocol is the compounding requirement for oral chemotherapeutic drugs; these liquid agents should only be administered at a veterinary hospital and not by the owner.

Palliative Chemotherapy

Palliative chemotherapy is used to diminish clinical signs in cases of unresectable, disseminated, or recurrent disease. When using chemotherapy with the goal of improved comfort and organ function, the agents are not usually administered based on a specific schedule but instead on the status of the patient and the discretion of the owner and client. Prednisone or prednisolone (PO), chlorambucil (PO), and L-asparaginase (SC), or a combination of the three, are used for this purpose because of their ease of administration and mild adverse effects.[56] Prednisone may be used alone to reduce tumor bulk and improve the ferret's appetite and attitude.

Doses may be used from published protocols with the dosing interval altered to best suit the patient. For treatment of lymphoma, prednisone has been used at dosages of 0.5 mg/kg PO every 12 hours,[78] 1 mg/kg PO every 24 hours,[3] 40 mg/m^2 PO every 24 hours,[29] and 2 mg/kg PO every 24 hours for 1 week and then 2 mg/kg PO every 48 hours or 1 mg/kg PO every 24 hours.[56] L-asparaginase has been used at doses of 10,000 IU/m^2 SC and 400 IU/kg IM.[56] Chlorambucil has been used in ferrets at 1 tablet (2 mg) PO every 24 hours or ½ tablet (1 mg) PO every 24 hours for 2 days in a row.[56] One of the authors (N.W.) has used prednisone (1 mg/kg PO every 24 hours) and L-asparaginase (400 mg/kg SC) for palliative treatment of lymphoma. Additionally, the author (N.W.) uses oral prednisone and an initial dose of L-asparaginase to decrease tumor size in patients and then a second dose of L-asparaginase when the tumor regrows.

Adverse Effects of Chemotherapy

As with other species, adverse effects of chemotherapy in ferrets are gastrointestinal damage, myelosuppression,[29] and loss of pelage.[3] After certain immunosuppressive chemotherapeutic agents such as cyclophosphamide are administered, evaluate a complete blood count within 7 to 10 days for evidence of leukopenia, specifically neutropenia (which often manifests as diarrhea in affected animals). Administration of antimicrobials and gastroprotectants may be required for severely neutropenic animals. In cases such as these, even diminished doses of the same agent may result in precipitous drops in leukocyte numbers, requiring a change to a different chemotherapeutic agent. Another common adverse effect of prednisone/prednisolone is hyperglycemia, requiring glucose monitoring (and possible dose reduction) while this agent is being used.

The proteinaceous nature of L-asparaginase may result in anaphylaxis; hence, it is not recommended for use more than three or four times in the same patient. Pretreatment with diphenhydramine (1 mg/kg IM) may be beneficial. Note that the period of asparagine depletion in ferrets is unknown.

Nausea is a common adverse effect of many chemotherapeutic agents. Pretreatment with antiemetics such as metoclopramide, ondansetron, or maropitant citrate is recommended in most cases; GI protectants may also be beneficial.

Radiation Treatment

Lymphoma is highly responsive to radiation therapy. With the advent of more advanced equipment such as linear accelerators, radiotherapy offers a safe modality for either primary or adjunctive treatment. It is most beneficial in a single neoplasm in the abdominal cavity but can also be used on a single peripheral lymph node. Although multiple treatments to a site are preferred, even a single dose of radiation will shrink most tumors and greatly improve outcomes. Radiation can also be used as a rescue treatment for solid masses not responding to chemotherapy. Half- and total-body irradiation protocols are used in other species, but only limited data is available for its use in ferret.[56] Radiation therapy may also be used as a palliative therapy for patients that have localized disease such as rectal lymphoma, mediastinal lymphoma (when dyspnea or precaval syndrome is present), or focal bone involvement.[85]

Ancillary Treatments

The most important ancillary treatment in any cancer patient is the provision of proper nutrition.[62] Cancer cachexia is a well-documented paraneoplastic syndrome in all species, consisting of progressive weight loss despite adequate nutritional intake.

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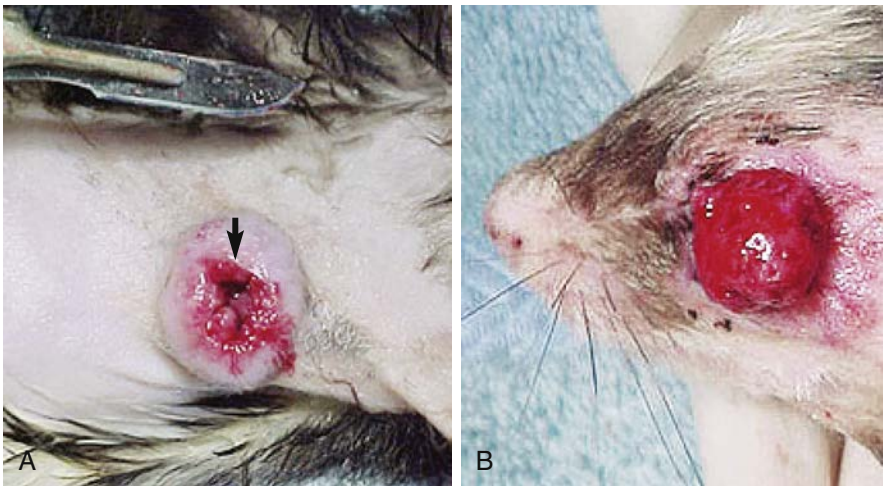


Fig. 8.7 Multiple sebaceous adenomas in a ferret on the thorax (A) and face (B). The neoplasm on the face did not involve the orbit. Occasionally, the centers of these neoplasms may be cavitated *(arrow)*. Although these lesions were impressive in appearance, surgical removal was curative.

Maintaining nutritional status improves immune response, GI function, and surgical healing and may also improve a cancer patient's chances of remission. Most high-quality ferret diets are ideal because of their high protein and fat content. Supplementation can also be provided with formulas available for ferrets (Carnivore Care, Oxbow Animal Health, Murdock, NE; Emeraid IC Carnivore, EmerAid LLC, Cornell, IL) or, in their absence, commercial gruel diets used for cats. Most ferrets can be encouraged to eat or are easily force-fed.

Although clients often ask about holistic or herbal therapies, free radical scavengers, or immune stimulants, avoiding these products is recommended for patients receiving chemotherapy. The goal of chemotherapy is to suppress the immune system and often to induce cell death and free radicals; immune stimulants may interfere with this process. If necessary, consult with both a veterinary oncologist and a veterinarian trained in holistic/herbal medicine before initiating any alternative therapies. In addition, ferrets that have received chemotherapy should not be vaccinated for the remainder of their lives, because vaccines stimulate the immune system, which may terminate remission.

Other types of hematopoietic neoplasms are rarely seen, with the spleen as the most common site of origin. Myelolipoma, a benign neoplasm of immature leukocytes admixed with well-differentiated adipocytes, may occasionally present as a space-occupying mass in the spleen, but it is of no clinical significance.[51] Histiocytic sarcoma, a malignant hematopoietic tumor of histiocytes, is a rare aggressive malignancy most often arising in the spleen. In a recent report of four ferrets with this tumor, splenomegaly or splenic nodules, as well as mesenteric lymphadenopathy were common findings. Surgical and chemotherapeutic intervention resulted a survival time of 9 days to 5 months.[84] Thymoma, a neoplasm involving the epithelial elements of the thymus, may present as a mass lesion of the anterior thorax and can be easily confused for thymic lymphoma; presenting signs include vomiting, lethargy, and dyspnea.[83] Malignant plasma cell tumors are rarely documented in ferrets. In a study of six cases, the most common clinical sign was hind limb paresis (5/6), the most common hematologic abnormality was hyperglobulinemia (5/6), and osteolysis was seen on radiographs of 3 of 4 ferrets. Most ferrets (5/6) had tumors in more than four locations. Chemotherapy was attempted in one ferret that showed no response to treatment. Prognosis was poor, with most (4/6) ferrets being euthanized less than a week after diagnosis, although one survived for 107 days after diagnosis.[14] Osteolytic lesions have been reported in several other cases.[29,53,54]

TUMORS OF THE SKIN AND SUBCUTIS

The skin and subcutis is the third most common location for neoplasia in ferrets, accounting for approximately 20% of cases in most reports.[52,64,95] Most neoplasms of the skin are benign and can be successfully treated with surgical excision alone or together with radiation therapy.[46] A single ferret can have multiple cutaneous tumors that are the same or a differing type.[46,87] Mast cell tumors and tumors of basal cell origin are the two most commonly diagnosed skin tumors.

Unlike mast cell tumors in the dog and cat, ferret mast cell tumors are universally benign, do not metastasize, and warrant a good prognosis.[46,87] Recent studies have shown a preponderance in males with an average age of 4.5 to 5 years,[46] and 30% of ferrets had more than one mast cell tumor.[87] Grossly, these neoplasms are discrete, flat, round, plaque-like, and crusted[87] and are often pruritic. Mast cell tumors can be readily diagnosed by cytologic examination, but slides must be viewed with non-Wright's stains (including Diff-Quik) to properly demonstrate granules.[87]

Tumors of basal cell origin, including sebaceous adenoma and sebaceous epithelioma, are warty, exophytic neoplasms (Fig. 8.7) that may attain a large size and ominous appearance (largely as a result of self-trauma) but are almost invariably benign. These tumors are common on the head and neck and occur in ferrets at an average age of 5.2 years with no apparent sex predilection.[46] Tumors occasionally cause irritation, and the resulting self-trauma may result in local inflammation and infection. In very rare cases, these tumors may give rise to squamous cell carcinoma.[95] Surgical excision is curative and should be accomplished early.

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Neoplasms of apocrine scent glands are the third most common neoplasm seen in the skin and subcutis in ferrets. Unlike the above-described neoplasms, tumors of apocrine glands are largely restricted to the deeper layers of the skin and subcutis and have a distinct predilection for malignant behavior. Apocrine neoplasms are most common in areas where scent glands are concentrated (head, neck, prepuce, and vulva). Approximately 75% of preputial neoplasms of apocrine origin (100% of the less common perianal and perivulvar tumors) are malignant, exhibiting aggressive infiltration of local tissues, metastasis to local nodes, and occasionally pulmonary metastasis. Complete surgical excision of apocrine malignancies is difficult because of their rapid and aggressive growth, as well as the distinct possibility of presurgical metastasis. To minimize the potential for metastasis, excise any suspected apocrine neoplasms with wide surgical margins. Use advancement flaps or Y-plasty, if necessary, to close or reconstruct the prepuce. In cases of apocrine carcinoma of the prepuce, appropriate surgical treatment may entail amputation of the prepuce and urethrostomy. Radiation therapy may be a valuable postoperative treatment to aid in eliminating any local residual malignant cells, and chemotherapy can be used as an adjunct to decrease the risk of metastasis.

Low-grade subcutaneous sarcomas are occasionally seen in the subcutaneous tissues. Many of these neoplasms arise from smooth muscle (erector pili) associated with hair follicles along the dorsal midline (piloleiomyosarcomas).[71] These raised, often ulcerated nodules occur most commonly on the head and neck in male ferrets with an average age of 3.1 years.[46] Although cutaneous fibrosarcomas may also be seen in the skin of ferrets[95] and have been reported in association with vaccination in this species,[60] these neoplasms do not manifest the aggressive behavior associated with vaccine-related sarcomas in cats.[60] Regardless of their derivation, subcutaneous sarcomas are generally low-grade malignancies with a slow growth rate and low metastatic potential; they all respond well to wide surgical excision.

Mammary gland neoplasms are rare in ferrets. One report of six cases described only benign mammary neoplasms[95]; a second report of nine cases described seven benign tumors and two malignancies (both in males).[46] Three cases of simple mammary hyperplasia have also been reported,[58] two of which were seen in conjunction with adrenal carcinoma.

A range of other neoplasms of the skin and subcutis have been reported in ferrets. Benign neoplasms seen in the skin include lipomas, squamous papillomas, and tumors of sebaceous or eccrine sweat glands.[80] Reported malignancies include adenocarcinomas of the ears[32] and lacrimal glands,[13] liposarcomas,[18,34] epitheliotropic lymphoma (as previously discussed), and squamous cell carcinoma (which may occasionally arise from the lining of the anal sac).[95]

Subcutaneous neoplasms of the ventral abdomen with marked morphologic and immunohistochemical similarities to adrenocortical tumors have been reported.[80] In each case, the ferret did not display systemic signs associated with endocrinopathy, and a primary adrenocortical tumor could not be identified.

General guidelines for treating cutaneous neoplasms in ferrets are similar to those in traditional pet species. Early surgical intervention is the rule with cutaneous neoplasms; most neoplasms are benign, and most malignancies are of low grade and can be successfully treated with early surgical excision with wide margins. Submit all neoplasms for histopathologic evaluation to provide an accurate diagnosis, as well as recommendations for additional treatment, if any. Surgically excise all preputial or perivulvar/perianal neoplasms as early as possible, after careful palpation and survey radiographs to detect potential metastasis. Follow-up radiation therapy may be useful in malignancies in which sufficient surgical margins cannot be obtained.

Vascular neoplasms (hemangioma, hemangiosarcoma) of the skin and subcutis are occasionally seen in ferrets. (See vascular neoplasms below.)



Fig. 8.8 Biliary cystadenoma in a ferret. Because of their aggressive nature, these histologically benign tumors *(arrows)* are best treated with lobectomy or, at a minimum, wide surgical excision.

TUMORS OF THE GASTROINTESTINAL TRACT

Neoplasms of the gastrointestinal tract are frequently seen in ferrets. The liver is a particularly common site for metastasis, particularly malignant lymphoma and adrenocortical carcinoma.[95] It is also a relatively common site for the development of primary neoplasms. Biliary cystadenoma/cholangioma is by far the most frequent; however, cholangiocarcinoma, hepatocellular carcinoma, and hepatoma are also observed.[95] In most cases, ferrets with hepatic neoplasia are presented for nonspecific signs or are asymptomatic. Increases in alanine transaminase or alkaline phosphatase activity are occasionally present, but clinicopathologic abnormalities are usually mild and nonspecific. A cranial abdominal mass may be identified by palpation or on radiographs but is most readily apparent on abdominal ultrasound scanning.

Diagnosis of biliary neoplasia is especially important in this species because of the predilection for neoplasms that appear benign to exhibit malignant behavior (replacing one or more lobes of the liver and ultimately resulting in hepatic failure) (Fig. 8.8). Biliary cystadenocarcinomas are differentiated from biliary cysts or cystadenomas (a common incidental finding in this species) by one or more of the following: the presence of clinical signs, abnormalities

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in liver-specific biochemical results, or expansive growth over time documented by serial abdominal ultrasound scanning. Hepatic carcinoma and cholangiocarcinoma will, over time, result in high hepatic enzyme levels, eventual hepatic failure, and other clinical signs such as profound anemia, hemoperitoneum, and ascites.

When possible, biopsy all hepatic neoplasms, especially those involving multiple liver lobes. Peripheral indices of clotting are recommended before any invasive procedure, including fine-needle aspirate; if this is not possible, pretreatment with vitamin K may be prudent to minimize the risk of bleeding.

If a neoplasm is confined to one lobe of the liver, lobectomy is recommended. Lobectomy of two lobes is possible but may lead to further compromise of the patient. Because of the aggressive nature of biliary tumors in ferrets, remove any cystic lesion of the liver with wide surgical margins or lobectomy. Neoplasms involving multiple lobes warrant a poor long-term prognosis; however, survival times of several months or more may be seen with hepatocellular carcinoma in ferrets. Ferrets with malignancies of the biliary system usually die within a short time frame.

Neoplasms of the exocrine pancreas are occasionally seen in ferrets and are most often malignant, exhibiting infiltrative growth, explantation, compression of ducts within the pancreas and liver,[42,70,90] and metastasis to additional organs.[90] Complete surgical excision of these tumors is unlikely before they begin to extend into other areas of the abdominal cavity.

Malignant lymphoma is the most common neoplasm affecting the GI tract. This is understandable considering that (1) the GI tract contains more than half of all lymphoid tissue in the body of ferrets, and (2) the high prevalence of chronic inflammatory disease in the stomach and intestine. In lymphomas arising in the gastrointestinal tract, the intestine is the most common site of origin, followed by the stomach, liver, colon, and oral cavity. Lymphoma of the intestine carries a poor prognosis because of the disruption of the intestinal barrier and absorption of toxins from the GI tract; therefore it can be refractory to treatment.[9] The incidence of intestinal lymphoma may be even higher than reported, because many ferrets with variable GI signs do not undergo biopsy and remain undiagnosed. In some cases, steroids likely are used to alleviate clinical signs without biopsy, which may lead to incorrect assumptions regarding potential survival times and response to therapy.

Adenocarcinomas develop primarily in the stomach and intestines and are locally aggressive, often infiltrating multiple layers of the wall with metastasis to local lymph nodes. Intestinal adenocarcinoma tends to incite a prominent scirrhous response, often resulting in obstruction (as opposed to intestinal lymphomas, which do not result in a scirrhous response). This same scirrhous response, however, tends to entrap the malignant epithelial cells, allowing visualization of the tumor margins and facilitating complete excision. Prognosis is heavily influenced by the presence or absence of presurgical metastasis. These masses can be identified by palpation and diagnostic imaging such as ultrasound, computed tomography, or a GI contrast study. Perform a resection and anastomosis whenever solitary intestinal masses are present without gross evidence of metastatic disease. Other uncommon tumors of the GI tract, including colonic polyps[12] and gastrointestinal stromal tumors,[35] have been reported.

Tumors of the oral cavity are occasionally seen, are commonly malignant, and are usually associated with a poor prognosis. Squamous cell carcinoma, the most common, is an aggressive neoplasm of the alveolar lining epithelium that invades underlying bone, resulting in tooth loss, disfigurement, and inappetence. In treating ferrets with this neoplasm, reports of chemotherapy[37] and combined surgical and radiation therapy[38] showed poor to equivocal results. Intralesional chemotherapy may also be attempted, following current recommendations for companion animals. Early, aggressive treatment provides the best opportunity for resolution of squamous cell carcinoma. Other malignancies, including fibrosarcoma[9] and melanoma,[19] have been reported in the oral cavity and respond poorly to all forms of treatment.[9]

TUMORS OF THE REPRODUCTIVE TRACT

Whereas earlier reports indicated a high prevalence of these neoplasms,[6,17] the common practice of early neutering makes them a rarity today. Clinical signs of reproductive neoplasia in ferrets vary and are often nonspecific; many are found as incidental finding during neutering procedures. In most cases, surgical excision of affected gonads is curative.

Testicular neoplasms are most common in retained testes. Affected males may show signs of hyperestrogenism, including intact sexual behavior, aggression, a prominent musky odor, and a poor, greasy hair coat. Multiple neoplasms may be seen in retained testes; in one testis, four distinct neoplasms (interstitial cell, seminoma, Sertoli cell, and a carcinoma of the rete testis) were seen.[95] Smooth muscle tumors of the testis have also been reported.[45]

Ovarian tumors often result in no overt signs; in a few cases, affected animals exhibit reproductive failure or abnormal reproductive status.[55] Ovarian tumors (granulosa cell tumors, teratomas, thecoma,[55] Leydig cell tumors, and sex cord-stromal tumors)[95] have been reported, often as incidental findings during routine spays. Teratomas may attain a size that is obvious on routine palpation or may be identified via survey radiographs as a result of the presence of bone within the tumor mass. One reported Leydig cell tumor metastasized to a regional lymph node.[95]

Most neoplasms of the ferret uterus are of smooth muscle origin. Whereas approximately 75% are malignant based on histologic appearance,[95] metastatic disease has not been reported, and surgical excision is curative. Nonmuscular tumors of the uterus are extremely rare in ferrets. One uterine adenocarcinoma and one deciduoma have been seen by the author (B.W.). On histologic examination, regressing implantation sites in female ferrets may be mistaken for uterine carcinoma as a result of the profound atypia of maternal presymplasmal cells.

TUMORS OF THE MUSCULOSKELETAL SYSTEM

Neoplasms of the skeletal system are occasionally seen in ferrets and generally result in a clinical appearance that is

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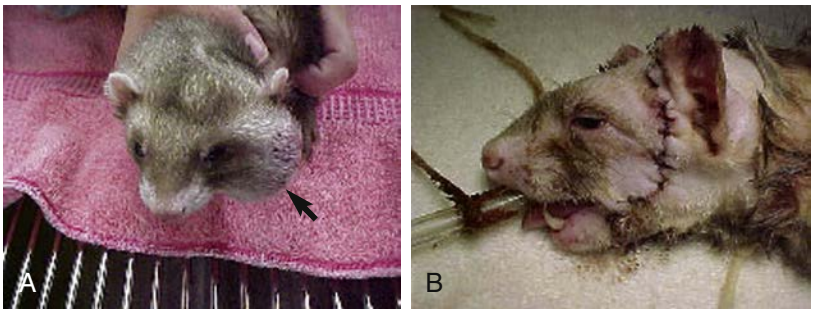


Fig. 8.9 Preoperative (A) and postoperative (B) images of a malignant peripheral nerve sheath tumor *(arrow)* in a ferret. Removal was achieved with cryosurgery; however, facial nerve paralysis was encountered after surgery. (Courtesy Dr. Darrell Kraft, Pet's Choice Animal Hospital, Woodinville, WA.)

obvious to both owner and practitioner. Chordomas are the most common neoplasm of the musculoskeletal system in ferrets.[95] They most commonly appear as irregularly round, whitish gray, firm, club-like swellings of the tail tip. This low-grade malignancy (arising from primitive notochord) also may develop in a vertebrae in any region of the spinal column.[21] These neoplasms are locally aggressive, destroy the vertebral body in which they arise, but only rarely metastasize.[33,93] Radiographs reveal a focally extensive vertebral lesion that is both lytic and proliferative. Tail tip chordomas may be easily cured by amputation, but they carry a poor prognosis when they affect other parts of the spinal column because of their infiltrative nature.

True bone tumors (osteomas, osteosarcomas, and chondrosarcomas) are seen occasionally. Osteomas most commonly arise on flat bones, including the skull and ribs, and progress slowly. Surgical removal may be accomplished with the help of radiographic imaging to more easily delineate margins; however, many osteomas regrow when excision is incomplete. Osteosarcomas are rarely reported in ferrets[91] and may arise on either flat or long bones. If possible, amputate the affected limb, because these malignancies are locally destructive, and incompletely excised neoplasms can recur. Noncore biopsy of malignant bone tumors may result in an erroneous diagnosis because of the pronounced periosteal reactions surrounding these neoplasms.

Tumors of skeletal muscle are extremely rare in ferrets.[95] Rhabdomyosarcomas (malignant tumors of skeletal muscle) have been reported.[52,95] These neoplasms are treatable by radical excision or amputation if present on the limbs.

TUMORS OF THE NERVOUS SYSTEM

Neoplasms of the nervous system are rare, accounting for fewer than 0.5% of reported tumors in ferrets.[95] These tumors equally affect the central nervous system (brain and spinal cord) and peripheral nervous system (peripheral nerves and ganglia). Tumors of the central nervous system (CNS) generally lead to the development of neurologic signs, including ataxia and seizures, whereas those of the peripheral nervous system result in body-surface masses that owners usually notice before any neurologic signs develop.

When the cause of neurologic signs in ferrets is being considered, intracranial tumors are very unlikely, ranking as only the third most common cause of neurologic signs. Hypoglycemia due to insulinoma is by far the most common cause of neurologic signs in ferrets, followed by bacterial infections of the CNS.

Clinical signs associated with intracranial tumors vary and are often nonspecific. Lateralizing signs, such as turning toward the side of the lesion, head tilt, ataxia, cranial nerve deficits, normocellular cerebrospinal fluid, and uncontrolled seizure activity in the presence of normal blood glucose levels suggest an intracranial neoplasm, although nonspecific. Hindlimb weakness and ataxia, although suggestive of a spinal cord tumor, are extremely common presenting signs for a wide variety of diseases in ferrets. Currently, successful treatment of CNS tumors has not been reported.

The most common neoplasm of the CNS (including the eyes) in ferrets is malignant lymphoma. Primary tumors of the brain and spinal cord are rare and usually result in severe neurologic deficits over time. Astrocytomas are the most common primary brain tumors, followed by granular cell tumors,[79] meningiomas,[52,95] primitive neuroendocrine tumors, and a choroid plexus papilloma.[86] Primary spinal cord tumors are more rare, with a single intradural teratoma reported.[48] Of all primary brain tumors, meningiomas show the most promise for surgical excision because they are discrete neoplasms arising from the meninges and tend not to infiltrate the neuropil. Antemortem diagnosis of meningioma is a significant challenge; computed tomography scanning or magnetic resonance imaging is used to detect the presence of the tumor; meningioma should be suspected when any tumor is located along the meninges.

Neoplasms of the peripheral nervous system carry a significantly improved prognosis over those in the CNS, as they tend to be restricted to the skin and subcutis. Prognosis is based on the degree of malignancy and infiltration of local tissue. In one review, both benign and malignant peripheral nerve sheath neoplasms were identified.[95] Malignant peripheral nerve sheath tumors generally exhibit rapid growth and tend to infiltrate adjacent tissue to a higher degree than their benign counterparts, rendering complete excision more difficult (Fig. 8.9). In many cases, repeat surgery is required to effect a cure. Although these neoplasms may be seen at any site in the body, the head (and, interestingly, the eyelids) appear to be a common site. Tumors of nerve sheath origin may be misdiagnosed as fibrosarcoma or leiomyosarcoma when immunohistochemical procedures are not used. Excise these tumors with wide surgical margins as soon as possible after diagnosis,

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because growth in areas with high skin tension may result in large defects that are difficult to close. Moreover, incomplete excision of these tumors often results in a recurring neoplasm that shows both increased cytologic and behavioral malignancy, to include more rapid growth and infiltration. Radiation therapy may help minimize or prevent recurrence at the surgical site or may be used to reduce tumor size before surgery.

Ganglioneuromas are rare neoplasms of the peripheral nerve ganglia.[52,95] These well-differentiated neoplasms with neurons and glia in a matrix of neural tissue are reported close to the right adrenal gland. Close examination is required to differentiate these nodules from normal ganglia on a histologic basis; however, these tumors tend to be much larger than ganglia, ranging up to 1.5 cm in diameter. These tumors have no apparent clinical signs and on gross inspection are often misjudged to be adrenal tumors.

TUMORS OF THE URINARY SYSTEM

Although rare (comprising less than 1% of tumors in one study),[9] primary neoplasms of the kidneys and bladder have been reported in ferrets. As with other species, signs of neoplasia in the urinary system include hematuria and stranguria or dysuria. Diagnostic workups should include abdominal radiographs, ultrasound, and urinalysis (with urine culture if warranted) to rule out more common causes such as adrenal-associated prostatic cysts, crystalluria, or urolithiasis.

As with other systems, the most commonly reported tumor in the urinary system is lymphoma.[95] The most common primary neoplasm of the urinary tract is transitional cell carcinoma and has been reported in the kidneys[7,95] and bladder.[9] In the bladder, transitional cell carcinoma is generally associated with a poor prognosis. Because the presenting signs are vague, diagnosis is generally achieved only after extensive local invasion has occurred.[9] Once identified, these tumors likely would be a surgical challenge, especially in the area of the trigone. For unresectable tumors, chemotherapeutic agents that inhibit COX-2 enzymes have shown promise in dogs and may ameliorate clinical signs and prolong life in ferrets; other, more traditional agents such as doxorubicin, cisplatin, and cyclophosphamide may also be useful, but appropriate dosages in ferrets have not been defined.

Renal carcinomas and adenomas have been reported in ferrets.[47,52] These unilateral neoplasms of the kidney are most often encountered at necropsy, because most tend to be slow-growing with low metastatic potential. In one case, metastasis was noted in multiple organs.[47] On ultrasound examination, renal neoplasms generally present as cystic areas within the kidney, similar to benign renal cysts. If biopsy is not feasible, serial ultrasound examinations are recommended to monitor for continued growth and a change in echogenicity.

TUMORS OF THE RESPIRATORY SYSTEM

Neoplasms involving the lung are generally of metastatic origin, although one undescribed primary neoplasm of the lungs has been reported.[52] The lungs are a common site for the metastasis of lymphoma; clinical signs may include marked pulmonary edema or effusion, which may be significant enough to mask the radiologic signs associated with a disseminated tumor. Pulmonary metastasis of other neoplasms would likely go unnoticed in most cases. Chemotherapy may be of benefit in metastatic lymphoma.

VASCULAR NEOPLASMS

Hemangiomas and hemangiosarcomas are occasionally seen in ferrets. Most arise in the skin or subcutis,[95] although endothelial neoplasms are also seen in the liver,[15] spleen, pancreas, lymph nodes, and free-floating in the abdomen. The incidence is equal in male and female ferrets, and the average age is 4 years.[46] Although more than half of cutaneous vascular neoplasms exhibit histologic evidence of malignancy, they are low-grade malignancies with slow growth, and metastasis is not seen.[95] Excision of cutaneous neoplasms is curative. Coat color and pigmentation do not appear to be risk factors in the development of this neoplasm (as in other domestic species).

However, the prognosis for animals with visceral hemangiosarcoma is significantly worse. These tumors tend to grow more aggressively within abdominal organs and may rupture at any time, seeding the abdomen with metastatic tumors[16] or resulting in fatal hemorrhage. For ferrets with visceral hemangiosarcomas, prognosis is guarded, and early surgical intervention is indicated when the neoplasm is restricted to a single site.[16] One report of combined surgical/metronomic chemotherapeutic treatment of a hepatic hemangiosarcoma is available.[67]

MISCELLANEOUS NEOPLASMS

Mesotheliomas are uncommon malignancies of ferrets that bode extremely poorly for any affected animal.[94] These tumors arise in the abdominal cavity and spread extensively before the appearance of clinical signs. The most common clinical sign is profound ascites ("malignant" ascites).[94] Abdominocentesis is recommended in such cases; identifying rafts of atypical mesothelial cells may accomplish diagnosis. Because normal mesothelial cells may be seen in any abdominal tap, exercise care to avoid misdiagnosis.

Anaplastic neoplasms are those in which the level of cellular differentiation is below that needed to identify a cell of origin by its microscopic resemblance to normal tissue. Sophisticated techniques such as immunohistochemistry or electron microscopy may yield clues to a tumor cell's origin even if it does not resemble the parent tissue. In a retrospective study from a large referral laboratory using advanced diagnostic techniques, the tissue of origin could not be identified in only 2% of cases; however, in 80% of cases, a broad category of epithelial versus mesenchymal origin was obtained.[95] Even this limited classification has therapeutic importance, as epithelial and round cell tumors tend to be significantly more responsive to chemotherapy than sarcomas are. Sarcomas of the skin were the largest single classification of poorly differentiated tumors but likely the most responsive to treatment (i.e., surgery). Because skin sarcomas tend to have low metastatic potential, definitive identification of cell of origin (smooth muscle, skeletal muscle, fibrocyte, etc.) is of little clinical importance. However, the remainder of the poorly differentiated neoplasms generally carry a poor prognosis, especially those present in abdominal organs.

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9

Dermatologic Diseases of Ferrets

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The clinical workup of ferrets with dermatologic diseases is very similar to that for dogs and cats. First, collect a detailed general history that incorporates the following information: the pet's signalment (e.g., sex, reproductive status, age, weight, source, etc.), lifestyle (e.g., housing, diet, other pets in the household, etc.), health management (e.g., vaccination status, medications, etc.), and general health condition, as well as specific history regarding the skin disorder (e.g., previous treatments, duration of clinical signs, etc.) and health conditions of cohabitant pets and owners (e.g., presence of skin lesions, pruritus, etc.).

Perform a physical examination to assess the general health of the ferret and identify the presence of systemic conditions that could be associated with the dermatologic signs. Next, perform a dermatologic examination by using a methodical approach that will identify the appropriate diagnostic tests needed for a definitive diagnosis. Evaluate exudates by cytologic examination and submit samples for bacterial culture and sensitivity testing as indicated. To identify cutaneous or aural parasites, perform a skin scraping, coat brushing, adhesive tape collection, or hair plucking followed by microscopic evaluation.

In the case of a cutaneous or subcutaneous mass, perform fine-needle aspiration (FNA) and cytologic evaluation.[44] Submit blood for at least a minimum database, including a complete blood count (CBC), plasma biochemical analysis, and hormonal panel to determine plasma androgen and estrogen levels. Perform a skin biopsy (punch or excisional) to achieve a histopathologic diagnosis of the mass. Depending on the refined differential diagnoses, consider performing diagnostic imaging tests (e.g., radiography, ultrasonography, computed tomography, etc.) or additional laboratory tests (e.g., polymerase chain reaction, cultures, etc.).

ANATOMY, PHYSIOLOGY, AND HUSBANDRY CONSIDERATIONS

Compared with other small pets, ferrets have relatively thick skin, especially over the neck and shoulders. The skin contains numerous sebaceous glands under androgenic control, which are larger in intact animals.[36,44] Particularly during the breeding season (March through August in the northern hemisphere), intact and sexually mature male ferrets increase sebaceous secretions in response to elevated hormone levels; this results in an increased musky odor, oily fur, and a yellowish undercoat.[44] Neutering decreases much of the skin odor by reducing androgenic stimulation.[44,46] Ferrets have two prominent scent glands located lateral to the anus, which produce a secretion when the ferret is frightened, excited, or in estrus.[44] Although breeding farms usually perform anal sacculectomy in conjunction with neutering, scent gland removal is not recommended (except in case of gland impaction) because of possible complications and because it does not affect the musky odor.

Similar to other pet carnivores, ferrets have epitrichial (apocrine) sweat glands on the body and atrichial (eccrine) sweat glands on the footpads.[36] Ferrets are predisposed to hyperthermia when exposed to high environmental temperatures.[44]

Ferrets have a fine undercoat and longer, coarser guard (primary) hairs that define the coat color. Under natural conditions, ferrets usually molt in the spring and autumn.[6,14,44,46] The molting process is also under hormonal control.[20] Therefore bilaterally symmetrical alopecia involving the tail and the perianal area may be seen during the breeding season and is more marked in females and intact animals.[44]

Nutrition may also influence coat quality. An inappropriate diet—e.g., one that is low in fat—may result in a dry, dull

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haircoat.[44] Avoid clay cat litter, which can also dry a ferret's haircoat.[5] Environmental factors, such as low humidity, may also predispose to skin scaling and pruritus.[6]

Traumatic cutaneous lesions may be seen in ferrets kept with inadequate bedding or nesting. A lack of hiding places may be associated with facial abrasions in ferrets that rub their faces on the floor in an attempt to hide. These lesions must be differentiated from scratches, bite wounds, and self-mutilation, especially during the breeding season.[44] Intact females may pull hair from their bodies to use as bedding material, thus mimicking pruritic skin diseases.[20] During the initial stages of hair regrowth (e.g., after hair clipping for surgery or adrenal gland disease treatment), the skin may take on a bluish appearance that can be mistaken for bruising or cyanosis.[6] This bluish coloration disappears as soon as hairs erupt from the skin.[44]

DISEASES

Ectoparasites

Ferrets are susceptible to most of the ectoparasites that affect dogs and cats. However, other than fleas and ear mites, ectoparasites are rarely seen in this species.

Fleas

Ctenocephalides felis (the cat flea) commonly affects ferrets.[46] In addition, *Paracaras meli* (the badger flea), *Ceratophyllus sciurorum* (the squirrel flea), and *Ceratopyllus vison* (the mink flea) have also been reported occasionally in ferrets.[5,31,47,59] The primary clinical sign of flea infestation in ferrets is pruritic erythema on the dorsal cervical and interscapular areas, which may or may not be associated with alopecia. However, some flea-infested ferrets are symptom free.[37,44] Others may develop signs of flea-bite hypersensitivity, including pruritic papulocrustous dermatitis over the tail base, ventral abdomen, or caudomedial thighs.[47]

The diagnostic workup and treatment of flea infestation or hypersensitivity is very similar to that used for dogs and cats. However, with the exception of imidacloprid 10%/moxidectin 1% spot-on (Advocate/Advantage Multi for Cats; Bayer, Shawnee, KS), no antiparasitic treatments are specifically licensed for ferrets.[1] In ferrets with established flea infestations, Advocate/Advantage Multi dosed at 0.4 mL per ferret and applied to the interscapular skin resulted in a therapeutic efficacy of 100% on day 1 after treatment and a preventative efficacy of >90% for up to 4 weeks.[59] Topical imidacloprid alone (Advantage 40 for Cats, Bayer, Shawnee, KS) can also be administered at a dose of 0.4 mL per ferret.[17] Because of its rapid flea adulticide activity, imidacloprid was effective in eliminating an established flea population and protecting against flea challenge for 3 weeks.[17] In conjunction with environmental control, one application of imidacloprid may be sufficient to control a flea problem.[44] Selamectin (Revolution/Stronghold; Zoetis, Parsippany, NJ) administered at a dose of 6 to 18 mg/kg was also proven effective in the treatment and prevention of flea infestation in ferrets. Monthly applications resulted in an effective preventive action lasting up to 21 days after treatment.[16] Anecdotally, selamectin may also help prevent heartworm infections, as well as ear mite and sarcoptic mange mite infestations in ferrets. Topical application of fipronil (Frontline; Merial, Duluth, GA) has also successfully treated flea infestations in ferrets.[15] Along with an adulticide (e.g., imidacloprid, selamectin, or fipronil), insect growth regulators (e.g., s-methoprene, pyriproxyfen, or lufenuron) are used to treat the environment infested by flea larvae.[5] Of these, lufenuron for cats (Program; Elanco, Greenfield, IN) can be administered to ferrets orally once a month.[5] However, because Program has a lag time of 6 to 8 weeks, use it in conjunction with a flea adulticide.[5]

Mites

Ear Mites. *Otodectes cynotis* is the ear mite that affects dogs, cats, and ferrets, often causing chronic otitis.[47] Mite transmission occurs mainly by direct contact with other infested animals. Although some mite infestations are asymptomatic, affected ferrets generally develop clinical signs of external otitis, such as head shaking and ear scratching. Otitis externa, excoriations, and periaural crusting may be seen on physical examination. The ear canal is filled with a dark brown, coffee ground–like exudate and eventually blood clots. Although aural debris and cerumen may be present in nonaffected animals, pruritus and head shaking are not seen in healthy ferrets.[44] Contrary to ear mite infestations in dog and cats, ear mites may colonize other areas of the ferret's body (e.g., the perineum).[7] Occasionally, heavy mite infestations may predispose to a secondary bacterial or fungal otitis, causing severe pruritus and a head tilt.

Diagnosis is the same as for dogs and cats. If the tympanic membrane is intact, use an otic cleaning solution before using a local antiparasitic treatment. The authors commonly use Advocate/Advantage Multi (Bayer) or Revolution /Stronghold (Zoetis) for the treatment of ear mites in ferrets. In an efficacy and safety study of Advocate/Advantage Multi, two or three treatments administered at 14-day intervals to ferrets infested with ear mites eradicated 100% of the parasites after 56 days.[32] Similarly, selamectin was reported to be safe and efficacious when applied topically at a dose of 45 mg in the dorsal interscapular area every 30 days.[40] Also, ivermectin administered at a dose of 0.2 to 0.4 mg/kg subcutaneously (SC) repeated every 2 weeks for three treatments is successful in most affected ferrets.[44] In a study that compared three protocols for treating ear mites in ferrets (parenteral ivermectin [1% ivermectin diluted 1:4 in propylene glycol; 0.4 mg/kg SC], aural topical administration of ivermectin [1% ivermectin diluted 1:10 in propylene glycol; 0.4 mg/kg divided between each ear canal, then repeated 2 weeks later], and aural topical administration of an otic preparation of thiabendazole, dexamethasone, and neomycin [Tresaderm, Merial, Iselin, NJ; 2 drops in each ear canal every 24 hours for 7 days, untreated for the next 7 days, then treatment reinstituted for 7 days]), treatment with either the thiabendazole product or aural topical ivermectin was more effective in eliminating mites than parenteral ivermectin.[48] Remember that concurrent use of topical and parenteral ivermectin is discouraged to reduce systemic toxicity in all animals.[44] In addition, administration of ivermectin in pregnant jills has been reported to have teratogenic effects on kits.[47] Finally, fipronil (Frontline, Merial) administered

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topically (1 drop in each cleaned external ear canal) was effective in treating a 3-year-old ferret with ear mites.[3]

To interrupt the mite life cycle, treat all contact animals and clean the entire environment. If secondary infections are identified, institute antibiotic or antifungal therapy or both as indicated.[44]

Sarcoptic Mange. Ferrets are rarely infested with *Sarcoptes scabiei*.[10,44] Two clinical forms of sarcoptic mange have been described in ferrets: the more common generalized form, which is characterized by focal or diffuse alopecia and intense pruritus; and a less common localized form, which is characterized by a pruritic, crusting pododermatitis, thus giving it the name "foot rot." In the latter form, the feet are generally swollen and painful, and the claws may become dystrophic before falling off.[47] The diagnosis can be achieved, as in dogs and cats, by mite or mite egg identification on skin scraping. However, because of the small number of mites on the skin, false-negative results are common; therefore a clinical diagnosis may be based on the response to treatment.

Treatments for sarcoptic mange in ferrets include topical or injectable parasiticides. Ivermectin can be administered at a dosage of 0.2 to 0.4 mg/kg SC every 14 days for three times.[37] Alternatively, 2% lime sulfur dips can be performed once weekly until 2 weeks after the signs resolve[56]; however, lime sulfur has a strong odor and discolors the fur. Other efficacious treatments for dogs and cats, which are anecdotally reported to be effective against *S. scabiei* in ferrets when used off label, are 10% imidacloprid/1% moxidectin (Advocate/Advantage Multi, Bayer) and selamectin (Revolution/Stronghold, Zoetis).[12,19]

Treat secondary bacterial infections with topical or systemic antibiotics as indicated and relieve pruritus by using antiinflammatory doses of glucocorticoids.[12] Treat animals affected by the localized form of sarcoptic mange with warm-water soaks, gentle debridement of crusts, and trimming of affected claws.[12,44] Treat all ferrets and cohabitant pets, as well as the environment, including cages and bedding. Because of the zoonotic potential, instruct owners to avoid direct contact with affected animals by wearing gloves.

Demodectic Mange. Demodicosis, which has been rarely reported in ferrets, occurs primarily in immunosuppressed individuals. Several cases have been described in ferrets with adrenal disease and systemic lymphoma,[2] and in animals receiving glucocorticoid treatment (e.g., prednisone) for neoplastic, inflammatory, or parasitic diseases.[43,44] *Demodex* species have also been found within the hair follicles and sebaceous glands in the perianal, vulvar, preputial, facial, and caudal abdominal regions in healthy ferrets.[36]

Clinical signs of demodicosis include alopecia, pruritus, and comedones; skin discoloration of the face or ventral abdominal, inguinal, and periaural areas; and erythema and brown ceruminous debris in the external ear canal.[12,44] Small plaques containing mites in the preputial skin have also been reported (Fig. 9.1).[44]

Diagnosis is made by direct observation of *Demodex* mites in skin scrapings and smears of aural exudate.[44] Treatment includes 10% imidacloprid/ 1% moxidectin spot-on (Advocate/ Advantage Multi, Bayer) once monthly for several months, oral ivermectin (50–300 µg/kg every 24 hours until 1 month after negative skin scrapings), or amitraz dips (0.0125% solution at 7-day intervals for three treatments and local topical application of the same solution in the ears every other day).[2,43]

Other Mite Infestations. Infestation by the fur mite, *Lynxacarus mustelae,* was reported in five ferret kits with ulcerative dermal lesions on the face.[54] Topical application of a powder containing permethrin along with cleaning the animals'

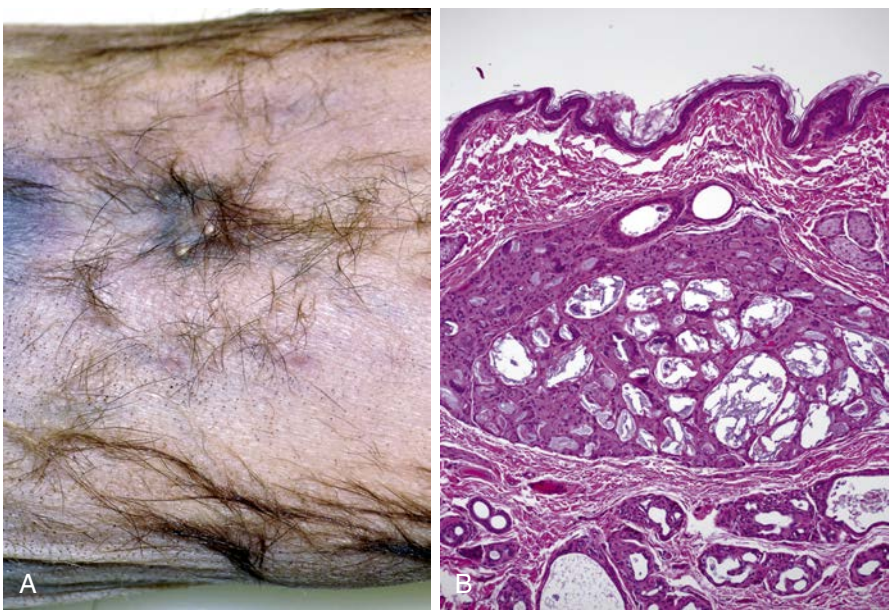


Fig. 9.1 Demodicosis in a geriatric male neutered ferret on chronic treatment with prednisone for presumptive inflammatory bowel disease. Several small plaques in the skin surround the prepuce (A). Histopathologic examination revealed a granulomatous reaction and cystic apocrine glands containing numerous cross sections of mites that were found in longitudinal section to be morphologically consistent with *Demodex* species (B) (hematoxylin and eosin stain; original magnification × 10). (Photographs courtesy Dr. Pamela Mouser.)

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cage with a permethrin-containing shampoo were effective in treating the animals and eliminating the mites from the environment.[44]

Ticks

Ticks can affect ferrets housed outdoors, living with infested cohabitant pets, or used for outdoor hunting.[47] Diagnosis and manual removal is the same as for dogs and cats. For ferrets living in tick-infested areas, monthly use of a tick preventative, such as fipronil (Frontline, Merial), is recommended.

Cutaneous Myiasis

Uncommon external parasites associated with infestations in ferrets include *Cuterebra* species and *Hypoderma bovis.* In both cases, subdermal cysts or granulomatous masses with an open pore containing the larvae may be seen.[47]

Fly strike, or infestation by *Wohlfahrtia vigil* (the flesh fly), has been reported by commercial mink and ferret ranchers and by owners who keep ferrets outdoors, mainly during the summer months.[47] Fly eggs laid on the face, neck, or flanks of the kits bore into the skin and cause irritation. Larvae localized in subcutaneous tissues can produce abscess-like lesions.[47]

Diagnosis is made by parasite identification. Treat by removing the larvae, debriding wounds, and administering topical and systemic antibiotics for secondary bacterial infections. Allow wounds to heal by second intention.[44]

Viral Disease

With the exception of canine distemper, viral dermatopathies are rare in ferrets. Canine distemper results in a pruritic rash, which starts under the chin and spreads to the inguinal or perianal regions. This is associated with orange-tinged discoloration of the skin and, in some cases, superficial pyoderma.[49] Less commonly, generalized desquamation is reported.[11,64] Brown crusts develop on the facial area secondary to mucopurulent nasal and ocular discharge, and swelling and hyperkeratosis are often seen on the footpads (Fig. 9.2). Refer to Chapter 5 for further discussion of canine distemper.



Fig. 9.2 Canine distemper in an adult male neutered ferret with hyperkeratosis and crusting of foot pads. (Photograph courtesy Dr. David Perpiñán.)

Fungal Disease

Dermatophytosis is rarely reported in ferrets. The most common etiologic agents are *Microsporum canis* and *Trichophyton mentagrophytes*.[37] Although infection may be seen in animals of any age, young and immunosuppressed animals appear to be predisposed.[12] Fungal pododermatitis was described in a 7-year-old ferret undergoing chemotherapy for lymphoma. *Microsporum nanum* was isolated as the causative agent.[44] Transmission occurs through direct contact with infected animals or carriers, infected cohabiting pets (e.g., cats), or fomites.

Clinical signs of dermatophytosis may include annular alopecia, broken hairs, diffuse scaling, small papules that spread peripherally, erythema, and crusting. The skin may also become lichenified, erythematous, and hyperkeratotic with superficial crusts.[44] Pruritus is not normally a clinical feature.[44,46]

A presumptive diagnosis can be made by evaluating clinical signs together with microscopic visualization of fungal arthrospores and hyphae in hair plucks that have been mixed with 10% potassium hydroxide or mineral oil. A Wood's lamp examination may also be helpful in identifying fluorescence by *M. canis*; however, only 50% of *M. canis* strains may fluoresce, whereas *Trichophyton* species do not.[22] Definitive diagnosis can be achieved only by isolating the causative fungus on a fungal culture of hair, scales, and crusts collected by plucking, combing or brushing. Macroscopic and microscopic fungal identification should always be made after fungal colony growth, generally within 2 to 4 weeks. Histologic examination of skin biopsy samples may also help identify fungal elements through the use of special stains, such as periodic acid-Schiff.

Ferret dermatophytoses have a zoonotic potential. A survey of zoonotic dermatoses conducted in Italy by the authors showed that both *Microsporum* spp. and *T. mentagrophytes* were isolated from pet ferrets living in close contact with owners.[10]

Although spontaneous remission of clinical signs of dermatophytosis is reported in ferrets,[22] always recommend medical treatment in definitively diagnosed cases to limit the zoonotic potential and persistence of spores in the environment. Therapy includes topical, systemic, and environmental approaches. A topical antifungal (e.g., enilconazole or miconazole cream) can be used, but ferrets generally will remove it during self-grooming; therefore shampoos, sprays, or mousses may be more appropriate. Lime sulfur dips can be applied weekly to the ferret's entire body.[44] Systemic oral antifungals include griseofulvin (25 mg/kg every 24 hours for 21–30 days),[46] fluconazole (10 mg/kg PO every 12 hours),[24] and itraconazole (5–10 mg/kg PO every 24 hours).[25,51] Periodically measure plasma liver enzyme concentrations during treatment with itraconazole and perform CBCs during therapy with griseofulvin to monitor for liver and bone marrow damage, respectively.[44] Although clinical signs may improve before full resolution of the infection, treatment is ideally continued until two fungal culture results are negative.[44]

Disinfect the environment to eliminate infectious spores by using dilute chlorine bleach (1:10), employing high-temperature professional steam-cleaning of carpets, changing air conditioning filters, cleaning heating ducts, and vacuuming with prompt disposal of vacuum bags.[44] Evaluate all animals in the household for infections and treat them topically with or without systemic therapy as required.

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Other Fungal Infections

Systemic fungal infections with dermatologic involvement, such as blastomycosis, coccidioidomycosis, and histoplasmosis, have been described rarely in ferrets. *Blastomyces dermatitidis* was diagnosed in one ferret affected with pneumonia and an ulcerated footpad.[56] Subcutaneous nodules have been observed in ferrets affected with histoplasmosis and coccidioidomycosis.[46] Mucormycosis, with *Absidia corymbifera,* was reported in a ferret from New Zealand raised for fur; the mycosis manifested as pruritic dermatitis of the pinnae.[22] A case of systemic infection with *Candida parapsilosis* was diagnosed in an 18-month-old castrated male ferret suffering from severe necrotizing encephalitis, granulomatous mediastinal lymphadenitis, and ulcerative dermatitis.[35]

Diagnosis can be made by physical evaluation of ferrets, as well as skin cytology or histopathology to identify the fungal organisms, especially in those animals unresponsive to treatment and or showing systemic clinical signs (i.e., hypothermia, pneumonia, etc.).[62] Oral ketoconazole and intravenous amphotericin B have been used for the treatment of systemic mycoses[44,56]; however, potentially significant adverse effects (e.g., liver and renal damage, respectively) must be considered.

Bacterial Disease

Bacterial dermatoses most often develop as a result of traumatic lesions (e.g., bite or puncture wounds) sustained during playing, mating, or fighting. However, bacterial infections can also develop as a result of oral disease, such as oral wounds incurred during ingestion of bones. Abscesses, pyoderma, or cellulitis are generally caused by *Staphylococcus aureus* or *Streptococcus* spp., although *Escherichia coli*, *Corynebacterium* spp., and *Pasteurella* spp. may also be isolated.[46,56] Clinical signs include fluctuant, warm, and sometimes painful masses that may be found anywhere on the body.[46,56] Abscesses can also involve the anal glands (Fig. 9.3).[44] Pyoderma may present as skin erosions, ulcerations, crusts, and erythematous macules.[30] Although dermatologic lesions are generally localized, some animals may develop systemic signs, such as hyperthermia and leukocytosis.[44]

Rarely, nodules or abscesses in the cervical area discharging green-yellow pus may develop after contamination by *Actinomyces* spp., causing "lumpy-jaw."[57] Markedly enlarged nodules may cause dyspnea. In some cases, superficial and follicular lesions, as well as areas of furunculosis, may develop instead of abscessation.[46]

Diagnosis is based on observation of clinical lesions and cytologic evaluation of samples from skin lesions or FNAs from masses. Infection can be confirmed by bacterial culture and sensitivity testing. In some instances (e.g., with fastidious bacteria), definitive diagnosis may be achieved only through molecular methods (i.e., polymerase chain reaction testing). Histologic examination of skin biopsy samples may help confirm pyoderma.[30]

Treatment depends on the type and location of the lesions. Always drain and surgically debride abscesses. In all cases, administer antibiotic therapy based on results of culture and sensitivity testing. Broad-spectrum systemic antibiotics, such as penicillin (40,000 IU/kg SC every 24 hours) or tetracycline (25 mg/kg PO every 12 hours), may be administered in cases of actinomycosis while sensitivity test results are pending.[37] Provide antiinflammatory and supportive treatment as needed for pruritus and pain.

Neoplasia

The integumentary system is the third most common body system affected by neoplastic disorders in ferrets.[34] Benign lesions predominate. The most common benign skin neoplasms in ferrets are mast cell tumors, basal cell tumors, sebaceous adenomas, epitheliomas, and cystadenomas.[28,44,58] These tumors may appear as small, darkly pigmented areas of skin or nodular lesions (mast cell tumors) (Fig. 9.4); nodular or plaque-like lesions (basal cell tumors); nodular, wart-like, or plaque-like masses; or verrucous, inflamed, or ulcerated lesions (sebaceous adenomas/epitheliomas).[21,28,34,45,50] The most commonly reported malignant skin tumors are squamous cell carcinoma,[26,52,61] adenocarcinoma,[23,42,44,45] and cutaneous (nonepitheliotrophic) lymphoma (Fig. 9.5).[28,29,33,53] These tumors tend to be nodular or plaque-like and can be located in the skin of the head, trunk, or limbs or involve the preputial gland.[28]



Fig. 9.3 Anal gland abscess in a ferret. Anal sacculectomy was performed, and the abscess contents were submitted for aerobic culture. No bacteria were isolated. (Photograph courtesy Dr. Connie Orcutt.)

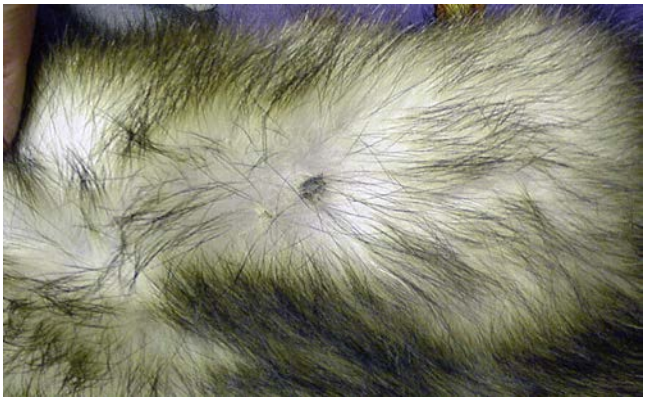


Fig. 9.4 Superficial, black, crusted debris overlying a dermal plaque in a ferret. This is a common clinical manifestation of both mast cell and sebaceous cell tumors. (Photograph courtesy Dr. Connie Orcutt.)

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Fig. 9.5 Severe ulcerative lesions in a ferret with cutaneous lymphoma. (Courtesy Stephen White, DVM. Picture from the case files of the Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of California. Used with permission.)

Epitheliotrophic lymphoma has also been reported in ferrets, but it is rare.[28,53] As in other species, it may manifest as chronic pruritus, diffuse generalized alopecia, erythema, erosions, crusts, and ulcerated plaques.[28,44,53] Malignant tumors commonly result in local invasion and metastasis to other sites, such as lymph nodes.[44]

Other benign or malignant neoplasms involving the skin or subcutis, which are less frequently reported in ferrets, include amelanotic melanoma,[28] angiokeratoma,[63] extraskeletal osteosarcoma,[4,28,41] fibroma and fibrosarcoma,[41,45] hemangioma,[45] hemangiosarcoma,[28,45] histiocytoma,[21] leiomyosarcoma,[4,39] lipoma,[28] liposarcoma,[9] mammary gland adenocarcinoma,[28] myxosarcoma of the subcutis,[21] myelosarcoma,[21] neurofibroma,[21,28,45] neurofibrosarcoma,[21] papilloma,[21] piloleiomyoma,[38] rhabdomyosarcoma, and vaccination-associated sarcoma.[45]

When a skin mass is detected, perform an excisional biopsy, being sure to attain wide surgical margins in the case of malignant tumors suspected on cytologic analysis of a FNA sample. Histopathologic and immunohistochemical evaluation of skin biopsy samples provide a definitive diagnosis. Transmission electron microscopy has been used to demonstrate viral particles in keratinocytes (e.g., multicentric squamous cell carcinoma in situ associated with papillomavirus).[52]

As with other species, perform preoperative staging by means of a CBC and biochemical analysis, diagnostic imaging, and lymph node biopsy.[12] Based on staging, consider chemotherapy or radiation as adjunct treatment for malignant tumors in ferrets.

Endocrine Disease

Progressive, bilaterally symmetrical alopecia can be seen in neutered ferrets affected with adrenocortical hyperplasia and neoplasia (see Chapter 7). Other clinical signs may include pruritus and serpentine and annular erythematous macules (Fig. 9.6).[55,56] Affected ferrets may develop a strong odor from androgenic stimulation of sebaceous glands in the skin.[44] Estrus, retained ovarian remnants, and ovarian neoplasms may also cause alopecia in both intact and neutered ferrets.[44]



Fig. 9.6 Gyrate erythema in a ferret after adrenalectomy for adrenal disease. (Photograph courtesy Dr. Stephen White.)



Fig. 9.7 Apocrine cyst in a ferret. These fluid-filled lesions are benign but can become very large.

Although adrenalectomy can be performed, it may not result in remission of clinical signs (e.g., cutaneous telangiectasia).[60] Medical therapies may be considered as alternatives to surgical treatment. Refer to Chapter 7 for further discussion of the diagnosis and treatment of endocrine disease in ferrets.

Other Dermatologic Diseases

Apocrine cysts are benign lesions but can become quite large. Lesions are usually firm and filled with pale yellow or colorless fluid (Fig. 9.7).[44]

A pemphigus foliaceus-like skin disease was reported in a 6-year-old neutered male ferret that presented for progressive skin lesions, loss of appetite, and lethargy.[13] The ferret had pustules and bilaterally symmetrical crusting around the mouth, chin, eyes, foot pads, and prepuce. Thick, yellow-brown crusts were observed around the nose, commissures of the mouth, and tarsal pads. Results of analysis of a skin scraping and fungal culture were negative. Skin biopsy results revealed epidermal hyperplasia, as well as a focal pustule containing eosinophils, neutrophils, and occasional acantholytic keratinocytes. These findings, along with a lack of response to treatment with antibiotics and antifungals and a positive response to therapy with prednisolone (2 mg/kg PO every 12 hours), were consistent with pemphigus foliaceus-like disease. Discontinuation of treatment with prednisolone resulted in relapse, and clinical signs resolved when prednisolone therapy was reinstated.[13]

Contact dermatitis has been seen in ferrets after frequent use of shampoos or insecticide sprays.[8] As with other companion species, avoid frequent bathing (more than once a month) and

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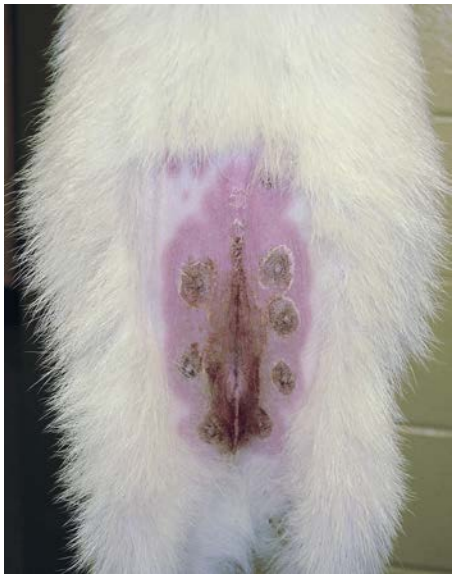


Fig. 9.8 Erythema multiforme in a ferret. This 5-year-old castrated male had markedly elevated estradiol and androgen levels. Bacteria and yeast were found on a skin scraping. (Photograph courtesy Dr. Connie Orcutt.)

aggressive shampooing, as well as use of concentrated topical antiseptics (e.g., povidone-iodine).[56]

Food hypersensitivity was diagnosed in a ferret showing clinical signs similar to atopic dermatitis. The animal responded to feeding a hypoallergenic diet for cats (Innovative Veterinary Diets [venison]; Royal Canin, St. Charles, MO).[56]

A pruritic dermatosis resembling atopic dermatitis was described in a ferret presenting with self-induced alopecia involving the trunk, rump, and paws.[56] After ruling out ectoparasite infestations and food hypersensitivity, the ferret responded to treatment with glucocorticoids or chlorpheniramine.

Erythema multiforme was described in a 5-year-old neutered male ferret presenting with a sudden onset of crusting and erythema on the ventral inguinal area (Fig. 9.8).[18] After initial treatment with cefadroxil, the initial lesions progressed to involve the axillary regions and the ventromedial aspect of the limbs; additionally, pad thickening and hyperkeratosis appeared on all four feet. Results of skin biopsy revealed severe multifocal to confluent and moderate to severe keratinocyte necrosis and bulla formation, severe superficial interface dermatitis, and mild to moderate hyperkeratosis and parakeratosis of the skin; these findings were consistent with erythema multiforme.[18] Underlying adrenal disease was postulated as the potential predisposing factor. Clinical signs improved after treatment with prednisolone but never completely resolved.[18]

Alopecia involving the back, neck, abdomen, and tail was reported in a 3.5-year-old male cryptorchid ferret affected with testicular leiomyosarcoma.[27] The animal also demonstrated pronounced sexual behavior and weight loss. After removal of the cryptorchid testicle, the haircoat completely regrew, which indicated that alopecia was likely the result of hormone production by hyperplastic interstitial (Leydig) cells.

A figurate erythema over the dorsolateral lumbosacral region and tail, which was clinically and histopathologically similar to erythema annulare centrifugum in humans, was reported in a 3-year-old spayed female ferret with adrenocortical adenocarcinoma and elevated levels of serum estradiol.[55] Lesions were successfully treated with a commercial omega-3/omega-6 fatty acid–containing product. Diffuse cutaneous telangiectasia was also reported in a ferret with adrenal-associated endocrinopathy.[60] Alopecia associated with chemotherapy treatment was reported in one ferret.[1]

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10

Musculoskeletal and Neurologic Diseases

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Ferrets can manifest with neurologic signs as a result of various conditions that may be of nervous or muscular origin; however, suggestive signs can also originate from weakness, cardiac conditions, or orthopedic abnormalities. Therefore, before neurologic evaluation, conduct a thorough general physical examination. In cases of altered mentation, check for signs of shock, such as tachycardia, delayed capillary refill time, and pale mucous membranes. Perform laboratory evaluations (e.g., a complete blood count, plasma biochemical analysis, etc.) as part of the complete physical assessment. In ferrets with gait abnormalities, perform a complete orthopedic evaluation. If results of the orthopedic and laboratory tests are normal, perform a neurologic examination to identify functional deficits.

NEUROLOGIC EXAMINATION

Neurologic examination of ferrets follows the same principles as for dogs and cats.[51] First, assess the level of consciousness, posture, and gait. Normal ferrets are hyperactive and have a characteristic hunchback posture while taking small steps. Cranial nerve examination is also performed in the same way as in dogs and cats. Ferrets normally have a keen sense of smell, but olfactory assessment is rarely performed. A ferret's vision is adapted to a crepuscular lifestyle and is presumed to be inferior to dogs and cats.[28] Ferrets generally do not have a menace response; therefore, vision is difficult to assess. Albino ferrets reportedly have a poorer ability to detect motion by sight compared with other ferrets.[23,38] Assess pupillary size as well as physiologic nystagmus during head movement. Keep in mind that ophthalmic examination can be difficult to perform in ferrets because of the reduced size of the globe, the relatively large lens, and the darkly pigmented iris.

Jaw tone is easily assessed in ferrets. To assess facial sensitivity and response, begin by gently placing the tip of a cotton-tipped applicator on the corneal surface to elicit the corneal reflex. Test the palpebral reflex by touching the medial or lateral canthus, and trigger nasal stimulation and facial sensitivity by touching a naris with a pointed instrument.

Hearing is difficult to evaluate in ferrets. The owner may report a lack of response to vocal stimuli or difficulty in training. Congenital deafness appears to be a problem in certain ferrets. In an epidemiologic study of 152 ferrets,

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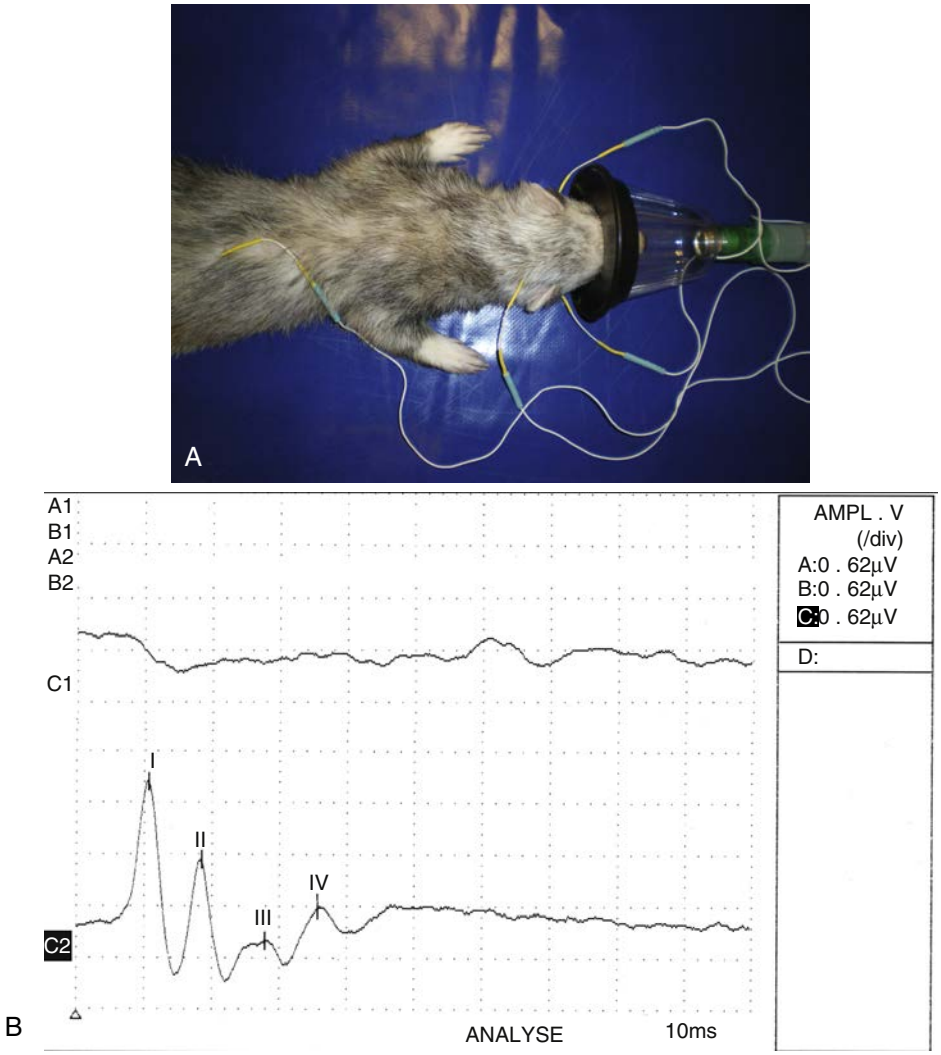


Fig. 10.1 (A) Setup used for brainstem auditory-evoked response (BAER) measurement in a ferret. (B) BAER recording in a unilaterally deaf ferret. The lower curve (C2) represents the normal hearing ear and includes peaks I, II, III, and IV. The upper curve (C1) represents the deaf ear with absence of the expected peaks.

the high prevalence of deafness (29%) was strictly associated with coat color patterns, specifically white markings and premature graying.[67] All panda, American panda, and blaze ferrets were deaf.[67] It is important for breeders to have a keen awareness and understanding of this defect to reduce its prevalence. Brainstem auditory evoked response (BAER) is the only reliable method for clinical evaluation of hearing in ferrets (Fig. 10.1).[67] The procedure can be performed easily in anesthetized ferrets as young as 8 weeks of age. A reliable routine protocol for BAER in ferrets has been established.[68]

Perform postural tests to assess proprioception and motor nerves. In very active animals, performing hopping and wheel barrowing may be easier than proprioceptive placing. Evaluate the presence of voluntary movement. Tests of spinal reflexes, which include withdrawal in all four limbs, are easy to perform and reliable. However, the patellar reflex is difficult to assess, primarily because the patellar ligament is reduced in ferrets. If voluntary movement is absent, assess nociception by using a hemostat.

ABNORMAL NEUROLOGIC SIGNS

Paresis

Pelvic limbs paresis, or paraparesis, is a common presentation in ferrets and has several possible causes (Table 10.1). Because of the elongated body of ferrets, generalized weakness is often more pronounced in the rear legs. It is important to rule out hypoglycemia, orthopedic conditions, abdominal pain (e.g., from foreign body ingestion, cystitis, or prostatitis), and organomegaly (e.g., splenomegaly or lymphadenopathy) as possible causes.

Pelvic limb paresis can involve upper motor neuron (UMN) or lower motor neuron (LMN) deficits. Upper motor neuron deficits involving both pelvic limbs (with normal thoracic limbs) reflect a T3-L3 spinal cord lesion, and differential diagnosis includes a focal or diffuse, intramedullary or extramedullary lesion in this segment of the spinal cord. Further diagnostic testing involves imaging and analysis of cerebrospinal fluid (CSF). Subsequent to survey radiography of the vertebral column, computed tomography (CT) can be performed to enhance

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TABLE 10.1 Pelvic Limb Paresis: Differential Diagnosis in Ferrets

Classification	Examples
Immune-mediated	• Disseminated myofasciitis • Myasthenia gravis
Infectious	• Toxoplasmosis • Sarcocystosis
Toxicity	• *Clostridium botulinum* endotoxin
Spinal defects	• Congenital (spina bifida, vertebral defects) • Acquired (trauma, luxation)
Metabolic	• Hypoglycemia
Neoplasia	• Chordoma/chondrosarcoma • Lymphoma • Fibrosarcoma • Histiocytic sarcoma • Plasmacytoma • Teratoma
Degenerative	• Intervertebral disk disease

three-dimensional visualization. Myelography or myelo-CT can be performed to identify spinal cord compression. The spinal cord can be delineated, and external compression and focal intramedullary swelling can be differentiated by injecting contrast medium (e.g., iohexol at 0.25 to 0.5 mL/kg) with a 25-gauge spinal needle into the subarachnoid space. When the spinal needle is inserted, a CSF sample can also be obtained for cytologic analysis and further testing (e.g., polymerase chain reaction [PCR]). Sites for CSF tap and myelography are the atlantooccipital and lumbar (L5-L6) regions (Fig. 10.2).

Lower motor neuron deficits of the pelvic limbs can reflect a lesion in the spinal cord at the level of L4-S2 or a neuromuscular disorder (e.g., a neuropathy, junctionopathy, or myopathy). Perform a complete systemic evaluation, including assessing results of routine blood tests, before considering primary neurologic disease. Ferrets suffering from systemic disease, such as hypoglycemia, may appear to have posterior paresis. If the lesion is suspected to involve the vertebral column, use the diagnostic approach suggested for UMN deficits. However, if an abnormality involving the peripheral nerves or neuromuscular junctions is suspected, perform electromyographic and nerve conduction velocity tests (Fig. 10.3). Normal values have been published in ferrets.[5]



Fig. 10.2 (A) Cerebrospinal tap from the cisterna magna in a ferret. With the ferret in lateral recumbency at the edge of the table, the head is flexed so that the point of the nose is at 90 degrees to the long axis of the body. The wings of the atlas and the point of the occipital condyle are used a landmarks. (B) Lumbar cerebrospinal fluid (CSF) collection at L5-6. Only a few drops of CSF can be collected; therefore, to maximize the sample, the fluid can be collected directly into a microtainer (C) or hematocrit tube (D).

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Fig. 10.3 Electromyographic and electroneurographic study in a ferret. The figure demonstrates measurement in the thoracic limb only; however, both thoracic and pelvic limbs are evaluated. The technique is described by Bianchi et al.[5]

Tetraparesis (i.e., paresis involving all four limbs) can reflect a C1-T2 abnormality or an intracranial or multifocal disorder. Spinal lesions cranial to C5 often manifest with UMN deficits in all four limbs, whereas a C6-T2 lesion often results in LMN deficits in the thoracic limbs and UMN deficits in the pelvic limbs; LMN deficits in all four limbs reflects a neuromuscular disorder.

Ataxia

Ataxia is incoordination; it can be characterized as either cerebellar, vestibular, or proprioceptive in origin. Cerebellar ataxia (e.g., hypermetria, intention tremor, broad-based stance) is caused by a lesion in the cerebellum. Because the cerebellum does not initiate motor activity but rather coordinates it, affected patients will have intact strength but will demonstrate abnormal rate, range, or force of movement. Paresis is not present with cerebellar dysfunction. Vestibular ataxia (i.e., peripheral or central vestibular disease) occurs when the vestibular system (i.e., inner ear, vestibular nerve, and vestibular nuclei) is damaged or diseased (e.g., otitis media, tumor). The vestibular system refines and coordinates motor activity by controlling muscles used to maintain head position, eye movement, and equilibrium. Dysfunction results in loss of balance; animals often list or fall to one side and may have a head tilt. Proprioceptive ataxia is caused by spinal disease, which will result in proprioceptive deficits that can be localized to the affected region of the spinal column. In the differential diagnosis, consider trauma, intervertebral disk disease, and tumors arising within or compressing the spinal cord or nerves.[42,62] In the diagnostic workup, a CT scan will provide important information about bone abnormalities, whereas magnetic resonance imaging (MRI) provides better imaging of soft tissue abnormalities of the spinal cord and brain (Fig. 10.4).

Seizures

Seizures in ferrets are most commonly caused by hypoglycemia secondary to insulinoma, particularly in middle-aged and older ferrets. The other possible causes are an intracranial lesion, another metabolic abnormality, or an idiopathic condition. The anamnesis must be reviewed critically when the ferret is not presented in status. Many presentations, such as gastritis, may mimic tremors and salivation, which may be mistaken for neurologic signs.

In any seizing ferret, direct the initial treatment toward arresting seizure activity. Check the blood glucose concentration immediately in any ferret presenting with seizures, ataxia, or other neurologic signs. If the glucose level is lower than 60 mg/dL, administer an intravenous (IV) bolus of 50% dextrose solution (diluted 1:1 in crystalloid fluid) at a dose of 2–5 mL/kg, or titrate to effect.[18] Begin a dextrose drip infusion adequate to maintain normoglycemia while performing further diagnostic testing. Some ferrets require as much as 10% dextrose added to IV fluids to achieve normoglycemia. Administer prednisone or prednisolone to hypoglycemic patients to enhance hepatic gluconeogenesis and inhibit glycogenolysis. If an insulinoma is suspected, consider initiating additional treatment, such as diazoxide.

If seizures persist and the blood glucose concentration is normal (or has been restored to normal), begin aggressive seizure management, extrapolating from treatment protocols developed for traditional small animals.[69] Administer diazepam (0.5–1.0 mg/kg IV) or midazolam (0.25–0.5 mg/kg IV); if venous access is not readily available, administer diazepam or midazolam intramuscularly, intranasally (for more rapid absorption), or rectally. Double the dose for rectal or nasal administration. Repeat up to three times to arrest seizure activity. If generalized or focal seizures persist, begin a constant-rate infusion (CRI) of midazolam (0.1–0.3 mg/kg per hour) or, if not accessible, use diazepam (0.1–1.0 mg/kg per hour); however, diazepam molecules tend to adsorb to plastic tubing. At the same time, to prevent seizure reoccurrence, initiate phenobarbital by bolus; use 3 mg/kg slow IV up to a total dose of 18 to 24 mg/kg over the first 24 hours, then 3 mg/kg every 12 hours. Phenobarbital and diazepam can be administered concurrently. Levetiracetam (20 mg/kg IV) can also be considered, using a high initial dose (60 mg/kg once) to provide rapid seizure control.

Use of propofol is controversial and should be considered only as a last resort in an attempt to control seizure activity.[53] Administer in aliquots of 2 mg/kg to effect, then 6 mg/kg per hour via CRI to effect. If increased intracranial pressure is suspected (e.g., as evidenced by stupor, anisocoria, bradycardia in the presence of systemic hypertension), use mannitol (0.5–1.0 g/kg IV over 20 minutes) or hypertonic saline solution (NaCl 7.5% dosed at 2–4 mL/kg over 5–10 minutes). Dexamethasone can be used in case of meningoencephalitis (0.2 mg/kg) or in case of vasogenic edema (e.g., in the presence of a brain tumor).

When no seizures have occurred for 6 hours, taper the diazepam or midazolam infusion slowly. Once seizures are controlled, use oral phenobarbital (1–2 mg/kg orally [PO] every 12 hours or levetiracetam (10 mg/kg PO three times daily), if necessary, for long-term seizure management. Potassium bromide can also be used for seizure control; it is administered at 70–80 mg/kg PO per day if used alone or at 22–30 mg/kg per day in combination with phenobarbital. Check blood levels of phenobarbital within 2 to 3 weeks after starting therapy; however, potassium bromide levels may not reach steady state for 60–90 days. Adjust dosages based on blood levels and clinical signs. To date, no pharmacokinetic study results are available

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TABLE 10.2 Seizures: Differential Diagnosis in Ferrets

Classification	Classification
Immune-mediated	• Meningoencephalitis • Eosinophilic syndrome
Infectious	• Viral • Aleutian disease • Coronavirus • Distemper • Rabies • Parasitic • Toxoplasmosis • Sarcocystosis • Bacterial • *Streptococcus zooepidemicus* • Fungal • Cryptococcosis • Blastomycosis
Toxicity	• Ibuprofen • Permethrin • Organophosphate • *Clostridium botulinum* endotoxin
Trauma	• Traumatic brain injury
Congenital	• Skull / brain defect
Metabolic	• Hypoglycemia • Hypocalcemia
Idiopathic	• Idiopathic epilepsy
Neoplasia	• Osteoma • Granular cell tumor • Lymphoma
Degenerative	• Neuronal vacuolation

in ferrets for the use of phenobarbital, gabapentin, zonisamide, imepitoin, or levetiracetam. Investigate any underlying disease stimulating the seizure activity after the patient is stable (see Table 10.2 for differential diagnosis). A full complete blood count and plasma biochemical panel, including electrolytes, is recommended. Magnetic resonance imaging has better resolution than a CT scan for brain evaluation in exploring structural changes. Administer a contrast agent IV to enhance brain lesions. Whenever meningoencephalitis is suspected, attempt to collect a CSF sample.

SPINAL DISORDERS

Spinal Defects

Spinal defects can be either congenital or acquired. The most common congenital vertebral lesion in ferrets is a transitional vertebra.[70] Block and wedge vertebrae are also found (Fig. 10.5).[70] Spina bifida was described in one stillborn ferret.[27] Congenital vertebral lesions are not always clinical but may predispose to intervertebral disk herniation.[49] One case in a 3-month-old ferret involved congenital occipitoatlantoaxial malformation that caused severe neurologic signs, including nonambulatory tetraparesis and head tilt.[10] Acquired spinal deformities include trauma and luxations. Because of the increasing popularity of raw-meat diets, ferret kits can be affected by nutritional secondary hyperparathyroidism, which can result in the spontaneous fracture of long bones and severe spinal deformities (Fig. 10.6). Metabolic bone disease was also reported in association with a congenital vitamin D deficiency in a young ferret.[75]

Intervertebral Disk Disease

There are several reports of intervertebral disk disease (IVD) in ferrets.[21,49,55,63,77] The most commonly affected site is L2-L3.[49,55,77] Clinical signs are similar to those seen in other mammals with IVD and may range in severity from mild postural deficits to complete paralysis. Predisposing factors, such as vertebral abnormalities or subluxation, are sometimes reported.[55,63] In two cases, ferrets with prolapse or herniation of an intervertebral disk presented with paresis or paralysis accompanied by postural reaction deficits caudal to the lesion.[49,77] The ferrets affected ranged in age from 7 months to 6 years. Diagnosis of IVD is usually made with myelography, alone or in combination with CT (Fig.10.7).

Surgical decompression is the treatment of choice for IVD. In two of the ferrets reported, hemilaminectomy was performed successfully and resulted in ambulatory recovery within 1 and 2 months after surgery, respectively.[49,55] One case was successfully managed medically with physotherapy and hydrotherapy.[77] For ferrets with paresis or paralysis, begin passive range-of-motion exercises with the affected limbs three to four times daily to prevent contracture. Gently massage muscles to enhance blood flow. Implement active exercise as early as possible to preserve muscle tone and stimulate neural return.[3] Use guidelines for prognosis in IVD in companion animals based on the presence or absence of nociception and the duration of clinical signs.

Spinal Neoplasia

Chordomas and Chondrosarcomas

Chordomas are tumors that arise from remnants of notochord.[20] In ferrets, these tumors develop most commonly at the tip of the tail, but they have also been described in the cervical and thoracic regions (Figs. 10.4 and 10.8).[1,13,14,22,35,71,83] Ferrets with cervical or thoracic chordoma can present with posterior paresis and ataxia localized to the area of the lesion (Fig 10.8).[71,83] In such cases, perform spinal radiography and myelography to identify a site for surgical approach.

Depending on the location, chordomas may be amenable to surgical resection; however, the one reported case of recurrence and metastasis of a chordoma in a ferret was that of a cervical chordoma that had been surgically excised.[83] Another ferret that was euthanized after presentation with a large cervical mass and a 1-week history of abnormal ambulation was diagnosed postmortem with a cervical chordoma that had metastasized to the lung.[22] In the case of a ferret with a thoracic chordoma, clinical signs persisted in spite of decompressive surgery.[71]

In the tail, chordomas appear as lobulated, firm, nonencapsulated, ulcerated masses at or near the last caudal vertebra. Microscopically, these tumors consist of lobules of

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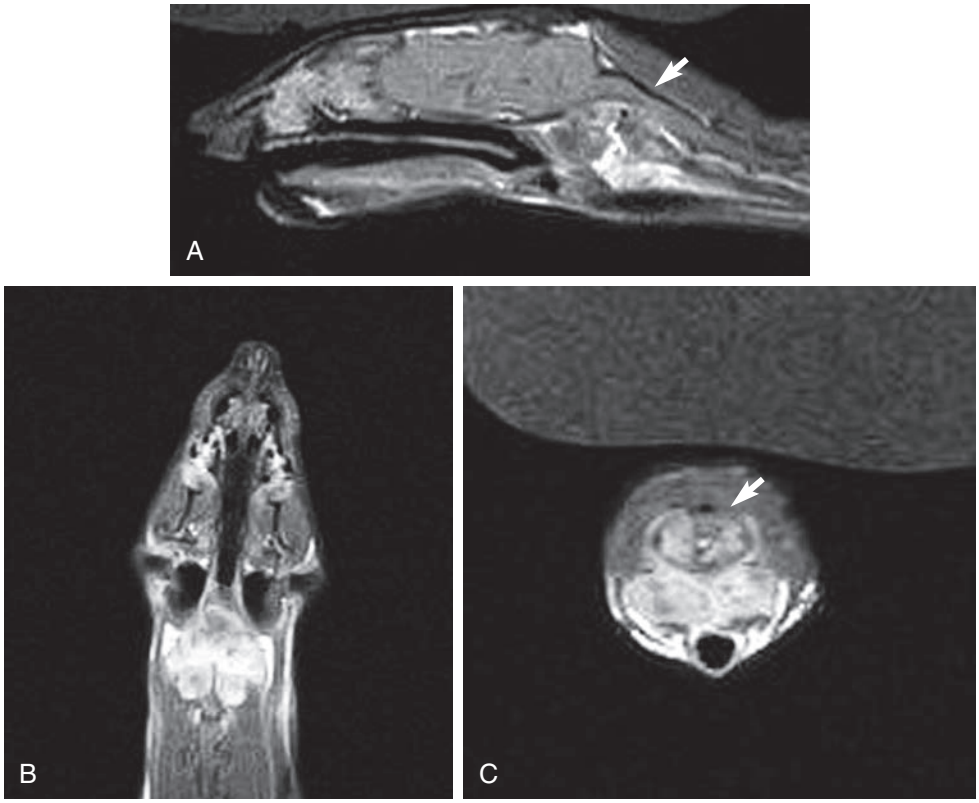


Fig. 10.4 (A–C) MRI of a ferret exhibiting ataxia with a cervical chordoma of C2-3. The spinal cord is compressed ventrally by the mass *(arrow,* A*)*, which also caused lysis of the vertebral body *(arrow, C)* and extended into the base of the skull.

physaliphorous cells with areas of well-differentiated bone or cartilage throughout.[14,36,83]

Chondrosarcoma of the tail has also been described in ferrets.[35] Clinical and morphologic descriptions are almost identical to those of chordoma. Differentiation must be made on the basis of immunohistochemical staining, with positive uptake of low-molecular-weight cytokeratin occurring in chordoma but not in chondrosarcoma.[14,35] In ferrets with any distal tail mass, amputate several vertebrae proximal to the lesion. In cases of chordoma and chondrosarcoma, this is considered curative. Recurrence has not been reported.

Other Neoplasia

Invasion of the vertebral body and subsequent spinal compression have also been reported with lymphoma, fibrosarcoma, and histiocytic sarcoma (Fig. 10.9).[34,61,81] A fibrosarcoma originating at T15-L2 metastasized to the lungs.[61] A case of plasmacytoma eventually resulted in a fracture of the cranial articular vertebral process and spinal compression.[47] Treatment with surgical decompression and prednisone resulted in adequate mobility.[47] One case of adrenal neuroblastoma and one case of adrenal carcinoma in ferrets were reported to invade the vertebrae.[37,54] Two cases of intramedullary neoplasia have been reported in ferrets: one case was a lymphosarcoma and the other a lumbosacral teratoma.[39,42] Both carried a poor prognosis.

INTRACRANIAL DISORDERS

Neoplasia

In ferrets, osteomas of the skull can arise from the zygomatic arch, parietal bone, or occipital bone (Fig. 10.10).[40] There is also a report of a multilobular osteoma originating from the neck and extending from the base of the skull to C5, causing extradural compression of the spinal cord.[32] Although these are benign neoplasms, clinical signs are related to physical displacement or compression of normal structures. Diagnosis is made via radiography. Biopsy may be difficult without surgical removal of the mass because of the extreme density of the tumor. Histopathologic evaluation usually reveals compact lamellar bone, bony trabeculae, and mild to moderate osteoblastic and hematologic activity.[40] Surgical removal is the treatment of choice and is usually curative if excision is complete.

A primary granular cell tumor (sometimes called a *myoblastoma*) was reported in the cerebrum of a ferret. Presenting signs included progressive head tilt, ataxia, and circling followed by refractory seizures.[76]

Neuronal Vacuolation

Neuronal vacuolation was reported in one ferret that presented with rapidly progressive convulsions and incoordination.[30] Characteristic lesions were identified on histologic examination of tissue samples collected during postmortem examination.

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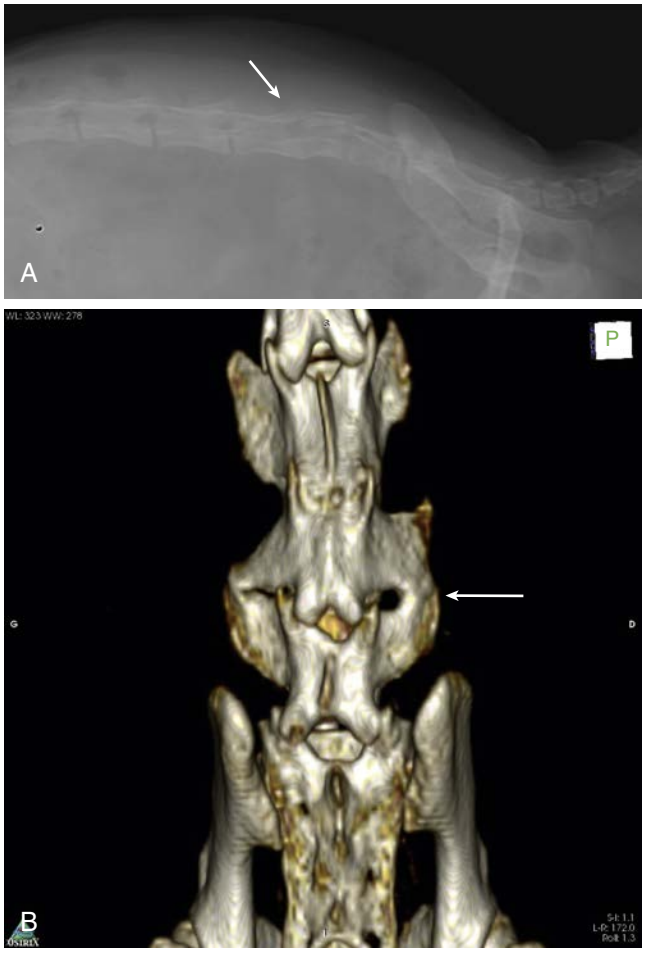


Fig. 10.5 Radiograph (A) and CT scan 3D reconstruction (B) of a bloc vertebra *(arrow)* between L4 and L5 causing hindlimb paresis in a ferret.

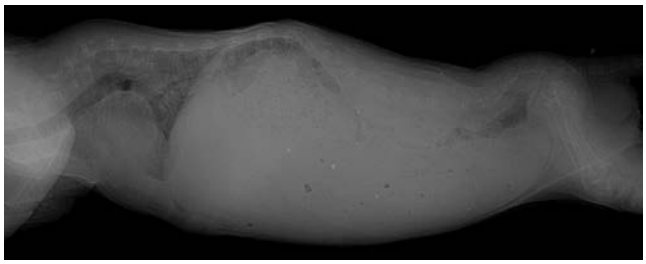


Fig. 10.6 Radiograph of a paretic ferret kit affected with metabolic bone disease from nutritional secondary hyperparathyroidism. Note the severe loss of bone density throughout, as well as vertebral deformities.

METABOLIC DISEASE

Hypoglycemia

Hypoglycemia is one of the main causes of neurologic signs in ferrets, with insulinoma being the most common cause. However, hypoglycemia potentially can be caused by various other diseases, including other forms of neoplasia, sepsis, starvation, hepatic disorders, or polycythemia vera. Notably, in a case series of lymphoma in ferrets, 4 out of 22 individuals exhibited low glucose levels.[16] Four of nine ferrets affected with megaoesophagus were hypoglycemic, presumably secondary to starvation and chronic regurgitation.[6]

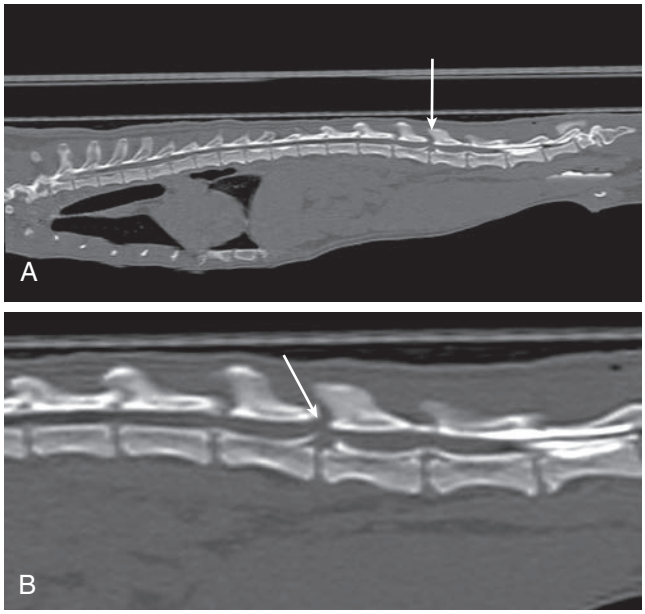


Fig. 10.7 (A) A contrast myelo-CT scan demonstrating an intramedullary compression secondary to intervertebral disk prolapse at L2-L3. (B,) Closeup of disk prolapse *(arrow)*.

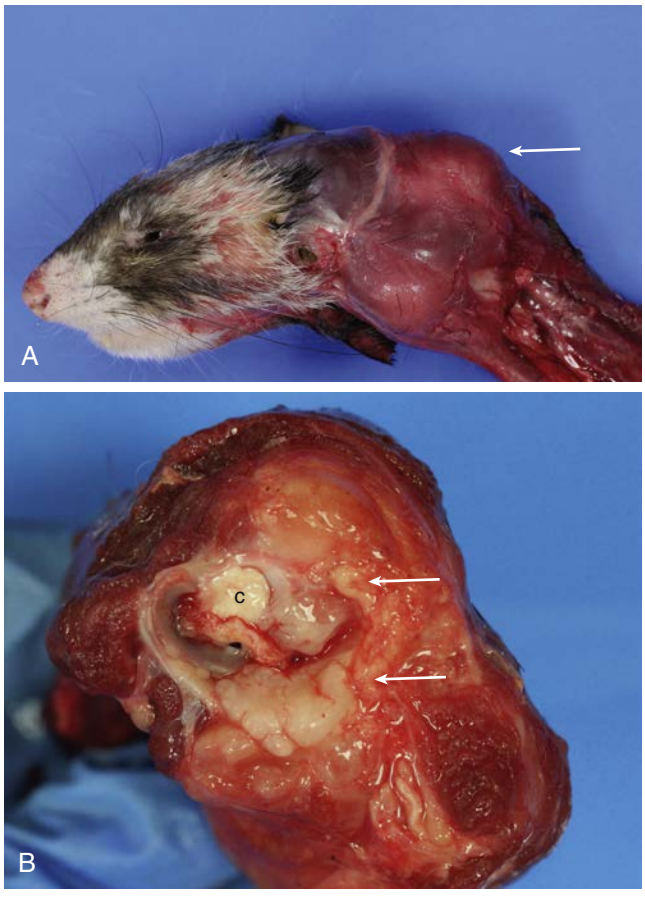


Fig. 10.8 (A) Ferret with a chordoma within the muscle of the neck, caudal to the skull *(arrow)*. (B) Cross-section of the skull showing the chordoma infiltrating the epaxial muscles, cervical vertebra *(arrows)*, and vertebral canal and impinging on the spinal cord *(c)*. Photo courtesy K. Quesenberry.

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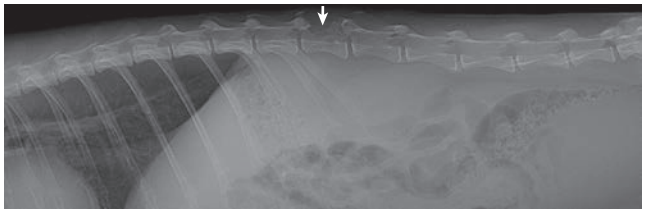


Fig. 10.9 Vertebral tumor affecting L1. Note the osteolysis of the vertebral process *(arrow)*.



Fig. 10.10 Osteoma of the zygomatic arch in a ferret. Osteomas usually cause neurologic signs when located on a cervical vertebra or on the parietal bone.

Hypocalcemia

Primary hypoparathyroidism has been described as a cause of hypocalcemia in ferrets.[11,52] Lethargy was reported consistently, in addition to intermittent seizures in one case. Diagnosis of primary hypoparathyroidism is supported by low total and ionized calcium levels, high phosphorus levels, and concurrent low parathyroid hormone (PTH) levels without renal impairment. Because PTH levels can vary throughout the day, it has been recommended in human medicine to collect samples at midmorning.[52]

Treatment of primary hypoparathyroidism is based on administration of calcium gluconate during the hypocalcemic episode followed by maintenance treatment with calcium carbonate (25–50 mg/kg PO every 12 hours) and dihydrotachysterol (6.6 µg/kg every 12 hours to 24 µg/kg every 5 days). A phosphate binder, such as aluminum hydroxide, may be used to reduce high plasma phosphorus levels. Survival of 21–24 months was reported in response to daily supplementation.[11,52]

Another condition called pseudohypoparathyroidism has been described in a ferret.[84] In this syndrome, plasma PTH levels are very high, but there is a lack of response to the hormone.

Nutritional secondary hyperparathyroidism can affect ferrets fed a meat-only diet that is not adequately supplemented with vitamins and minerals. A common cause in young, primiparous jills late in gestation is toxemia of pregnancy. Long bone fractures and deformities usually precede neurologic signs. In fact, although hypocalcemia, hypophosphatemia, and ketosis may develop, neurologic signs are rare unless hepatic lipidosis is so severe that encephalopathy is present.[4] The differential diagnosis includes hypomagnesemia, hypoalbuminemia, acute pancreatitis, renal disease, and tumor lysis syndrome.

Toxicosis

There are very few reports of ferrets with neurologic signs secondary to toxin exposure. However, ibuprofen toxicosis can typically cause neurologic signs such as ataxia, tremors, and weakness, as well as renal compromise.[73] Doses greater than 200 mg/kg can be lethal.[73] *Clostridium botulinum* type A, B, and C endotoxin were reported to cause ataxia and ascending LMN paralysis in ferrets within 12–96 hours after ingestion of contaminated feed.[78] Anecdotally, permethrin toxicosis can produce neurologic effects in ferrets; however, there are no published case reports to support this assertion.[15]

INFECTIOUS DISEASE

Viral Disease

Rabies

Ferrets, as any carnivores, are susceptible to rabies.[31,59,60] Clinical disease includes ascending paralysis, ataxia, cachexia, bladder atony, fever, hyperactivity, tremors, and paresthesia. Although usually fatal, one ferret experimentally inoculated with a rabies virus of skunk origin survived with paraplegia until being euthanized 180 days post infection.[31] Rabies should remain in the differential list of any ferret with neurologic disease. Vaccination is strongly recommended—and, in some locales, mandated—to prevent rabies. Note that legislation may vary among states and countries regarding rabies vaccination and surveillance in ferrets (see Chapter 2).

Canine Distemper

As discussed in more detail in Chapter 6, ferrets are sensitive to infection by canine distemper virus (CDV), with clinical signs generally becoming apparent within 7–10 days after exposure. Neurologic signs appear in the late stage of the disease, usually after respiratory, dermatologic (inconsistent), and digestive signs. In the neurotropic phase, ferrets exhibit hyperexcitability, tremor, seizures, and coma.[44] The disease mortality rate approaches 100%, usually 12–16 days after infection with a ferret-adapted CDV strain and 21–35 days after infection with a canine CDV strain.[43] Diagnosis relies primarily on a thorough anamnesis (e.g., a ferret unvaccinated against CDV) and suggestive clinical signs. In addition, severe leukopenia is often noted one week after infection. Additional supporting clinical data include demonstration of eosinophilic nuclear inclusions on conjunctival scraping or lymphoid tissue samples, and increased protein levels and lymphocyte counts on CSF analysis. Definitive diagnosis is based on positive findings of reverse

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transcription PCR testing of peripheral blood, conjunctival scrapings, CSF, or urine. To protect other hospitalized dogs or ferrets, isolate ferrets suspected of CDV. Ferrets should be protected by vaccination against CDV (see Chapter 2).

Aleutian Disease

Aleutian disease is caused by Aleutian disease virus, a parvovirus that was originally reported in mink but can also infect ferrets (see Chapter 5). Some infected ferrets may be asymptomatic but remain persistently infected, or the disease may be self-limiting and nonpersistent.[82] In other ferrets, associated neurologic signs may vary from mild incoordination to posterior ataxia, ascending paresis, persistent tremors, and quadriplegia.[79] Clinical signs in one outbreak developed as soon as 24 hours or as long as 90 days after exposure.[79] The most significant biochemical abnormality is hypergammaglobulinemia, with gamma globulin concentrations increased to greater than 20% of the total serum protein concentration. However, not all affected ferrets have high gamma globulin concentrations.[82] Histopathologic changes involving the brain and spinal cord include perivascular cuffing with lymphocytes and sometimes plasma cells, nonsuppurative meningitis, astrocytosis, mononuclear cell infiltration, and focal malacia.[82] Tentative diagnosis is based on a positive result of Aleutian disease virus serologic testing, high gamma globulin concentration, and the presence of compatible clinical signs; however, definitive diagnosis relies on demonstration of positive testing by PCR or enzyme-linked immunosorbent assay. Disease in suspected ferrets is confirmed by demonstration of lymphocytic and plasmacytic infiltrates on histologic examination of tissue samples collected at necropsy. The overall incidence of Aleutian disease in ferrets appears to be low; in one serologic study of 446 ferrets, the incidence of seropositive animals was 8.5%.[82] Treatment consists of supportive care and isolation of suspected animals from unaffected ferrets.

Coronavirus

Systemic coronavirus (see also Chapter 3), which was first described in ferrets in 2004, has similarities to feline infectious peritonitis.[24] Although the disease is predominantly visceral; neurologic lesions may be present, associated with clinical signs such as hind limb paresis, ataxia, and seizures.[24,66] An initial description of systemic coronavirus in 23 ferrets reported nonsuppurative meningoencephalitis in five animals and one case of pyogranulomatous lesions in the brain.[24] Diagnosis can be achieved with PCR or immunohistochemistry applied to biopsy samples. One case was more completely described on a CT scan that revealed contrast-enhancing extraparenchymal lesions.[26] Pyogranulomatous lesions were identified and systemic coronavirus infection was confirmed with immunohistochemistry.[26] Treatment is typically unsuccessful and relies primarily on controlling signs of inflammation with corticosteroids and supportive care.[66]

Bacterial Disease

Streptococcus equi subspecies *zooepidemicus* has been isolated in a ferret as a cause of pneumonia and meningitis.[58] The ferret initially presented for head tilt and facial tics. The neurologic status deteriorated rapidly, and the ferret was euthanized. Histologic findings were consistent with meningoencephalitis, and *S. equi* subspecies *zooepidemicus* was cultured from brain tissue.[58]

Fungal Disease

Various fungal diseases are associated with neurologic manifestations in ferrets. Disseminated cryptococcosis can cause granulomatous meningoencephalitis and exudative chorioretinitis.[29,74] Blindness, ataxia, and incontinence can be also be present, although lethargy, respiratory signs, and lymph node enlargement are more common.[17,33,50,74] Diagnosis can be achieved by demonstration of intralesional yeast on fine-needle aspirates of infected lymph nodes and subsequent identification by PCR. In ferrets with granulomatous lesions, MRI studies may reveal a compressive mass in the spinal cord.[74] Treatment includes antifungal drugs, such as fluconazole (10 mg/kg PO every 24 hours) and itraconazole (15 mg/kg PO every 24 hours). In cases of chorioretinitis, prednisone 0.5 mg/kg every 24 hours may be added.

In one case of blastomycosis in a ferret, granulomatous lesions were present in the meninges and brain; however, clinical signs were predominantly respiratory.[45] Histoplasmosis has also been described in two ferrets, one of which exhibited seizures.[19,41] However, most cases of histoplasmosis in ferrets are subclinical.[19]

Parasitic Disease

Toxoplasmosis

Ferrets are sensitive to toxoplasmosis (*Toxoplasma gondii*), although the disease is rarely reported and clinical manifestation appears to be rare. Farmed ferrets infected with toxoplasma cysts were reportedly asymptomatic.[65] In colonies of black-footed ferrets with toxoplasmosis, neurologic manifestations included posterior weakness, disorientation, depression, head tilt, and circling.[8] Necrotizing nonsuppurative or granulomatous meningoencephalitis was found on postmortem examination.[8]

Toxoplasma may encyst in various tissues, including the brain, liver, muscles, and retina.[65] Transmission occurs when raw meat with encysted stages is ingested or by contact with cat feces containing oocysts. Serologic or PCR testing of CSF is used for antemortem diagnosis; however, histologic examination is the gold standard for definitive diagnosis. Treatment is sulfadiazine and pyrimethamine or clindamycin.[65]

Sarcocystosis

One ferret infected with *Sarcocystis neurona* was presented for rhinitis and hindlimb paresis.[7] Disseminated disease was diagnosed on histologic examination of brain tissue. *Sarcocystis* species are known to induce nonsuppurative meningoencephalitis in mink.[65]

VESTIBULAR SYNDROME

Vestibular syndrome can be classified as peripheral or central. Peripheral vestibular syndrome, which involves the inner ear or the vestibular nerve, is primarily explored with

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Fig. 10.11 CT scan of a ferret with a head tilt. Note the filling of the right tympanic bulla with radiodense material consistent with otitis media.

TABLE 10.3 Vestibular Syndrome: Differential Diagnosis in Ferrets

Classification	Examples
Inflammatory	• Meningoencephalitis
Infectious	• Otitis media/interna • *Otodectes cynotis* • *Toxoplasma* • *Streptococcus zooepidemicus*
Toxicity	• Ototoxic drugs
Traumatic	• Traumatic head injury
Congenital	• Congenital vestibular syndrome
Neoplasia	• Vestibular papilloma • Granular cell tumor • Cholesteatoma

otoscopy, CT, and/or MRI (Fig. 10.11). Central vestibular syndrome can arise from a brainstem, cerebellar, or thalamic lesion and is most reliably investigated with MRI.

Vestibular syndrome is rarely described in ferrets. The differential diagnosis is presented in Table 10.3. Otitis externa is relatively common in ferret, and infection with *Otodectes cynotis* infection has been implicated.[46] Complications include otitis media and otitis interna. Systemic antibiotic and antiinflammatory drugs are needed. Primary otitis interna was diagnosed in a 4-year-old ferret.[12] No cause was identified and the ferret responded favorably to antibiotic and steroid therapy. Congenital vestibular syndrome with asymmetry of the inner ear, identified by MRI, was described in a 2-year-old ferret.[56] A choroid plexus papilloma originating from the fourth ventricle in a 6-year-old ferret caused head tilt, ataxia, and hemiparesis.[80] The mass was located by use of contrast-enhanced CT, and the diagnosis was confirmed by histologic examination of tissue samples. Another case involved a cerebral granular cell tumor in a ferret that presented for head tilt.[76]

TABLE 10.4 Disseminated Idiopathic Myofasciitis: Treatment Plan[66]

Drugs	Dosage
Prednisolone	• 1 mg/kg every 12 hours for 1 month and then every 24 hours until recovery
Cyclophosphamide	• 10 mg/kg SC on day 1 and day 14, then every 4 weeks for 3 months or until DIM is resolved
Chloramphenicol	• 50 mg/kg PO every 12 hours for 6–8 weeks

DIM, Disseminated idiopathic myofasciitis; *PO,* orally; *SC,* subcutaneously.

MUSCULOSKELETAL DISORDERS

Disseminated Idiopathic Myofasciitis

Disseminated idiopathic myofasciitis, also known as myofasciitis or polymyositis, was first described in 2003.[24] This disease affects young ferrets ranging from 5 to 24 months of age.[24] The clinical presentation can be very diverse and nonspecific, with signs including lethargy, inappetence, enlarged lymph nodes, a subcutaneous mass effect, green diarrhea, nasal and ocular discharge, coughing, or seizures.[25] Myofasciitis is often painful; thus most clinical signs are believed to be a consequence of hyperesthesia.[72] Dysesthesia has also been described.[72] Disease is usually acute or subacute in onset, and ferrets frequently present with a high fever (e.g., 104°F–108°F).[25] Some individuals may decline rapidly, whereas others remain in poor condition for months and ultimately die.[72]

Hematologic findings are characterized by anemia and a marked neutrophilia with an occasional left shift. However, creatine kinase levels, which are usually a marker of muscle necrosis, are generally not elevated in affected ferrets. One theory for this unusual finding is that, although muscles are severely inflamed, histopathologic examination shows minimal muscle necrosis.[72] Diagnostic imaging findings are nonspecific and usually performed to rule out other causes of hyperthermia. Antemortem diagnosis relies primarily on muscle biopsy. Open surgical biopsy samples collected from several sites are usually recommended, focusing especially on atrophied muscle and avoiding sites of previous injections. The vastus lateralis, cranial tibial, and triceps brachii muscles are the most easily accessed sites. Gross lesions can be subtle in acute cases but more obvious in chronic cases. Microscopic lesions are multifocal and include mild to severe suppurative to pyogranulomatous lesions involving the fascia between muscle bundles. A pathognomonic lesion is a circumferential transmural infiltrate in the muscular tunics along the entire length of the esophagus.

Several treatments have been attempted. In three confirmed cases, ferrets recovered after being treated with a combination of prednisolone, cyclophosphamide, and chloramphenicol (Table 10.4).[72] Supportive care is crucial and includes nutritional management, fluid therapy, pain management, and gastrointestinal protectants. Acupuncture may be beneficial in some cases.[72]

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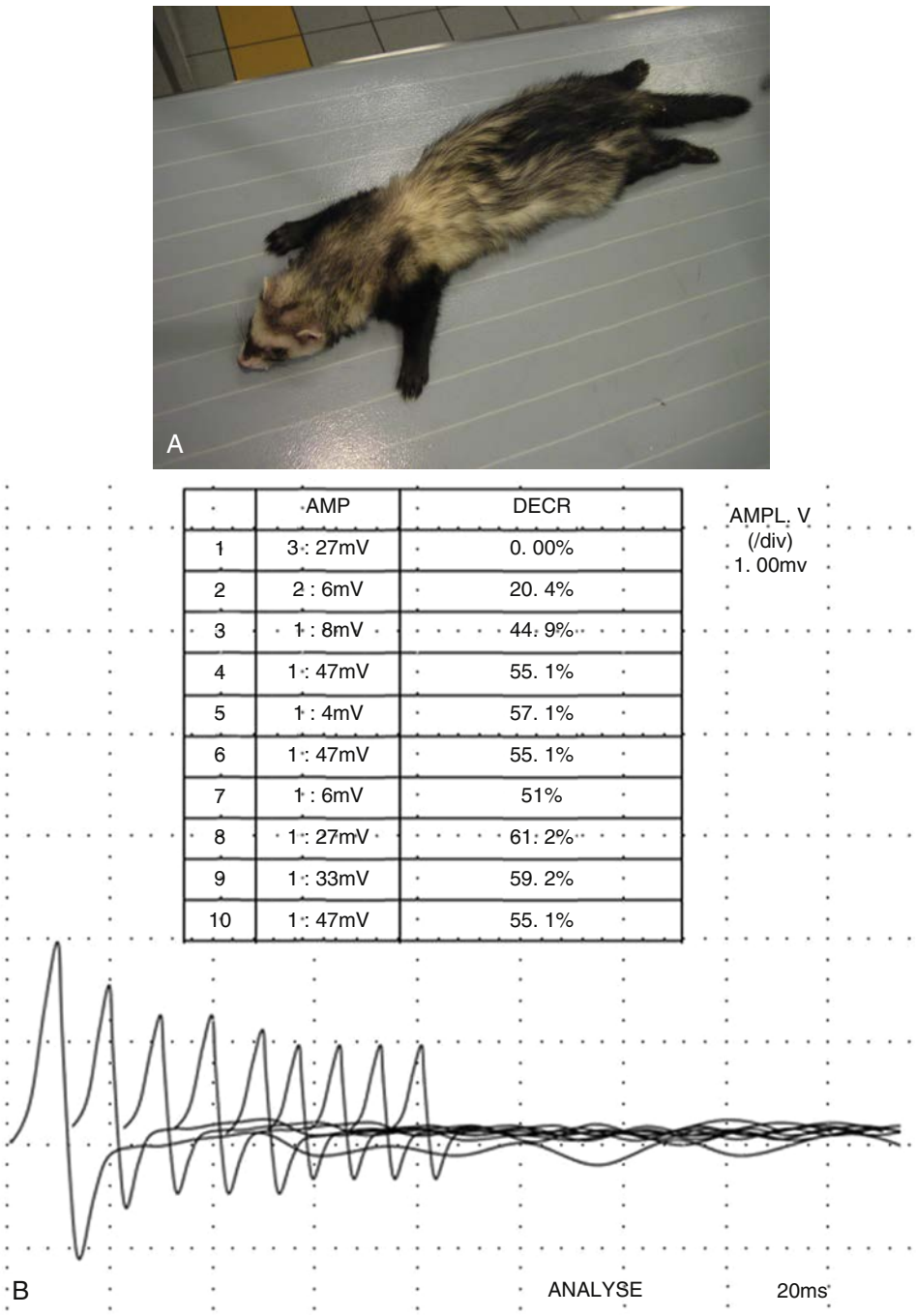


Fig. 10.12 Ferret affected by myasthenia gravis (A). Repetitive nerve stimulation (B) demonstrated a severe decremental response (>50%) of the compound action potential.

The cause of disseminated idiopathic myofasciitis remains unidentified.[72] Similar lesions were inadvertently induced in ferrets during an experimental vaccine trial, and affected ferrets were known to have received at least one dose of canine distemper vaccine.[25] One distemper vaccine (Fervac-D; United Vaccines, Madison, WI) was suspected to induce the disease, especially after the number of cases decreased dramatically subsequent to removal of the product from the market in 2006. However, no clear relationship was established because of considerable variability between vaccination and the onset of disease. Furthermore, additional cases have been identified since the vaccine was discontinued in the United States, as well as in Europe where the vaccine is not available.[48,57]

Myasthenia

Myasthenia gravis is characterized by a defect in the neuromuscular junction caused by either an immune-mediated disease (acquired myasthenia) or a congenital defect of the acetylcholine receptor. The literature includes three case reports involving a 7-month-old ferret, a 4.5- year-old ferret, and a 6-year-old ferret, respectively.[2,9,64] Clinical presentation included generalized weakness and paraparesis that progressed to tetraparesis (Fig. 10.12).

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Diagnosis was made by nerve conduction velocity testing, which showed a characteristic decremental response of the compound muscle action potential with repetitive nerve stimulation.[9,64] In all ferrets, response to cholinesterase inhibitor administration induced a dramatic resolution of the locomotor deficit. Levels of antiacetylcholine receptor antibodies were also elevated in all animals (normal value <0.06 nmol/L based on 5 normal ferrets).[2,9,64] In one case, resolution of the condition has been associated with a return to baseline antibody titer.[64]

Treatment with pyridostigmine bromide (0.5–1 mg/kg every 8–12 hours) may achieve normal mobility. However, overdosing may mimic signs of myasthenia gravis; therefore regular reassessments are necessary.[2] Because this condition may have an immunologic component, prednisolone may be beneficial in some cases.[2] The prognosis is guarded. In reported cases, one ferret died within 1 month and the other was managed for more than 2 years on medical therapy.[2,9] Finally, one case recovered fully with pyridostigmine and prednisone therapy despite a lack of clinical response within the first 2 months, which suggests that supportive care and patience are crucial during the initial stage of the disease.[64]

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11

Basic Anatomy, Physiology, and Husbandry of Rabbits

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INTRODUCTION

Etymology

The mammalian order Lagomorpha consists of two living families—Leporidae (rabbits and hares) and Ochotonidae (pikas) (Fig. 11.1). The scientific name for the Old World or European rabbit from which all domestic breeds originate is *Oryctolagus cuniculus*. The genus name is derived from the words *orukter* [Greek: a tool for digging] and *lagos* [Greek: a hare], and the species name is derived from *cuniculus* [Latin: a rabbit or an underground passage]. In contrast to most other species in Lagomorpha, rabbits are a burrowing animal.

Through human mediation, wild European rabbits have been dispersed to all continents except Antarctica. This has led to some confusion with the common name "rabbit." The family Leporidae splits broadly into two groups: the hares of the genus *Lepus* containing 32 species, and the rabbits in the remaining 10 genera that include *Oryctolagus* (Fig. 11.2).[34] However, these vernacular names are often used synonymously and applied to the wrong animals; for example, African red rock hares (*Pronolagus* species) and the endangered hispid hare (*Caprolagus hispidus)* are rabbits, whereas the snowshoe rabbit (*Lepus americanus*) and the various species of North American jackrabbits are hares. Even more confusing, North American cottontails, comprising 17 *Sylvilagus* species, are commonly called rabbits. Both the European rabbit and Eastern cottontail (*S. floridanus*) are unique because of their great diversity of habitat: fields, farms, woodlands, deserts, swamps, and forests. However, in North America, the European rabbit has not become feral and is only found domesticated; all wild rabbits in North America are cottontails.

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The English word "rabbit" (from Middle English "rabbet"; Middle French dialect "rabbotte"; Walloon "robète" [baby rabbit], diminutive of Middle Dutch "robbe") arose in the 14th century to mean the young of the species. The adult was a *coney* (from Anglo-Norman "conis," plural of "conil" from Latin "cunicula") until the 18th century and can be found in the King James Bible [Leviticus 11:5; Proverbs 30:26]. In 16th-century British slang, a coney was someone to cheat or rob, and doing so was known as "coney-catching"[18]; the Lancashire expression "coney-fogle" meant "to lay plots."[5] Despite the pronunciation of "coney" (rhyming with honey, money) being changed from a short to long vowel (rhyming with boney),[17] the word "rabbit" gradually pushed out "coney" in common usage. The similarity of present-day European words for "rabbit" to the English "coney" can be seen: coniglio [Italian], conejo [Spanish], konijn [Dutch], Kaninchen [German]. Although specific English words describe the young of a species (e.g., dog/puppy; hare/leveret; cat/kitten), there is no word for the young of rabbits, although they are often called a "kit" or by the hypocoristic term "bunny."

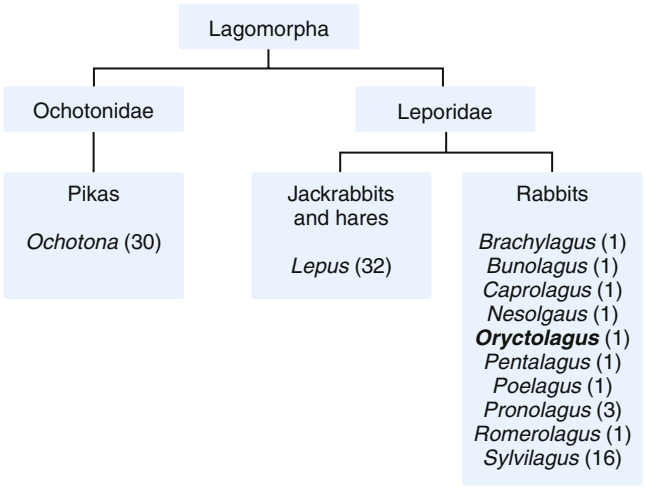


Fig. 11.1 Relationship of domestic rabbits (*Oryctolagus cuniculus*) within the family Leporidae (hares and rabbits). Approximately 90 living species of lagomorphs, placed in 2 families and 13 genera, are currently recognized. (Modified from Fontanesi L, Di Palma F, Flicek P, et al. LaGomiCs-Lagomorph Genomics Consortium: an international collaborative effort for sequencing the genomes of an entire mammalian order. *J Hered* 2016;107:295-308.)

Taxonomy and Similarities to Rodents

In both rabbits and rodents, the anterior incisors in the upper and lower jaws are modified to form chisel-like cutting organs.[26] Enamel is deposited on the anterior surfaces only, with the back surface being dentin. Because enamel is harder than dentin, the front surface wears down more slowly, and the incisors remain in a permanently sharp condition from gnawing. This modification is associated with a loss of teeth between the last incisor and the first cheek tooth—a toothless interval called the diastema.

Karl von Linne (*Latin* Linnaeus, 1717–1738), who originated the systematic classification of plants and animals, recognized the similarities of rabbits and rodents. In his *Systema Naturae* (10th ed., 1758), he assigned rabbits and rodents to a group called *Glires* (*Latin* glis = dormouse). Later naturalists designated *Glires* as the mammalian order Rodentia. Within this order, rabbits, hares, and pikas were grouped in the suborder Duplicidentata because they possessed a second pair of incisors in the upper jaw. Most rodents, which have only a single pair of upper incisors, were grouped in the suborder Simplicidentata. However, in the 20th century, a strong consensus evolved that the similarities of rabbits and rodents are an example of convergent evolution (i.e., the development of a similar adaptive morphological trait by two or more unrelated species). Naturalists now designate the Duplicidentata as the mammalian order

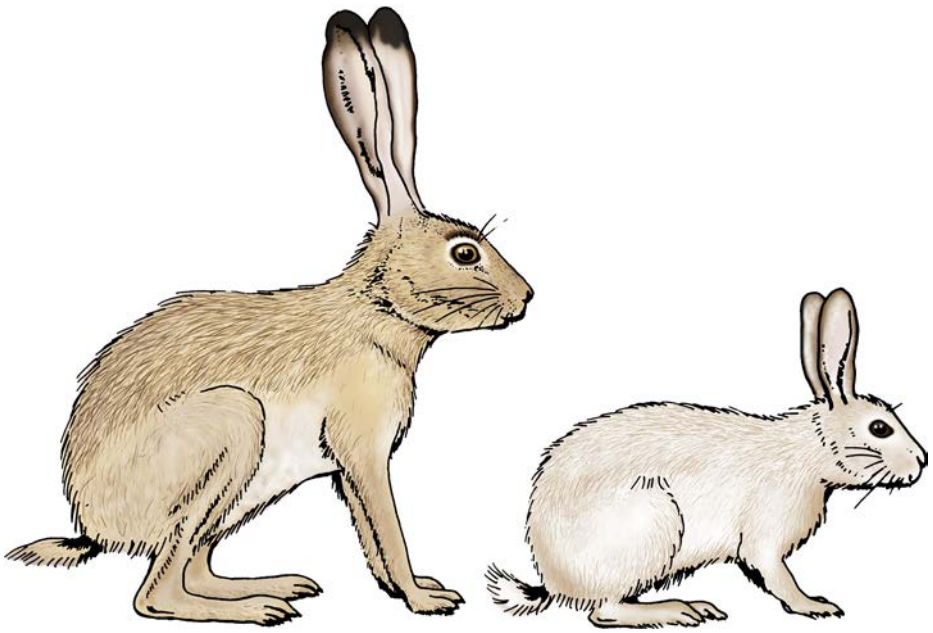


Fig. 11.2 Diagram comparing the bodies of a hare (left) and a rabbit (right). Note the differences in size and length of legs and ears.

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Lagomorpha (to which rabbits belong) and restrict the order Rodentia to the larger group of mammals with only one pair of upper incisors. Based on results of mitochondrial plus nuclear DNA sequences, the concept that the two orders are in fact related has resurged.[28] The term Glires from Linnaeus is now used to describe the infraclass that encompasses these two orders.

Breeds and Varieties

Rabbits are commonly thought to have been domesticated in the 5th century by French monks.[12] This appeared to have been triggered inadvertently by Pope Gregory I in CE 600 when decreeing that "laurices," a delicacy consisting of unborn or newly born rabbits, were not considered meat and thus permissible to eat during Lent and other Christian fasts.[9] Unfortunately this popular fallacy can be traced to the German zoologist Nachtsheim[76] and the British archaeologist Zeuner,[117] both of whom miscited a late 6th-century Latin manuscript by St Gregory of Tours.[52] It seems likely that rabbits were domesticated somewhere in southwest France, because the genetic evidence demonstrates a close affinity between domestic rabbits and wild French rabbits. The archaeological evidence shows rabbits were exploited in southwest France long before elsewhere in Europe, except in Iberia. The historical evidence shows a long association between French monks and rabbits.

It was not until the 16th century that breeds were developed. However, the development of most breeds dates back no further than 200 years. Many breeds bear little resemblance to the original wild stock—some are small (dwarf rabbits) weighing 1 kg, but those bred for meat production may weigh as much as 7 kg. Rabbits are divided into more than 60 fancy and fur breeds.[7] The fur group is divided into normal fur breeds, rex breeds, and satin breeds. In normal fur breeds, the coat is made up of an undercoat and projecting guard hairs; the rex breeds have short guard hairs that do not project above the undercoat; and satin breeds have an abnormal hair fiber that produces a sheen.[95] *Variety* describes a color (e.g., black, blue, steel gray, tortoiseshell) within a breed. More than 500 varieties are described. For a list and images of domestic rabbit breeds, refer to the American Rabbit Breeders Association (www.arba.net) or the British Rabbit Council (www.thebrc.org).

Body conformation and ear size vary widely among rabbit breeds, and rabbit fanciers have coined some unusual terms to describe types of lagomorph body shapes and ears. The small and chunky body of a dwarf rabbit, like a cobblestone, is called a *cobby*; the long and lean body of a Belgian hare is described as *racy*; and giant rabbits are described as *mandolin-shaped* because of the high, curved top line over their hindquarters.[113] Most rabbit breeds have upright ears that are long or short. However, some breeds have soft pliable ears that hang downward and are incapable of erection; we know these as *lops*.

Life Span

Records for life span of rabbits in captivity are 9, 10, and 18 years.[11] Veterinarians often report seeing pet rabbits that are 10 to 12 years of age, and one of the authors has seen a 15-year-old pet rabbit. Wild rabbits in an enclosure and receiving supplementary winter feed were recorded as surviving a maximum of 7.7 and 8.7 years (female and male, respectively).[107] The longest life span recorded for a female European rabbit in the wild is 7.6 years.[88]

ANATOMY

Several books have been published on the anatomy of the rabbit. *A Colour Atlas of the Anatomy of Small Laboratory Animals: Rabbit, Guinea Pig* has been republished three times since its first print in 1990 and is found in many libraries.[90] The *Atlas of Rabbit Anatomy* is only found in selected university libraries because of its limited print run in 1973.[3]

Body Size, Condition, Surface Area, and Fat

Body condition has been calculated in meat rabbits for reproduction and feeding. Because obesity is an emerging problem in pet rabbits, an easy-to-use adipose tissue measurement has been developed. In medium-size rabbits, the body weight to distal forelimb length ratio is most strongly associated with body condition score, where 5 is obese, 2.5 to 3.5 is ideal, and 1 is emaciated.[103] A formula for body surface area has been calculated by using modeling guided by computed tomography.[116] The formula is body surface area = $(9.9 \times [\text{body weight in grams}]^{2/3})/10{,}000$.

Most of the brown fat in newborn and young rabbits is located in three subcutaneous lobes in the neck and interscapular region.[22] Yellow-fat has been reported in many rabbit breeds and is a simple Mendelian recessive trait due to a novel AAT-deletion mutation at codon 248 of the BCO2 gene.[102] Yellow-fat, ranging from pale, waxy yellow to deep orange, should not be confused with jaundice or steatitis (pansteatitis).

Skin and Hair

Rabbit skin is very delicate. Unless care is taken when clipping fur for surgery, it is easy to tear or rip the skin. Electric clippers require thin blades (size 50, 1/125″/0.2 mm or size 40, 1/100″/0.25 mm) because rabbit hairs are so fine. Hair growth in rabbits occurs in periodic orderly waves originating on the head and ventrum and spreading dorsally and caudally.[112] This is most noticeable when hair regrows after clipping. Adult rabbits usually molt twice a year (spring and fall).[43]

Intact female rabbits have a large fold of skin over the throat known as the *dewlap*. Breeding does pull fur from this area to line their nests before kindling. Moist dermatitis often develops in this area.

Rabbits do not have footpads; instead, coarse fur covers the front and hind toes and metatarsal areas. When a rabbit is sitting undisturbed, the plantar surface of the lower hindlimb from the toes to the hock is in contact with the ground. Rabbits housed on wire or hard smooth floors often develop an ulcerative pododermatitis of this area called sore hocks. Large breeds and obese, emaciated, or pregnant rabbits are more at risk. Guard hairs provide the normal protective barrier between the feet, the plantar surface of the lower hindlimb, and the substrate. Therefore do not clip hair from the base of the feet or hocks. Whereas the rex breed has been hypothesized to be prone to pododermatitis

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due to the lack of protective guard hairs on the feet and hocks, a retrospective study of skin disease in pet rabbits found that rex rabbits had no greater incidence than other breeds.[99] The claws of rabbits are very sharp, and a rabbit picked up without appropriate support of its hindquarters can inflict painful scratches on the handler.

Tactile vibrissae present on the face aid in food discrimination and underground navigation. The only glabrous areas of the rabbit are the nose tip, scrotal sacs, and inguinal folds.

Scent Marking Glands

Rabbits are strongly territorial, and both sexes have three glands used in scent-marking behavior: the chin glands, which are specialized submandibular glands opening onto the underside of the chin; the anal glands; and a pair of pocket-like perineal glands called the inguinal glands that are relatively large and often harbor a normal yellowish-brown deposit. The size of the glands and degree of marking is androgen-dependent and related to the level of sexual activity.[71] Males mark more frequently than females, dominants of both sexes mark more frequently than subordinates, and dominants mark most in the presence of subordinate rivals. When a rabbit becomes dominant, a new compound appears in the chin gland secretion, 2-phenoxyethanol.[46] This compound is a fixative used in the perfume industry and slows the release rate of compounds in chin gland secretions, enabling the scent to persist in the environment and not dissipate. The dominant rabbit thus reigns over the olfactory environment, as it does the physical environment.

Sense Organs and Nervous System

Rabbits are subject to a high degree of predation, and consequently their sense organs are well developed. They are sensitive to catecholamines and have evolved for flight rather than fight. Temperature, heart rate, and respiratory rates increase notably in a frightened animal; therefore obtain these values early in the physical examination because the stress of handling, transport, or the hospital environment may alter these parameters. Washing your hands clean of "predator" animal odors (dog, cat, or ferret) before starting the consultation can minimize stress.

Eye

Prince has described the anatomy and physiology of the rabbit eye in great detail in *The Rabbit in Eye Research*.[92] The rabbit cornea is large, occupying 30% of the globe, and the eyes are directed more laterally than those of most mammals. These two features give rabbits a panoramic field of vision to readily detect predators.[51] However, their eyes cannot visualize the small area beneath the mouth (blind spot), and rabbits depend on the sensitivity of the lips and vibrissae for food discrimination. During clinical examination, avoid touching the rostral aspect of the muzzle because it involves contact with the blind spot and startles the rabbit. Humans blink once every 5 seconds but rabbits rarely make spontaneous blinks (2–4 per hour).[68]

As in most rodents and other lagomorphs, the lens is spherical and large. The ciliary body is small and poorly developed. These two features suggest that rabbits have a limited need to alternate near and far focus (i.e., accommodation).

The optic nerve is above the horizontal midline of the eye, and fundus examination involves looking upward into the eye. Retinal vessels spread out horizontally from the optic disc; also, rabbits have a depression or physiologic cup in their optic disc, as do dogs. Rabbits do not have a tapetum lucidum.[92]

The nictitating membrane or third eyelid is prominent, found in the medial canthus of the eye, and associated with the superficial (nictitans) and deep (harderian) orbital glands. Behind and separated from the deep cartilage of the nictitating membrane is the harderian gland, which has a small, white upper lobe connected to a large pink lower lobe by a narrow strand medial to the optic nerve. The lower lobe is known as the deep gland of the nictitating membrane. Although both the superficial and deep glands of the third eyelid can prolapse, it is the deep gland that most frequently prolapses. [53] The clinical condition and treatment is similar to cherry eye in dogs.[10]

The horseshoe-shaped harderian gland is wrapped behind the eyeball and is phylogenetically and anatomically associated with the nictitating membrane. The single excretory duct opens at the base of the nictitating membrane, and the milky secretion is made up of a complex mixture of lipids, protein, and the pigment protoporphyrin that provides lubrication for the edges of the eyelid.[29] Epiphora in rabbits often presents as a milky white overflow of tears because of impaired drainage or obstruction of the nasolacrimal drainage system—the tears are normal harderian gland secretions.[57] Other orbital glands are the lacrimal and accessory lacrimal glands located caudodorsal and ventral to the orbit, respectively.

A few millimeters posterior to the limbus and under the bulbar conjunctiva, the rectus dorsalis muscle is visible.[45] Placing an anchoring suture under or around this muscle stabilizes the globe during surgery; in other species, dissection is necessary to find extraocular muscles.

In rabbits, the primary channel for return of venous blood from the head, including that from the eye, is the external jugular vein[91]; in contrast, in people the primary drainage of the eye and head is via the internal jugular vein. In other species, such as dogs, significant anastomoses exist between the branches of the internal and external jugular veins. In rabbits, such anastomoses are minor, and ligation or long-term catheterization of the external jugular vein results in swelling and protrusion of the eyeball for about 24 hours, after which its normal appearance returns.[50] The same pattern of vascularity also applies to the arterial blood supply of the rabbit's eyes, but ligation of the external carotid artery results in ipsilateral ocular necrosis.

Rabbits, like rodents, have an extensive orbital venous plexus.[106] Because of possible severe hemorrhage, enucleation of the eye is difficult compared with other species. Bilateral exophthalmos can occur in rabbits secondary to engorgement of their orbital venous sinuses (retrobulbar venous plexus). Rabbits with either compromised heart function or a cranial thoracic mass[108] such as thymoma can present with marked "cranial vena cava" signs such as bilateral exophthalmos. Occasionally, bilateral exophthalmos can also be seen in rabbits exhibiting extreme fear.

The nasolacrimal drainage system provides a conduit for tears from the lacrimal lake to the nasal cavity. In rabbits, a

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single ventral lacrimal punctum (about 3 to 4 mm ventral to the lid margin), canaliculus, sac, duct, and nasal meatus form the drainage system for each eye. The diameter of the nasolacrimal duct is small and narrows in two places, where it changes course. These two sites, the proximal maxillary bend and the apex of the main upper incisor, are important in developing nasolacrimal obstruction (dacryostenosis) (see Chapter 40).[65] Dacryocystitis and dacryostenosis often cause epiphora, one of the most common ocular problems seen in rabbits.

Ear

The pinnae are highly vascular and have the largest arteriovenous shunts in the body. At rest, the pinna of leporids is a thermoregulatory organ. Heat flow from the pinna oscillates synchronously in both ears. A warm environment (25°C) results in a general vasodilation of the pinnae, and a cool environment (15°C) leads to a general vasoconstriction, but the thermal pulsing continues independent of temperature.[73] The Australian population of the European rabbit has responded to its warmer environment by increasing the mean length of its pinna from 71 mm, as found in English and French wild rabbits, to 79 mm.[85]

Anatomists have hypothesized another role for the pinna of leporids, as a part of a suspensory system for the greater portion of the head, absorbing shock that might otherwise interfere with vision during high speed locomotion.[101] This is certainly the case with European hares. However, because the rabbit is semi-fossorial and does not rely on sustained fast running to avoid predation as do hares, the significance of the ears in capital shock absorption is not as important.

In large-eared rabbits, the veins of the ear margins (medial and caudal auricular veins) are easily accessible for venipuncture. However, in small-eared rabbits such as dwarf breeds, venipuncture of the ear veins can lead to vasculitis, vascular necrosis, and sloughing of ear pinna. During anesthesia, the central auricular artery and auricular veins are good sites to obtain noninvasive measurements such as pulse oximeter blood oxygen saturation and laser-based systolic and diastolic arterial blood pressure.[47]

The vertical ear canal has a natural diverticulum separated by a cartilaginous bridge called the *tragus*. Lop-eared breeds have a stenosis in their ear canals at the point of flexion that may predispose to otitis externa. Surgical intervention to treat otitis externa and media is becoming more common (see Chapter 31).[19] Knowledge of rabbit ear anatomy is critical in understanding ear pathophysiology and treatment options. Rabbits do not have distinct vertical and horizontal ear canals but have a vertical-leaning ear canal. For any bulla osteotomy surgery, be aware of the location of the facial nerve, as temporary or permanent facial nerve paralysis (lack of palpebral reflex, ipsilateral drooling, ipsilateral facial contraction) is common.[19]

Muscles and Skeleton

Bones of rabbits are relatively delicate compared with their muscle mass. The skeleton represents only 7% to 8% of body weight in rabbits, whereas the skeletal muscle comprises around 50% of the body weight.[59,96] By comparison, the skeleton of a cat constitutes 12% to 13% of body weight. However, the dry matter and percentage calcium is higher in rabbit bones than in cat bones.[1] The infraspinous fossa of rabbits is sharply triangular, whereas that of cats is more rounded; also, the suprahamate process of the acromion is hook shaped in rabbits, whereas it is blunted in cats.[24] Good drawings of these skeletal differences are found in Okerman's *Diseases of Domestic Rabbits*.[81] The color of the muscles also distinguishes the two: rabbit muscles are pale pink, whereas those of cats are deep red.[24]

The acetabulum of rabbits is formed by the ilium, the ischium, and a small accessory bone, the os acetabuli, which excludes the pubis. In other animals, the acetabulum comprises the ilium, the ischium, and the pubis. The trochanteric fossa of the femur is a good site for intraosseous catheter placement and is easily located by palpating the prominent greater trochanter.[8] The trochanteric fossa can potentially be misinterpreted as a bone lesion on computed tomography (CT) images.[109]

Scientists have studied skeletal muscle architecture in different species to determine the force, velocity, and displacement properties of a muscle. The rabbit has a pelvic limb muscle mass of 13% (of total body mass), reflecting its need to evade predators by accelerating quickly and maintaining high-speed locomotion.[114] Forelimb muscle mass accounts for 9% of total body mass, highlighting the predisposition toward hindlimb propulsion. The bulk of the fore and hindlimb muscle mass is proximal—the distal limbs (e.g., carpi and tarsi) have little musculature, and in the hindlimb this adaptation decreases rotational inertia.[60] Spinal musculature accounts for 9% of body mass—a substantial portion of the total locomotor muscle mass (≈30%).[114] Much of the back musculature extends the lumbar spine and increases the distance from the hind foot to the rabbit's center of mass. When normalized for body mass, the back muscles are much larger than those of the dog and horse. The powerful hind legs and lumbar muscles mean that rabbits can kick violently. If rabbits are not held securely when picked up, their kicking can result in a vertebral fracture (usually at the seventh lumbar vertebra) and damage to the spinal cord. Clinically, the large lumbar and proximal hindlimb muscles are the best sites for intramuscular injections.

The normal vertebral formula, as found in 44%–75% of rabbits in two studies is C7/T12/L7/S4.[41,93] Seven vertebral formulas can be identified: cervical (C) is always 7, but thoracic (T), lumbar (L) and sacral vertebrae varies from 11–13T, 6–8L, and 4–6S.[93] The spinal cord ends within S2 in 79%, S1 in 19%, and S3 in 2% of rabbits.[41] This feature is unusual, because the spinal cord ends in most other species within the caudal lumbar region.

Digestive System

The definitive references on the anatomy and physiology of the digestive tract of rabbits are Cheeke's *Rabbit Feeding and Nutrition*[14] and the more recent *The Nutrition of the Rabbit* by Blas and Wiseman.[6] Most of the information described in this section is from these books unless otherwise noted.

Teeth

All the teeth of rabbits are classified *elodont* (continuously growing, with no anatomic "roots") and *hypsodont* (long crowned).

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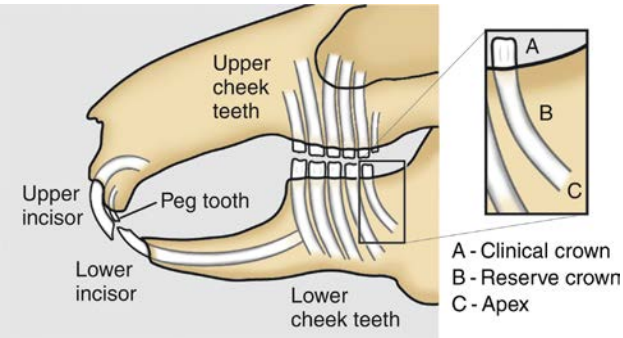


Fig. 11.3 Cross-section schematic of a rabbit skull showing dentition of mandible and maxilla and of an individual tooth. (Courtesy Marise Watson).

The teeth can also be classified as aradicular. This type of dentition also allows for a concurrent increase in teeth size with growth of the animal.[26]

The rabbit dental formula is *2 (I2/1 C0/0 PM3/2 M3/3) = 28*. It is useful clinically to divide rabbit dentition into two groups, the *incisor teeth set* and the *cheek teeth set* (premolars and molars). There is no anatomic difference between premolars and molars. Each cheek teeth arcade can be divided into *quadrants* (upper and lower, right and left). Each tooth can be further divided into the *clinical crown* (region of tooth exposed above the gingival margin) and the *reserve crown* (region of tooth buried below the gingival margin), which is often misnamed the "root" of the tooth. The growing portion at the tip of the reserve crown is the *apex*, which is open in rabbit elodont hypsodont teeth (Fig. 11.3) Further discussion of rabbit dental anatomy and physiology is found in Chapter 36.

Mouth

The diastema allows the lips to fold inward (inflexa pellita) and come together behind the incisors.[1] The infolding brings fur inside the mouth and effectively forms an antechamber in the rostral part of the mouth.[26] A median cleft of the upper lip, commonly known as harelip, allows easy exposure of the incisors rostrally (Fig. 11.4).[26] The lower jaw is narrower than the upper jaw, a feature known as *anisognathism*. Rabbits have no bony union between the two halves of the mandible. However, the existence of broad symphyseal plates with highly interdigitating rugosities, united by dense connective tissue, render the symphyseal joint virtually immobile.[48] The rigid symphysis converts the mandibles into a single unit and permits the masticatory muscles on both sides of the head to shift the jaw laterally and generate the force required for grinding. Because the articular process forming the temporomandibular joint is elongated longitudinally, the mandible can move forward, backward, and vertically but less so from side to side.

The mouth opening is small. The gape of maximal jaw opening in rabbits is only 20° to 25°,[110] compared with 65° to 70° in small felids.[32] These characteristics mean that examination of the rabbit mouth can be relatively difficult. Muscles of the jaws extend both forward and backward. This confers a deceptively large appearance to the oral cavity, which is actually smaller than the size of the jaws suggests.

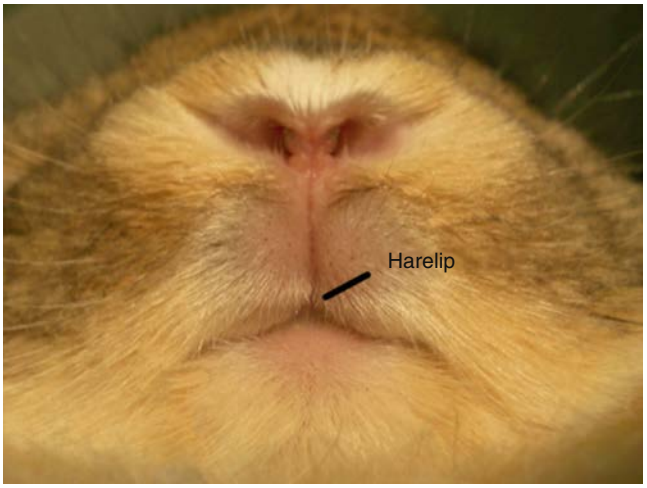


Fig. 11.4 In rabbits, the pars supralabialis (supralabial part) of the musculus orbicularis oris (literally, the little circular muscle of the mouth) is reduced ventrally and a cleft divides the upper lip. This cleft is called the upper lip cleft or "harelip."

The rabbit has four pairs of major salivary glands: the parotid, mandibular (also known as submaxillary or submandibular), sublingual, and zygomatic. Saliva is produced continuously by the mandibular glands and in response to food intake by the parotid, mandibular, sublingual, and zygomatic glands.[21] There is a marked taste preference for glucose and its disaccharide constituent maltose, suggesting that these saccharides are likely to add to the taste sensation while feeding on starchy plants.[58] Salivary gland ducts and their openings are not well described in the rabbit, except for the mandibular gland duct that opens into an elongated sublingual caruncle on the floor of the mouth, under the tongue caudal to the mandibular incisors.[64]

The tongue is large for the size of the skull. The large tongue and small mouth make visualizing the epiglottis unrealistic without endoscopic equipment. The dorsal surface of the tongue is covered by multiple small elevations termed papillae, which give it a roughened surface. The dorsal surface of the tongue can be divided into the rostral, middle, and caudal parts. The rostral part contains the lingual apex and makes up almost half of the tongue. The middle part has a conspicuous lingual prominence (torus linguae) located at the intermolar region close to the caudal half area of the tongue (Fig. 11.5).[80]

The caudal tongue is a narrow region located at the lingual root. The presence of a lingual prominence is a characteristic structure of herbivores and is effective for grinding food between the tongue and the upper palate. Large, spearhead-like filiform papillae on the rostral edge and branched filiform papillae on the caudal area of the prominence facilitate movement of ingesta within the mouth.[80]

Abdominal Cavity

Rabbits are true herbivores with a large abdominal cavity and are classified as hindgut fermenters, like horses. The gastrointestinal tract is relatively long, and its contents make up 10% to 20% of the body weight. The largest organs are the stomach and cecum, with their combined contents accounting for 10% (range 5%–19%) of the total body weight. Preanesthetic

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Fig. 11.5 Rabbits have large tongues with a noticeable prominence, known as the torus linguae (black arrow), found in the intermolar region. This structure aids in grinding food between the tongue and the upper palate.

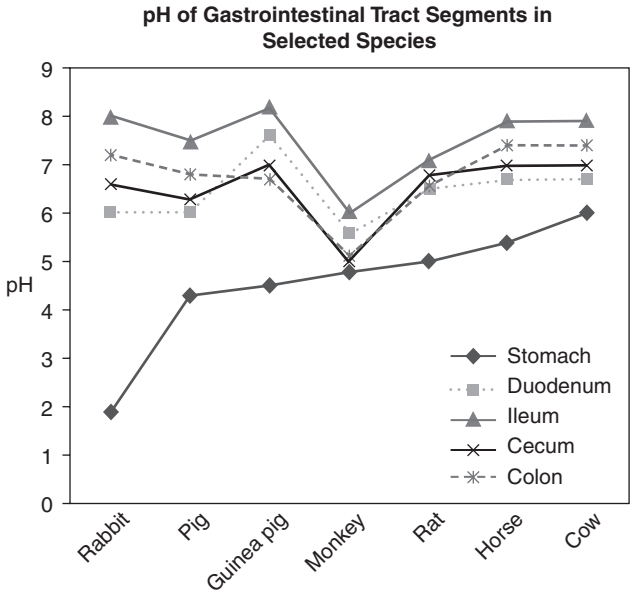


Fig. 11.6 The pH of segments of the gastrointestinal tract in selected species. Note the low stomach pH (2) of the rabbit.

fasting is sometimes recommended to partly empty the intestinal tract—not to prevent vomiting. The radiographic anatomy of dwarf rabbit abdomens has been described with normal measurements.[27]

Stomach. The stomach serves as a reservoir for much of the ingested feed. It typically contains 15% of the alimentary tract ingesta, and food and fecal pellets are usually present. The stomach lacks specialized regions, is thin walled, and often appears ruptured at necropsy because of gas distention during autolysis. However, the cardia and pylorus are well developed. The lower esophagus contains a massive muscular sphincter and a serrated mucosal rosette at the cardiac orifice—these two structures form a perfect closing mechanism between stomach and esophagus, and rabbits are unable to vomit. The pylorus is easily compressed by the duodenum, which exits at an acute angle. Gastric distention or compression due to a fur mat, gas, or hepatomegaly contributes to pyloric compression and prevents emptying.

The rabbit stomach is extremely acidic (pH 2), which effectively kills bacteria and other microorganisms, so that the stomach and small intestine are essentially sterile. In suckling rabbits, the stomach acidity is higher (pH 5–6.5), but drops after weaning (pH 2–3) (Fig. 11.6). This is why weanling rabbits are so susceptible to diarrhea—because the stomach pH is not low enough to kill ingested bacteria.

Small Intestine. The small intestine is shorter in rabbits than in other species and makes up about 12% of the total gastrointestinal tract volume. The duodenum and jejunum have a relatively small lumen. Peyer's patches are absent from the duodenum and the first half of the ileum. No correlation exists between the number of Peyer's patches and intestinal length, and only three to nine Peyer's patches may be visible in the first one-quarter of the jejunum and last one-quarter of the ileum.[72,94] The

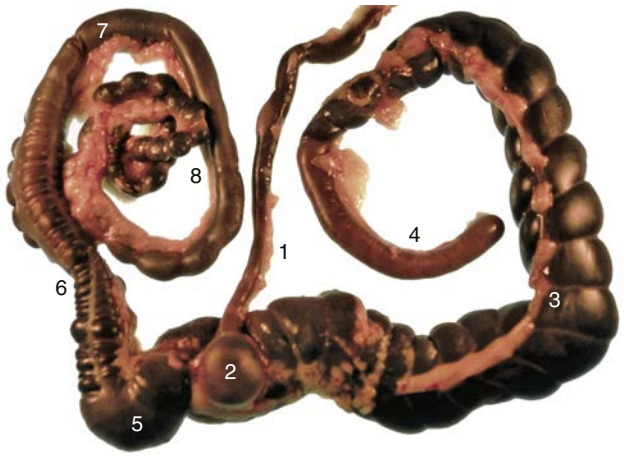


Fig. 11.7 The dissected large intestine of a rabbit. 1, Ileum; 2, sacculus rotundus; 3, body of cecum (note the long spiral fold along its length); 4, vermiform appendix; 5, ampulla coli; 6, proximal colon; 7, fusus coli; 8, distal colon.

terminal portion of the ileum ends with the rounded *sacculus rotundus* at the ileocecocolic junction. The sacculus rotundus, sometimes referred to as the *ileocecal tonsil*, has a honeycombed external appearance owing to the presence of numerous lymph follicles. The terminal portion of the ileum is a common site of foreign body impaction due to luminal narrowing.

Large Intestine. Rabbits have a large, thin-walled, coiled cecum that displays 18 to 22 haustra-like bulges or pouches, delineated by a spiral running constriction.[98] The cecum holds about 40% of the ingesta (Fig. 11.7) and ends in a finger-like, thick-walled, pale *vermiform appendix* that is characterized, like the sacculus rotundus, by abundant lymphatic tissue. The cecum is the largest and most prominent organ in the abdominal cavity of rabbits. It folds onto itself three times as it constricts around most of the inner surface of the abdominal cavity wall. The cecal contents are generally semifluid.

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Sacculations and the presence of bands characterize the colon. These start at the bulbous cecal *ampulla coli,* from which the proximal colon emerges. The *fusus coli,* a thickened section of colon heavily supplied with ganglion cell aggregates, separates the proximal from the distal colon. The fusus coli acts as a pacemaker that controls the contractions for excreting the two distinct types of feces that rabbits produce: a dry, hard fecal pellet, which is discarded; and a soft fecal pellet, which is contained within a strong mucous envelope (also known as soft feces, night feces, or cecotropes) (see Chapter 13). The cecotropes attach to hairs around the anus and are ingested directly and swallowed without mastication.

The large intestine is rich in goblet cells that coat the cecotropes with mucus. This mucilaginous membrane that surrounds cecotropes acts as a barrier to the low pH of the stomach and permits their reabsorption in the small intestine. Multiple zones of proliferating cells exist at multiple levels in the crypt column of the distal colon and rapidly differentiate as they migrate toward the surface epithelium. Consequently, populations of proliferating cells in the distal colon have a rapid turnover.[40] Inflammation of the large intestine will increase crypt populations of goblet cells; consequently, mucus associated with feces is a normal inflammatory response in the rabbit. The presence of mucus is not pathognomonic, and the disease mucoid enteropathy is descriptive only (not etiologic) in its name.

Liver, Gallbladder, Pancreas, and Spleen. The liver lays caudal to the diaphragm mostly within the caudal ribcage. It is divided into two major lobes, a larger left and smaller right, separated by a deep median cleft. The left lobe is subdivided into lateral and medial lobes. The right lobe has subdivisions of lateral and medial lobes, plus smaller quadrate and caudate lobes, giving a total of six lobes. The *caudate lobe* has a narrow attachment or stalk to the dorsal, hilar region of the liver. This stalk is prone to displacement, and torsion of the caudate lobe has been reported.[39] In recent years, early surgical intervention has recognized that other liver lobes can be torsed. In a survey of 16 rabbits with liver lobe torsion, 56% involved the caudate lobe, (28%) the right lateral lobe, (11%) the left lateral lobe, and (5%) the right medial lobe; 2 rabbits had more than one torsed liver lobe.[39]

The gallbladder is deceptively deep within the abdominal cavity and is located between the right medial and quadrate lobe within the fossa of the quadrate lobe. Gallbladder (absence, duplication, variation in size) and extrahepatic biliary tract anomalies are found in ≈1% of rabbits.[42] Rabbits secrete mainly biliverdin, rather than bilirubin, in their bile, as do most nonmammalian species. Similar to dogs, in rabbits the bile and pancreatic ducts have separate openings in the duodenum. The bile duct empties into the proximal part of the duodenum, whereas the single pancreatic duct opens at the junction of the ascending and transverse loops of duodenum. Ligation of the pancreatic duct does not result in pancreatic insufficiency. Although the pancreas of rabbits is closely associated with the duodenum, it is diffuse and often difficult to differentiate from surrounding mesentery.

Gut-associated lymphoid tissue constitutes about 50% of the total lymphoid tissue mass. Therefore the spleen is relatively small compared with other species. The spleen is elongated and flat and lies along the greater curvature of the stomach. The frequency of accessory spleens in rabbits is 9%.[37]

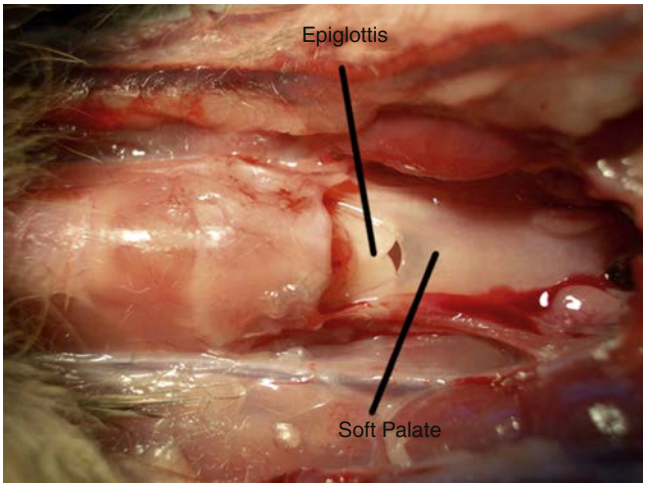


Fig. 11.8 Dissection of the ventral view of the oropharynx and glottis of the rabbit. Rabbits are obligate nasal breathers because the larynx is dorsal in the oropharynx, and the epiglottis opens directly into the soft palate.

Respiratory System and Thymus

Rabbits are obligate nasal breathers. Their larynx is placed high in the oropharynx where it has direct access to the nasopharynx. The epiglottis normally lies dorsal to the soft palate (Fig. 11.8), which has important clinical and anesthetic consequences. Mouth breathing is a poor prognostic sign, and inflammation of the upper respiratory tract increases the risk of anesthetic-related death in nonintubated animals.

Rabbits can be challenging to intubate. Their small mouth and large cheek teeth restrict direct visualization of the larynx. Subglottic soft tissue trauma results in a thickened tissue response in young rabbits, not seen in adult rabbits.[89] Traumatic or prolonged endotracheal intubation can cause mechanical abrasion, pressure necrosis, and subsequent ulceration of the laryngeal and tracheal mucosa. Average tracheal diameters of rabbits weighing 2.3 to 5.1 kg are 5.8 mm (ventral-dorsal) by 5.4 mm (lateral) at the level of the cricoid, and 4.7 mm (ventral-dorsal) by 5.9 mm (lateral) at the eighth tracheal ring.[61] The dimensions of the rabbit subglottis appear consistent independent of weight, whereas tracheal size at the level of the eighth tracheal cartilage varies significantly by weight.

Hyperemia of the trachea is a normal endoscopic finding in rabbits.[54] The deep red color of the epithelium does not involve the dorsal tracheal membrane and vanishes relatively abruptly at the level of the carina.

Rabbits have three left lung lobes (cranial, middle, caudal) and four right lung lobes (cranial, middle, caudal, accessory). The left lung is about two-thirds the size of the right lung. Unlike rats and mice, the left lung of rabbits is lobed. In rabbits (and rodents), the lungs do not have connective tissue septae, which in other animals divide the lungs into the pyramidal portions of pulmonary tissue known as lobules. Therefore "lobular pneumonia" is not described in rabbits and rodents. Lobular

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pneumonia is classically bronchogenic in origin compared with lobar pneumonia, which can be hematogenous or bronchogenic in origin. Pneumonia in rabbits and rodents is always lobar.

The lungs of rabbits and rodents differ from those of people and dogs in total lung volume changes. In people and dogs, residual volume (air that remains in the lung after expiration) increases with age at the expense of vital capacity (maximal volume of air that can be expelled from the lungs). Short, shallow, sometimes labored breathing is seen in geriatric people and dogs. In rabbits and rodents, the lung volume changes with age, whereas the ratio of residual volume to vital capacity does not change. Any signs of dyspnea in rabbits and rodents are always cause for a poor prognosis.

The thoracic cavity of rabbits is relatively small; in contrast, the abdominal cavity is large, and the rabbit breathes primarily by contraction of the diaphragm. These characteristics allow for an efficient method of artificial respiration: suspend the rabbit horizontally in midair, holding the forelimbs in one hand and back legs in the other hand, and gently rock the rabbit from a head-up to a head-down position every 1 to 2 seconds.

The thymus is "sail shaped," reaches maximum weight around 4 to 5 months, and then progressively decreases in size, although it persists into adult life.[67] It consists of three lobes: one main left thoracic lobe and the dorsal and ventral right thoracic lobes. The thymus lays cranioventral to the heart and extends forward to the thoracic inlet. It is not unusual to have a large thymus occupying the cranial thorax (from ventral to the heart to the thoracic inlet) in rabbits.

Cardiovascular System

The size of the rabbit's heart is directly related to its body size. Because the size limits blood volume, the tissues cannot be supplied with oxygen by means of increased ventricular volume pumped out in one beat. Instead, heartbeat frequency is the major modifying variable, and consequently, heart rates are higher in smaller animals than in larger ones. In rabbits, the heart rate can vary from 180 to 250 beats/min. Despite the small size and rapid contraction rate of rabbit hearts, quantitative Doppler echocardiographic methods have been validated to evaluate structural and functional abnormalities (see Chapter 19).[35,36]

The heart lies in the cranial thorax and is normally positioned between the third and sixth ribs. Rabbits have a relatively small heart, which accounts for about 0.3% of body weight. The small size of the thorax may paradoxically create the impression of an enlarged heart radiographically. The vertebral heart score system is not used in rabbits to measure heart size radiographically because soft tissue shadows (thymus or intrapleural fat) make accurate evaluation of the cardiac border difficult. Furthermore, differences between the cardiac long axis length and vertebral heart score vary according to body weight.[82]

Rabbits have a left and right cranial vena cava. The left carinal vena cava and coronary veins terminate in a coronary sinus that may be misinterpreted as a congenital defect or early right-sided heart failure.[86] A limited collateral coronary circulation can predispose the heart to ischemia induced by coronary vasoconstriction—a significant causative factor in ketamine/xylazine-induced myocardial fibrosis.[66] The right atrioventricular valve is uniquely composed of two, rather than three, cusps. The rabbit aorta has a rhythmic contraction that is neurogenic in origin.

The veins have thin walls, and peripheral veins are susceptible to hematoma formation, which can be avoided by judicious use of Teflon catheters and gentle pressure. Muscle swelling in the pulmonary artery of rabbits make this vessel thicker and more muscular than it is in any other species. Pulmonary hypertension causes death from anaphylaxis, and at necropsy, severe constriction of the pulmonary arteries and dilatation of the right side of the heart are observed.

Urinary System

Most mammalian kidneys are multipapillate, but those of rabbits and rodents are unipapillate. Only one papilla and one calyx enter the ureter directly.

The plasticity of the rabbit urinary system has not been fully recognized. Rabbits from Australian desert zones have large kidneys with powerful urine-concentrating ability, small adrenal glands, and low levels of circulating aldosterone, whereas those from alpine zones have small kidneys (at least 25% less in weight than those of desert rabbits), large adrenal glands, and high levels of circulating aldosterone.[75] In desert-dwelling rabbits, which live on a high-fiber, high-salt, low-protein plant diet and have limited access to water, the medulla is long. In contrast, in alpine rabbits, which enjoy a high-protein diet of lush grasses that are low in sodium, the renal medulla is short. A main reason that rabbits have succeeded in colonizing diverse geographic regions may be that their urinary system can vary its developmental pattern under different environmental conditions and with different digestive strategies.

Urine concentrating ability refers to the water-sparing effect of the kidney by the corticomedullary gradient, which is partially created by urea. Urea concentration relies on other mechanisms such as glomerular filtration, tubular secretion, and reabsorption. The two processes are different, although the effects of one impact the other. A frequently cited article on the effect of urea loading on volume and concentration of urine in rabbits showed that an increase in urea load is associated with an increased amount of urine production.[100] However, this holds true only in rabbits eating a low-salt diet. The article's conclusion has led to the frequently quoted error that rabbits have limited capacity to concentrate urea.

The serum calcium level of rabbits is unusual because it is not regulated in a narrow range but reflects the level of dietary calcium. Urine is a major route of calcium excretion, which varies directly with the serum calcium level. Whereas the fractional excretion of calcium in most mammals is less than 2%, the range for rabbits is 45% to 60%. Increases in dietary calcium directly increase urinary calcium excretion (Fig. 11. 9). Urine consistency is often thick and creamy because of a white calcium carbonate precipitate. Prolonged intake of a diet high in calcium results in calcification of the aorta and kidney. High vitamin D intake intensifies this effect.[55]

Biologic pigments from the breakdown of endogenously synthesized compounds (e.g., bile pigments, porphyrins, flavins,

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Comparative calcium metabolism		
Item (%)	Rabbits	Rats
Ingested Ca in feces	19.8	92.7
Ingested Ca in urine	59.0	2.0
Apparent Ca digestibility	80.2	7.3

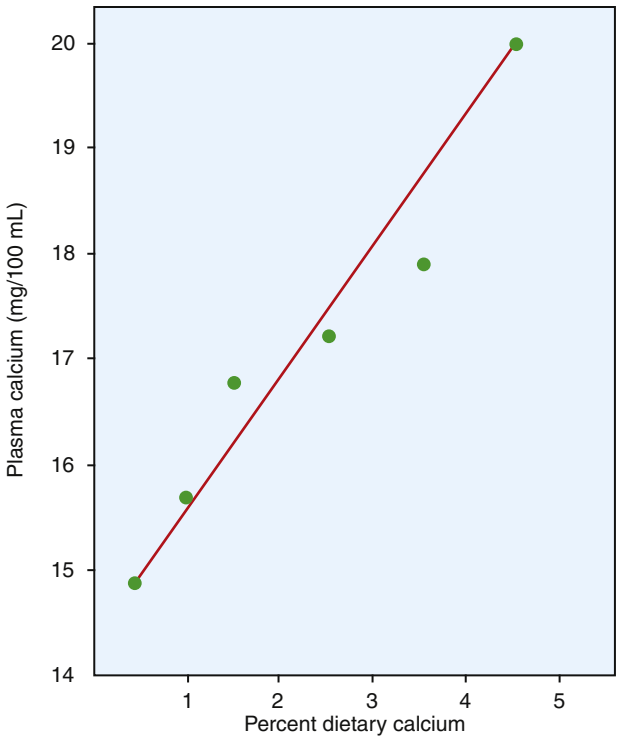


Fig. 11.9 Table of calcium digestibility versus ingested calcium in urine and feces for rats and rabbits. Graph of plasma calcium concentration versus ingested (dietary) calcium for rabbits. In contrast to many species, the blood calcium level of rabbits readily reflects dietary calcium intake (see graph). Most mammals regulate intestinal calcium absorption to metabolic need. In a rat, little calcium is absorbed, and most of it is passed in the feces, whereas a rabbit absorbs most of the calcium ingested independent of metabolic needs (see table). When serum calcium exceeds the renal threshold in a rabbit, excess serum calcium is excreted in the urine, whereas other mammals excrete little calcium in the urine (see table). Rabbit kidneys have a high calcium fractional excretion (approximately 2.25 mmol/L) compared with other mammals (approximately 1.5 mM). (Modified after Cheeke PR. *Rabbit Feeding and Nutrition*. Orlando, FL: Academic Press; 1987.)

melanins, pteridines) or ingested plant pigments are excreted in urine and, with fluid volume (hydration status), give urine a characteristic color. Among the pigments, a group of yellow, brown, and red pigments, generally designated as urochromes, are considered metabolic breakdown products. The red pigment was first named *uroerythrin* by Simon in 1840[97] and was known to increase with certain metabolic states such as high fever or tissue degradation. Uroerythrin is a breakdown product or a precursor of heme[4] and is related to the bile pigment biliverdin. Urine pigments can be bile pigments such as bilirubin, biliverdin, or bilicyanin; or they can be derivatives of bile pigments that appear singly, as compounds, or as compounds with a peptide (e.g., urochrome B is a compound of urobilin or urobilinogen and a peptide). The color of normal rabbit urine varies from yellow to red. Red is a normal variation of urine color, but rabbit owners often erroneously report it as the presence of blood in their pet's urine. Certain types of feed (e.g., alfalfa, the tropical legume Leucaena, beet, carrot, spinach, and cruciferous vegetables such as cabbage, radish, turnip, mustard, cauliflower, and broccoli) increase the intensity of the red pigmentation.[15] Some feeds may contain plant pigments that directly color urine various shades of red. Alternatively, certain foods (e.g., cruciferous vegetables) may induce selective cytochrome P450 enzymes in the liver that affect how bile pigments and their urinary derivatives (e.g., bilirubin, urobilin, urobilinogen) are metabolized.

PUBERTY AND BREEDING LIFE

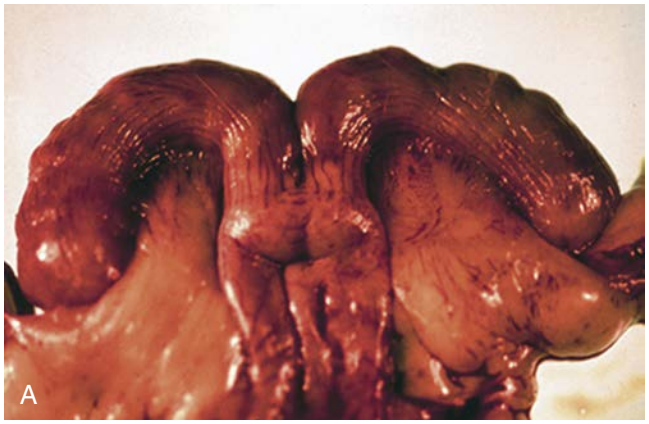
The age at which rabbits attain sexual maturity varies considerably according to the breed. However, if the biologic pattern of growth is plotted graphically, puberty occurs just after maximal growth rate. On the growth velocity curve, sexual maturity occurs at the point at which growth is still taking place, but its rate is decelerating rapidly. Therefore bodyweight is more important than age in determining sexual maturity. Small breeds develop more rapidly and are mature at 4 to 5 months of age, medium-sized breeds mature at 4 to 6 months, and large breeds reach maturity at 5 to 8 months of age.[87] Does mature earlier than bucks, which do not achieve optimal sperm production and reserves until 40 to 70 days after puberty. Among New Zealand white rabbits, females reach maturity at approximately 5 months of age and males at 6 to 7 months of age. The reproductive life of a rabbit depends on its breed but is about 5 to 6 years for the buck and up to 3 years for the doe.

FEMALE REPRODUCTIVE SYSTEM

Anatomy and Physiology

The reproductive tract of a doe lacks a uterine body; instead, each of two separate uterine horns has its own opening into the vagina. If a cesarean section is performed, remove the fetuses

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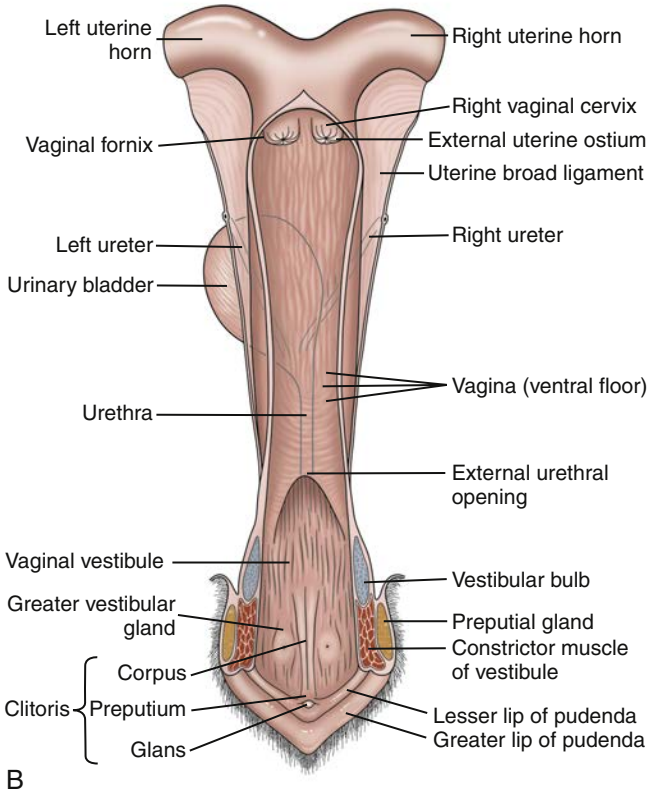


Fig. 11.10 (A) Dorsal surface of a dissected postparturient rabbit uterus. Note the abundant mesometrial fat, which makes identification and ligation of uterine vessels difficult. (B) Diagram of rabbit vagina. The rabbit's vagina is long and characterized by a well-developed, complex musculature. It forms a single canal by which does copulate, give birth, and urinate. In contrast to rodents, in which the vagina opens into the vulvar cleft on the external surface of the body, in the rabbit the vagina ends several centimeters beyond the caudal edge of the pubic bone, and the distal urethra opens midway along the length of the vagina (≈ 4 cm from the vaginal orifice) into the anterior pelvic vagina. Never express the bladder during ovariohysterectomy, because urine will pool in the vagina; then, when the uterocervical tube is severed, urine can flow anterograde and contaminate the abdominal cavity.

through separate incisions in each horn. The mesometrium is a major fat storage site, and identifying and ligating the uterine vessels in the mesometrium can be difficult (Fig. 11.10A).

The vagina of rabbits is long and flaccid. The surgical procedure of neutering a female rabbit is actually an ovariohysterovaginectomy, because the incision is made through the vagina distal to the vaginal fornix. Do not manually express the urinary bladder before surgery, because urine will pool in the vagina, and when the vagina is cut, the urine may flow out and contaminate the abdominal cavity (Fig. 11.10B).

Like cats and ferrets, rabbits are induced ovulators and do not have an estrous cycle. However, does vary in their sexual receptivity, and a certain rhythm can be detected. In domestic rabbits, this rhythm has been reported as having intervals of 4 to 6 days. Ovulation occurs after coitus or after the injection of luteinizing hormone. The time of ovulation is approximately 10 hours after copulation compared with 30 hours in cats and ferrets.

Female Sexual Behavior

Sexual receptivity in a doe is characterized by lordosis, a reverse bending or flattening of the back, raising of the pelvis, or presenting of the perineum in response to attempts by a buck to mount. Generally, receptive does are hyperactive and brace themselves when touched. When not receptive, does do not allow males to mount. Depending on cage space, nonreceptive behavior often takes the form of running away, cornering, biting, and vocalizing.

In natural conditions, rabbits exhibit distinct breeding seasons that are influenced by both day length and temperature. In the northern hemisphere, conception rate in rabbits under natural conditions is highest in spring and lowest in autumn. When environmental conditions are controlled, male rabbits mate at any time. Maximal sexual receptivity in does is often accompanied by enlargement of the vulva, which becomes reddish purple and moist. Although females will almost invariably mate in this condition, they also occasionally mate even when these changes have not occurred. Vaginal smears do not provide useful information on receptivity. The most reliable indicator is lordosis, which occurs when the female is firmly clasped in the lumbar region. Ovulation occurs between 10 and 13 hours after copulation. To ensure successful ovulation, give a single intravenous injection of 100 IU of human chorionic gonadotropin to does after mating to induce ovulation. Transportation of female rabbits may also result in spontaneous ovulation, with a resultant pseudopregnancy that lasts approximately 18 days' duration.

Does will mate at the postpartum estrus. When the young from the previous pregnancy are removed, the willingness to mate persists for at least 36 days after parturition. If suckling of the young is permitted, however, sexual receptivity wanes. One study found that 100% of rabbits will copulate on the first day after parturition, 71% on the fourth day, only 42% on the eighth day, and only 11% on the 12th day.[44] After the 12th day, all does studied refused to copulate until they became receptive again when the young began to wean 50 to 60 days after parturition. Reproductive behavior is therefore minimal to absent if the mammary glands are actively functioning.

Lactating does seldom conceive when mated before the eighth day after parturition. If a small litter of only one to two young is left to a suckling doe, conception usually occurs; that is, the percentage of fertile matings is inversely related to litter number.

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Pregnancy and Nursing Behavior

The gestation period in rabbits varies with the breed but is approximately 30 to 32 days. Litter size depends on the breed and on parity. Primiparous animals tend to produce smaller litters. Small breeds produce small litters of 4 or 5 young, whereas larger breeds produce large litters of 8 to 12 young. If pregnancy does not reach full term (for any or all of the fetuses), then the fetus(es) may be resorbed rather than aborted. There are two peaks for fetal resorption—days 11 to 15 and day 21. Fetal resorption is closely related to dominance and tends to be limited to subordinate does. Fetal resorption may have an advantageous role in energy preservation and masking signs to predators. Mummified fetuses, often floating in the peritoneal cavity or within the uterus, can be an incidental finding.[83] Does have four pairs of mammary glands distributed within the fatty tissue of ventrolateral axillary, thoracic, abdominal, and inguinal areas.[115] However, the number of teats can vary from 8 to 10. Suckling rabbits do not fix on any one teat. Consequently, does can rear a large number of offspring in comparison with the number of teats, and rabbit producers selectively breed for supernumerary teats.[33] Milk is stored mainly in the secretory alveoli. The milk ducts unite until there are six to eight main ducts or galactophores, each draining a sector of the mammary gland, and these pass separately through the nipple. This arrangement allows for rapid secretion of milk during the brief daily nursing period.

Several days to a few hours before parturition, the doe collects hay, straw, or other similar material, which carries to the nest site. In nature, this would be one of her burrows; in the domestic situation, it is usually the nest box. The doe then plucks hair from the abdomen, sides, and dewlap and interweaves it with the hay or straw to line the maternal nest.[38] Normally the hair is tightly adhered to the skin but becomes loose near the time of parturition under the influence of negligible progesterone levels and high levels of testosterone and prolactin.[38] Pregnant animals show a marked increase in hair loosening between 5 days prepartum and the day of parturition. The increase in hair loosening is also seen in pseudopregnant rabbits at the termination of pseudopregnancy.

The hollowed-out center of the nest is where the young are generally born. In an excellent nest, the top is roofed over with nesting material, which effectively helps the neonates maintain their body temperature. Does usually give birth in the early morning. Normal parturition takes approximately 30 minutes. As the young are born, the doe usually eats the fetal placenta (placentophagia) and membranes and severs the umbilical cord.[70] Placentophagia persists up to postpartum day 5 in about 50% of all rabbits. Occasionally the doe will inadvertently eat an offspring's limb or ear during placentophagia, but the affected neonate usually survives.

Rabbits are born altricial and weigh about 50 g (1.75 oz) at birth. They are sensitive to touch, temperature, and smell from birth. Their ears are functional at 7 days, and their eyes open at 10 days. Neonatal rabbits recognize their mother by the scent of feces that she deposits in the nest. A gland in the region of the nipple produces a pheromone (2-methylbut-2-enal) that attracts the neonate.[63] At birth, the neonates first suckle and then burrow deep into the nest material. Thereafter, a regular 22-hour cycle of behavior is followed. The doe feeds about once every 24 hours, with nursing occurring between the hours of 8:00 p.m. and 6:00 a.m., corresponding to the normal activity period of adults. Does nurse only once a day for 3 to 5 minutes. However, during this brief period, a young rabbit may drink 20% of its body weight. A healthy, well-fed litter bursts out of the nest like popcorn when it is examined. Within 15 minutes of nursing, all of the young have reburied into the depth of the nest and group together for warmth. They conduct a continual slow circular movement to regulate differences in temperature at different levels of the nest. This is important, as neonatal rabbits cannot thermoregulate on their own. After 22 hours, activity increases, and they move to the surface of the nest, sniffing the air for the doe's return. Once attached to a nipple, they paddle with their forelimbs to stimulate milk let-down. Ejection of milk occurs toward the end of nursing period. Immediately after nursing, all the young urinate on the surface of the nest before reburrowing. Unique among altricial young, neonatal rabbits do not require stimulation to urinate. At about 8 days, they commence nibbling nest material and by 12 days, they often have eaten most of it—including the doe's fecal pellets. The ingestion of fecal pellets may aid in the colonization of the gut with important microflora. By day 18, they begin leaving the burrow to explore. Until the 18th day of nursing, the doe "plugs" the entrance hole to nest, but after the 18th day, she ceases to perform this activity, thus encouraging the young to emerge. By 24 days, the pregnant doe abandons the young rabbits, and they must fend for themselves.

Olfactory cues are critical during the nursing period. Does mark their offspring with chin and inguinal gland secretions and are openly hostile to young rabbits that are not their own. Does harass young from their own colony but pursue and kill young rabbits from other colonies. A doe will attack and kill her own offspring if it is smeared with an odor from other rabbits. Successful cross-fostering requires that the young are healthy, have the energy to suckle, and have their scent camouflaged by placing them on the bottom of the litter pile and rubbing them in the nest bedding.[25]

Hand-Rearing of Baby Rabbits

Baby pet rabbits may require hand-rearing because of the death of the mother or because of poor nursing, which often occurs with a doe's first litter. Most baby wild rabbits that are found, including cottontail rabbits in North and South America, are not abandoned or orphaned. Nursing does leave their nest, returning only once or twice a day to care for the young. Therefore, unless the wild neonate is injured, it should be left undisturbed in the nest.

Orphaned baby rabbits are very susceptible to hypothermia. Warming the neonatal rabbit is critical if its body temperature drops to less than 97°F (36°C). A rabbit can be warmed by immersing it in a warm (100°F [37.8°C]) bath and gently massaging it while keeping its head above the water. Because warming can worsen any dehydration, the neonate may require administration of isothermic (100°F [37.8°C]) crystalloid fluids (10–15 mL/100 g subcutaneously).

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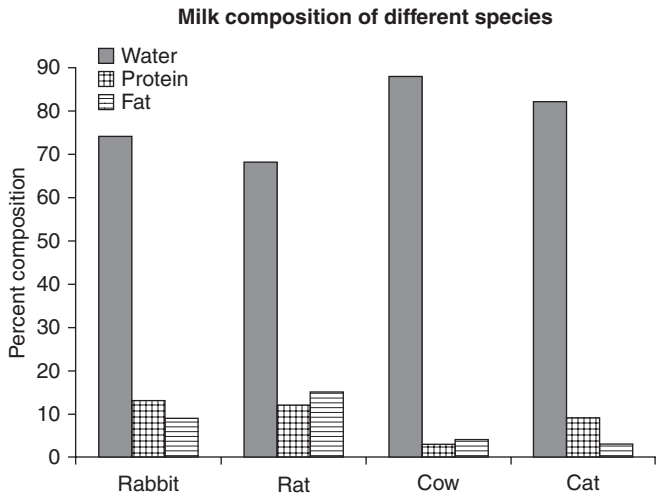


Fig. 11.11 Milk composition of the rabbit, rat, cow, and cat. Notice how the protein and fat content of the rabbit and rat is higher than that of the cow and cat.

BOX 11.1 Recipes for Rabbit Milk Replacer

Cheeke's Milk Replacer[69]
- 1 part evaporated milk
- 1 part water
- Add to 1 cup of the mixture
- 1 egg yok
- 1 tablespoon corn syrup

Taylor's Milk Replacer 1[105]
- 1 part Esbilac powder
- 0.25 parts heavy cream
- 1 part water

Taylor's Milk Replacer 2[105]
- 2 parts KMR liquid
- 1 part Multi-Milk powder

Taylor's Milk Replacer 3[105]
- 6 parts Esbilac
- 4 parts Multi-Milk powder

Taylor's Milk Replacer 4[105]
- 1 part Esbilac
- 1 part Multi-Milk powder
- 1.5 parts water

Despite warming and fluid administration, weak neonates are often unable to nurse from a teat or syringe and require orogastric tube feeding. For this, use a 5-Fr or smaller feeding tube and try to provide about 4 mL of milk replacement formula for newborns. Increase the volume appropriately for weight gain and body size. Tube feeding permits control of how much milk the neonate receives and avoids the problem of aspiration of milk into the lungs.

Numerous studies have looked at the quantity and composition of milk produced by lactating does. Neither breed nor pregnancy status affect milk composition. However, the stage of lactation significantly affects the major components of milk, except lactose.[30] Rabbit milk is higher in protein, fat, and ash than that of other species except rats. The milk of both rabbits and rats is high in fat and protein but low in carbohydrates (Fig. 11.11). Several recipes for rabbit milk replacer have been published (Box 11.1).

Milk replacer for rabbits is commonly a combination of Esbilac or KMR (Kitten Milk Replacer) and Multi-Milk (all available from PetAg Inc., Hampshire, IL). Prepare enough fresh milk replacer daily to allow for 1 day of feeding, and refrigerate between feedings. Rabbit breeders and wildlife rehabilitators often like to add a probiotic and infant multivitamin drops to the rabbit milk replacer; however, their effectiveness has not been established.

Although does feed their young only once a day, feed neonates three times a day to reduce bloat yet still provide adequate calories. Baby rabbits can take 2 to 3 days before they settle into a feeding pattern. Record the neonate's body weight daily (or at every feeding time) and the amount of milk replacer consumed at each feeding. A neonate that drinks a small amount of milk replacer at one feeding may be greedy at the next.

Although neonatal rabbits do not require stimulation of the perineum to urinate and defecate, postfeeding stimulation by gently stroking the anogenital area with a warm, wet, cotton-tipped applicator or gauze sponge is recommended in orphan rabbits. Generally, this procedure is no longer necessary after 1 week of growth.

Neonatal rabbits depend totally on milk until day 10. They can digest a small amount (5%) of solid feed by day 15, and by day 20, coprophagy is taking place, and solid feed represents most of the feed intake.[2] Hand-raised rabbits may take slightly longer to achieve these time points. By day 21, rabbits should be nibbling on hay and eating some solid feed. By day 28, rabbits should be weaned from milk replacement but can be offered water from a bottle.

MALE REPRODUCTIVE SYSTEM

Anatomy and Physiology

Unlike most other placental mammals but similar to marsupials, the penis is caudal to the testes. Rabbits do not have a scrotum but two hairless scrotal sacs; they do not have an os penis. Male rabbits have very small nipples that are not apparent under their fur.

The testes descend at about 12 weeks of age, and the inguinal canals do not close. The technique for castration must consider measures to prevent inguinal herniation. Each testis is made up largely of closely packed seminiferous tubules. In many species, the tubules are arranged in lobules separated by bands of fibrous tissue. However, in rabbits (and many rodents), there are no subdivisions, but tightly coiled tubules that apparently lie at random throughout the testis. When the testicular capsule is cut, the underlying tubules spill out like spaghetti. In species with lobular separation of tubules, testicular biopsy is possible without damaging the testis; this is not so in species like the rabbit without lobular subdivisions.

The morphologic arrangement of the accessory sex gland complex of the male rabbit is unique. The terminology used for the accessory glands lacks uniformity: glandula vesicularis (glandula seminalis, vesicular seminalis); proprostata (glandula vesicularis, coagulating gland, prostata); prostata,

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paraprostata (glandula Cowperi superior); and glandula bulbourethralis (glandula Cowperi inferior). The English equivalents are the vesicular, proprostate, prostate, paraprostate, and bulbourethral glands. Holtz and Foote have described the anatomy of the male rabbit reproductive system in great detail.[49]

The vesicular gland (seminal vesicle) lies between the prostate and bladder. The cranial end of the hollow vesicular gland is bilobed and thick walled. Its size is extremely variable, and sometimes it becomes extraordinarily dilated due to the amount of fluid it contains. On ultrasound scanning, enlarged vesicular glands have a honeycomb appearance suggestive of the cecal appendix and sacculus rotundus.

Male Sexual Behavior and Reproduction

Bucks show a constant libido after puberty. Initiation of copulation in rabbits is confined to basic patterns such as sniffing, licking, nuzzling, reciprocal grooming, and following the doe. Bucks may also exhibit tail flagging and enurination: emitting a jet of urine at a partner during courtship display. Experienced males usually initiate copulation within minutes after a receptive female is introduced. Inexperienced males generally require longer.

The species-specific copulatory patterns of the male are related to the ovulation and corpus luteal function of the female. Copulatory behavior of bucks may be understood by considering that the doe ovulates spontaneously after coitus. The stimulus of coitus is necessary only for ovulation and not for the maintenance of the corpus luteum, which always follows ovulation. Bucks rapidly mount receptive females and accomplish intromission after a series of rapid copulatory movements. Reflex ejaculation follows immediately on intromission. The copulatory thrust is generally so vigorous that the buck falls backward or sideways and may emit a characteristic cry. Vigorous bucks may attempt to copulate again within 2 to 3 minutes. A problem often encountered in male rabbits trained to use artificial vaginas is a reduced ability to induce lordosis during natural mating attempts. These conditioned bucks fail to grasp and apply pressure to the flanks of the female when attempting to copulate and thus fail to induce lordosis.

Bucks deposit semen into the anterior vagina, and the sperm pass individually through the cervical mucus. This pattern also occurs in sheep, cattle, and people. If a rabbit is inseminated during an active corpus luteal phase (e.g., early pregnancy, pseudopregnancy), then sperm transport does not take place. During this period, when blood progesterone levels are increasing in rabbits (as in humans), the cervical secretions are thick and mucoid and inhibit sperm transport.

BEHAVIOR

The behavior of wild and domestic rabbits is very similar. The major difference is their response to confinement: wild rabbits do not adapt well to cages, often fail to breed, and exhibit abnormal behavior not seen under natural conditions. Other wild lagomorphs (e.g., hares) resist domestication and cannot be raised successfully in cages. In contrast, domesticated rabbits are not stressed by confinement, retaining most of the behavioral repertoires of their wild ancestors. The genomes of wild and domestic rabbits differ minimally in actual protein sequences but do differ in how gene and protein expression is regulated. Tame behavior in rabbits (and other domestic animals) has evolved by shifts in allele frequencies at many loci, rather than by critical changes at only a few domestication loci.[13] The genetic shifts are generally associated with regions of the genome involved in the development of neurons and the brain that allows rabbits to tolerate humans and the domestic environment. Frequent handling of rabbits by owners results in more compliance to being lifted, transported, and examined.[104]

Eating, Drinking, and Elimination Behavior

Wild rabbits are selective feeders with a wide food range. They prefer to eat tender, succulent plant parts as the major portion of their diet and consume small quantities of coarse roughage to stimulate gastrointestinal motility (see Chapter 13). Wild rabbits can consume a large volume of fiber without the need for a large gut like ruminants because of the rapid digestive time. Furthermore, the small, herbivorous gut does not interfere with the ability for swift evasion of carnivorous predators.

The primary feeding times for rabbits are in the early morning and at night, with coprophagy commencing 3 to 8 hours after eating.[14] Rabbits like sweet materials and select diets containing molasses or sucrose over similar diets without added sugar.[14] This preference can be used to advantage when an anorectic rabbit is encouraged to eat.

Compared with other companion animals, rabbits have a high water intake. A rabbit's average daily water intake is 50 to 150 mL/kg of body weight; a 2-kg rabbit drinks about as much water daily as does a 10-kg dog.[16] When food is withheld from rabbits, they develop polydipsia, and after 3 days of food deprivation can increase their water intake by 6.5 times.[16] With water deprivation, food consumption declines; after 3 days of deprivation, anorexia results.[16]

Wild rabbits use latrines or earth closets, which are special patches of ground used to defecate near the burrow. Latrines serve social functions such as the recognition of their own or familiar odors, which may have a "comforting" effect, and as loci for the indirect exchange of olfactory information between members of the same social grouping.

Pet rabbits tend to void their droppings at one particular site, such as the corner of the cage. They can be trained to use a litter tray if they are constantly placed in the litter tray every few minutes when first acquired. However, adult bucks deposit strong-smelling feces in scattered places to mark their territory. Intact male house rabbits will mark their territory with a strong-smelling secretion by rubbing their chins on furniture, carpets, and household items.

Group Behavior

A unique aspect of rabbit behavior is the ability to form large groups or warrens. Rabbits are the only leporid that live in large, stable groups, sometimes numbering several hundred.[84] Although rabbits dig burrows that serve as a primary

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haven and restrict their home ranges, they are active above ground, hopping, running, chasing, and playing. Rabbits also engage in "amicable" activities such as lying together, grooming, and nuzzling, which may occupy much of the activity each day.[62] Rabbits are fastidious groomers and spend about 16% of their daily activity on grooming. Rabbits will lick their forepaws and wipe this over their face and ears. They will also use their incisors and tongue to groom their back, legs, haunches, and ventrum. Mutual grooming (allogrooming) is also performed. This usually occurs on the face, head, and ears of the companion. This may help to both relax and strengthen the social bond between rabbits.

Vocalization, Auditory, and Visual Signals

Rabbits are considered silent animals with a limited vocal repertoire. However, a range of vocalizations and auditory signals may denote pleasure, pain, aggression, or fear. Some examples of these are soft clicking when contented; quiet teeth chatter while relaxing; loud teeth grinding when in pain; growl or hiss to denote aggression; soft humming by bucks before mating; loud shrill scream in intense pain or fear; and thumping of the hindfoot to signal threats or danger.

Visual signals are not a major part of a rabbit's communication repertoire, primarily because rabbits spend much of their time in darkness. Signs of visual communication are as follows: a relaxed rabbit may lie on its side with its hindlimbs stretched out; a submissive or fearful rabbit may lay flat to the ground, adopting a small stature and flattening its ears to its body; facial muscle contraction may give the appearance of wide eyes; head shaking may denote an irritation or dislike of a smell or taste; head bobbing may indicate novel environmental stimuli; and displaying the white underside of the tail by raising the hindquarters while running signals other rabbits to seek the safety of the burrow.

HUSBANDRY

Rabbits require daily regular exercise to maintain good health. Regular exercise may also stimulate normal defecation and urination, thus promoting gastrointestinal and urinary tract health. Access to unfiltered sunlight is beneficial to rabbits because it produces vitamin D. Hypovitaminosis D may play a role in nutritional osteodystrophy of the skull and acquired dental disease.[26] Indoor rabbits exposed to ultraviolet radiation produced by artificial light significantly increase their vitamin D blood levels.[31]

Rabbits can be given free rein of a house, but if this is practiced, the home should be rabbit proofed. Rabbits like to chew and scratch objects found in a home; two of the greatest hazards are electrical cords and poisonous plants. Electrical wires should be placed out of reach of rabbits. The decorative houseplant dumbcane (*Dieffenbachia seguinae*) and the ornamental shrub oleander (*Nerium oleander*) are poisonous to rabbits.[15] The alternative to rabbit proofing a home is to provide rabbits with supervised out-of-cage exercise/play time.

In any housing or free-roam situation, provide rabbits with places to run and hide. Their natural tendency when frightened, especially from perceived predators, is to bolt underground into the safe haven of a burrow. These bolt holes can be simulated by placing overturned boxes/containers or pipes around their area. If a pet rabbit is given free range in a house, it must have a cage or box in which to escape.

Divide the cage area into two functional spaces: a space for lying and sleeping, and a space for activities. A free-roam indoor rabbit requires a cage that allows it to stretch out when lying on its side. A cage with a plastic bottom and a wire top is suitable because it can be easily cleaned and is well ventilated. If two or more pet rabbits are kept indoors, each animal should have its own cage, as fighting can result when two rabbits are kept in the same cage.

An important feature of any rabbit enclosure is the substrate or flooring. The ideal substrate for rabbits simulates the compliant texture of earth that allows the nails to grasp. Many commercial hutches come with wire-mesh flooring, and the rabbit *must* be protected from this type of flooring. Rabbits are vulnerable to developing pododermatitis from wire flooring and other noncompliant substrates such as hardwood floors. Provide rabbits with thick layers of soft substrate such as straw or grass hays on top of any flooring. Change bedding materials regularly, especially if they become soiled or wet.

Rabbits are sociable animals, so housing them with other rabbits is encouraged. Suitable groupings include mixes of neutered rabbits or intact females. Monitor any attempted introductions closely because rabbits can inflict serious wounds on each other and even fight to the death. Rabbits can be housed with other species; pet birds such as parakeets cohabitate well with rabbits. Take care when housing with some cats or dogs because they can harm a rabbit. More often, rabbits reign supreme in mixed-species households. It is often recommended not to house rabbits with guinea pigs, because rabbits may transmit *Bordetella bronchiseptica*, which is pathogenic in guinea pigs. However, this statement has never been proven. There are no references on transmission of *B. bronchiseptica* from rabbits to guinea pigs. The original statement comes from the 1996 edition of the *Guide for the Care and Use of Laboratory Animals*, but it was removed from the 2010 edition of the book.[77, 78] Owner-directed aggression and stranger-directed aggression are greater for intact does and neutered males than for intact males.[20] Bucks are more likely to seek contact with their owner.

Outdoor rabbits should be housed in hutches that provide shade and shelter from wind and cold below 39.2°F (4°C). Plans for the construction of hutches are available from libraries, feed manufacturers, and agricultural extension agents; assembled cages are available from farm supply stores or on line sources. Minimally, the length of the hutch should have space for a rabbit to complete three hops[23]; a fully grown New Zealand white rabbit moves forward 1.5 to 2.0 m in three hops. The hutch should be tall enough for a rabbit to stand up on its hind legs. Laboratory rabbits have been observed to climb onto raised platforms and shelves placed 2 m above the cage floor; these have been used successfully for rabbit housing.[23]

With a grazing ark, indoor and hutch rabbits can feed on lawn.[74] The ark can be a mesh indoor rabbit cage without the floor or a solid tent-type frame with wire mesh and door. Move the grazing ark every day to a fresh area of grass. Provide a

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shaded area within the ark and peg the ark down so the rabbit cannot tip it upward. Weed killers used on lawns can be poisonous to rabbits.

If rabbits are housed outdoors or given free rein of a yard, then take measures to prevent escape via digging, jumping, or climbing. Predator proofing is essential. Subterranean wire mesh and adequately high fences with wire mesh "roofing" may be useful. Female rabbits more often than bucks perform digging, and pregnant or pseudopregnant females attempt to dig deep tunnels as part of their maternal behavior.[38,56]

Provide behavioral enrichment by varying the environment. Penned rabbits often dig shallow holes in which they lie or sleep. Hide fresh, green food or treats in hay or soil for rabbits to root out. Cardboard boxes to explore-and-gnaw, as well as varying straws, grass hays, tree branches, and wooden toys, can be supplied for chewing.

Ideally, protect rabbits from flies and mosquitos—such insect vectors can spread the viral diseases myxomatosis and rabbit calicivirus. Rabbits tolerate cold better than heat.

Because they do not possess brown fat, they shiver when exposed to cold. Shivering works well in the short term, and rabbits can tolerate cold weather if properly acclimatized and sheltered. Rabbits are unusually sensitive to elevated temperatures higher than 82°F (28°C) and have little protection against high ambient temperatures. They cannot sweat except through sweat glands confined to the lips; also, they pant ineffectively, and when sufficiently dehydrated, they stop panting. Rabbits do not increase water intake when the ambient temperature becomes high; heat actually seems to inhibit drinking. Rabbits can tolerate a water loss equivalent to 48% of their body weight. In contrast, when water loss reaches 11% to 14% of body weight in dogs, circulatory failure occurs. Although rabbits use their ears to dissipate heat, they actively seek shade and burrow to conserve water and to shelter themselves from heat. The heart rate of rabbits increases only mildly in response to an increase in body temperature. Shelter from direct sunlight is essential in the design of any rabbit housing. The response of rabbits to high and low ambient temperatures is also important during transportation. The risk of death is greater in hot weather or in the presence of excessive indoor heating than in cold weather.

Results of one UK survey suggested that many rabbit owners were not aware of their pets' needs.[79] More than 50% of respondents believed that the average rabbit lives for only 3 to 4 years, and 71% did not know that fiber, in the form of hay and grass, was a vital component of a rabbit's diet. A recent large survey of rabbit owners in and outside North America found increasing attachment and regular veterinary check-ups were associated with a higher knowledge of rabbit care.[111] These results suggest that acquisition sources, veterinarians, and companion-animal professionals can have a key role in the developing the knowledge of rabbit care for pet owners and in promoting the importance of neutering.

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12

Basic Approach to Veterinary Care of Rabbits

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Rabbits are popular companion animals that frequently are presented to veterinary clinics for routine and emergency care. Clinics equipped for seeing dogs and cats can be easily adapted to accommodate rabbits. This chapter will review common clinical procedures specific to rabbits.

HOUSING

Housing requirements can be readily met for rabbits. Hospitalized rabbits can be kept in standard hospital cages designed for dogs and cats or in caging designed specifically for exotic small mammals. Line the cage floor with absorbent paper or toweling to provide a nonslip surface to prevent back injuries. A rubberized mat with small crosshatches placed on the cage floor will provide traction and has the added benefit of allowing urine and feces to fall through. The rabbit's feet lack plantar pads, and the plantar surface of the foot is protected by thick fur. Surfaces that prevent damage to the fur are preferred, because fur removal can lead to significant damage to the foot, particularly the hock.

Keep a supply of good-quality hay and pellets available for hospitalized rabbits. Types of hay differ in composition, fiber content, and palatability. Providing fresh leafy greens to hospitalized rabbits may encourage eating in otherwise anorectic patients. A rapid change of diet, even a change from a poor diet to a proper one, may cause gastrointestinal upset and anorexia (see Chapters 13 and 14).[10]

Historically, there was an idea that rabbits do not drink water.[28] This wrong assumption may have been derived from the fact that rabbits consume less water when supplied with an abundance of fresh greens.[28] Indeed, rabbits drink more water when the dietary dry matter increases, mainly when fed hay only.[44] Fresh water should always be available for rabbits. Rabbits prefer drinking from open dishes, even if previously conditioned to drink from sipper bottles.[50] For hospitalized rabbits, provide water in bowls, with additional sipper bottles provided for animals unaccustomed to bowls. Water bowls should be made of a heavy ceramic so they are not easily tipped over. For rabbits with large dewlaps, bowls with high sides are recommended to prevent the dewlap from contacting the water when they drink. Chronic wetting of the dewlap can lead to "wet dewlap" disease, which is an easily preventable moist dermatitis most often associated with colonization by *Pseudomonas* species.

If possible, hospitalize rabbits in an area separate from potential or perceived predators. Sounds and even smells from hospitalized dogs, cats, or ferrets may stress sensitive rabbits.[30] Results of one study showed that exposure of wild European rabbits to red fox (*Vulpes vulpes*) odor caused an increase in the rabbit's fecal corticosterone metabolites.[41]

Take care to avoid overheating hospitalized rabbits. Healthy New Zealand white rabbits housed at 107.6°F (42°C) and 45% relative humidity for 1 hour had decreased feed intake lasting 5 days, as well as changes in multiple blood analytes.[1] Immune cell proliferation and immunoglobulin synthesis were reduced for 30 minutes after exposure to stress.[1] Warm areas appropriate for sick birds or reptiles may cause heat stress in euthermic or hyperthermic rabbits.

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Fig. 12.1 Restrain a rabbit with one hand under the thorax and the second hand supporting its hindquarters.



Fig. 12.2 Restrain a stressed rabbit by covering its eyes and supporting its hindquarters.



Fig. 12.3 To help facilitate physical examination or the administration of medicines to a rabbit when an assistant is not available, a towel can be wrapped around the rabbit to restrain it.

HANDLING AND RESTRAINT

The rabbit skeleton represents only 7%–8% of the body weight (as opposed to 12%–13% in cats).[33] With the powerful musculature of their hind limbs and the delicate nature of their skeleton, rabbits are prone to fractures of the back and hind limbs. Rabbits are easily stressed, and care should be taken to reduce stress to the patient during examination. Estimates from surveys suggest that 57% of rabbits struggled at least slightly when being lifted, whereas 61% and 75% of rabbits showed signs of fear when "handled" by the owner and by an unfamiliar adult, respectively.[8] Proper handling and housing of patients is necessary to avoid injury.

Supporting the hindquarters is vital when moving rabbits to prevent injury. Rabbits that are used to handling can be carried with one hand under the thorax or holding the scruff and the second hand supporting the hindquarters (Fig. 12.1). Fractious rabbits should be carried with the head under the handler's arm to minimize stress by covering the eyes; the hindquarters are supported at the same time (Fig. 12.2). To reduce chances of injury from kicking away while putting a fractious rabbit in a cage, place it rear end first into the cage while supporting the hindquarters. When examining a rabbit or placing it in a cage, use a nonslip mat to avoid sliding and injury. Maintain control of the rabbit at all times during transport and examination. A towel can be used to wrap the rabbit and cover its head to prevent struggling when transferring it from a carrier to a table for examination. Similarly, if an assistant is not available, a towel can be wrapped around the rabbit to help facilitate physical examination or medication administration (Fig. 12.3). However, take care to prevent the rabbit from overheating when using a towel to facilitate handling. Because rabbits radiate body heat through their ears, avoid covering the ears to minimize risk of hyperthermia. As an alternative, place a hand over the eyes of a fractious rabbit to calm it. Rabbits are obligate nasal breathers; avoid obstructing the nostrils with the towel or hand. Rabbits may appear calmer when placed on their backs, and the handler can sit in a chair or on the floor with the rabbit in his/her lap, with the hindquarters toward the handler's body. The incisors, abdomen, genitalia, and feet can then be examined. Some research suggests that in laboratory rabbits this position induces tonic immobility and is associated with changes in cardiac rate and function, respiratory rate, and increased corticosterone levels.[19,37]

PHYSICAL EXAMINATION

In general, physical examination of a rabbit is performed similar to that in other mammals.[24] Observe the rabbit at a distance before starting the examination. If the patient is stable, allow the rabbit to move around the room. Take note of its movement and document any visible neurologic or musculoskeletal abnormalities. A common presentation in sick rabbits is gastrointestinal stasis. These animals tend to be painful and appear uninterested in surroundings. If dyspnea is observed, place the rabbit in a quiet, oxygenated cage before examination. Occasionally a

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Fig. 12.4 Use a nonslip surface to prevent the rabbit from slipping and injuring itself while it is being examined.

rabbit may be too stressed to undergo an examination without sedation. A sedative such as midazolam (0.5–1.0 mg/kg intramuscularly) is often very effective in calming a patient.[20]

Measure the body temperature early in the examination because temperature may increase from the stress of the examination.[2] Rectal temperature may be a prognostic indicator in terms of overall survival.[12] Risk of death before or within 1 week after hospital discharge was three times higher in rabbits with hypothermia than in normothermic rabbits.[12] For each 1.8°F (1°C) decrease in admission rectal temperature, the odds of death were doubled.[12] In hot or humid climates, rabbits may become hyperthermic during even a short transport to the veterinary office. In these animals, often the ears will feel very warm, an indication of hyperthermia. To measure body temperature, as well as to examine the ventrum or trim nails, the rabbit can be cradled on its back in a "C-shape," with the hind end supported.

A systematic approach is needed for physical examination. When examining the rabbit, use a nonslip surface on the table to avoid injury (Fig. 12.4). Measure the heart and respiratory rates before the rabbit is stressed. Differentiating heart and lung sounds on auscultation can be challenging; respiratory sounds superimposed over the heart beats may create the false impression of a heart murmur. Note any ocular or nasal discharge when examining the head. Examine the ears, including the pinna, otic canal, and the tympanic membrane. Lymph nodes are located as in other species, but lymphadenopathy is rare in rabbits. Document skin and coat quality and examine the plantar surface of the feet for pododermatitis or fur loss.

A complete oral examination is an important part of patient assessment. Palpate the face and ramus of the mandible for any evidence of swelling or tooth elongation. The mouth can be partially examined by using an otoscope and cone or nasal speculum; however, rabbits are often reluctant to allow access to their oral cavity, and light sedation or general anesthesia may be needed for a thorough examination. If using an otoscope for initial examination, take care to select a proper cone size, and check for potential sharp edges of the cone tip to prevent damage to the oral mucosa and gingiva. A nasal or vaginal speculum with attached light source gives a better field of view than an otoscopic cone (Fig. 12.5) for dental assessment (see Chapter 36).



Fig. 12.5 The oral cavity of a rabbit is examined with a nasal speculum. The speculum can be placed in the center of the mouth and the speculum blades opened fully laterally to view the oral cavity, or the blades can be placed on either side of the mouth to more fully view the upper or lower dental arcades of one side.

Palpate the abdomen for masses, distention, gas, or other abnormalities. A firm, dough-like, or distended tympanic stomach, increased gas or fluid within the intestinal tract, or absence of normal intestinal sounds on auscultation may be noted with gastrointestinal disorders.[45] Document and investigate any suspect organomegaly. Tensing of abdominal muscles or teeth grinding may be signs of discomfort. A pain scale, called the *rabbit grimace scale*, was developed in rabbits in a study that explored the analgesic effect of a topical anesthetic cream containing 2.5% prilocaine and 2.5% lidocaine during ear tattooing.[27] The pain scale assessed changes in rabbit facial expressions to rate pain, such as orbital tightening, cheek flattening, pointing of the nose, and whisker changes.[27] Incorporating a grading scale into postprocedural monitoring of wellness in laboratory rabbits has been suggested,[21] and this may be useful in pet rabbits. However, other parts of the body should also be assessed when using behavioral indicators of pain.[32]

SAMPLE COLLECTION

Blood Collection

Sites used for venipuncture in rabbits are the lateral saphenous, cephalic, jugular, and marginal ear veins and the central ear artery. Use of the ear veins, and in some breeds the central ear artery, is not ideal because hematoma formation, bruising, or thrombosis and skin sloughing can result, especially in small-eared breeds. To improve visibility of the vein, use alcohol to part the fur; plucking the fur or careful clipping may be useful in some cases.

The lateral saphenous vein is an ideal site for venipuncture in rabbits (Fig. 12.6). Have the handler restrain the rabbit laterally on its side and extend the top back leg. If needed, the rabbit can be restrained in a towel with its head covered. The handler

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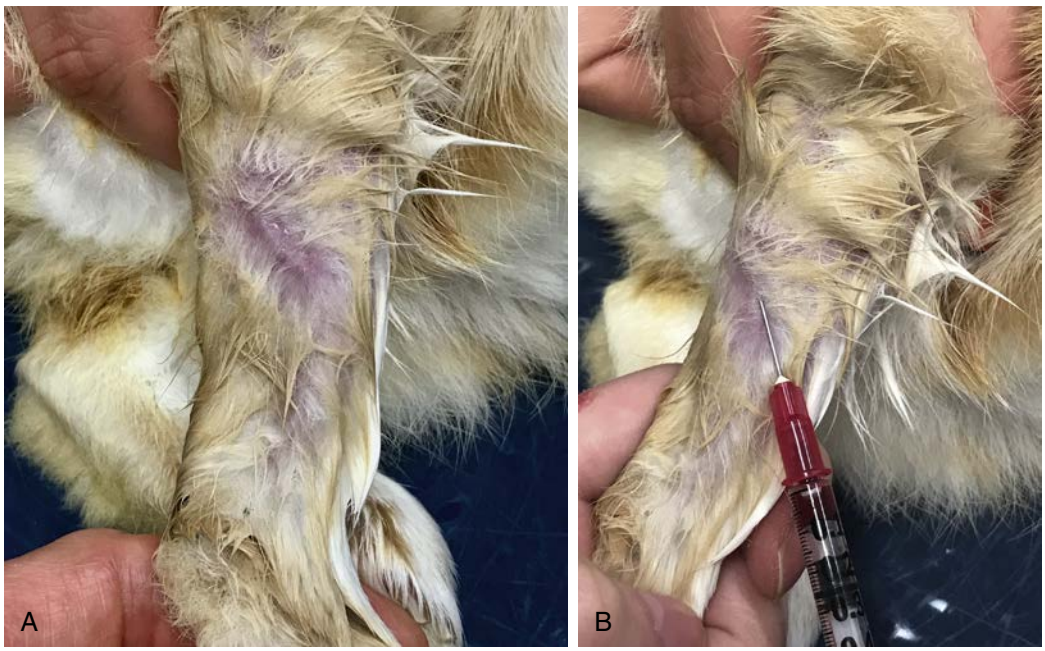


Fig. 12.6 (A) The lateral saphenous vein of the rabbit is best seen by wetting the area with alcohol or gently plucking the fur. This is the most accessible vein for venipuncture for blood sample collection. (B) A small-gauge needle and 1- to 3-mL syringe are used to avoid collapse of the vein.

holds off the saphenous vein by compressing across the back of the proximal thigh or just above the knee only; encircling the entire leg may compress the vein. The vessel is readily accessible across the lateral surface of the tibia just proximal to the hock. After the sample is collected, apply gentle digital pressure or a pressure wrap over the venipuncture site to prevent hematoma formation.

Cephalic veins are accessible in rabbits but occasionally can be difficult to locate and occlude in small breeds. Additionally, venipuncture of the cephalic veins may be more stressful for the patient because the handler is working near the head of the rabbit. Avoid using this vein for blood collection if a catheter needs to be placed to preserve the integrity of the vein.

Rabbits have large paired jugular veins that are often a preferred venipuncture site for very calm or sedated rabbits or when collecting a larger amount of blood (e.g., for blood transfusion). However, visualizing the jugular vein can be difficult in overweight rabbits or in females with a large dewlap. For jugular venipuncture, shave the mid-neck area cranial to the thoracic inlet. Position the rabbit with the front legs held over the edge of the table and the head extended up, avoiding overextending the head. Alternatively, wrap the rabbit in a towel and place it in the dorsal recumbency position, extending the head and neck to allow visibility of the jugular vein. Cranial vena cava venipuncture is rarely performed in rabbits and is not recommended.

Hematologic and Biochemical Testing

Tables 12.1 and 12.2 contain reference ranges for hematologic and biochemical values in rabbits. Several point-of-care units are available that allow a quick assessment of select biochemical parameters. Human and veterinary portable blood glucose meters (PBGM) have been compared with a veterinary benchtop analyzer for accuracy in rabbits.[48] Human PBGMs underestimated blood glucose concentration, had decreased accuracy at high hematocrit levels, and had the lowest total error. Veterinary PBGMs overestimated blood glucose concentration, had decreased accuracy at low hematocrit levels and at high blood glucose concentrations, and had the highest total error.[48] Recently, the use of continuous interstitial glucose-monitoring devices has been shown to be feasible in rabbits.[36] Assessing blood glucose concentration can be useful and provide prognostic value. In one study, blood glucose concentration, food intake, signs of stress, and severity of clinical disease were shown to be significantly related.[23] Severe hyperglycemia (>360 mg/dL [>20 mmol/L]) was associated with conditions with a poor prognosis.[23] Results also suggested that mean blood glucose concentration was significantly higher in rabbits with confirmed intestinal obstruction (445 mg/dL [24.7 mmol/L]) than in rabbits with confirmed gut stasis (153 mg/dL [8.5 mmol/L]).[23] However, preliminary data by other authors suggest that blood glucose level is not an accurate diagnostic tool for gauging surgical need, nor does it correlate with the degree of gastrointestinal disease when compared with radiographic and physical examination findings.[46] Instead, the degree of hyperglycemia may be correlated to a stress response similar to that seen in cats, as well as the presence of concurrent disease.[46] Plasma sodium levels in pet rabbits decrease in conditions of hyperglycemia, similar to people.[7] Because hyperglycemia is common in rabbits, simultaneous measurement of plasmatic sodium along with glucose levels in ill rabbits is advised.[7] In-house blood analysis using portable units is commonly performed with the i-STAT analyzer (Abbot Point of Care Inc., Abbott Park, IL), and reference values for rabbits using this unit have been reported (Table 12.3).[4] Limitations of this analyzer have been reported.[47] Concentrations of whole blood L-lactate measured by a portable analyzer and a blood gas analyzer have

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TABLE 12.1 Reference Ranges for Hematologic Values in the Rabbit

Analyte	Reference Interval[a]	Mean ± SD[b]	Range (Min–Max)[b]
Hematocrit, %	31.3–43.3	32.1 ± 2.7	20.6–39.6
Erythrocytes, $\times 10^6/\mu L$	4.5–6.9	5.7 ± 0.5	3.9–7.0
Hemoglobin, g/dL	11.0–14.4	12.3 ± 1.0	7.8–15.4
Mean corpuscular hemoglobin, pg/cell	19.4–23.8	21 ± 1	18–23
Mean corpuscular hemoglobin concentration, g/dL	32.3–34.5	33.6 ± 0.6[a]	31.1–37.0[a]
Mean corpuscular volume, μm^3	59.0–70.1	63.7 ± 3.1[a]	59.0–70.1[a]
Platelets, $\times 10^3/\mu L$	134–567[c]	400 ± 89	192–662
White blood cells, $\times 10^3/\mu L$	4.1–10.8[c]	7.2 ± 2.5	2.4–12.8
Neutrophils, $\times 10^3/\mu L$	—	4.5 ± 2.3	1.1–7.4
Neutrophils, %		52 ± 12	21–73
Lymphocytes, $\times 10^3/\mu L$	—	2.1 ± 1.4	0.5–6.5
Lymphocytes, %		29 ± 14	9–64
Monocytes, $\times 10^3/\mu L$	—	1.1 ± 0.6	0–3.7
Monocytes, %		15 ± 5	1–32
Eosinophils, $\times 10^3/\mu L$	—	0.01 ± 0.01	0–0.03
Eosinophils, %		0 ± 0.1	0–0.7
Basophils, $\times 10^3/\mu L$	—	0.1 ± 0.1	0–0.4
Basophils, %		2 ± 1	0–7

[a]Data from Hewitt et al,[26]except where noted; n = 110 young male New Zealand white rabbits, 2.5–97.5 percentile values.
[b]Data from Archetti et al[3]except where noted; n = 58 nulliparous does.
[c]Data from Gallego[18]; 90% confidence intervals; n = 54 mixed sex pet rabbits, age range 5 months–10 years.
SD, Standard deviation.

TABLE 12.2 Reference Intervals for Select Biochemical Values in the Rabbit

Analyte	Reference Interval[a]	Mean ± SD[a]	Min–Max values[c]
Albumin, g/dL	2.8–4.0	3.4 ± 0.3	—
Alkaline phosphatase, U/L	6–14	10 ± 2	—
Alanine transferase, U/L	52–80	66 ± 7	—
Amylase, IU/L	82–343[d]	—	—
Aspartate aminotransferase, U/L	48–96	72 ± 12	—
Bile acids, µmol/L	26–34[d]	—	—
Total bilirubin, mg/dL	0.1–0.5	0.3 ± 0.04	—
Calcium, mg/dL	7.6–12.2	10.0 ± 1.2	
Chloride, mEq/L	—	102 ± 3[c]	96–109[c]
Cholesterol, mg/dL	6–65[d]	—	—
Creatine kinase. U/L	23–247	135 ± 56	—
Creatinine, mg/dL	1.0–2.2	1.6 ± 0.3	—
Gamma-glutamyltransferase, U/L	0–7	3 ± 2	—
Globulin, g/dL	2.1–3.7[d]	—	—
Glucose, mg/dL	109–161	135 ± 13	—
Lactate dehydrogenase, U/L	59–205[b]	107 ± 44[b]	—
Lipase, IU/L	38–210[d]	—	—
Magnesium, mg/dL	1.9–3.2[d]	—	—
Phosphorous, mg/dL	3.0–6.2[b]	4.7 ± 0.8[b]	—
Potassium, mEq/L	—	4.2 ± 0.3[c]	3.4–5.1[c]
Total protein, g/dL	6.1–7.7	6.9 ± 0.4	-
Sodium, mEq/L	—	143 ± 3[c]	138–148[c]
Triglycerides, mg/dL	22–188[d]	—	—
Urea nitrogen, mg/dL	9–29	19 ± 5	—

[a]Data from McLaughlin et al.,[38] except where noted; n = 120 adult males.
[b]Data from Hewitt et al[26]; plasma samples, 2.5 and 97.5 percentile values, n = 110 young adult males.
[c]Data from Hewitt et al[26]; plasma samples; min–max values given if n < 100; n = 60 young adult males.
[d]Data from Gallego[18]; 90% confidence interval; plasma samples; n = 60 mixed-sex pet rabbits, age range 5 months–10 years.
SD, Standard deviation.

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TABLE 12.3 Reference Intervals for Venous Blood Samples Analyzed With the *i-STAT* EC8+[a] in Rabbits

Analyte	95% Reference Interval
pH	7.25–7.53
Pco_2, mmHg	28.9–52.9
HCO_3^-, mmol/L	17.0–32.5
TCO_2, mmol/L	18 –34
BE_{ecf}, mmol/L	–10 to 8
Na, mmol/L	136–147
K, mmol/L	3.4–5.7
Cl, mmol/L	93–113
AnGap, mmol/L	11–26
Hematocrit, %	29–46
Hemoglobin, g/dL	9.8–15.5
Blood urea nitrogen, mg/dL	9–33
Glucose, mg/dL	93–245

[a]Abbot Point of Care, Princeton, NJ.
Data from Ardiaca M, Bonvehi C, Montesinos A. Point–of–care blood gas and electrolyte analysis in rabbits. *Vet Clin North Am Exot Anim Pract* 2013;16:175–195.

been compared with those measured by high-performance liquid chromatography.[31] Results showed L-lactate values were higher in rabbits than in other mammals, and good correlation was found between the portable and blood gas analyzers.[31] In a study in pet rabbits of the association of L-lactate levels with morbidity and death at 2 weeks after initial examination, a better prognosis was associated with a 3.3 mmol/L increase in L-lactate concentration within 48 hours after initial examination.[5] These results suggest that, in contrast to other species, sustained low concentrations of L-lactate in pet rabbits are associated with increased morbidity and mortality rates, whereas increased concentration of L-lactate is associated with a good prognosis.[5] This may be related to a different metabolism of L-lactate in rabbits. Blood hormone levels in neutered male and female rabbits are presented in Table 12.4.[13]

Urine and Fecal Collection

A rabbit's bladder can be gently expressed to obtain a urine sample during examination. To decrease chances of iatrogenic bladder rupture, however, cystocentesis may be preferable to manual bladder expression. Cystocentesis in the rabbit is similar to that in other small animals and has been described.[9] Although sometimes unnecessary, sedation or anesthesia reduces the risk of struggling and damage to internal structures, especially in stressed rabbits. Ultrasound scanning can help to visualize the bladder and detect any bladder abnormalities, and ultrasound-guided cystocentesis reduces risk of damage to other organs, including the cecum. Ultrasound scanning should always be used if the bladder is small. A small-diameter needle (22- to 25-gauge) attached to a sterile 6-mL syringe provides an adequate sample for complete urinalysis. With the animal restrained in the dorsal or lateral recumbency position, locate the bladder on ventral midline just cranial to the pelvic brim and insert the needle after sterile preparation of the antepubic region. Urinalysis reference values are presented in Table 12.5.

Urethral catheterization can be performed in sedated or anesthetized patients to collect a urine sample, for therapeutic flushing of the bladder in cases of urinary sludge, or to place a urinary catheter. For most rabbits, a well-lubricated 9-Fr sterile catheter is used. For the female, place the animal in sternal recumbency and locate the urethral opening on the floor of the vagina. For the male, placing the rabbit in a sitting position allows for extrusion and catheterization of the penis. In a research setting with anesthetized male New Zealand white rabbits, manual retrograde urinary catheterization proved to

TABLE 12.4 Blood Hormone Levels in Spayed/Neutered Rabbits (n = 29)

Hormone	Mean ± SD (ng/mL)	Range (ng/mL)
Androstenedione	2.47 ± 0.22	0.8–4.0
Cortisol	7.28 ± 0.40	4.64–11.2
17-Hydroxyprogesterone	6.40 ± 1.35	0.75–22.2
Progesterone	0.25 ± 0.02	0.11–0.46
Testosterone	0.02 ± 0.0	0.02–0.04

SD, Standard deviation.
Data from Archetti I, Tittarelli C, Cerioli M, et al. *Serum chemistry and hematology values in commercial rabbits: preliminary data from industrial farms in Northern Italy.* 9th World Rabbit Congress: 2008;1147–1152.

TABLE 12.5 Reference Values for Urinalysis in the Rabbit

Analyte	Reference Values
Urine volume	
Large breeds	20–350 mL/kg per day
Medium breeds	130 mL/kg per day
Specific gravity	1.003–1.036
pH	8-9[a]
Bilirubin, mg/dL	0[a]
Erythrocytes	0[a]
Glucose, mg/dL	0[a]
Ketones, mg/dL	0–15[a]
Leukocytes	0–25[a]
Nitrates	Negative [a]
Proteins, mg/dL	0–30[a]
Urobilinogen, mg/dL	0–1[a]
Crystals present	Ammonium magnesium phosphate, calcium carbonate monohydrate, anhydrous calcium carbonate, calcium oxalate
Casts, epithelial cells, or bacteria present	Absent to rare

Data from Gallego[18]; 90% confidence interval; n = 43 mixed sex pet rabbits, age range 5 months–10 years.
From Quesenberry KE: Rabbits. In Birchard SJ, Sherding RG, eds. *Saunders manual of small animal practice.* 2nd ed. Philadelphia: WB Saunders; 2000.

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be difficult because of frequent misplacement of the catheter into the ejaculatory canal and vesicular gland. To minimize this complication, the "digital pressure" catheterization technique was developed.[51] In this technique, the anesthetized male rabbit is placed in dorsal recumbency. Using sterile technique, the tip of a lubricated 10-Fr catheter is introduced into the penile urethra. The tip of the index finger is placed immediately caudal to the pubic symphysis, and while the catheter is threaded slowly into the urethra with the opposite hand, the operator applies pressure to this point with the index finger. The advancing tip of the catheter can be felt at the fingertip during this step. Once the catheter is advanced into the bladder lumen, placement is confirmed by aspirating urine.

A direct smear of fresh feces in saline solution should be examined microscopically for the presence of protozoal organisms. Several nonpathogenic protozoa may be found normally. Fecal flotation is used to diagnose coccidia, cryptosporidia, and helminths. Coccidiosis is a common cause of diarrhea in young rabbits (see Chapter 14).

Dermatologic Sampling

Rabbit mites may be visualized under low magnification of skin brushings. *Cheyletiella*, bacteria, and yeast can be found on acetate tape strips applied to the skin and examined microscopically.[22] As in other mammals, skin scrapings can be obtained in rabbits to diagnose some parasitic conditions, including sarcoptic or demodectic mange. Fungal and bacterial cultures, as well as biopsy specimens, can be obtained from skin lesions (see Chapter 17).

Cerebrospinal Fluid Tap

Cerebrospinal fluid collection may be indicated to help diagnose neurologic disease. Anesthesia is mandatory. The techniques are similar to those used in cats. The best site to collect spinal fluid is the cerebellomedullary cistern. Position the rabbit in lateral recumbency with the head flexed toward the chest at a 90-degree angle to the vertebral column. Shave the fur on the nape of the neck from the occipital protuberance to the level of the third cervical vertebra and laterally past the margins of the atlas. The cranial margins of the wings of the atlas and the occipital protuberance are the landmarks for needle placement. Insert a 22-gauge, 1.0- to 1.5-inch-long spinal needle in the skin midway between these points and direct it perpendicular to the skin, toward the patient's nose. A stylet is usually not necessary because of the relatively small size of most rabbits. After the needle has penetrated the dura and arachnoid membranes, watch carefully for the appearance of spinal fluid. Allow the fluid to drip into empty glass or plastic tubes; do not attach a syringe or a manometer, since the movements caused by syringe attachment will likely cause bleeding, contaminating the fluid. If the fluid cannot be submitted to the laboratory immediately, one drop of serum from the rabbit added to 10 drops of cerebrospinal fluid (CSF) will preserve the cells for cytologic evaluation. In this case, another 10 drops of CSF need to be collected in a separate tube for cell counts and protein analysis if serum is added for cell preservation. Only 10 drops are needed if the fluid can be analyzed immediately. Reference values for constituents of CSF in rabbits are presented in Table 12.6.[29] A lumbar puncture, not a cerebellomedullary injection, should be used if myelography is to be performed because contrast media generally will not flow past an extradural obstruction if the injection is made cisternally.

TABLE 12.6 Reference Values for Cerebrospinal Fluid Analysis in the Rabbit

Analyte	Concentration
Alkaline phosphatase	5.0 U/dL (King-Armstrong)
Calcium	5.4 mg/dL
Carbon dioxide	41.2–48.5 mL%
Chloride	127 mEq/L
Cholesterol	33 mg/dL
Creatinine	17 mg/dL
Glucose	75 mg/dL
Lactic acid	1.4–4.0 mg/dL
Magnesium	2.2 mEq/L
Nitrogen, nonprotein	5.6–16.8 mg/dL
Phosphate	2.3 mg/dL
Potassium	3.0 mEq/L
Protein, total	59 mg/dL
Sodium	149 mEq/L
Urea nitrogen	20 mg/dL

Data from Kozma C, Macklim W, Cummins LM, Mauer R. The anatomy, physiology, and the biochemistry of the rabbit. In Weisbroth SH, Flatt RE, Kraus AL, editors. *The biology of the laboratory rabbit*. New York: Academic Press; 1974.

TREATMENT TECHNIQUES

Catheterization and Fluid Therapy

Although some hospitalized rabbits can be managed with subcutaneous fluids, critically ill patients require intravenous fluids via a catheter in the cephalic vein (Fig. 12.7) or, alternatively, the lateral saphenous or lateral ear vein. A 24-gauge catheter can be placed in small rabbits, whereas a 22-gauge catheter usually can be placed in rabbits over 2 kg. Mild sedation (e.g., midazolam) is often necessary when placing a cephalic catheter. If an intravenous catheter cannot be placed, use a butterfly catheter taped in place for short-term or bolus fluid therapy. Jugular catheters are rarely used, and anesthesia is needed to facilitate placement. Many clinicians use intravenous catheters in the marginal ear vein in large-eared rabbits without complication, but placing ear catheters potentially can cause sloughing and necrosis of the ear margin in small-eared rabbits. If an ear vein catheter is used, only administer intravenous fluids through the catheter, and do not administer drugs that can cause irritation or inflammation. Take care when administering intravenous fluids to rabbits to avoid volume overload: 50 to 70 mL/kg per day can usually be tolerated intravenously, with volumes of 1.5 to 2 times maintenance used without complication in the absence of underlying cardiac disease. Normal water consumption of rabbits is estimated to be 100 to 150 mL/kg per day, with urine production at 20 to 250 mL/kg per

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Fig. 12.7 (A) A 22-gauge intravenous catheter is placed for fluid administration in the cephalic vein of a rabbit sedated with midazolam. (B) The catheter is securely taped in place.

24 hours.[52] Infusion pumps help regulate fluid delivery. A combination of crystalloids and colloids can be used to treat hypovolemic shock (see Chapter 41).

If peripheral vessels are collapsed from dehydration, intraosseous catheters can be placed in the proximal humerus, greater trochanter of the femur, or the tibial crest. The intraosseous route is particularly useful in young or very small rabbits in which intravenous access is difficult. Intraosseous administration of crystalloid fluids in rabbits allows sufficient flow of fluid to rapidly reverse hypotension caused by hemorrhage, with results similar to the intravenous route.[42] Fluids injected into the tibial marrow cavity of rabbits reach the heart in as little as 10 seconds after injection.[49] Before inserting an intraosseous catheter, clip the fur and surgically prepare the selected site in the sedated rabbit. Use an 18- to 23-gauge, 1.0- to 1.5-inch spinal needle or intraosseous catheter, depending on the size of the rabbit. Using sterile gloves, palpate the site of insertion, and insert the needle into the medullary cavity parallel to the long axis of the bone. Remove the stylus, flush the catheter gently with sterile saline solution, and attach a male adapter. Apply antimicrobial ointment to the insertion site with a light dressing applied to hold the catheter in place. Administer fluids via the intraosseous catheter until the patient is adequately rehydrated or an intravenous catheter is placed. In an animal model study, intraosseous catheters were placed in the tibias of rabbits, and the bones were evaluated at 1 and 21 days after catheter placement.[6] Gross and microscopic changes were confined to metaphyseal bone and completely resolved after 3 weeks.[6] Based on this information, bone damage associated with intraosseous catheter placement appears to be minimal and quickly resolves.

Subcutaneous fluid administration can be used on most hospitalized rabbits that have normal blood pressure and plasma protein levels and are accepting oral feedings. Rabbits can easily tolerate 100 to 120 mL/kg/day of subcutaneous fluids divided into 2-3 treatments daily. The loose skin located on the dorsum of the rabbit is an ideal location for subcutaneous fluid administration (Fig. 12.8). Monitor for development of dependent edema if fluids are administered subcutaneously for a prolonged period or if the rabbit is immobile; decrease or stop fluid administration if edema develops.

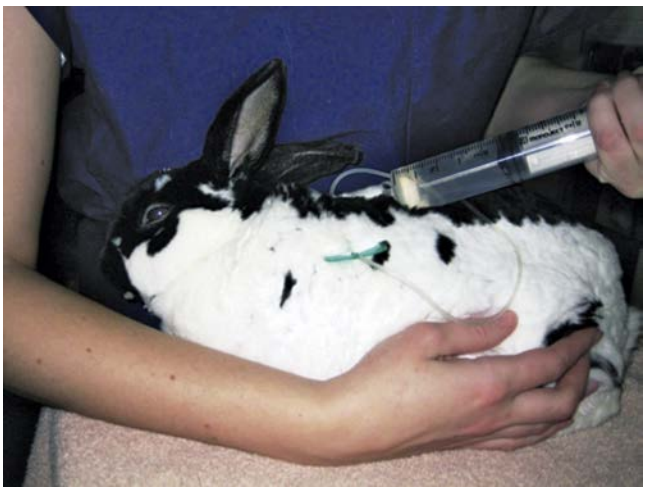


Fig. 12.8 Subcutaneous fluid administration is done in the loose skin located on the rabbit's dorsum.

Injection Techniques

Injection techniques in rabbits are similar to those used in cats. Intraosseous, intravenous, and subcutaneous routes are described under catheterization and fluid therapy. Intramuscular injections can be given into the large lumbar muscles on either side of the spine, just cranial to the pelvis (Fig. 12.9). One person can restrain and administer an intramuscular injection in a rabbit by tucking the rabbit under an arm as described under handling. If the hindlimbs are used for injection, the cranial

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Fig. 12.9 Intramuscular injections are done in the large lumbar muscles on either side of the rabbit's spine, just cranial to the pelvis.



Fig. 12.10 To administer oral medication, the rabbit can be wrapped in a towel in "burrito" fashion. The syringe is placed at the side of the oral cavity to administer food or medication.

aspect of the rear leg (i.e., the quadriceps) should be used to avoid damaging the sciatic nerve. Because some medications, including enrofloxacin, may cause pain, necrosis, or abscessation when given into subcutaneous or muscular tissues, dilute such medications with fluids and administer subcutaneously. Also, avoid repeat administration of benzathine or procaine penicillin in the same subcutaneous location, because localized injection reactions can occur.

Oral Medications

Suspensions are much preferable to tablets when administering medications orally to rabbits. Medications available only in tablet form can be made into suspensions by compounding pharmacists. Use of a towel to wrap the rabbit in a "burrito fashion" may be helpful when giving oral medications to fractious animals. Give the medications into the side of the mouth as far back as possible to prevent the rabbit from spitting it out (Fig. 12.10).

If necessary, some tablets can be crushed and placed into a favorite treat, hand-feeding formula, or jam and offered slowly. Alternatively, small tablets can be given without dissolving. Restrain the rabbit as previously described, hold the head, and introduce the tablet through the mandibular diastema. Place the tablet over the tongue and use one finger to push the tablet into the mouth. The use of a small pet piller may be useful and prevent bite injury to the person administering the medication.

Enteral Feeding Support

Anorectic rabbits are commonly presented for medical evaluation. Dental disease, gastrointestinal disease, neurologic disease, and other systemic diseases are often complicated by secondary anorexia.[43] Failure to provide nutritional supplementation to an inappetent rabbit can result in hepatic lipidosis in as little as 2 to 3 days.

Several commercial formulas for support feeding of rabbits are available (Oxbow Critical Care, Oxbow Animal Health, Murdock, NE, USA; Recovery Plus, Recovery, Supreme Petfoods Ltd, Suffolk, UK; Emeraid Sustain Herbivore, Lafeber Co, Cornell, IL, USA). These are usually timothy hay–based formulas that are mixed with water to provide a high-fiber mixture that can be syringe-fed long term. These products generally have good fiber levels at 19% to 25% and are highly palatable. Oxbow Critical Care Fine Grind (Oxbow Animal Health) was developed for ease of use with nasogastric feeding tubes. Emeraid Intensive Care Herbivore (Lafeber Company) is a high-fiber cellulose and soy-protein food that also can be used with feeding tubes short term in critically ill animals. An alternative to the commercial diets is to soak and blend pellets and greens with water, but this is more time consuming and generally results in a less homogenous mixture.

Syringe-feeding an anorectic rabbit can be stressful to some patients. One of several methods can be used, depending on the size and demeanor of the rabbit.[20] It is easiest to feed a rabbit directly out of a catheter-tip syringe if the animal will tolerate it. The tip of the syringe is introduced into the diastema, and contents are fed slowly. In smaller patients or those rabbits that resist feeding, 1-mL syringes or small oral feeding syringes can be used to deliver the food directly into the oral cavity. This method is more time consuming but can be very effective in some rabbits that otherwise refuse feeding. Rabbits are easiest to syringe-feed when wrapped in a towel with the head facing away from the handler or held in one's lap; the feeding syringe is then introduced into the side of the mouth.

Orogastric tubes can be used for single dosing but are inappropriate for long-term use. Sedation or anesthesia is required to minimize stress to the patient while passing an orogastric tube. To pass a tube, premeasure and mark a 14- to 22-Fr round-tip rubber catheter for the distance from the mouth to the last rib. Keep the rabbit's mouth open with a mouth gag, flex the rabbit's neck, and pass the lubricated tube through the oropharynx into the stomach. Test the tube placement by auscultating as air is injected through the tube into the stomach or checking for negative pressure when the tube is backed into the esophagus. This technique is also used to remove liquid gastric contents in rabbits with fluid-distended stomachs caused by gastrointestinal obstruction; in these cases, extra holes are cut into the distal tube tip (see Chapter 14).

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Fig. 12.11 A nasogastric tube placed in an adult male Flemish giant rabbit for force-feeding.

Nasogastric tubes are used clinically but may be more stressful compared with oral syringe feeding. Nevertheless, nasogastric tubes are a good option for long-term management if syringe-feeding is not feasible, and, depending on the rabbit's behavior, restraint may not be needed for feeding. Measure the tube as described for orogastric tubes, using the tip of the nose and the last rib as landmarks. A pediatric feeding tube (3.5 to 5 Fr) can be used for most rabbits. Place a topical anesthetic such as 2% lidocaine gel or several drops of proparacaine in the nasal opening several minutes before placement. Insert the tube through the ventral medial nasal meatus and pass it ventrally and medially with the head flexed. Check tube placement with a lateral radiograph or as described for orogastric tube placement. Secure the tube with a drop of cyanoacrylate glue on the furred area above the nose and with tape glued or sutured to the top of the head (Fig. 12.11). Further description of the technique has been reported elsewhere.[34]

Vaccinations

No routine vaccinations are recommended for pet rabbits in the United States. In Europe, vaccines against myxomatosis and rabbit viral hemorrhagic disease are recommended.

Pain Control

Pain control is important for successful recovery of the compromised rabbit patient. Pain assessment is difficult in rabbits because they typically do not vocalize when experiencing pain. A painful rabbit may sit very still in the back of the cage in a hunched position while teeth grinding. Other clinical signs of pain are decreased fecal production, head elevation, aggression, isolation, and rapid shallow breathing. The rabbit grimace scale (see above) may provide additional parameters to assess pain in rabbits.[21,27,32] Preemptive analgesia is recommended whenever possible.

Nonsteroidal antiinflammatory drugs are estimated to last for 12 to 24 hours in rabbits. Based on pharmacokinetic data, meloxicam dosing at 1 mg/kg by mouth every 24 hours is required to achieve clinically effective circulating concentrations in rabbits.[17] This dosage has been administered to healthy rabbits for a total of 29 days without significant changes observed on plasma biochemical analyses or on histologic examination of tissues.[11] Buprenorphine is effective for 6 to 12 hours, whereas butorphanol is effective for 2 to 4 hours. Transdermal fentanyl patches can also be used in rabbits (25 μg/h in 4 kg rabbit).[16] Patches must be placed in non-haired areas, such as the ear pinna, or after using depilatory cream in furred areas. Abdominal or visceral pain may respond better to opioid analgesia, whereas nonsteroidal antiinflammatory drugs are generally more effective for somatic or integumentary pain. Multimodal analgesia, combining agents from different classes, may be more effective than a single agent alone, and allows the agents to be used at lower doses. For hospitalized patients, many analgesic agents, both non-opioid and opioid, can be administered by intravenous continuous rate infusion and titrated to effect. See Chapter 37 for more detailed information regarding analgesia.

Anesthetic Delivery

Anesthetic agents are administered to rabbits in a variety of ways, including topical, injectable, inhalant, and combination protocols (See Chapter 37 and Appendix).[15,25] Anesthesia involves many considerations such as stability of the patient, monitoring, and anesthetic agents used.[39,40] Critically ill patients should be stabilized before anesthetic administration.

Topical anesthesia may be useful before procedures such as catheter placement. A topical cream containing lidocaine 2.5%/prilocaine 2.5% enables percutaneous insertion of catheters into rabbit veins without causing any detectable pain or discomfort.[14] These topical preparations may take 45 to 60 minutes to be fully effective.

Nasolacrimal Cannulation

Nasolacrimal duct flushing is indicated to determine and restore patency of the nasolacrimal ducts when rabbits present with an ocular discharge. Common causes of nasolacrimal duct obstruction include infectious agents and dental disease.[53] See Chapter 40 and Figure 40.2 for description of this technique and further discussion.

Ear Cleaning

Ear cleaning is indicated in cases of otitis externa (see Chapter 17). Otitis externa may be caused by primary bacterial infections or an extension of otitis media through a ruptured tympanic membrane. Minor ear cleaning can be done in unsedated animals by using ear-cleaning solutions and cotton swabs, making sure to massage up from the base of the ear to loosen debris. For severe otitis, sedate the rabbit to allow more aggressive cleaning. Use a flexible (plastic) ear curette or cotton-tipped applicators to gently remove purulent and waxy debris. To flush the ear canal, insert a red rubber catheter into the canal, then flush with warm saline solution and remove debris with mild suction. Avoid flushing if the tympanic membrane is ruptured. Use an otoscope for visualization to minimize trauma to the ear canal or tympanic membrane. Ear cleaning should be accompanied by appropriate medical diagnostic tests to determine the cause of disease.

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Ear mites (*Psoroptes cuniculi*) can cause mild to very severe otitis externa. This large, nonburrowing mite typically causes inflammation and crusty exudates secondary to a hypersensitivity reaction from the mucus and feces of the parasite.[35] See Chapter 17 for discussion of treatment.

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13

Gastrointestinal Physiology and Nutrition of Rabbits

Susan M. Smith, PhD

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The rabbit is a monogastric, hindgut-fermenting herbivore with a complex and unique digestive physiology that relies heavily on cecotrophy. Given the wild rabbit's ecologic role as a small prey species, its digestive strategy has evolved to permit efficient digestion of fibrous vegetation without the need to store large volumes of food within the body. The gastrointestinal tract features a simple stomach, a well-developed cecum, and a particle-dependent separation mechanism within the proximal colon. Digestible fiber particles and solutes that are not immediately digested and absorbed enter the colon and are selectively retained as substrates for microbial fermentation within the cecum, whereas nondigestible fiber is rapidly expelled. The production and ingestion of cecotropes (packets of cecal contents) is a significant complement to the animal's nutrition and enhances the nutriture of the forage-based diet.

An appreciation of normal gastrointestinal physiology is essential to formulate appropriate diets, understand the pathophysiology of common diseases, interpret diagnostic tests, and aid formulation of effective treatment plans. The importance of nutrition in the maintenance of health in the pet rabbit cannot be overstated. Inappropriate nutrition is a significant contributory factor in the development of many common dental, gastrointestinal, urinary, and obesity-related disorders. Much of the published literature related to rabbit nutrition is derived from the production industry and emphasizes growth and reproduction. Nutrition of the pet domestic rabbit, as well as the laboratory rabbit, emphasizes maintenance and reduction of chronic disease risk. This chapter summarizes the current understanding of rabbit gastrointestinal physiology and focuses on the dietary requirements of the pet domestic rabbit.

RABBIT GASTROINTESTINAL PHYSIOLOGY

Ingestion of Food

Feed intake of the juvenile and adult rabbit is driven by the food's energy density and gastric fill. The wild diet on which domestic rabbits evolved is seasonably variable and low in energy density, with grasses dominating. Rabbit feeding preferences are shaped by nutrient needs, and they will seek more energy-dense diets when offered a choice.[12,34] Palatability and variety are also important modulators. The adult rabbit feeds >20 times across the 24-hour cycle in short sessions of 2 to 8 g of food consumed over 4 to 6 minutes.[57] Rabbits are crepuscular, and feeding is more frequent around the light/dark cycle transitions.[41] Rabbits do not see their food as they eat because of the lateral position of their eyes, and food selection relies on olfactory cues and tactile information obtained via the sensitive vibrissae around the nose and lips.[18] Food choice is also crucial to healthy dentition, because rabbit teeth grow continuously, and the upper incisors grow as much as 2 mm per week.[18] Foods are initially sliced vertically by the three pairs of incisors (two upper, one lower) into smaller pieces. These are then masticated by the 22 premolars and molars operating in a lateral grinding pattern that also keeps the occluding surfaces in correct alignment. The large

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tongue circulates the food particles through the molar grinding surfaces. Breakdown of fibrous foods into fine particles suitable for fermentation requires chewing actions up to 120 times per minute.[6]

Stomach

The rabbit's alimentary tract features a simple stomach comprising approximately 15% of total gastrointestinal volume.[18] There is a well-developed cardiac sphincter that prevents vomiting. Hydrochloric acid and pepsin are secreted into the stomach and initiate the digestive process in much the same way as in other species. The gastric pH varies diurnally but is generally very acidic compared with that of other species; postprandially, it can drop to as low as 1.0 to 2.0, whereas after ingestion of cecotropes, it rises to 3.0.[5] This low pH effectively sterilizes ingesta. Juvenile (preweaned) rabbits have a much higher gastric pH (5.0–6.5), which promotes the survival and passage of ingested bacteria, facilitating the establishment of the vitally important large intestinal flora.[5] The stomach usually contains hair, food, and fluid even after 24 hours of fasting or anorexia. Gastric transit time is approximately 3 to 6 hours.[10] *Cyniclomyces guttulatas (Saccharomycopsis guttulata)* a symbiotic yeast, has been found to line the stomach of domestic and feral rabbits and likely proliferates there rather than in the cecum or large intestine.[64]

Small Intestine

The small intestine is the primary site of nutrient digestion and absorption and is similar to that of other monogastric animals. Bicarbonate is secreted into the proximal small intestine and functions to neutralize the acidic digesta leaving the stomach. The duodenum is enriched in enteropeptidase, aminopeptidases, and oligosaccharidases and disaccharidases. Host digestive enzymes are upregulated during the developmental transition to solid foods and include pancreatic amylase and lipase, proteases such as trypsin and chymotrypsin, and a shift in the jejunum from lactase to maltase and sucrase.[10] Nutrient absorption occurs within the jejunum and ileum. Digestion and absorption of nutrients from the ingested cecotropes also occurs here. Digestion is efficient, and 80% to 100% of dietary starch and amino acids are absorbed by the time they reach the distal ileum.[37,61] Nutrient-dense foods with high digestibility, such as commercial rations, have higher bioavailability than vegetative foods and grasses. The bulk of the rabbit's diet consists of vegetative forage, which mastication breaks into small particles largely comprised of cellulose, hemicellulose, lignin, oligosaccharides, and protein, all bound in a biomatrix. These particles pass through the small intestine largely undigested. Dry matter in the distal ileum is ~70% fiber and ~15% nitrogenous.[27,29,61] Transit time through the small intestine is rapid: 10 to 20 minutes through the jejunum and 30 to 60 minutes through the ileum.[10] The ileocolic valve at the distal ileum prevents retrograde motion of ingesta from the colon and cecum into the ileum.

Gut-Associated Lymphoid Tissue (GALT)

Functional interactions between the intestinal microbiota and host are essential for maturation and maintenance of the intestinal mucosa and immune system. In the rabbit, the GALT consists of Peyer's patches, which are lymphoid follicles associated with the jejunum and distal ileum, and two structures that are unique to rabbits: the sacculus rotundus at the ileocecal junction, and the vermiform appendix at the distal terminus of the cecum (Fig. 13.1).[18] Both are enriched in lymphoid nodules that are sites of lymphocyte expansion.[24,58] Similar lymphoid follicles are also present along the colon. Roles for the GALT are incompletely understood, but, as in other mammals, they provide barrier functions, stimulate oral tolerance, mediate antigen presentation of microbial proteins, and influence enterocyte development.

Large Intestine

The rabbit large intestine is comprised of a cecum and colon. Its complex structure reflects its role in fermentation and cecotrope formation. The thin-walled cecum constitutes 49% of the digestive tract volume and is the primary site of digestible fiber fermentation.[18] It occupies more than half of the abdomen and is positioned on the rabbit's right side in a coiled structure. The cecum terminates in a vermiform appendix that, in addition to its lymphoid tissue, secretes water and bicarbonate into the cecum for fermentation.[6, 10] The colon has four regions that are structurally and functionally distinct. The most anterior region (approximately 10 cm) of the proximal colon is longitudinally striated by three thick muscular bands, or taeniae, that are interspersed with three sacculated haustra providing a high lumenal surface area. The next ≈ 20 cm are characterized by a single longitudinal taenia and haustrum. Demarcating the proximal and distal colon is a structure unique to lagomorphs, the fusus coli. This 4-cm-long structure is densely innervated and banded circumferentially with muscle. It lacks both taeniae and haustra, and its luminal surface is rich in goblet cells. The distal colon is 80 to 100 cm long and extends from the fusus coli to the rectum. It is thin walled, and its luminal surface features short crypts and numerous goblet cells. Connecting the ileum, cecum, and proximal colon at the base of the cecum is a specialized chamber called the *ampulla caecalis coli*.

The primary function of the proximal colon is to mechanically separate digested particles by size for either cecal fermentation or fecal excretion. The luminal surfaces of the haustra are lined with dense mucosal protrusions called "warzen" (or warts), each averaging 0.5 mm in diameter. Smaller (< 0.3 mm) fiber particles penetrate the spaces between the warzen and are preferentially retained along the haustra. Larger particles (> 0.3 mm) are excluded from these spaces and remain in the central lumen. A complex sequence of contractions separates these particles for either cecal fermentation or fecal excretion as described below (Fig. 13.2).[20,40] In the postprandial period, the larger, nonfermentable particles are propelled aborally. The hormone aldosterone mediates the resorption of water, potassium, and sodium from this fibrous material. Passage of this material through the muscular fusus coli compacts the material into the familiar rounded pellets. Additional water, electrolytes, and volatile fatty acids are extracted during fecal passage through the distal colon. The excreted feces are mostly compressed nondigestible fiber (dry matter, 52.7%) with very little water.

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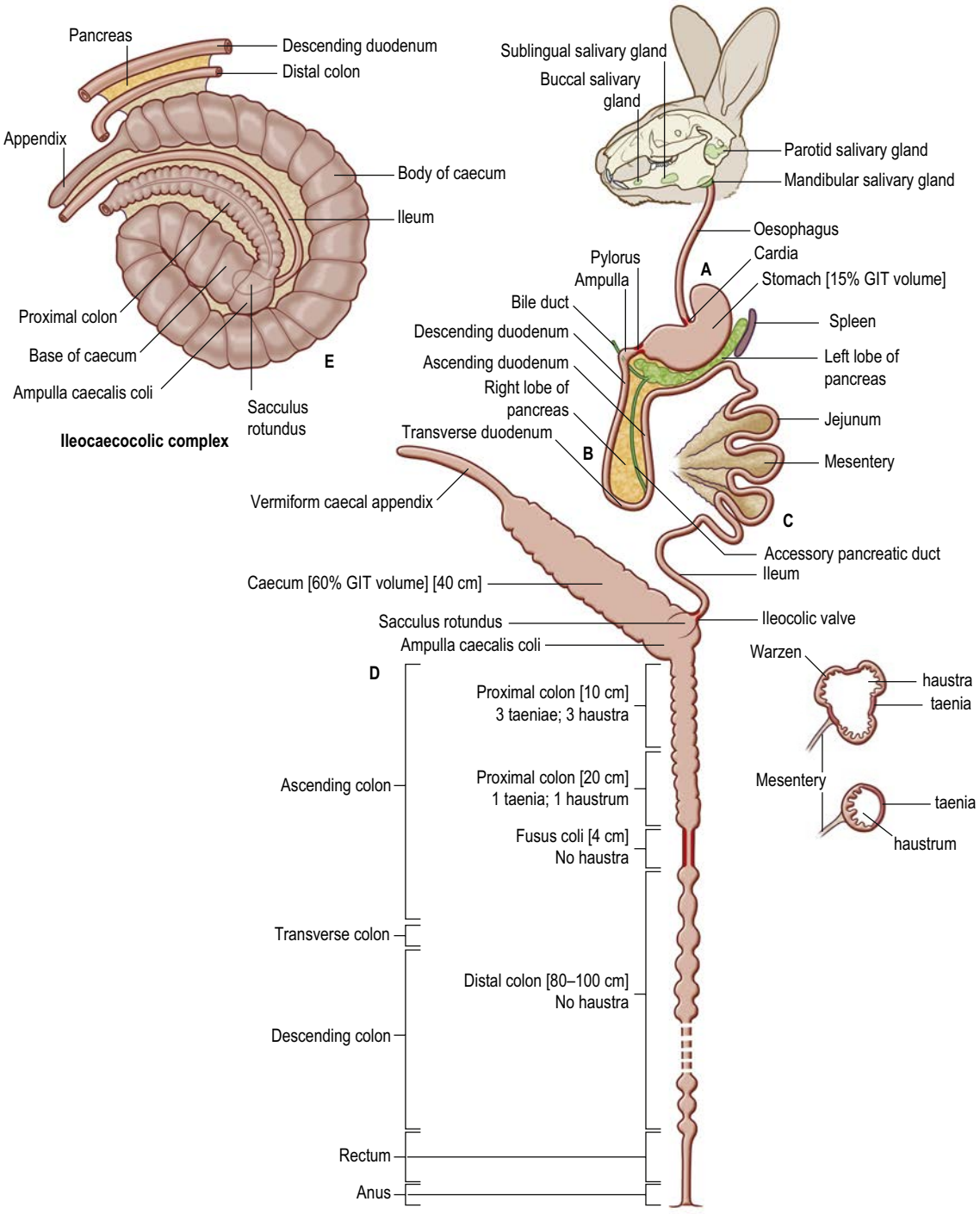


Fig. 13.1 Anatomy of the rabbit digestive tract. Reprinted by permission from F. Harcourt-Brown. *Textbook of Rabbit Medicine, Second edition.* Oxford: Elsevier, 2013.

Although the indigestible fiber does not contribute metabolizable energy, its bulk properties promote gastrointestinal motility, cellular regeneration, and muscle tone and help regulate microbiota composition. Thus indigestible fiber is essential for healthy gastrointestinal function.

Hindgut Flora and Fermentation

Wild rabbits subsist on a forage-based diet that is low in energy density and nutrient yield. They therefore evolved highly specialized hindgut fermentation coupled with coprophagy to extract maximal nutrients and energy from otherwise nondigestible forage.[59] This fermentation occurs predominantly in the cecum, although the distal ileum and proximal colon also contain microbial populations and may contribute pectinases and xylanases for conversion of soluble fiber.[29] New analytical methods that use DNA sequencing of microbial ribosomal genes reveal that the rabbit's complex microbiota is genetically unique to this species.

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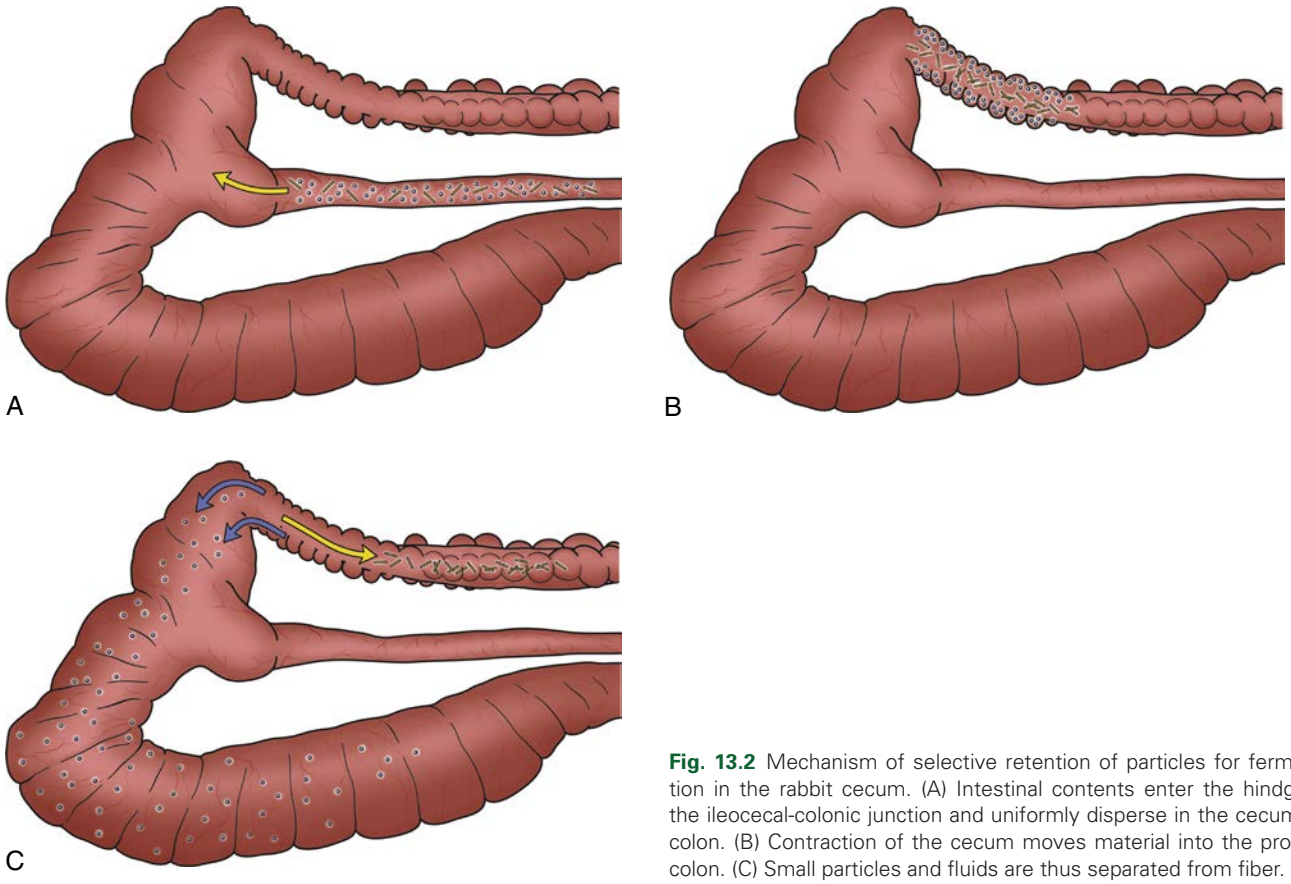


Fig. 13.2 Mechanism of selective retention of particles for fermentation in the rabbit cecum. (A) Intestinal contents enter the hindgut at the ileocecal-colonic junction and uniformly disperse in the cecum and colon. (B) Contraction of the cecum moves material into the proximal colon. (C) Small particles and fluids are thus separated from fiber.

A gram of cecal content contains 10^{10} to 10^{12} bacteria and approximately 10^7 copies of 16S RNA from archaea (prokaryotes).[15,24] The microbiota appears to lack eukaryotic protozoa and anaerobic fungi, and the presence of yeast *(C. guttulatus)* in the cecum is debated.[15] However, *C. guttulatus* symbiotic yeast have been found to line the stomach of domestic and feral rabbits.[64] The *Firmicutes* (> 90%) phylum dominates the bacterial cecal microbiota, with fewer *Bacteroidetes* (4%). The most abundant *Firmicutes* are in the families *Ruminococcaceae* (45%) and *Lachnospiraceae* (35%). Facultative anaerobes (*Streptococcus* species, *Escherichia coli*) are abundant postnatally and largely disappear postweaning.[24] Rabbits are unique in lacking *Lactobacillus*.[24] Most of the gut microbiota represent new species not previously identified.[1,51] In an adult healthy rabbit, the cecal community is remarkably stable over time.[16] Interrabbit variability is also relatively low,[16] although this may reflect genetics or limited diet variability.[49,50] The bacterial and archaeal population in the cecotrope largely reflects the cecal population, whereas the fecal community is more divergent.[49,50] Thus the cecotrope profile compositionally reflects the cecal environment.

Fermentation in the cecum converts forage into energy and nutrient forms that the rabbit can utilize. A gram of cecal material contains 10^7 colony-forming units of cellulolytic bacteria and 10^9 to 10^{10} colony-forming units of pectinolytic and xylanolytic bacteria.[15] Thus cellulose, pectin, and hemicellulose can all be fermented, although the latter two dominate. Available nitrogen sources for the microbes include plant proteins and plasma urea.[23,61] Mucin production by cecal goblet cells also modulates microbial growth.

The digesta entering the cecum from the ileum is predominantly fiber (70%) and nitrogenous compounds (15%). Hydrolysis of plant oligosaccharides by microbial hydrolases liberates monosaccharides that are fermented by the microbes to volatile fatty acids (VFAs), with a typical abundance of 75% acetate, 10% propionate, and 15% butyrate.[28,29] The fermentation efficiency is pectin > hemicellulose > cellulose. Other compounds produced by the microbiota include ammonia, intermediate organic acids (lactate, succinate, formate), and small quantities of gas (H_2, CH_4, CO_2). The VFAs and organic acids are efficiently transported into the mucosal cells, where they are a preferred energy source for the colon, particularly butyrate.[46] The remainder are exported to the bloodstream for use predominantly by the liver. The VFAs contribute 30% to 50% of the rabbit's basal metabolic needs.[28,46]

The proportion of the three volatile fatty acids varies according to the time of day, the diet, and the rabbit's developmental stage. The indigenous intestinal microbiota serves a protective role in relation to potential pathogens. *Clostridium* species represent < 1% to 0.1% of the total bacterial population in normobiotic rabbits.[24] Energy is the limiting factor for the cecal microbial population. Disruption of the normal balance of microbiota in the gut, usually with overgrowth of known or potential pathogens, is termed *dysbiosis* and is a common and

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Fig. 13.3 Rabbits produce two types of feces. Cecotropes, or "soft feces," (A) are produced by the rabbit according to a circadian pattern of intestinal motility and are usually eaten directly from the anus. They are soft and arranged in clusters and have a mucous coating. The appearance and composition of hard feces (B) are distinctly different from that of cecotropes; hard fecal pellets are predominantly composed of indigestible fiber and are generally round and dry.

serious clinical problem in rabbit medicine.[44] This may occur as a result of inappropriate therapeutic antibiotic administration, exposure to pathogenic organisms or toxins, increased glucocorticoid levels (iatrogenic or secondary to stress), gastrointestinal hypomotility, and poor dietary composition (low fiber, high carbohydrate, and high protein levels) (see Chapter 14).

Suckling rabbits are unique among nursing neonates in that they feed for only 3 to 4 minutes and just once or twice every 24-hour period.[63] For this reason, rabbit milk is energy dense (8.5 MJ kg-1) and contains 10% to 15% protein and 12% to 15% lipid, whereas the lactose content is quite low (5% of dry matter).[34,62] In the stomach, the milk is enzymatically converted to a curd that is slowly digested over the 24 hours; other milks do not confer this property. The milk is rich in medium-chain triglycerides, particularly octanoic and decanoic acid, which confer antimicrobial properties.[9] Ingestion of maternal hard feces begins at postnatal (PN) days 4 to 6 to begin cecal microbiota colonization and is facilitated by the stomach's higher pH.[10,34] Solid food consumption begins at PN days 16 to 18 and increases sharply around PN day 25. Weaning occurs between 5 to 6 weeks old and occurs sooner if the mother is pregnant.

Cecotrophy

Whereas hard feces are produced in response to a meal, cecotrope production is actively regulated and occurs in a circadian rhythm that is the inverse of food intake and fecal synthesis.[10] In pet rabbits, cecotrope production is often diphasic and typically occurs four hours after a meal, during a period of quiet. The frequency is also modulated by age, light cycle, and feeding pattern.[10,45] Cecotrope production is not a response to nutritional stress. Cecotrophy in rabbits is a normal physiologic process that enhances the nutrient content of poor-quality foods through the reconsumption of fermented digesta enriched with microbe-derived nutrients.

The cecotrope is comprised of the cecal contents, compressed into a soft pellet and coated by mucus (Fig. 13.3). The signals that initiate cecotrope production are incompletely known but may include cecal pH and its content of volatile fatty acids. The fusus coli acts as an "intestinal pacemaker," controlling segmental, peristaltic, and haustral colonic motility.[6] In response to those signals, endogenous prostaglandins minimize the antiperistaltic contractions within the haustra of the proximal colon to reduce the mechanical separation process.[20,54] The prostaglandins also stimulate motor contractions in the distal colon, and indomethacin blocks this peristaltic switch.[54] Aboral peristaltic waves now dominate and rapidly propel the cecal contents through the proximal colon. Passage through the fusus coli compresses the loose cecal material, and goblet cells within the lumen coat the small pellets with mucin. The resulting pellets average 5 mm in diameter and emerge from the anus in a grapelike cluster. The rabbit directly consumes the cecotropes from the anus without chewing (Fig. 13.4).[33] The sensory signal that triggers



Fig. 13.4 The rabbit in the foreground is demonstrating cecotrophy (i.e., the ingestion of cecotropes directly from the anus). Given the posture required to perform this normal physiological function, rabbits with mobility problems or spinal issues, or those that are overweight, frequently have difficulty practicing cecotrophy.

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cecotrophy is unknown and does not appear to involve rectal or olfactory signals.[26] The transit time for cecotropes through the colon is 1.5 to 2.5 times faster than that for hard feces.[22]

The cecotrope contains 34% dry matter by weight.[10,40] This dry matter is 18% fiber and 30% protein, and roughly 80% of this protein is microbial in origin.[10,35] It also contains a rich microbiota of mostly bacteria (10^{10}/g dry matter) and some archaea.[15,59] Most of the cecotrope's nutrient richness comes directly from the microbiota and its cecal fermentation of plant forage. From the digestion of these microbes within the small intestine the rabbit obtains essential amino acids (notably lysine, threonine, and sulfur amino acids), several vitamins (thiamin, riboflavin, niacin, pantothenate, pyrodixine, folate, B12, biotin, vitamin K), and minerals released from the plant biomatrix (especially phosphorus, magnesium, iron, copper, zinc).[12] The cecotrope protein contributes from 10% to 23% of the daily amino acid requirement.[12,61] Reingestion of cecotropes enables these nutrients to be absorbed in the jejunum and ileum. The ingested cecotropes reside largely intact within the stomach for 3 to 6 hours.[33] Cecotropes have a buffering action on stomach pH, raising it from 1 or 1.5 to 3.0. During this time, lysozyme secreted by the colon and incorporated into the cecotropes breaks down the peptidoglycans in the microbial cell walls and releases their protein and micronutrients for digestion.[8] The microbes may further ferment the fiber content of the cecotropes, because the mucus layer protects them from the stomach pH. Although the preponderance of the cecotrope microbiota is digested, small quantities may survive passage and reach the cecum. Feeding healthy cecotropes could benefit rabbits that have cecal dysbiosis. The percentage of cecotropes eaten varies depending on feeding regime and dietary composition. For example, fewer cecotropes are consumed on a high-protein diet compared with a high-fiber diet. A cecotrope may occasionally pass intact into the intestine.

Motility

Normal gastrointestinal function relies on a complex and highly coordinated pattern of intestinal motility. Postprandial motility in the small intestine is under the influence of the autonomic nervous system, hormones, and nutritional content (especially indigestible fiber levels). During the interdigestive phase, motilin released from endocrine M cells within the duodenojejunal mucosa stimulates the migrating motor complex, which propels materials aborally and serves to limit bacterial overgrowth.[56] Motilin receptors are present in the rabbit small intestine, colon, rectum, and central nervous system and are absent from the cecum.[6] Its activity is mimicked by motilide pharmacologic agents and macrolide antibiotics such as erythromycin.

In the cecum and colon, a complex, circadian motility pattern governs fermentation and coordinates the production of cecotropes and feces.[6] Formation of hard feces coincides with feeding activity, whereas cecotrope formation occurs several hours after feeding, typically during a period of rest. This rhythm is influenced by diet, age, and reproductive status.[10] In the cecum, peristaltic and antiperistaltic waves move from base to apex and back at a frequency of 1 to 2 contractions per minute. These slow waves create backflow to mix the cecal contents and enhance fermentation.[20] In the proximal colon, shallow aboral contractions of the haustra (13.8–16.2 per minute) mix the digesta and drive particle size separation. Retrograde contractions along the single-haustrated colon propel small particles and liquid back to the triple-haustrated colon and the cecum. This supplies the cecal microbiota with substrate for fermentation. At the same time, migrating segmenting contractions propel the large particles aborally to the fusus coli for concentration and excretion. These haustral contractions are suppressed when cecotropes are produced. Giant rhythmic contractions stimulated by prostaglandins expel the cecal contents through the proximal colon for processing into cecotropes as described above.[54]

NUTRITIONAL REQUIREMENTS

Rabbit nutrient requirements are imprecisely known. A nutritionally adequate diet provides fiber substrate for cecal fermentation and gastrointestinal motility and meets nutrient and energy needs in excess of that provided by fermentation and cecotrophy, as these latter are nutritionally inadequate, particularly with respect to energy, protein, and micronutrients. The diet should also promote normal foraging behavior throughout the day. Inappropriate diet is a significant predisposing factor for acute and chronic disease in this species.

Energy Requirements

Energy requirements are influenced by age, body size, and environment. Recent estimates of the digestible energy (DE) requirement suggest 400 kJ/day^{-1} per kg^{-1} LW$^{0.75}$ (96 kcal/day^{-1} per kg^{-1} LW$^{0.75}$) for maintenance (DE_m) and 430 kJ/day^{-1} per kg^{-1} LW$^{0.75}$ (103 kcal/day^{-1} per kg^{-1} LW$^{0.75}$) for growth, pregnancy, and lactation, where LW is live weight in kilograms.[12,62] Assuming thermoneutrality and moderate energy expenditure, and using a value for DE_m of 96 kcal/day^{-1} per kg^{-1} LW$^{0.75}$, an adult, nonbreeding, 1-kg Netherland dwarf rabbit would require 96 kcal/day^{-1} of digestible energy for maintenance and a 7-kg Flemish giant rabbit would require 413 kcal/day^{-1}. This reflects that energy requirement does not linearly increase with body weight, and that small breeds require more energy per kilogram LW because of their higher basal metabolic rate and smaller gut capacity.[36] Environmental temperature also affects energy need, and temperatures below and above thermoneutrality (21°C–25°C) increase or decrease energy intake, respectively.[11] Although rabbits typically self-regulate food intake in response to energy status and diet composition, boredom and the need for gastric fill can promote overeating.[2] For environments characterized by low energy expenditure (cage housing, indoor pet rabbits), foods with low energy density (i.e., forage) should dominate, and energy-dense foods (i.e., commercial pellets) are fed in a restricted manner to reduce obesity risk. This is discussed further below.

Protein

Protein is required for growth and lactation, maintenance, and fur production. Dietary protein requirements are 16% for growth, 12% to 14% for maintenance, and 18% for lactation; intakes of 16% to 18% may be necessary for angora

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breeds that continuously produce fur.[53,61] Essential amino acids for rabbits are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. These must be supplied by the diet and from ingested cecotropes (28% protein); essential amino acids from cecotropes will not meet requirements when dietary protein quality is poor.[13] The urea cycle supplies sufficient arginine. Forage contains sufficient sulfur-containing amino acids to meet needs. Protein digestion in the small intestine is efficient even for forages such as alfalfa (72% to 83%) and fresh grass (78%).[43,48,60] Rabbits poorly utilize nonprotein nitrogen, and dietary urea can be toxic.[12] Rabbits voluntarily regulate cecotrophy to balance protein intake, and more uneaten cecotropes are observed when rabbits are fed high-protein diets. Excess dietary protein elevates plasma urea and cecal ammonia content, which raises the cecal pH and creates an environment more permissive for *Clostridia* and *Escherichia* overgrowth.[12,21,23] Cereal grains such as corn, barley, oat, and rye are low in lysine and methionine, and commercial diets add complementary protein sources such as alfalfa to address that insufficiency.

Carbohydrate

Rabbits efficiently digest carbohydrate, both starch and simple sugars, and it is their major source of energy. Ileal digestibility averages 97% and ranges from 93% for wheat to 99% for maize starch.[5] Starch digestibility is lower in young rabbits and rises as pancreatic amylase levels increase through at least 12 weeks of age.[19] It has been assumed that high intakes of rapidly fermentable carbohydrate cause enteritis.[14] More recent work shows this risk reflects a commensurate reduction in fiber intake.[31,32] Thus rabbits may tolerate greater starch intakes than currently recommended (150–1555 g/kg dry matter), provided that fiber intake exceeds 10% to 12%.[30] However, this is not the case for young rabbits because of their greater ileal flow of starch, and high carbohydrate increases their risk for enteritis.[5,10]

Fiber

As hindgut fermenters, rabbits are evolutionarily adapted for a high-fiber diet, and thus fiber is essential for their health. The dietary fiber content of commercial pellets should be 20% to 25% for pet or maintenance rabbits and 18% to 20% for those in production.[29,43,48] Both digestible and nondigestible fibers are required, and these provide both physical and metabolic benefits. Long-strand fibers, as in hay, promote healthy dentition because the plant silicates and large particles keep the constantly growing molar surfaces in proper occlusion. The long fibers also propel ingested fur through the digestive tract and reduce the risk for trichobezoars in the stomach. The larger particles from nondigestible fiber stimulate gut motility and enterocyte turnover. At the metabolic level, fermentation of predominantly digestible fiber, but also some cellulose, provides 30% to 50% of daily energy, and the volatile fatty acids are a preferred energy source for the colon.[28,36] Fiber digestibility is a function of fiber source, diet composition, and breed, and values range from 10% to 27% for cellulose and lignins and 11% to 46% for hemicellulose and pectins.[12,29,60] The efficiency is lower than for other hindgut fermenters such as horses.[12,60] Reingestion of the cecal product provides vitamins and essential amino acids via cecotrophy. Fiber promotes microbial diversity and reduces the risk for enteritis.[15] In the form of ad libitum hay, it satisfies the need to forage frequently without promoting obesity or unwanted behaviors such as fur pulling.[3,4] Diets low in fiber are associated with increased gastrointestinal disorders, death, and reduced voluntary food intake.[2,29,31]

Fat

Fat contributes a small percentage of daily calories, and the requirement is imprecisely known. The recommended intake is 20 g/kg (2%) and is not to exceed 30 to 35 g/kg (3%–3.5%).[12,53] Triglyceride digestion is similar to that of other nonruminants and uses pancreatic lipases, bile acids, and duodenal absorption of micelles. Fats promote absorption of the fat-soluble vitamins. They also provide essential fatty acids (linoleic, linolenic, eicosapentanoic, docosahexaenoic) that are the precursors for the eicosanoid hormones that modulate inflammation, blood pressure, and thrombosis. The essential fatty acid requirement for rabbits is unknown, and omega-3 forms should be emphasized over omega-6 forms. Lipids promote food palatability.[12] Companion rabbits are prone to obesity, hepatic lipidosis, and atherosclerosis, and high-fat diets must be avoided.

Vitamins and Minerals

Vitamin and mineral requirements are summarized in Table 13.1.[12,47,53] These values are for production; maintenance requirements are imprecisely known and may be slightly lower. In the healthy rabbit, cecotropes provide vitamin K and most of the B vitamins. Vitamin D is obtained from sun-cured hay (as ergosterol) or direct sunlight exposure (as cholecalciferol). Vitamin E is found in alfalfa meal and seed oils. Rabbits efficiently synthesize vitamin A from plant carotenoids and do not store carotenoids. Toxicosis is more likely than deficiency and can result from feed misformulation and carrot overconsumption.[25] Rabbits synthesize vitamin C and do not require a dietary source. Vitamin supplementation above requirements has not been shown to improve health and may increase risk for toxicosis. Vitamin deficiencies are uncommon but may be a consequence of poor diet quality, intestinal parasite infestation, failure to consume cecotropes, or chronic disease.

Minerals must be obtained from dietary sources. Microbial phytases in the cecum significantly improve the bioavailability of plant-based calcium and phosphorus, as well as divalent metals (magnesium, copper, zinc, manganese). Calcium metabolism in the rabbit is unusual in that its intestinal absorption is directly proportionate to intake and is independent of both phosphorus intake and vitamin D action.[12,47] Serum calcium levels directly reflect dietary intake. Vitamin D and parathyroid hormone regulate serum calcium, and excess calcium is excreted through the urine rather than the bile. The urine's alkalinity (pH 8.2) precipitates the urinary calcium as insoluble white or yellowish carbonate deposits, which can be seen

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TABLE 13.1 Summary of Vitamin and Mineral Requirements of Domestic Rabbits

Vitamin/Mineral	Dietary Requirement (kg^{-1} diet)	Comments
Vitamin A	6000 IU/kg[a]	Deficiency is rare. Toxicosis can result if overfed carrots or overfortified feed. Symptoms of toxicosis mirror deficiency and include ataxia, enteritis, weight loss, neurologic symptoms, hyperostotic polyarthropathy, keratitis, iridocyclitis, and fetal malformations.
Vitamin B complex	Biotin—0.2 mg/kg[a] Cyanocobalamin—0.01 mg/kg[a] Folate—5 mg/kg[a] Niacin—50 mg/kg[a] Pantothenate—20 mg/kg[a] Pyridoxine—2 mg/kg[a] Riboflavin—6 mg/kg[a] Thiamine—2 mg/kg[a]	Produced in the cecum; supplied by the cecotropes. Deficiency unlikely if microbiota is healthy. Cecal dysbiosis may pose deficiency risk. Dietary cobalt is necessary for cobalamin synthesis.
Vitamin C	0 mg/kg[a,b]	No requirement; synthesized endogenously.
Vitamin D	900 IU/kg[a]	Provided in sun-cured hay or synthesized in sun-exposed skin. Although calcium absorption is vitamin D independent, vitamin D enhances calcium absorption when intake is low. Excess intakes (> 2300 IU/kg) can cause fetal death, appetite depression, diarrhea, ataxia, paralysis, calcification of soft tissues, and death; deficiency leads to hypophosphatemia and osteomalacia.
Vitamin E	50 mg/kg[a]	Deficiency leads to muscular dystrophy, infertility, abortions, and stillbirths.
Vitamin K	Unknown. Some sources suggest 1–2 mg/kg.[c]	Deficiency unlikely because cecotrophy and green leafy vegetables are good sources. Unknown whether long-term sulfa drug use may increase need.
Calcium	4.0 g/kg for maintenance (acceptable range 3.0–6.0 g/kg)[c] 10.5 g/kg for lactation (acceptable range 10.0–12.5 g/kg)[c]	Calcium metabolism is unique; see text for details. High bioavailability because of phytase activity in cecum. Deficiency leads to rickets, tetany, and death, may increase risk for dental disease. Excess calcium causes urolithiasis, renal disease, and soft tissue calcification (aorta, kidney).
Chloride	1.7–3.2 g/kg[c,d]	Deficiency unlikely.
Choline	200 mg/kg—imprecisely known; range is 100–300 mg/kg.[c]	Not a vitamin. Endogenous synthesis is insufficient to meet needs. Deficiency leads to skeletal muscle wasting, fatty liver, and renal necrosis.
Cobalt	0.25 mg/kg[c,d]	Essential for cobalamin synthesis by cecal microbiota and propionate metabolism
Copper	5–10 mg/kg[c,d]	Deficiency leads to abnormal and greyed fur, bone anomalies.
Iodine	0.25–0.5 mg/kg[c,d]	Raw *Brassica* species contain goitrogens and high intakes may increase iodine needs. Microbial action can enhance goitrogen potency.
Iron	35–50 mg/kg[c,d]	Deficiency causes anemia.
Magnesium	3 mg/kg[c]	Requirement is imprecisely known. Deficiency leads to poor growth, alopecia, hyperexcitability, convulsions, myocardial fibrosis, and fur chewing.
Manganese	8–15 mg/kg[c,d]	—
Phosphorus	3.0 g/kg for maintenance (acceptable range, 3.0–4.5 g/kg) [c] 6.0 g/kg for lactation (acceptable range, 5.5–7.0 g/kg) [c]	Calcium-to-phosphorus ratio of 1.5:1 to 2:1 is acceptable but does not affect calcium absorption. High bioavailability due to microbial phytases. Deficiency leads to rickets and osteomalacia.
Potassium	6–10 g/kg[c,d]	Hypokalemia risk from diarrhea or kidney failure.
Selenium	0.05 mg/kg[c,d]	Does not spare vitamin E in rabbits. Toxicity at 2.5 mg/kg.
Sodium	2–2.5 g/kg[c,d]	Hyponatremia risk from diarrhea or kidney failure; hypernatremia from salty snack foods.
Sulfur	2.0 g/kg[c]	Requirement unclear. Content in dietary components is typically adequate. Microbiota can convert inorganic sulfur to organic forms.
Zinc	50–60 mg/kg[c,d]	Deficiency leads to dermatitis, alopecia, weight loss, and reduced hematocrit.

[a]Recommendation from Institut National de la Recherché Agronomique.[42]
[b]Recommendation from National Research Council.[53]
[c]Recommendation from Mateos et al.[47]
[d]Requirement is imprecisely known. Values represent the range of intakes that are known to be adequate and are below maximum intakes.

on the cage wire or litterbox. Excess calcium intake increases the risk for uroliths and soft tissue calcification. However, the continuously growing teeth have a high calcium demand, and inadequate calcium intake may increase the risk for dental disease.[38,39] Because calcium is drawn from the bones and teeth when intake is inadequate to meet plasma and cellular needs, urolithiasis should not be treated by completely removing calcium from the diet. A salt or mineral lick is unnecessary

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because minerals are provided by forage, vegetables, and commercial pelleted chows.

DIETARY COMPONENTS

Hay

Hay is an essential part of the pet rabbit's diet and should be provided ad libitum. It satisfies satiety needs, has a low energy density, promotes gut motility and cecal fermentation, and reduces the risk for dental disease.[17,32,39] Hay comes in two broad classes: leguminous and grass. Because of their higher protein (15%–25%) and calcium (1.2%–1.5%) content, leguminous hays, such as alfalfa and clover, are suitable for lactating does and young growing rabbits, whereas grass hays—with a lower energy and nutrient density—are preferred for mature or nonbreeding rabbits. The higher protein and calcium content of leguminous hays may increase risk of cecotrope overproduction and urolithiasis, respectively. Suitable grass hays include brome, fescue, orchard, rye, and timothy. Their nutrient content varies with growth stage at harvest; typical ranges are 7% to 15% protein and 25% to 35% fiber.[52] First-cut hay generally is higher in fiber, whereas second-cut hay generally is higher in protein and lower in fiber; fiber content increases and nutrient content decreases as a plant matures. Grain-based hays such as oat, wheat, and barley are less desirable because they can contain seed heads that encourage poor dietary habits and weight gain. Feeding silage is not recommended because it reduces growth and food intake.[55] Anecdotal reports suggest that a straw-only diet for 2 or 3 days may help reestablish the cecal microbiota and reduce enteritis risk; however, straw should not be a regular dietary feature because its poor nutrient content can cause deficiencies.[12]

Quality hay smells fresh and is not musty. It should be stored in an air-tight container away from sunlight, heat, and moisture. Hay can be obtained directly from farmers or from horse stables (grass hay is preferred for horses). It is also sold in small packages that can be ordered online from both large commercial and small local suppliers. Hay should be refreshed daily because rabbits prefer to select favored strands. It is typically offered in an open rack; mounting the rack above the litter pan encourages good litterbox habits. If offered in the litter pan, it should be changed daily.

Fresh Vegetables ("Greens")

Extensive experience with pet rabbits has demonstrated that they tolerate fresh greens well. Fresh vegetables and leafy greens provide many (but not all) micronutrients and modest fiber amounts. The high water content of greens provides satiety while contributing few calories. Fresh greens, especially novel items that have not been given before, should be introduced to a rabbit's diet gradually to allow the gut microbes to adapt, thereby avoiding gastrointestinal dysbiosis. Suitable greens and vegetables include green and red leaf and romaine lettuces (not iceberg); celery leaves, chard, chicory, endive, escarole, radicchio, spring greens, green and sweet red peppers; carrot, beet, and radish tops; herbs such as cilantro and fennel; broccoli, Brussels sprouts, cauliflower, cabbage, and carrots (small quantities).[7] In some rabbits, high calcium intake enhances the risk for urolithiasis, and high-calcium greens and herbs such as dandelion, collard, and mustard greens, kale, bok choy, spinach, watercress, basil, mint, and parsley should be offered in moderation, or not at all if the rabbit has a history of uroliths. Occasional wild plant offerings can include bramble, chickweed, fresh clover, dock, plantain, sunflower, wild strawberry and raspberry leaves, violet, and yarrow. Offering a rotating range of choices is key for nutrient variety and essential to prevent overfeeding of vegetables with high calcium, carotenoid, or carbohydrate content. As a rough guide, 2 cups of varied fresh vegetables or edible plants daily is considered appropriate for a 2.3-kg (5-lb) rabbit. Fruit should be offered very sparingly, if at all, because of the high sugar content and potential for carbohydrate overload in the hindgut, as well as obesity: a small amount (e.g., up to 1 tablespoon for a 2.3-kg [5-lb] rabbit) as a treat one or two times per week is unlikely to be problematic.

Perishable vegetables and greens must be stored refrigerated. Rinsing in fresh water before feeding is advised to remove any contaminants (fertilizers, insecticides, feces, urine, parasite eggs) from the outer surfaces of the food.

Commercial Mixes and Pellets

Pelleted food concentrates are widely used in the pet rabbit industry, as well as in commercial and laboratory settings. A good-quality pellet provides complete micronutrients, protein, and energy in a convenient form. Traditionally, these concentrates are high in energy, protein, and calcium and lower in fiber to address needs for commercial breeding and production. The popularity of pet rabbits stimulated development of concentrates that address the specific needs of adult, nonbreeding rabbits. These maintenance-style diets are higher in fiber (20%–29% vs 18%–20%) and are lower in protein (13%–14% vs 16–18%), calcium (<1% vs >1.5%), and digestible energy (1.6 vs 3.8 kcal/g) than breeding and production diets. The changes in nutrient composition are designed to reduce risk for obesity, cecotrope overproduction, and urolithiasis. These diets may be timothy-based or a timothy/alfalfa blend. Examples include Essentials Rabbit Food (Oxbow Pet Products, Omaha, NE), Science Selective Rabbit Food (Supreme Pet Foods, Ipswich, United Kingdom), and Kaytee Timothy Complete Rabbit Food and Forti-Diet Pro Health (Kaytee Products, Inc, Chilton, WI). Timothy-based pellets are not always available, and alfalfa-based pellets are acceptable when fed in restricted quantities. Examples include Laboratory Rabbit Diet HF no. 5326 and Prolab Hi-Fiber Rabbit diet (both from LabDiet, St. Louis MO), and Rabbit Chow Complete (Purina Mills, St. Louis, MO).

Concentrates should be offered ad libitum to growing, pregnant, and lactating rabbits and to rabbits that have difficulty maintaining weight. For adult, nonbreeding rabbits, offer pellets in limited quantities to reduce obesity risk and encourage hay consumption between meals. The serving size is individually determined and reflects the rabbit's size, age, activity level, and the pellet's energy density. A good guide is ¼ cup given twice daily per 2.3 kg LW (5 lbs). Because the energy density of pellets ranges widely (1.6–3.8 kcal DE/g), an appropriate daily intake for a 2.3-kg rabbit with a DE_m of 179 kcal/d could range from 47g (3.8 kcal DE/g) to 112 g (1.6 kcal DE/g). Serving size can be reduced further to facilitate weight loss in overweight rabbits; a

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safe rate of body mass loss is approximately 100 g (3.5 oz) per week. A meal of vegetables and greens substitutes for a pellet serving. There has been some debate about whether concentrate rations should be fed to adult pet rabbits. However, a diet comprised solely of ad libitum hay, a variety of greens, and normal cecotrope intake is nutritionally incomplete, particularly with respect to essential fatty acids, minerals, and some fat-soluble vitamins. For those diets, pellets should be considered a complementary and necessary nutritional supplement. Pellets are also a good food source for rabbits that cannot consume hay or vegetables because of loss of teeth associated with severe dental disease or that cannot consume cecotropes because of mobility or balance issues; a high-fiber pellet mash freshly prepared with warm water is a good feeding option in these animals.

The nutritional composition of commercial feeds varies enormously but, at a minimum, should meet nutrient requirements. Long fiber particles (>0.5 mm) stimulate gut motility, whereas small particles (<0.3 mm) can lead to increased gut retention time, reduced gut motility, and enteritis.[27,29,43,48] An optimal pellet size that reduces wastage is suggested to be 0.63 cm long and 0.47 cm diameter.[48] Extrusion of grain components enhances their digestibility. Antioxidants such as vitamin E or benzoic acid prevent rancidity. Some pellets contain prebiotics or probiotics, but these are unnecessary.[15] Pelleted feeds should be stored in a cool, airtight container in a pest-free location and used before the manufacturer's expiration date.

Mixed or muesli-style rations contain flaked or rolled grains, nuts, or extruded biscuits that have a high energy density. They should not be offered because they promote selective eating and nutrient imbalances.[12] Rabbits offered mixed-ration diets tend to favor flaked peas and corn, which are high in starch and low in calcium and fiber and may promote risk for obesity, enteritis, and dental disease.[38] Because most owners tend to replenish the feed bowl regularly, discarding uneaten items, the complete mixture of ingredients is rarely consumed. Additionally, some ingredients in the mixed rations (e.g., locust beans) have been implicated in cases of intestinal obstruction.[12] Owner perception is an important factor in pet nutrition, and many owners easily become misguided by the appearance or even the packaging of certain concentrate foods.

Other Feed Items

Foods rich in digestible carbohydrate or fat should not be fed because they promote enteritis, obesity, and picky eating. Such foods include beans, peas, corn kernels, bread, breakfast cereal, nuts, seeds, chocolate, high-sugar fruits such as bananas, and some commercial "treats." Treat items such as carrots, low-sugar fruits such as strawberries or raspberries, or timothy-based treats with no added sugar can be used as a source of reward or environmental enrichment (e.g., suspending them from the cage roof to act as edible toys). Food treats can be used to modify behavior, deliver medications, provide food variety, and monitor appetite.

Water

Fresh, clean water should be available at all times—a 10% loss of body water is fatal. Normal consumption ranges widely from 0.25 to 0.57 L per day, and a good recommendation is ≈120 mL per kg body weight.[12,34] Intake is influenced by temperature and diet; water-rich foods such as vegetables reduce water intake. Potable water can be offered in a bowl or bottle; there is debate about which is preferable. Rabbits drink more from a bowl, and this promotes urinary calcium excretion. A ceramic crock is easier to clean and disinfect and less likely to tip. A bottle is less likely contaminated with spilled food or feces, and it may reduce the risk for moist dermatitis on the dewlap in intact females. Bottles and automatic watering systems must be checked at least daily for air bubbles that block the water flow.

SUMMARY OF DIETARY RECOMMENDATIONS

As obligate hindgut fermenters, rabbits require a specialized diet to remain healthy and reduce their risk for gastrointestinal, dental, urinary, metabolic, and behavioral disorders. The dietary needs of nonbreeding, adult pet rabbits differ from those in production. Unlimited access to fresh hay helps keep the dentition in proper occlusion and satisfies the need for frequent foraging. Grass hays are preferred over leguminous hays, but any hay is better than none. Feed a high-quality pellet in restricted quantities that are proportionate to the rabbit's age, size, and activity level. A good starting daily intake is ½ cup per 2.3 kg (5 pounds) body weight, adjusted for the pellet's energy density. Preferred pellets for adult pet rabbits should be timothy based or a timothy blend and contain ≥14% protein, 0.5% to 1% calcium, and 20% to 29% fiber. Offer a selection of fresh vegetables to provide diet variety in a low-energy form; a suggested intake is 2 cups per 2.3 kg (5 pounds) body weight and displaces a pellet meal. Pellet-free diets, although popular, should be avoided because a hay- and vegetable-only diet cannot meet all nutrient requirements, even with normal cecotrophy. Rabbits should not consume highly digestible, energy-dense foods (dried and fresh beans and peas, grains, nuts, whole corn) because these cause dysbiosis or cecal blockage. Mixed rations or muesli-style pellets may promote selective eating and result in unbalanced diets. Rabbits should have unlimited access to fresh water. Introduce dietary changes gradually so that cecal microbiota can adapt. Concentrate pellets and leguminous hays (e.g., alfalfa) are a useful way to meet the added nutritional demands of lactation, pregnancy, growth, and recovery from illness.

Overfeeding of energy-dense pellets and treats and the lack of unlimited hay is the most common mistake owners make in their pet rabbit's diet. It is therefore not surprising that inappropriate diet is foundational in the development of gastrointestinal and dental diseases in domestic rabbits. Regardless of the presenting problem, dietary advice should be given to any owner of a rabbit with a history suggestive of poor nutrition.

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Gastrointestinal Diseases of Rabbits

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GASTROINTESTINAL MOTILITY DISORDERS

Gastrointestinal Stasis Syndrome

Gastrointestinal (GI) stasis is the common term used to describe a syndrome of reduced or absent GI motility and its consequences in rabbits. It is by far one of the most common disorders seen in pet rabbits. Very often, it is caused by an inappropriate diet. However, stress is a common initiator of decreased GI motility, so any illness, painful condition, or stressful event can trigger an episode. Rabbits with GI stasis will eventually stop eating, and a lack of food in the intestinal tract will exacerbate GI stasis. Left untreated, GI stasis can rapidly become life-threatening.

The Role of Fiber

To understand the pathogenesis of GI diseases of the rabbit, the normal anatomic and physiologic aspects of rabbit digestion must be appreciated. Details of this are discussed in Chapter 13. In rabbits, the main driving force for normal intestinal motility is the presence of large quantities of indigestible fiber. Lack of this fiber, caused by either dietary inadequacies or conditions that cause anorexia, is a major cause of GI stasis.[18] Fiber stimulates cecocolic motility, either by a distention effect of the bulk or directly. Diets high in fiber promote the production of specific volatile fatty acids in the cecum that promote peristalsis.[18] Inadequate ingestion of coarse fiber will inhibit normal GI peristalsis. Rabbits ingest hair routinely in the process of grooming.

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However, they cannot vomit to eliminate accumulated hair. If GI motility is normal, ingested hair moves along with food out of the stomach at regular intervals and is ultimately expelled in the feces. If GI motility is impaired, hair and ingesta accumulate in the stomach. Fluid is absorbed from the stomach, further compacting the contents. Compacted ingesta causes discomfort, contributing further to anorexia and exacerbating GI hypomotility. A vicious cycle can result, until large amounts of hair and compacted ingesta accumulate in the stomach. This accumulation is erroneously referred to as a "hairball," "wool block," or "trichobezoar." These terms imply, incorrectly, that the hair accumulation is the cause of disease rather than simply being the consequence or a symptom of impaired intestinal motility.

The Effect of Diet and Cecocolic Motility

Cecal bacteria are vital to health. The cecum acts as a fermentation chamber and contains a complex milieu of microorganisms, including anaerobic organisms, such as *Bacteroides* species, large anaerobic metachromatic staining bacteria, and many as-yet unidentified species of bacteria.[14,23,40] Other bacteria normally present are gram-negative oval and fusiform rods, as well as yeast and several nonpathogenic species of protozoa and amoebas.[40] This combined microflora is responsible for processing fiber entering the cecum into digestible nutrients, which are then reingested as cecotrophs.

An inappropriate diet or GI stasis can disrupt the balance of this complex cecal microflora and the environment in which it grows. Diets low in fiber cause cecocolic hypomotility, prolonging the retention of digesta in the cecum and ultimately producing changes in cecal microflora. Populations of potentially pathogenic bacteria, primarily *Clostridium* and coliform species such as *Escherichia coli,* are normally present in small numbers in the cecum.[14,23] Slowing of cecocolic motility leads to the production of abnormal cecal fermentation products and alterations in the cecal pH. Even mild alterations in cecal pH cause an increase in these pathogens as the populations of normal organisms decrease. Overgrowth of these pathogens can cause a range of pathologic changes, from intestinal gas distention to death from enterotoxemia. Gas and toxin formation cause pain and stress, further decreasing appetite, and a cycle of pain, inappetence, and hypomotility ensues. Without intervention, all motility can be lost, leading to end-stage ileus. Other effects of fiber consumption are indirect. High-fiber diets have a low level of available carbohydrates and thus decrease the risk of enterotoxemia caused by carbohydrate overload of the hindgut. Carbohydrates provide an environment in which pathogens such as *E. coli* and *Clostridium* species proliferate. Glucose, a by-product of carbohydrate digestion, is necessary to produce iota toxin by *Clostridium* species. Thus diarrhea and enterotoxemia in pet rabbits are often caused by this disruption in microflora, commonly referred to as *dysbiosis*.

History and Clinical Signs

During physical examination, obtain a complete dietary history, including the type and amount of commercial pellets, hay, leafy greens, and treats. Rabbits with a regular diet consisting primarily of pellets without adequate fresh hay supplementation are at increased risk for development of GI stasis. The risk is even higher in rabbits fed rations consisting of a mix of dried fruits, vegetables, seeds, nuts, grains, and pellets. Acute episodes of GI stasis and dysbiosis are common in rabbits after ingesting a large volume of high-carbohydrate, high-fat treats. Rabbits at low risk are those fed diets of unlimited, good-quality, high-fiber grass or timothy hay, a moderate amount of fresh leafy greens, minimal pellets, and no or only occasional treats.

Stress alone, including stress caused by pain or concurrent disease, can cause GI stasis. Question the owner about recent potentially stressful events such as changes in housing, introduction of new rabbits or other pets, recent illness, trauma, or surgery, or any underlying disease processes. Common underlying disorders that may cause anorexia are dental disease, chronic upper respiratory tract disease, neurologic disorders, lower urinary tract disease, and renal or hepatic disorders. Many rabbits with stasis will have a history of little or no routine exercise.

In rabbits with GI stasis, the most common presenting complaint is a gradual decrease in appetite over 2 to 7 days and subsequent decrease in fecal production. Left untreated, rabbits will eventually stop eating entirely. Water consumption also is often decreased. Feces become scant, dark, dry, and small, eventually ceasing altogether. Owners may report a corresponding decrease in activity, due to abdominal pain. Rabbits in pain are reluctant to move, appear less social, may grind their teeth, may dig or scratch, and sit in a hunched position.

Physical Examination Findings

Rabbits with stasis generally appear alert and quiet, exhibiting little or no sign of lethargy. In suspect cases, palpate the abdomen with careful attention to the stomach contents, intestines, and cecum. The size and consistency of the stomach are key in differentiating GI stasis from obstructive disorders. With GI stasis, stomach size may vary with the duration of disease, but it always contains ingesta, as opposed to fluid and gas seen in rabbits with obstructive disorders. In GI stasis, fluid is pulled from the stomach, eventually leading to stomach contents that feel firm, doughy, and remain pitted on compression. Occasionally, stomach contents are very dehydrated and solid. No fluid and little or no gas is palpable in the stomach, whereas the intestines and cecum frequently contain variable amounts of gas. Little or no feces are palpable in the colon. Auscultate the abdomen, listening for borborygmus, because the character and frequency of gut sounds also will distinguish GI stasis from obstructive disorders. Rabbits with intestinal hypomotility have decreased or absent gut sounds. The remainder of the physical examination is usually unremarkable except for those findings related to any underlying disorder.

Diagnostic Testing

Other than evidence of dehydration, results of the complete blood count and biochemical profile will not change because of GI stasis. Radiographs are very helpful in the diagnosis and essential to differentiate GI stasis from obstructive disorders. Radiographic changes vary with the severity of illness, but in

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all cases, the stomach will contain ingesta. Presence of an ingesta-filled stomach in a rabbit that has been inappetent for several days is suggestive. As fluid is pulled from the stomach, ingesta will become compact and dense and may be surrounded by a small halo of gas (Fig. 14.1A–B). This appearance contrasts sharply with the dilated, fluid-filled stomach observed radiographically in rabbits with obstructive disorders (Fig. 14.2A–B). Moderate to severe gas distention of the cecum and scant fecal pellets are commonly seen.

Treatment

The key principles in the treatment of GI stasis are to rehydrate the patient and stomach contents, alleviate pain, provide nutrition, and treat any underlying disorders. Fluid therapy is essential to recovery. Administer fluids via either the intravenous or subcutaneous route, depending on the severity of dehydration. If stasis is mild or treated early, many rabbits respond well to oral and subcutaneous fluid administration and are less stressed when treated on an outpatient basis. If anorectic for more than

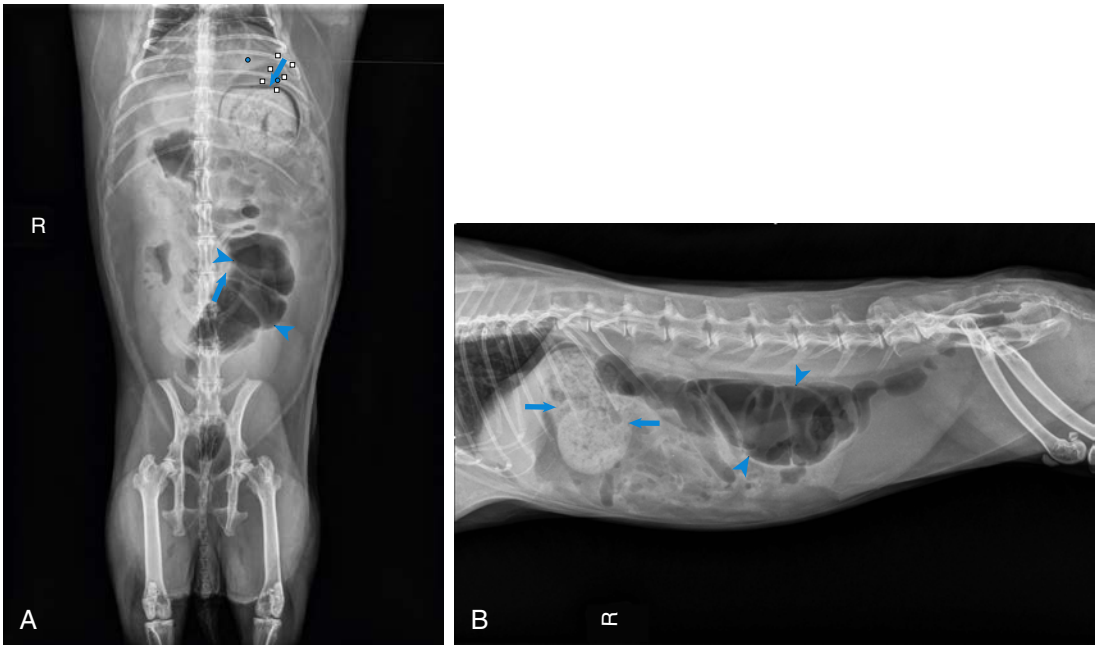


Fig. 14.1 Survey lateral (A) and ventrodorsal (B) radiographs of a rabbit with gastrointestinal stasis. Note the increased density of firm ingesta *(arrows)* and large amounts of gas within the in cecum *(arrowheads)*, characteristic of gastrointestinal stasis.

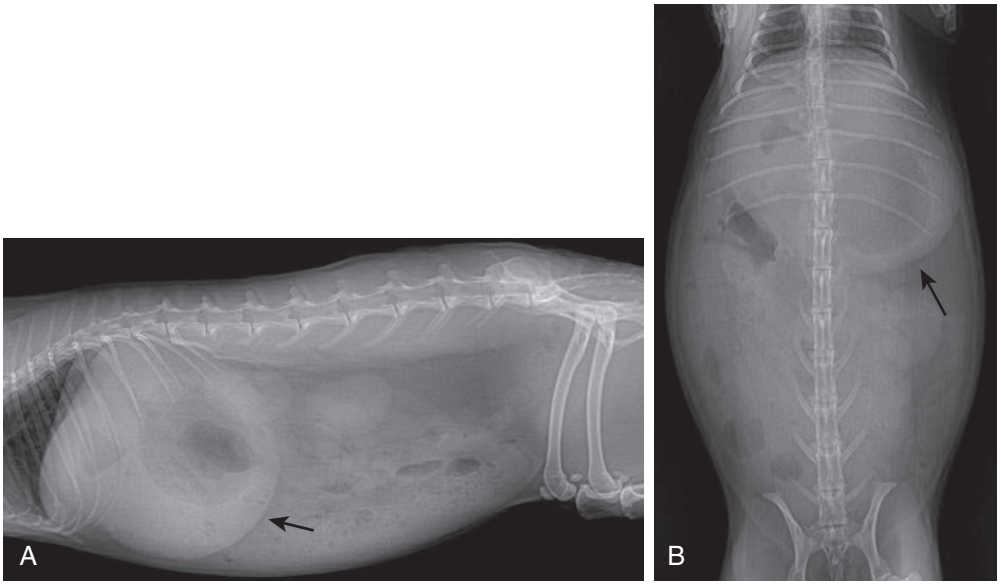


Fig. 14.2 Survey lateral (A) and ventrodorsal (B) radiographs of a rabbit with a proximal acute gastrointestinal obstruction. Note the severely distended, fluid-filled stomach with central gas cap ("fried-egg" appearance) and the lack of gas within the gastrointestinal tract distal to the stomach. This is consistent with an acute proximal small intestinal obstruction.

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1 to 2 days, rabbits are usually severely dehydrated and generally require hospitalization for intravenous fluid therapy. Rehydrate the stomach contents by assisted feeding with a syringe or by placing a nasogastric feeding tube (see Chapter 12) if the rabbit will not accept syringe feeding. Ensuring that the patient continues to eat during and after treatment is important. Continued anorexia will exacerbate GI hypomotility and cause further derangement of the gastrointestinal microflora. The act of eating itself stimulates gut motility. Maintaining caloric needs will prevent secondary hepatic lipidosis, which progresses quickly in anorectic rabbits. Several commercial nutritional products for rabbits are available for this purpose, and most rabbits will readily accept them when offered by syringe. Base the volume and consistency of the feeding formula on your palpation of the stomach and radiographic findings. For example, if the stomach is small with radiographically dense ingesta, feed a diluted formula. If the stomach is very full or even dilated with ingesta, withhold assist feeding until the stomach contents begin to move out of the stomach. Do not feed pineapple, pineapple juice, or papaya, because these are ineffective and can be detrimental (see below). Offer rabbits free-choice water in a bowl, fresh hay, and a variety of greens to provide every opportunity to self-feed. Ingestion of fibrous food is critical to reestablish GI motility.

Rabbits with GI stasis have moderate to severe gut pain, especially if the intestines are distended with gas. Most will not begin to eat until this pain is alleviated. If the rabbit appears painful (reluctant to move, hunched posture), administer an opioid such as buprenorphine (0.03–0.05 mg/kg subcutaneously [SC] or intravenously [IV] every 6–12 hours) or a nonsteroidal antiinflammatory drug (NSAID) such as meloxicam (0.5–1.0 mg/kg SC every 24 hours) or carprofen (1.0–2.2 mg/kg by mouth [PO] every 12 hours). Less painful rabbits may respond well to NSAIDs alone, but a combination of opioids and NSAIDS can be used in very painful rabbits. Before administering NSAIDs, be certain that the rabbit is fully hydrated and that no underlying renal disorders are present. Initially, always use a parenteral route for medications, because intestinal absorption is limited with ileus. A recent study compared the effects of IV buprenorphine and IV lidocaine continuous rate infusion (CRI) on gastrointestinal motility and evidence of pain in New Zealand white rabbits after ovariohysterectomy.[59a] Rabbits that received a lidocaine CRI (2 mg/kg loading dose, then 100 µg/kg/min CRI for 2 days) had higher gastrointestinal motility, food intake, fecal output, and normal behaviors and lower blood glucose levels than rabbits treated with buprenorphine (0.06 mg/kg IV q8h for 2 days). Therefore, a CRI of lidocaine may be useful in treating or preventing pain and associated stasis in rabbits.

Intestinal prokinetic agents are usually beneficial. Metoclopramide (0.2–1.0 mg/kg PO, SC, or Intravenously (IV) every 8–12 hours) should initially be administered parenterally. If IV fluid therapy is being administered, metoclopramide also can be administered as a constant rate infusion (2 mg/kg per day). Ranitidine (2–5 mg/kg PO, SC, or IV every 12–24 hours) has intestinal prokinetic effects in addition to protecting against gastric ulceration. If GI motility is sufficient to allow oral administration of medications, administer cisapride (0.5 mg/kg PO every 8 hours, available through compounding pharmacies). Antibiotics are only indicated if evidence of severe dysbiosis is present. Encourage movement to stimulate gut motility further by making the rabbit hop around on the floor one to two times daily.

Continue treatment for 3 to 5 days. Most rabbits will begin to eat and pass stool within 24 to 48 hours of treatment. Feces passed initially may be abnormal in shape, size, and consistency and may contain mucus or hair. If a rabbit is not responding to treatment, reevaluate the animal to identify underlying disorders contributing to anorexia.

Other remedies such as lubricants (e.g., petroleum laxatives), protein-digesting enzymes (e.g., pineapple for bromelain and papain), and simethicone have no beneficial effect because they do nothing to return function to the intestinal tract. Many rabbit associations and websites promote the use of simethicone, and it appears to have no ill effects. Caution owners against the use of protein-digesting enzymes, because these can be irritating to oral and potentially gastric mucosa. The risk of gastric ulceration is increased in anorectic rabbits, and use of these enzymes may exacerbate this.

Gastrointestinal Obstructive Disorders: Acute Gastrointestinal Obstruction and Moving Obstructions

Gastrointestinal obstructive disorders can be divided into two major categories: acute obstructions and moving obstructions. Acute GI obstruction (also referred to as GI dilation or "bloat") is an acute, life-threatening condition. The pathogenesis, history, and clinical findings differ considerably from those of GI stasis. Both acute and moving intestinal obstructions are usually caused by a compact mat or "felt" of hair, approximately 3 × 1 cm (size of an almond). Where these mats of hair are formed is not clear, but possibly they are compacted in the cecum, then ingested and swallowed whole with other cecal contents during normal cecotrophy.[31,32] Other foreign objects reported to acutely obstruct the intestinal tract include carpet or other cloth fibers, locust beans, and plastic.[31,32] Extraluminal compression of the intestinal tract by neoplasia, postsurgical adhesions, tapeworm cysts, abscesses, and hernias may also occur.[29,31,32,54]

The most common cause of death from an acute intestinal obstruction is hypovolemic shock, caused by a sudden loss of fluid into the lumen of the GI tract proximal to the obstruction. In studies of intestinal obstruction with rabbits used as models, ligating the intestinal tract results in rapid, active secretion of sodium, followed by water into the intestinal lumen proximal to the obstruction.[10,11,47,68] Within hours, as much as 200 to 250 mL of fluid accumulates first in the obstructed intestinal segments and then in the stomach.[10,11,47,68] Sodium and fluid secretion is most active in the first 25 to 30 cm of the duodenum, proximal to the entrance of the pancreatic duct.[10] Fluid resorption is impaired in obstructed segments, and this rapid loss of fluid leads to hypovolemic shock. Gas formation also contributes to GI tract distension proximal to the obstruction. Within 1 hour of ligation, gut pH and bacterial flora begin to shift. Eventually, bacterial flora completely reverses, with an overgrowth of Enterobacteriaceae and gas-forming clostridia, adding to gastrointestinal dilation.[9,14,68] Accumulated fluid in obstructed intestines and eventually stomach results in stretching of the intestines, compromise of venous outflow, and pressure necrosis

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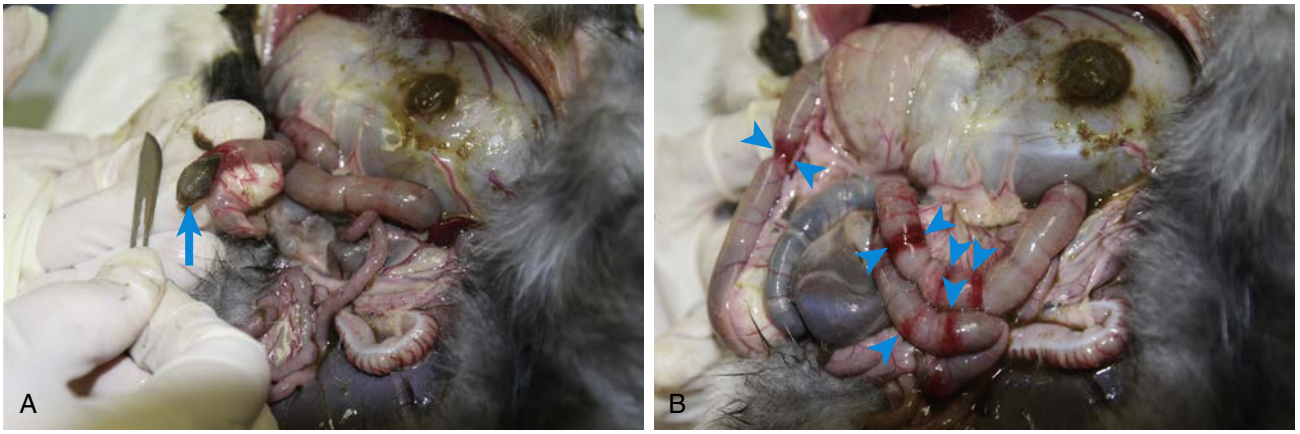


Fig. 14.3 Postmortem examination of a rabbit that died from gastric rupture due to an untreated, moving obstruction. (A) Note the typical appearance of acute gastrointestinal obstruction caused by a hair pellet *(arrow)*. (B) Note the hyperemic appearance of the intestinal serosa at multiple locations at which the hair pellet had previously lodged *(arrowheads)*.

of the affected segments.[47,68] In some cases, the stomach will acutely rupture. If the obstruction is not relieved, the affected intestinal loops will begin to necrose.[47,68] As this occurs, motility declines and secondary GI stasis develops.

The location of the obstruction determines the rapidity of the course of disease. The most common location is the proximal duodenum, approximately 2 to 5 cm from the pylorus where the lumen narrows. With a proximal obstruction, shock begins within hours and, if untreated, death occurs within 6 to 8 hours. If the obstruction is more distal, in the jejunum or ileocecocolonic junction, obstructed loops become progressively fluid or gas filled over a longer time. Experimental ligation in rabbits at the level of the jejunum results in death in 12 to 24 hours and at the ileum within an average of 21 hours.[11]

In contrast to GI stasis, the intestinal tract proximal to the obstruction becomes hypermotile. Studies of electrical activity in obstructed horses and rabbits demonstrate intense, irregular activity proximal to the obstruction.[11,17,35] This intestinal hyperactivity will often be successful in moving the obstruction distally. These "moving obstructions" are common (Fig 14.3A–B). The obstruction may pass with appropriate treatment, and small mats of hair may pass without treatment. Clinical signs of moving obstructions often resemble those of GI stasis.

History and Physical Examination Findings

A sudden onset of anorexia and depression is the hallmark feature of GI obstructive disorders. Some rabbits with proximal obstructions are found acutely moribund or dead with no premonitory signs. Affected rabbits suddenly refuse all food and abruptly stop producing feces. This contrasts with a gradual decline in appetite and production of small, dry fecal pellets with GI stasis. With moving obstructions, gut sounds may be audible from a distance, and the rabbit may stretch out and change positions frequently to get comfortable. With complete obstruction, they demonstrate signs of severe pain, such as reluctance to move and a hunched posture. As shock develops, affected rabbits become severely depressed, listless, laterally recumbent, and minimally responsive to external stimuli. With stomach rupture, they may suddenly cry out and die. On physical examination, the stomach will palpate as large, fluid-filled, or tympanic, in contrast to the firm, ingesta-filled stomach found with GI stasis. Rabbits may appear painful on palpation. Early on, before the affected segments become necrotic, gut sounds are increased, and sometimes gut motility is visible through the abdominal wall. Initially, affected animals are alert but quiet, tachypneic, and tachycardic. With the onset of shock, they become hypothermic, bradycardic, and hypotensive.

Always obtain body temperature in suspect cases. With the onset of shock, body temperature will decline. Rabbits with a body temperature of 98°–99°F (36.7°–37.2°C) are in early stages of shock. Temperatures below 98°F (36.7°C) indicate severe, life-threatening shock.[19]

Diagnostic Testing

Obtain radiographs to confirm the diagnosis. The radiographic appearance of a rabbit with acute GI obstruction differs sharply from that of a rabbit with GI stasis or a normal rabbit. The most prominent feature is that the stomach is distended with fluid as opposed to ingesta seen in rabbits with GI stasis. The degree of distension depends on the location of the obstruction and the time interval between presentation and the onset of obstruction. With proximal (duodenal) or late-stage distal obstructions, the stomach will appear severely distended with fluid and may have a gas cap, giving it a characteristic "fried-egg" appearance (Fig. 14.2A–B). If the obstruction is proximal, only the stomach is distended, and no organized gas is seen in intestinal loops. With distal obstructions, gas distention of intestinal loops from the point of obstruction proximal to the stomach are usually are noted (Fig 14.4).

Obtain a blood sample for a complete blood count and biochemical profile. Blood glucose concentration can be helpful in differentiating obstructive disorders from GI stasis.[30] Obstructed rabbits, especially at the onset of shock, often have blood glucose concentrations >300 mg/dL (15 mmol/L). This is in part due to stress, but glucose concentrations also will increase to maintain serum osmolality in the face of sodium loss into the GI tract.[8] Most rabbits with acute obstruction will have increased renal values, and some develop acute renal failure. If renal values are increased,

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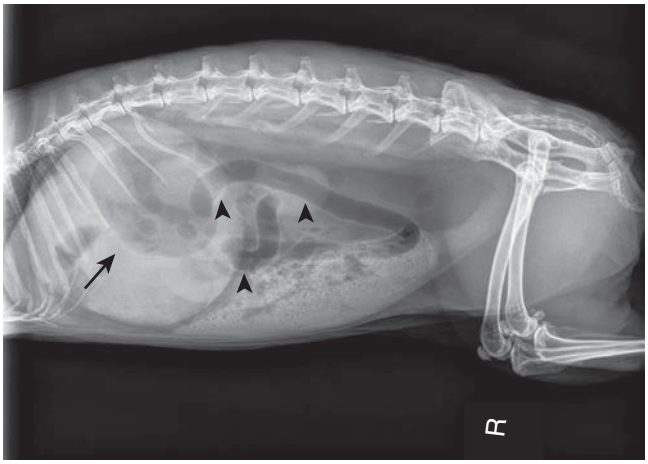


Fig. 14.4 Survey lateral radiograph of a rabbit with a distal intestinal obstruction. Note the severely distended, fluid-filled stomach (*arrow*) with central gas cap and gas distention of intestinal loops (*arrowheads*) leading to the point of obstruction.

monitor values after treatment. The biochemical profile will also help to rule out liver torsion, which may have a similar presentation.

Initial Medical Treatment

Begin treatment immediately, because this is a life-threatening disorder. Initial treatment goals are to warm the patient (if hypothermic), treat shock, decompress the stomach, correct any fluid and electrolyte imbalances, and control pain. If hypothermic, immediately begin external heat support. Place an intravenous catheter and begin treatment with a shock dose (60–90 mL/kg per hour for the first hour) of warmed, isotonic crystalloid fluids. When shock is controlled, reduce administration to a maintenance rate. If shock is severe and a response to crystalloid fluid therapy is not seen, administration of 7.5% NaCl or hetastarch (3 mL/kg over 5 minutes) may be effective (see Chapter 41). (Hetastarch is not available in the UK or Europe. In 2018, the European drug regulators announced the suspension of marketing authorizations for all hydroxyethyl starch [HES] plasma volume replacement solutions across the European Union and the UK.) Correct any electrolyte imbalances. To control pain, administer buprenorphine (0.02–0.05 mg/kg SC or IV every 6–12 hours), butorphanol (0.2–0.4 mg/kg SC or IV), or hydromorphone (0.1 mg/kg IV). Avoid NSAIDs until renal status is known.

Sedation is necessary to decompress the stomach in most cases. Sedation with midazolam (0.5–1.0 mg/kg IM, IV) or dexmedetomidine (0.03–0.05 mg/kg IM) or both, in addition to pain medications, may be sufficient if the patient is depressed, although the addition of gas anesthesia is often needed. A well-lubricated 18-Fr red-rubber catheter works well as an orogastric tube in most medium-sized rabbits; a smaller size may be needed in small breeds. Cut additional holes in the end of the tube to allow larger volumes of gas and fluid to pass. Measure the distance from the nose to the last rib (the distance to the stomach), and mark the tube. With the head held in ventroflexion, pass the well-lubricated tube gently by mouth into the stomach. If the tube becomes clogged, remove the tube and flush, then repass the tube to remove as much fluid and air as possible from the stomach. Percutaneous trocharization of the stomach is contraindicated as a method of decompression, because this will likely cause rupture of the stomach. The color and odor of the fluid are a prognostic indicator. The fluid should be brown to green and smell of food. If the fluid is odiferous and dark brown to red or black, the stomach is likely necrotic, and the prognosis is grave.

In many cases, the obstruction will pass after medical treatment and decompression. Palpate the abdomen frequently, monitor for signs of pain, and repeat radiographs to determine whether the obstruction is passing. The gas pattern will change, and gas will be visible in the distal intestines if the rabbit is passing the obstruction. These rabbits will appear comfortable and begin eating, drinking, and defecating, usually within 24 hours. If the patient does not improve, and the stomach begins to fill with fluid, decompression should be repeated. If no improvement is seen after a second orogastric decompression, the obstruction is either not moving or is caused by extraluminal intestinal compression. Surgical treatment is indicated, because the intestines will begin to necrose if the obstruction is not relieved.

Surgical Treatment

Exploratory laparotomy allows for diagnosis and possible treatment of intestinal obstructions caused by extraluminal compression (e.g., tumor, adhesions, hernia) and removal of complete, immobile intraluminal obstructions. Indications for surgery are a lack of response to medical treatment, an inability to decompress the stomach, or declining GI tract motility. These indicate that the obstruction is either extraluminal or is not moving. Surgery may also be indicated to quickly remove the obstruction if close monitoring of the patient is not possible after initial medical treatment. When possible, decompress the stomach and stabilize the patient for shock before attempting surgery. Because intraoperative gastric reflux may occur, always place an endotracheal tube for anesthesia. Provide IV fluids and heat support during surgery. A lidocaine CRI (loading dose 2 to 3 mg/kg, then 33–100 ug/kg/min) provides additional pain control, is antiinflammatory, and may help to prevent postoperative ileus.[59a,62]

Most acute intraluminal obstructions are in the proximal duodenum, 3 to 5 cm from the pylorus. When possible, avoid enterotomy by manipulating the foreign body into the cecum. If this is not possible, move it into the stomach and perform a gastrotomy rather than an enterotomy. Gastrotomies are generally better tolerated, with a lower probability of postoperative complications such as stricture, leakage, or GI stasis. Assess the viability of the obstructed portion of the intestine. If the portion of intestine surrounding the foreign body appears necrotic, an intestinal resection and anastomosis may be indicated. If large sections of obstructed intestinal loops have become ischemic, the prognosis is grave, and euthanasia may be warranted. If no intestinal foreign body is found, explore the abdomen for evidence of neoplasia, abscesses, or adhesions as the cause of obstruction. Provide postoperative supportive care, including fluid therapy and pain management. If GI motility has declined, provide promotility agents and assist feeding. With prompt removal of the foreign body, the prognosis is good. If intestinal viability is compromised, the prognosis is guarded to poor.

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Cecotrophy and Intermittent Diarrhea

Cecotrophs are nutrient-rich pellets resembling feces that contain the products of cecal fermentation. They are produced several times a day, usually in the morning and evening, and consumed reflexively directly from the rectum, a behavior termed *cecotrophy* (see Chapter 13). Because they are swallowed whole directly from the anus, most owners rarely see normal cecotrophs. If intact, cecotrophs appear as multiple, soft fecal pellets stuck together, resembling a blackberry, and have a strong odor. If cecotrophs are not eaten, they often stick to the fur around the perineum or are found smeared on the fur and flooring. This is often confused with diarrhea and is a common presenting complaint. Rabbits that do not consume their cecotrophs are either physically unable to do so or do not eat them because cecotrophs are abnormally formed. Obesity is a common cause of inability to consume cecotrophs because the rabbit cannot reach the anal region. Other causes are musculoskeletal disorders, vestibular disease, dental disease, pain, and physical barriers such as Elizabethan collars. Changes in normal cecal motility, pH, or flora result in the production of abnormal cecotrophs. These may be soft, malformed, pasty, or odiferous and are not eaten. Dietary deficiencies, as discussed above, are a common cause; however, other factors such as stress, concurrent disease, or antibiotic usage may also contribute.

Diagnosis is based primarily on history. Affected rabbits produce normal fecal pellets throughout most of the day. Soft feces are found on the fur or smeared on flooring. If the rabbit cannot reach the anus, the feces are pasted to the perineum, and secondary dermatitis often results. Obesity or signs of neuromuscular, dental, or other painful disorders are present on physical examination. Correcting the underlying disorder will allow a return to normal cecotrophy.

If the rabbit can reach the perineum and the cecotrophs are soft, fluid, or malformed, question the owner about the diet. Insufficient fiber (hay) or excessive carbohydrate intake is a common cause. In this case, correcting the diet will usually correct the problem. Feed only hay (preferably first-cut, high fiber) until uneaten cecotrophs are no longer seen. This can take days to weeks depending on the severity of cecal dysbiosis. Once no uneaten cecotrophs are seen for several days, gradually add back pellets, then greens to the diet. For some rabbits, the addition of greens will consistently cause abnormal cecotrophs and will need to be withheld permanently.

Cecoliths

Altered motility of the cecum, rate of transit in the colon, or abnormal diet (e.g., very short fiber length or feeding indigestible fiber, such as psyllium) can result in compaction and dehydration of cecal or colonic material and subsequent formation of "cecoliths," or abnormally hard lumps of cecal contents. Rabbits that form cecoliths often have a chronic history of large, malformed feces, recurrent cecal impaction, abdominal pain, and anorexia. Because these rabbits are unable to form normal cecotrophs, they are often underweight and lack normal muscle mass. A congenital progressive and eventually fatal disorder of sodium transport into the cecum is found in homozygous spotted (English Spot) and Checkered Giant breeds.[6] This is commonly referred to as "megacolon-syndrome" but involves primarily the cecum, not the colon. A presumptive diagnosis of cecolith formation can be made by palpation of doughy to very firm material in the cecum. Radiographs or ultrasound examination can confirm the presence of cecoliths. If the intestine is completely obstructed, gas will accumulate in the sacculated large intestine. Rabbits with cecal obstipation are in severe pain and may present moribund.

Treatment of cecoliths requires rehydration of inspissated cecal and colonic contents. Administer fluid therapy by the intravenous or subcutaneous route, depending on the degree of dehydration. Long-term administration of SC fluids may be helpful. Feed foods with a high water content (assist feeding slurries, wetted leafy vegetables) along with an appropriate fiber source, such as grass hay, to stimulate normal cecal motility and function. Intestinal promotility agents may also be of benefit. Provide analgesia, because these patients are often painful. The long-term prognosis is generally guarded to poor.

Rabbits with complete cecal obstipation are critically ill and in pain and require immediate treatment. Begin intravenous fluid therapy and pain medications. Occasionally, the obstructing cecolith can be softened and moved with a gentle enema. Take great care in administering enemas, because the colon may be necrotic at the point of obstruction. If the obstruction does not resolve with medical therapy, surgical removal will be required once the patient is stable.

DYSBIOSIS, ENTERITIS COMPLEX, AND ENTEROTOXEMIA

In clinical practice, the enteritis complex—with signs ranging from soft stool and diarrhea to enterotoxemia, sepsis, and death—is common in rabbits. Factors that allow pathogenic bacteria to proliferate are the usual causes. These factors involve stress, diet, antibiotics, and genetic predisposition to gut dysfunction. Epinephrine-mediated inhibition of gut motility is believed to cause stress-induced enteritis. Simple enteritis, resulting in a soft or pasty stool as the only clinical sign, may be caused by a minor disruption of cecal flora, pH, or motility. Correcting the diet, adding fiber in the form of hay, and decreasing stress will often correct the problem.

Enterotoxemia

Enterotoxemia in rabbits, which is characterized by more significant dysbiosis than with enteritis, is caused by the iota-like toxin from *Clostridium spiroforme*.[51] Newly weaned animals (3–6 weeks of age) are most often affected, and they have the highest mortality rate. These rabbits may develop enterotoxemia from simple exposure to *C. spiroforme*, likely because young rabbits have an undeveloped population of normal GI flora and a high gastric pH, which allows *C. spiroforme* to proliferate. Adult rabbits are more resistant and generally require some dietary, environmental, or other stress for dysbiosis to be induced and growth of the bacteria to occur. Rapidly multiplying *C. spiroforme* significantly alters the rabbit's normal cecal flora. Nursing does can develop "milk enterotoxemia" that is believed to be caused by *Clostridium* endotoxin produced in the does' cecum and passed to the bunnies in the milk.

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In acute disease, rabbits stop eating and become markedly depressed. Brown, watery diarrhea soils the perineum and rear legs, and it may contain blood or mucus. As the disease progresses, rabbits become hypothermic and moribund and die after 24 to 48 hours. Postmortem findings include petechial and ecchymotic hemorrhages on the serosal surface of the cecum; lesions can also involve the appendix and proximal colon. Various amounts of gas throughout the intestinal tract, cecum, and colon result from ileus. Hemorrhage, pseudomembranes, or mucus may be present in the mucosa of the cecum and proximal colon.

Mucoid Enteritis

Mucoid enteritis is a major cause of morbidity and death in young rabbits 7 to 14 weeks of age. It is characterized by anorexia, lethargy, weight loss, diarrhea, cecal impaction, and excessive production of mucus by the cecum. Its cause is unknown; however, studies have convincingly established the relation between bacterial dysbiosis and hyperacidity of the cecum and the symptoms of mucoid enteritis.[40] Alterations in cecal pH resulting from changes in the production or absorption of volatile fatty acids or from vigorous fermentation of carbohydrates can destabilize the cecal microbial population and stimulate mucus production within the cecum and colon. Feeding a diet high in fiber and low in simple carbohydrates is preventative.

Antibiotic-Induced Dysbiosis

Antibiotic administration can cause enteritis. Certain antibiotics suppress normal flora, allowing pathogens to proliferate. Clindamycin, lincomycin, ampicillin, amoxicillin, amoxicillin-clavulanic acid, cephalosporins, many penicillins, and erythromycin can induce enteritis in rabbits.

Treatment and Prevention of Dysbiosis and Enterotoxemia

Treatment of rabbits with severe enteritis, enterotoxemia, and mucoid enteritis consists of aggressive supportive care and efforts aimed at increasing cecal and colonic motility, discouraging the growth of pathogenic bacteria and the production of toxins, and supporting the growth of normal flora. Antimicrobial drugs have limited value in the treatment of the disease and are used primarily as supportive therapy. *Clostridium spiroforme* has been shown to be sensitive to metronidazole and penicillin G.[13] The use of metronidazole (20 mg/kg PO or IV every 12 hours) has been reported to reduce the number of deaths from enterotoxemia. Administration of cholestyramine (2 g in 20 mL water every 24 hours by gavage), an ion-exchange resin capable of binding bacterial toxins, has been reported to prevent death in rabbits with clindamycin-induced enterotoxemia.[41] Correcting dehydration and maintaining normal hydration are of paramount importance, and administration of intravenous or intraosseous fluids is indicated. If the rabbit is anorectic, assist feed and provide supportive care as described for treatment of GI stasis, above. Cecal transfaunation by means of retention enema with cecotrophs or feces from a healthy rabbit has been anecdotally reported and may be helpful.

To prevent enterotoxemia, maintain optimal husbandry and minimize stress. Feed a good-quality grass hay and limit or remove pellets from the diet. If a pelleted diet is fed, it should contain no less than 18% to 20% fiber and should be limited to less than ⅓ cup per 5 lb (2.3 kg) of body weight. Avoid sudden changes in the diet. Make hay available to weanling rabbits from 3 weeks of age; avoid early or forced weaning.

Primary Bacterial Enteritis

Bacterial enteritis may be seen occasionally in the adult pet rabbit. It is a common cause of mortality in commercial rabbit industry, where mortality rates ranging between 50% to 100% have occurred. Typically, however, enteritis is seen in neonates or rabbits under 16 weeks of age that are stressed by weaning, transport, or overcrowding.

Escherichia coli

Enterohemorrhagic *Escherichia coli*, a potential zoonotic pathogen, produces shiga toxins that cause hemorrhagic colitis with hemorrhagic diarrhea. Rabbits are susceptible to this common water- and food-borne pathogen by oral ingestion. Naturally infected rabbits develop thrombotic microangiopathy, the hallmark of shiga toxin, and this is believed to be the cause of the less frequently seen acute renal failure.[50] From the seven groups of pathogenic *E.coli,* enteropathogenic *E. coli* is a major cause of economic loss in the commercial rabbit industry. Rabbit enteropathogenic *E. coli* is an attaching and effacing *E.coli* strain, where bacterial adherence, via a fimbrial adhesin, results in destruction of the brush border and rearrangement of the enterocyte structure. Diarrhea, caused by the resultant villus atrophy and malabsorption, varies in severity depending on the age of rabbit and specific serogroup involved.

In infected does, subsequent litters may have passive immunity. The disease process is limited to the cecum and colon. The cecal wall may be inflamed with longitudinal "paintbrush" hemorrhages. In severe cases, intussusception and rectal prolapse may be present. Presumptive diagnosis may be based on isolation of *E. coli* from stool or tissue samples from affected animals; however, nonpathogenic *E. coli* routinely proliferates in any rabbit with dysbiosis. Confirmation of the diagnosis requires histologic examination of tissues and observation of *E. coli* attachment to the intestinal cells. Serotyping of *E. coli* isolated from rabbits is not available to clinical veterinarians and remains a research tool only.

Treat individual rabbits with antibiotics, guided by the results of culture and sensitivity testing, and supportive care including fluid therapy, assist feeding, and maintaining normothermia. Use trimethoprim-sulfamethoxazole (30 mg/kg PO every 12 hours) or enrofloxacin (15–20 mg/kg PO every 12 hours) until culture and sensitivity test results are obtained. The role of probiotics in the prevention and treatment of these cases is still unproven.

Proliferative Enteritis, Proliferative Enteropathy, Proliferative Enterocolitis

The obligate intracellular bacterium *Lawsonia intracellularis* has been reported as a cause of enterocolitis in rabbits both as a single pathogen and in association with an enteropathogenic strain of *E. coli* distinct from the prototypical rabbit diarrhea *E. coli* strain.[34,59] This intracellular bacterium is gram-negative, curved

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to spiral shaped, and found free in the apical cytoplasm of intestinal epithelial cells. The disease is most often characterized as an acute diarrheal disease of rabbits 2 to 4 months of age (weanlings). Proliferative enteritis or enteropathy is most reported in in swine and hamsters but also occurs in many species.[59] Histologic findings often show proliferative ileitis, with or without proliferative colitis, characterized by epithelial hyperplasia and mucosal inflammation. Similar disease in pigs and ferrets is caused by a different bacterium, *Desulfovibrio desulfuricans*.[26,44] Treatment of *L. intracellularis* in rabbits is challenging. Antibiotics used to treat *L. intracellularis* in other species include those of the macrolide family (e.g., tylocin, erythromycin, and lincomycin) that are not recommended for use in rabbits. Chloramphenicol (30 to 50 mg/kg PO or SC every 12 hours for 7–14 days) is generally efficacious. Florfenicol (20–30 mg/kg PO, IM or IV) has shown good efficacy, although more-frequent doses may be required to maintain plasma antibiotic levels above the minimum inhibitory concentration for longer than 6 hours.[22]

Tyzzer's Disease

Tyzzer's disease is caused by *Clostridium piliforme* (formerly *Bacillus piliformis*), a motile gram-variable, spore-forming, obligate intracellular bacterium.[21] Stress (produced by overcrowding, unsanitary conditions, high temperatures, or breeding) is an important component of this disease. Clinical signs of Tyzzer's disease are watery diarrhea, depression, and death. Morbidity and mortality rates may be especially high in weanling rabbits, whereas older rabbits can develop a more chronic form of the disease that results in chronic weight loss. Necropsy of rabbits with Tyzzer's disease may show characteristic foci of necrosis in the liver and degenerative lesions of the myocardium. More often, the intestinal wall is edematous, with areas of necrosis in the mucosa of the proximal colon. Treatment is palliative once clinical signs have been observed. The intracellular location of the bacteria may contribute to the difficulty in treatment. If exposed animals are treated early with preventative measures (isolation, good hygiene, supportive care, and a high-fiber diet), they may not develop the disease. Prevention depends on good husbandry. Clostridial spores are killed with a 0.3% sodium hypochlorite (bleach) solution, some disinfectants, or with heating to 173°F (80°C) for 30 minutes.

Other Causes of Bacterial Enteritis

Campylobacter species (*C. cuniculorum, C. jejuni, C.coli*) have been found in healthy and diarrheic rabbits. Although a pathogenic role of *C. cuniculorum* is not known, it has shown antibiotic resistance to fluoroquinolones and macrolides but is sensitive to chloramphenicol.[53]

Other causes of bacterial enteritis are *Salmonella* species, *Klebsiella pneumoniae, Klebsiella oxytoca,* and *Pseudomonas aeruginosa*. Because these are water-borne pathogens, outbreaks of disease can be seen when the watering system becomes contaminated. Salmonellosis is not common but can cause disease with high rates of both morbidity and mortality. *Salmonella typhimurium* is most often associated with salmonellosis in rabbits; however, other species and serovars have been reported.[7] Disease transmission is most often associated with contaminated food or water. Affected rabbits usually develop sepsis, which quickly leads to death; however, diarrhea may occur as well. Postmortem findings are consistent with septicemia and include vascular congestion of organs and diffusely distributed petechial hemorrhages. Lymph nodes and gut-associated lymphoid tissue may be edematous and contain similar foci of necrosis.

Mycobacteriosis, including *Mycobacterium bovis* and *Mycobacterium avium* subspecies *paratuberculosis,* can cause diarrhea and emaciation in rabbits. *Mycobacterium bovis* is zoonotic, whereas *M. a. paratuberculosis* has zoonotic capacity. Natural infections of *M. a. paratuberculosis* have been reported in wild rabbits examined from farms with a high prevalence of ruminant paratuberculosis (Johne's disease) in Scotland.[4] Fecal cytology and tissue biopsy can be useful to confirm the presence of acid-fast bacteria in suspect cases. Mycobacterial culture or polymerase chain reaction analyses are required for a definitive diagnosis. Speciation of the mycobacteria involved requires molecular diagnostic methods. Treatment is challenging and can be controversial.

VIRAL DISEASES OF THE DIGESTIVE TRACT

Papillomatosis

Rabbit oral papillomatosis is a benign disease caused by a papillomavirus. The disease has been reported only in colonies of laboratory rabbits, especially New Zealand white rabbits.[45,60] Lesions consist of small white growths on the ventral surface of the tongue but only rarely occur elsewhere in the mouth. Early lesions are sessile, later becoming rugose or pedunculated and ultimately ulcerated. Papillomas can exceed 4 to 5 mm at their greatest dimension but are typically smaller (1–3 mm). Lesions may persist up to 145 days, but they usually disappear within weeks.

Rabbit Hemorrhagic Disease Virus

Viruses of the *Lagovirus* genus within the family Caliciviridae that affect rabbits include rabbit hemorrhagic disease virus (RHDV), European brown hare syndrome virus, and the nonpathogenic rabbit calicivirus.[28] Although European brown hare syndrome virus affects European hares of the *Lepus* genus, RHDV specifically afflicts domestic rabbits worldwide but does not cause disease in wild cottontail rabbits, jackrabbits, or hares. Although RHDV is endemic in Europe, Cuba, Australia, and New Zealand, limited outbreaks have occurred in the Middle East, South America, Mexico, and the United States. The virus has been eradicated from Mexico. Sporadic outbreaks have taken place in the United States, the last of which occurred in Indiana in 2005. In 2010, a new variant, hemorrhagic disease virus 2 (RHDV2), was identified in mainland Europe and has been reported in the United Kingdom and Australia since 2015.[2] This variant affects both domestic and wild rabbits, and disease has been seen in rabbits vaccinated against the classic RHDV strain.

Clinical disease occurs in rabbits older than 2 months of age; younger rabbits appear unaffected, although this is not absolute.[3,24,43,58] Virus is shed in urine, feces, and respiratory secretions. Transmission of RHDV is by direct contact, contact with carcasses or fur from affected rabbits, or contact with fomites such as water, feed, utensils, clothing, or cages. Flies and other insects may serve as vectors, and virus can be found in

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feces from predators that have eaten infected rabbits. The disease is highly infectious and has traditionally been associated with high rates of both morbidity (40%–100%) and mortality (approaching 100%). Higher rates of morbidity and mortality are seen in naive populations. The incubation period is 1 to 3 days. During outbreaks, the number of rabbits affected peaks in 2 to 3 days, and the disease course may last 7 to 13 days. The variant RHDV2 is less virulent, with lower observed mortality rates than RHDV, and clinical signs tend to be more chronic.

Virus replicates in the liver, resulting in severe hepatic necrosis and death from disseminated intravascular coagulation.[12,42,43] In peracute disease, rabbits die with no premonitory signs, or they become febrile and lethargic and die within 12 to 36 hours of infection. In acute disease, rabbits are febrile and exhibit depression, lethargy, anorexia, constipation, or diarrhea. Some may show neurologic signs such as ataxia, opisthotonos, excitement, or seizures. At end-stage disease, tachypnea, cyanosis, and a blood-tinged, foamy nasal discharge are often seen. In some rabbits, the disease course is slower, with animals exhibiting jaundice, depression, anorexia, and fever, eventually dying within 1 to 2 weeks. In the subacute form, milder signs are seen, and many of these rabbits live. Persistent or latent infections may occur in asymptomatic rabbits.[2,24]

Hematologic testing often shows a lymphopenia and a gradual thrombocytopenia. In moribund rabbits, prothrombin and thrombin times are prolonged, and fibrin degradation products can be detected.[55] The most consistent postmortem changes are hepatic necrosis, splenomegaly, and evidence of disseminated intravascular coagulation. Congestion and hemorrhage may be seen in most organs but are most pronounced in the lungs. The liver is pale, and periportal necrosis with a fine reticular pattern is observed; the spleen is dark and thickened, and catarrhal enteritis is often identified.[20,55] Presumptive diagnosis is based on history, clinical signs, and pathologic findings. Definitive diagnosis requires identifying the virus by a variety of diagnostic tests, such as electron microscopy, reverse transcription polymerase chain reaction, Western blot, and enzyme-linked immunosorbent assay. The variant RHDV2 has been deciphered based on the major capsid protein (VP60) sequence. [58] In North America, on suspicion of disease, immediately contact state or federal regulatory agencies to report this disease, and send diagnostic samples only to authorized laboratories under secure conditions.

Several vaccines are available, including heat-killed liver extracts, VP60 protein, and a recombinant myxoma-RHD live virus. These vaccines do not provide protection against RHDV2.[58] Specific vaccines for RHDV-2 or combined RHDV-1/RHDV-2 are commercially available in mainland Europe and the United Kingdom. The virus can be inactivated by 0.5% sodium hypochlorite or 1% formalin.

Rabbit Enteric Coronavirus

In 1980, a coronavirus was found as a cause of diarrhea in laboratory rabbits.[39] This virus affects rabbits 3 to 10 weeks of age, but it is also found in clinically normal adult rabbits. In naturally occurring outbreaks, clinical signs are lethargy, diarrhea, abdominal swelling, and death. Pleural effusion and cardiomyopathy in rabbits have also been associated with coronavirus-like particles.[48] Morbidity and mortality rates can be high; in one described outbreak, 40% to 60% of rabbits were affected, and almost 100% died within 24 hours of the onset of clinical signs.[20] At necropsy, cecal contents are fluid, and histopathologic examination shows atrophy of intestinal villi. Tentative diagnosis is based on history, clinical signs, necropsy findings, and results of histopathologic analysis. The virus agglutinates red blood cells; evidence of hemagglutination activity in the feces therefore supports a tentative diagnosis. The diagnosis is confirmed by demonstrating the virus in feces or cecal contents.

Rotavirus

Rotavirus infection causes diarrhea in rabbits. Serosurveys have revealed that it is endemic within domestic rabbits, as well in wild *Sylvilagus* and *Lepus* lagomorphs in Europe, Asia, and the United States. Infant rabbits are most susceptible, because the virus targets terminally differentiated enterocytes lining the tips of villi of the jejunum and ileum.[3] Transplacentally derived maternal antibodies are protective, and some protection continues past 45 days, when antibody levels decline, so less severe or subclinical infections may be seen in weaned rabbits. Morbidity and mortality rates vary with age, host immunity, and environmental stressors. Coinfection with other pathogens, such as *E. coli,* can have an additive effect and greatly increase morbidity and mortality rates.[3] Diarrhea, dehydration, and sudden death are the main clinical signs. Necropsy findings include mild to severe villus blunting, villus fusion, and submucosal edema of the small intestines, and fluid cecal contents. The lamina propria is usually infiltrated with lymphocytes and occasionally with neutrophils. Definitive diagnosis is based on results of histopathologic examination of the intestine. Isolation of the virus or demonstration of antibodies is suggestive. Clinical signs and gross pathologic findings alone are not diagnostic.[20] Human enzyme-linked immunosorbent assay test kits will detect rotavirus group A in rabbits.[3] Preventing and controlling rotavirus infection is complicated by its highly infectious nature. Reducing stress (reducing crowding, stopping breeding, removing socially dominant animals, and adding fiber to the diet) along with appropriate treatment of concurrent disease and improved hygiene should reduce mortality rates.

Other Viral Causes of Enteritis

Adenovirus and astroviruses have been found in young rabbits with diarrhea and enteritis. Co-pathogens are often also present. Prevention and control is like that used for rotavirus. A novel bocaparvovirus, a parvovirus, was recently described in both healthy rabbits and rabbits with enteritis.[38] The prevalence and pathogenesis of this virus is unknown.

PARASITIC DISORDERS OF THE GASTROINTESTINAL TRACT

Coccidia

Coccidia are the most common parasites of the rabbit GI tract and are a frequent cause of illness in young rabbits less than 6 months old. Adult rabbits are rarely clinically ill, and identifying oocytes on fecal examination does not equate to disease. Twelve

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species, all members of the genus *Eimeria,* infect rabbits.[49] Only one species, *Eimeria stiedae,* which infects the liver, is found outside the intestinal tract. Two or more species of coccidia often are present in diseased rabbits; the exact role of different species as pathogens therefore is not clear.

Hepatic Coccidia

Eimeria stiedae, the coccidium responsible for hepatic coccidiosis, is ubiquitous in open rabbitries in which rabbits are not treated preventatively with coccidiostats. Infection results from ingesting sporulated oocysts that undergo excystation in the duodenum. Sporozoites then penetrate the intestinal mucosa and move to bile epithelial cells, where they undergo schizogony. Merozoites invade contiguous epithelial cells and undergo gametogeny, giving rise to microgametes and macrogametes. After being fertilized by a microgamete, the macrogamete develops into an oocyst. Oocysts rupture from the epithelial cells and are passed in the bile and eventually in the feces.[36] Many infections are asymptomatic; however, the disease can be fatal, especially in young rabbits. Heavily infected rabbits show signs related to decreased hepatic function and bile duct obstruction. These rabbits become anorectic and debilitated; diarrhea or constipation can occur in the terminal stages of the disease. The abdomen is occasionally enlarged, and the animal may be icteric. Serum biochemical testing reveals increased levels of alanine aminotransferase, aspartate aminotransferase, bile acids, and total bilirubin. On radiographs, hepatomegaly and ascites may be present. At necropsy, the liver is enlarged and has yellowish-white, nodular, abscess-like lesions of varying size, some of which are within a fibrous capsule. Diagnosis is by identifying oocysts in a sample of bile, by histologic examination, or by fecal examination.

Intestinal Coccidia

The most important species of intestinal coccidia are *Eimeria perforans, Eimeria magna, Eimeria media,* and *Eimeria irresidua,* with *E. perforans* being the most common. Infection is by ingestion of sporulated oocysts. Although rabbits are cecotrophic, the cecotrophs eaten from the anus do not contain infectious oocysts. Clinical signs vary widely depending on the age of the rabbit, the organism involved, the parasitic burden, and the relative susceptibility of the animal. Subclinical infection is common in both young and adult rabbits. The finding of oocysts in clinically normal rabbits does not warrant treatment. Clinical signs are most often associated with poor husbandry or overcrowding and generally occur in rabbits under 6 months of age. Severely immunosuppressed older rabbits may also become symptomatic. Mild intermittent to severe diarrhea that may contain mucus or blood, weight loss, and dehydration may be observed. Animals with severe diarrhea may develop intussusception. Death is most often attributed to dehydration and secondary intestinal dysbiosis. At necropsy, lesions are seen in the small or large intestine, depending on the agent involved, and intestinal epithelium may be ulcerated. The presence of organisms in fecal samples or intestinal scrapings in symptomatic animals supports a presumptive diagnosis. Definitive diagnosis is based on histologic findings.

Numerous drugs have been used to prevent and treat intestinal and hepatic coccidiosis. The addition of sulfadimethoxine to the diet in an amount to ensure intake of 75 mg/kg for 7 days or 0.02% sulfamerazine sodium to the drinking water is efficacious for treating groups of rabbits.[49] Amprolium 9.6% in drinking water (0.5 mL per 500 mL) also is effective. Treat individual pet rabbits with a single dose of toltrazuril (2.5 mg/kg PO)[56] sulfadimethoxine (15 mg/kg PO every 12 hours for 10 days) or trimethoprim-sulfamethoxazole (30 mg/kg every 12 hours PO for 10 days). The major role of antiparasitic agents is to limit multiplication until immunity develops. Instruct rabbitry, shelter, and pet store personnel in the practice of good husbandry to control outbreaks. Most healthy rabbits kept in clean, stress-free environments show no clinical signs after infection and develop immunity that may be lifelong.[49]

Cryptosporidia

Cryptosporidium parvum can cause a discrete and transitory diarrhea in young rabbits, peaking at 30 to 40 days, which may lead to growth retardation. Adult rabbits are unaffected. Clinical signs are diarrhea lasting 3 to 5 days, decreased appetite, depression, lethargy, exhaustion, and dehydration. The organism infects the intestinal tract, especially the ileum and the jejunum. Atrophy of villi of the ileum in young rabbits has been observed histologically.[46] Currently no effective treatment for cryptosporidiosis is recognized.

Other Protozoa

Several nonpathogenic flagellates may be found in the feces of rabbits. They occur more commonly in animals with diarrhea. *Giardia duodenalis* occurs rarely in the anterior region of the small intestine. *Monocercomonas cuniculi* and *Retortamonas cuniculi* are flagellates found in the cecum, as well as large ciliated protozoa such as those of the genus *Isotricha* in ruminants. *Entamoeba cuniculi* is commonly found in the cecum and colon of rabbits.[49]

Helminths

Nematodes

Passalurus ambiguus is the common pinworm of domestic rabbits, although *Passalurus nonanulatus* also is reported.[33] Occurrence is widespread in both wild and domestic rabbits; however, the presence of even relatively large numbers of pinworms is nonpathogenic. The adult parasite is found in the anterior portion of the cecum and colon. Adult worms are grossly visible in the lumen of the cecum and large intestine and when they are passed with fresh feces. The life cycle is direct, with infection through ingestion of infected eggs during cecotrophy. Juvenile stages are found in the mucosa of the small intestine and cecum. Pinworms are commonly seen during routine surgical procedures such as ovariohysterectomy. Diagnosis is made by identifying adult worms or by demonstrating the parasite's eggs in the feces.

Pinworm infections, even those with heavy worm burdens, are usually asymptomatic and do not require treatment. However, owners may notice the worms in rabbit feces and desire treatment. Advise owners that pinworms are species-specific and are not zoonotic. The benzimidazoles are effective in greatly reducing if not eliminating pinworms. Thiabendazole (50 mg/

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kg PO repeated in 10–14 days) and fenbendazole (10–20 mg/kg PO repeated in 14 days) are generally effective. Piperazine (200 mg/kg PO repeated in 14 days), to treat individual rabbits, or in drinking water (100 mg/100 mL of water for 1 day repeated in 10 days), to treat large numbers of animals, may also be effective.

Other helminths are extremely rare in pet rabbits. In farmed rabbits raised for slaughter, nematodes are more prevalent and include *Obeliscoides cuniculi, Graphidium strigosum*, *P. ambiguus*, *Trichuris leporis,* and *Trichostrongylus* and *Strongyloides* species.[61]

Cestodes and Trematodes

Clinical disease as the result of intestinal cestode or trematode infection has not been reported in pet rabbits. However, these parasites are present in wild rabbit species and are possible in laboratory animal populations.[1,5,33] The rabbit's GI tract can host several species of cestodes*: Cittotaenia variabilis, Mosgovoyia pectinata americana, Mosgovoyia perplexa, Monoecocestus americana,* and *Ctenotaenia ctenoide*s. Adult parasites are found in the small intestine. The life cycles of some species are not well known; however, oribatid mites or ants are believed to act as intermediary hosts. Rabbits are the intermediate host for several tapeworms that affect dogs and foxes, including *Cysticercus pisiformis,* the larval stage of *Taenia pisiformis*; *Coenurus serialis*, the larval stage of *Taenia serialis;* and *Echinococcus granulosus*.[57] Oral ingestion of the eggs, shed in carnivore feces, and then larval migration from the intestines leads to formation of cysts in various tissues, depending on their predilection site. Treatment of cestode parasites consists of the administration of a single dose of praziquantel (5–10 mg/kg PO). Prevent infestation of pet rabbits by avoiding feeding of wet grass clippings from areas where feces from possible natural hosts may be present.

NEOPLASIA

Neoplasms of the GI tract are uncommon and include adenocarcinoma and leiomyosarcoma of the stomach, leiomyoma and leiomyosarcoma of the intestine, papilloma of the sacculus rotundus, papilloma of the rectal squamous columnar junction, and bile duct adenoma and carcinoma. Metastatic neoplasia, most commonly uterine adenocarcinoma, can involve the GI tract. Surgical resection is the treatment of choice for many of these tumors. If diagnosed early, intestinal masses can be resected with good success.

Rectal papillomas (cauliflower-like, fungating masses arising from the anorectal junction) are benign and are not related to the papillomas of skin or the oral cavity. Removal of these lesions is curative.

Bile duct adenoma and adenocarcinoma occasionally occur in pet rabbits. These tumors are often multiple and consist of interlocking cysts filled with thick, viscous, myxoid fluid. A variety of noxious stimuli, particularly infection with *E. stiedae,* may be causative factors. Antemortem diagnosis in some rabbits is based on the results of radiography and ultrasonography. Surgical removal is often not practical. Metastatic disease is most often miliary and carries a grave prognosis.[64]

LIVER LOBE TORSION

Liver lobe torsion has been recognized as a problem in rabbits for some time, with published reports dating back to 1958 and occasional reports after.[16,26,65–67] The caudate lobe is most often affected; however, torsion of the right lobe, the quadrate lobe, and the posterior lobule of the left hepatic lobe have also been reported.[27,52,66,67] Both acute and chronic forms of liver lobe torsion are observed. With acute torsion, hemorrhage at the base of the torsed lobe is common, rapidly resulting in hemoabdomen and death if untreated.

Signs of acute liver lobe torsion generally progress rapidly. History resembles acute GI tract obsrtruction, as affected rabbits become acutely anorectic, demonstrate cranial abdominal discomfort, and become weak and depressed.[27,52] The stomach usually contains food and a small amount of gas, suggesting gastric stasis syndrome. An abnormal liver is sometimes palpable. Affected rabbits deteriorate over a short time; if not treated, they become obtunded and hyporthermic, with pale mucous membranes if hemoabdomen is present. Death may occur 12 to 72 hours from the onset of signs. The most common hematologic and biochemical abnormalities are anemia (packed cell volume, 16%–17%) and mild to severe increases in the liver enzymes alanine aminotransferase, aspartate aminotransferase, and gamma glutamyl transferase (GGT).[26,27,52,63,66] However, these values may be normal initially. On radiographs, rounded liver margins, hepatomegaly, increased density of the liver, or free abdominal fluid are sometimes visible. Ultrasonographic examination is diagnostic and demonstrates a heterogeneous appearance and lack of blood flow on color doppler in the affected liver lobe.[27,52] With hemoabdomen, free fluid is visible in the peritoneum, and fresh blood is obtained on abdominocentesis. Treatment of acutely ill rabbits initially is supportive care, including intravenous fluids, analgesia, and thermal support. Prompt surgical removal of the affected liver lobe in these rabbits is the treatment of choice.[27,52] However, if this is not feasible for the owner and hemoabdomen is not present, some affected rabbits will survive with supportive care alone.[27]

Signs of chronic liver lobe torsion are often nonspecific. These rabbits are often described as "poor doers" with a history of recurrent GI stasis. Liver lobe torsion has also been diagnosed as an incidental finding at necropsy in previously asymptomatic rabbits.[65,67] On physical examination, a firm, nonpainful mass is sometimes palpable in the cranial abdomen. Hematologic and biochemical abnormalities may include mild to moderate increases in liver enzyme activity, anemia, and azotemia. Diagnosis is based on ultrasonic examination of the affected lobe. Surgical lobectomy has been successfully performed in rabbits with this chronic presentation.[63]

AFLATOXICOSIS

Aflatoxins are secondary metabolites of fungi, produced primarily by *Aspergillus flavus* and *Aspergillus parasiticus*. The LD_{50} for aflatoxins in rabbits is among the lowest for any species studied.[15] In one described outbreak, affected animals

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showed anorexia, dullness, and weight loss followed by jaundice in terminal stages, and rabbits died within 3 to 4 days.[37] At necropsy, livers were congested and icteric, and gallbladders were distended and had inspissated bile. Liver sections showed degenerative changes of hepatic cells and dilatation and engorgement of sinusoids. Bile ducts had mild to severe periportal fibrosis. The level of aflatoxin B_1 in tested feed samples varied from 90 to 540 mg/kg of feed. Withdrawal of feed and supportive care resulted in gradual disappearance of signs and deaths.[37]

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15

Respiratory Disease

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Respiratory disease is common in pet rabbits and, as in other species, is caused by both primary and secondary etiologies. Rabbits are obligate nasal breathers because of the position of the elongated epiglottis engaged over the caudal margin of the soft palate. For this reason, mouth breathing indicates a severe abnormality. In general, diseases of the upper respiratory tract are more severe and stressful in rabbits than in other species. Respiratory disease can be classified as affecting the upper or lower respiratory tract, or both.

ANATOMY OF THE RESPIRATORY TRACT

The nasal cavities contain the paired conchae (also called *nasal turbinates* because of their highly complex arboreal structure); these structures with the surrounding nasal bones delineate the ventral, middle, dorsal, and ethmoidal meatuses. The ventral meatus continues to the rhinopharynx (Fig. 15.1). The paired, symmetrical paranasal cavities of rabbits are represented by the dorsal conchal sinus, the large, double-chambered maxillary sinus (composed of a dorsal and a ventral recess connected caudally by a large opening), and the sphenoidal sinus. The resulting large conchomaxillary cavity formed by the dorsal conchal sinus and both recesses of the maxillary sinus opens into the nasal cavities though a single, slitlike common opening, which makes the conchomaxillary cavity vulnerable to pathologic changes.[11] The nasolacrimal duct is closely associated with the nasal cavities and, from the orbital fossa, bends ventromedially, passes through the infratrochlear incisure and the foramen of the lacrimal bone, enters the bony nasolacrimal canal medial to the maxillary bone adjacent to the maxillary recess, and ends on the dorsomedial side of the naris (see Chapter 40, Fig. 40.2).[9,11] The nasal cavities are also closely connected to the tympanic bulla through the nasopharyngeal meatus and the eustachian tubes (which connect the rhinopharynx to the tympanic bulla medially).[45] Therefore disease of dental structures can directly or indirectly affect the paranasal sinuses, the nasal cavity, and the nasolacrimal duct, and disease of the nasal cavity can result in disease of the bullae.[9]

In normal position, the epiglottis is above the soft palate in rabbits and other obligate nasal-breathing species, preventing both mouth breathing and access to the trachea via the oral cavity. Hyperextension of the head causes the epiglottis to disengage and reposition below the soft palate, allowing access to the trachea (Fig. 15.2). The tracheal rings are normally incomplete dorsally in rabbits[29] and can also exhibit varying degrees of calcification.[1]

Each lung is divided into cranial, middle, and caudal lobes, with the right lung also possessing an accessory lobe. There are no septa to divide the lungs into lobules; for this reason, pneumonia is typically generalized rather than localized in this species.[28] The volume of the thoracic cavity of the rabbit is small, especially compared

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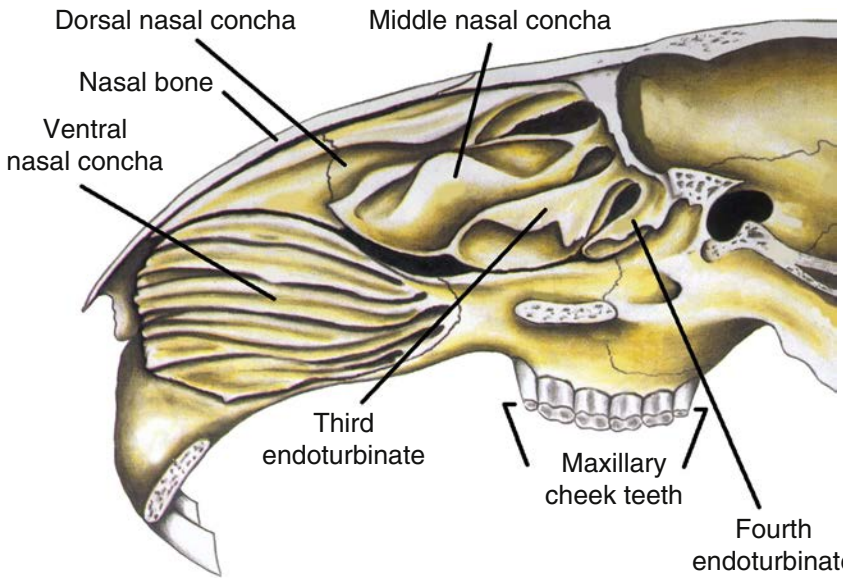


Fig. 15.1 Anatomy of the nasal cavities of the rabbit, median section through the head, lateral view. (Modified from Popesko P, et al: *A colour atlas of anatomy of small laboratory animals. Vol. I: Rabbit, guinea pig*. London: Wolfe Publishing, 1992; with permission.)

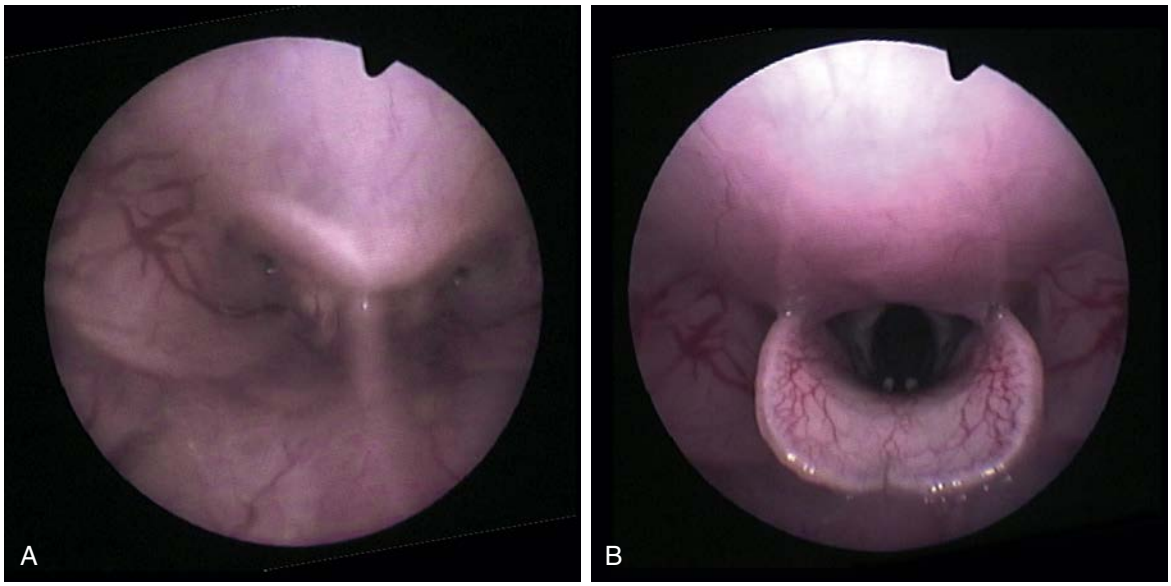


Fig. 15.2 Endoscopic view of the epiglottis and glottis of a rabbit. (A) The epiglottis is in the normal position engaged above the soft palate, a feature common in all obligate nasal-breathing species. (B) The epiglottis is disengaged below the soft palate, allowing introduction of the endotracheal tube. (Used by permission from Vittorio Capello, DVM.)

with the volume of the abdominal cavity.[22] The thymus lies ventral to the heart and extends forward into the thoracic inlet, persisting throughout adult life (see Chapter 20).[40]

PHYSICAL EXAMINATION

Symptoms of respiratory disease can be similar to those observed in other pet species; these include nasal and ocular discharge, nasal flaring when breathing, and increased respiratory effort and rate, often worsening with exertion. Rabbits with ocular or nasal discharge often attempt to remove the discharge with their forefeet, resulting in an accumulation of debris in the fur of the medial aspect of the feet.[22] Rabbits with tracheitis will often cough when the trachea is gently palpated. Because rabbits are obligate nasal breathers, diseases producing nasal discharge or other occlusion of the nares can lead to moderate to severe respiratory distress.[22] Other nonspecific symptoms that should arouse suspicion of respiratory disease are weight loss, decreased appetite, lethargy, and exercise intolerance.

Airway and lung sounds in a normal rabbit are similar to those in other small animals. However, the small thoracic cavity of rabbits can make identifying lung sounds challenging. Diseases affecting the upper airway often result in increased airway noise or wheeze, which is often referred to the thorax. Pulmonary

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disease produces predictable changes in lung sounds, including decreased or increased sounds, which may be bilateral or unilateral. Some rabbits under stress are particularly vocal and will produce a characteristic honking noise that should not be confused with a sign of respiratory disease.

As in other species, severe upper respiratory disease tends to increase inspiratory effort, whereas lower respiratory disease tends to increase expiratory effort. Rabbits with pleural disease (pleural effusion, pneumothorax) may demonstrate an asynchronous breathing pattern, with the thorax and abdomen appearing to move opposite to each other. One author (A.E.L.) has seen a case of hydrothorax in a rabbit where removal of fluid resulted in immediate restoration of synchronous breathing movements.

DIAGNOSTIC TESTING

Laboratory Analysis

In a rabbit with respiratory disease, hematologic and biochemical findings may be unremarkable, depending on the cause. Hematologic values may not reflect leukocytosis in rabbits with bacterial infections; however, an inverse shift in the heterophil/lymphocyte ratio (approximately 2:3) may be suggestive.[14] Results of biochemical analysis do not directly reflect respiratory disease.

Bacterial culture and sensitivity testing is useful, and common sources of samples include deep nasal swabs and nasal or tracheal washes. Culture of the external nares is more likely to reveal environmental pathogens. Deep nasal cultures offer a much more reliable reflection of pathogens of the nasal cavity. A deep nasal culture can be collected with a very small culturette introduced a distance of 2 to 3 cm into the ventral and common nasal meatus. The culturette should be introduced into both sides, because disease may be unilateral.

Occasionally, purulent material is present at the tip of the endotracheal tube after withdrawal, suggesting tracheitis. This material can be submitted for culture and sensitivity testing, as well as cytologic examination. Tracheal or lung washes can be collected by introducing a sterile red rubber catheter through the lumen of a sterile 2.0- to 3.0-mm endotracheal tube in place in an anesthetized patient. Choose a catheter size on the basis of the interior diameter of the endotracheal tube. Depending on patient size, introduce 1 to 2 mL/kg of sterile preservative-free saline solution and then aspirate. Because the amount of fluid collected back into the syringe may be scant to none, withdraw the catheter, fill the syringe with air, and then flush the catheter contents into a sterile tube for submission.

Flushing of the nasolacrimal duct can be both diagnostic and therapeutic (see Chapter 40).[22] Patency is demonstrated by the appearance of fluid at the nasal puncta. Alternatively, fluorescein stain may be observed at the nasal puncta if fluorescein dye is placed in the eye before flushing. Failure to flush may indicate temporary or permanent occlusion, rupture, or impingement. A dacryocystogram is useful to identify the duct radiographically or on computer tomography (CT).[22]

Fluid or specimens collected by ultrasound-guided aspiration of thoracic masses or by thoracocentesis can be submitted for cytologic examination and culture and sensitivity testing. In the case of thoracic abscesses, submission of purulent material for culture is often unrewarding. Certain culture techniques may enhance isolation of *Pasteurella multocida*; therefore consult the reference laboratory instructions on sample collection and handling.

Many laboratories offer molecular diagnostic testing, as well as serologic testing, separately or as part of a panel for specific pathogens, such as *P. multocida, Bordetella bronchiseptica,* and *Treponema cuniculi*. These tests are particularly helpful as screening tests in rabbits with nonspecific signs or where more invasive test methods are deemed too risky to perform.

Diagnostic Imaging

Radiography is extremely useful for the diagnosis of respiratory disease in rabbits but has several limitations, in particular for detecting lesions of the upper respiratory tract and characterizing lung lesions. As in all radiographic patients, excellent positioning and technique are essential to obtain images of diagnostic quality (see Chapter 38).[8] This is particularly true for radiographs of the skull, where rotation and asymmetry of lateral and dorsoventral views greatly complicate interpretation.

Radiographs of the nasal cavities are performed with the five standard projections of the skull: lateral, ventrodorsal or dorsoventral, right-to-left oblique, left-to-right oblique, and rostrocaudal. These are particularly advantageous when disease of the nasal cavity is secondary to acquired dental disease. Lesions of the nasal cavity are often subtle; however, marked and aggressive changes (abscesses, mineralization, masses, osteolysis) may be apparent (Fig. 15.3). Radiographs of the skull also serve to identify lesions suggesting dental disease and abnormalities of the tympanic bulla, which in some cases may produce symptoms of respiratory disease.[8] Plain radiography of the rabbit skull for detection of fluids is considered to have similar specificity and sensitivity as in cat and dog radiography; the dorsoventral view is most consistently useful.

In rabbits, the thoracic cavity is small compared with the abdomen. Structures visible in the rabbit thorax are the relatively large heart, the trachea and bronchi, a small portion of the cranial lung lobes, and a larger portion of the caudal lung lobes (Fig 15.4). Changes in normal radiographic patterns are similar to those seen in other small domestic mammals and can include discrete nodules, interstitial and bronchial patterns, and other abnormalities suggestive of pneumonia (Fig 15.5). Other changes can suggest pneumothorax, hydrothorax, mediastinal masses, and diaphragmatic hernia (Fig. 15.6).[8]

Ultrasound scanning is important for assessing cardiac size and function, distinguishing the heart from precardial masses such as thymomas, and identifying other pulmonary masses and pulmonary or pericardial effusion. Computed tomography (CT) is extremely useful for diagnosis of diseases of the respiratory system of rabbits. This includes diseases of the nasal cavities, including the maxillary recess, and tympanic bulla (Fig. 15.7),[6] and characterization of pulmonary and mediastinal masses (Fig. 15.8).[40]

In any rabbit with severe respiratory disease, use caution in restraint for diagnostic imaging. Anesthesia may pose substantial risk, and manual restraint can produce significant stress. In fractious animals exhibiting severe respiratory distress, mild sedation with midazolam (0.25 mg/kg intramuscularly [IM]) and butorphanol (0.2 mg/kg IM) will allow careful

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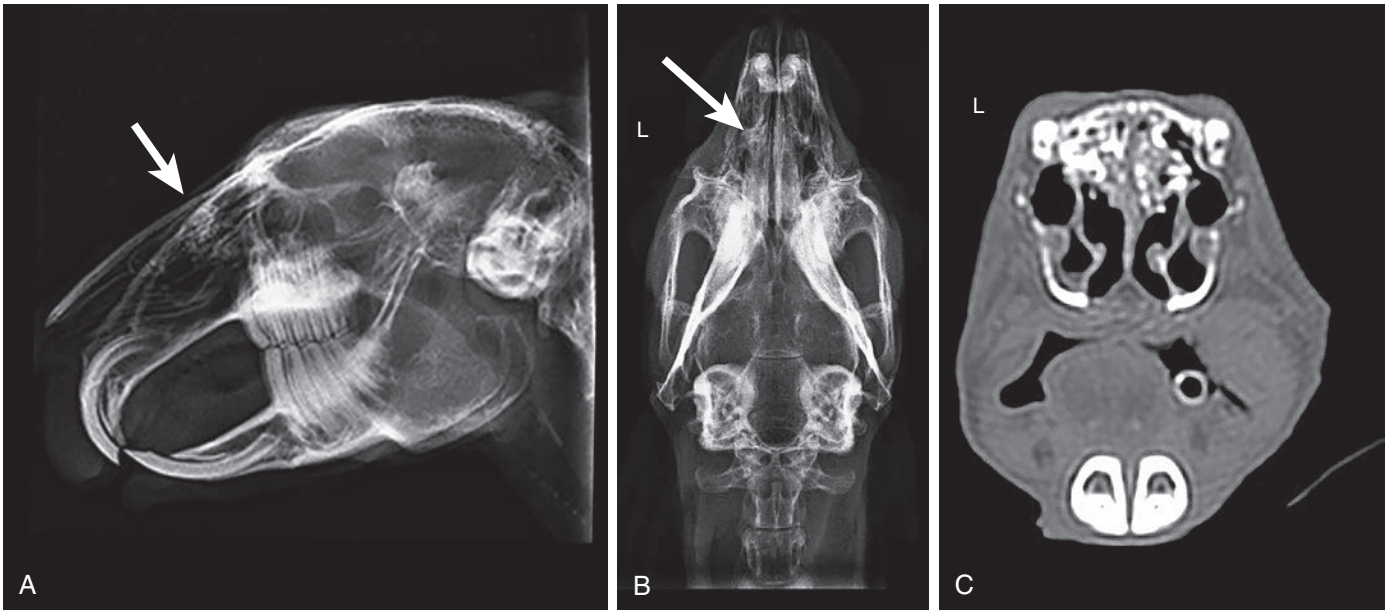


Fig. 15.3 Diagnostic imaging of the skull of a 10-year-old rabbit with chronic rhinitis. Lateral radiographic view (left) shows mineralization of the dorsal conchae *(arrow)*; dorsovental view (middle) indicates changes are most severe on the left side *(arrow)*. A computed tomography scan of the same patient, axial slice (right), confirms bilateral mineralization of the dorsal concha, which is more severe on the left side. Because disease was mild, medical management was selected for this patient. (Used with permission from Angela Lennox, DVM).

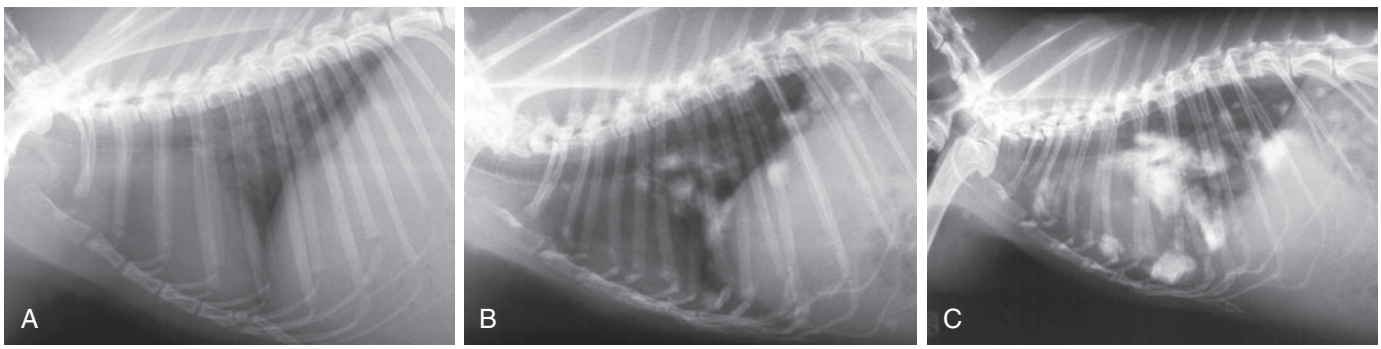


Fig. 15.4 (A) Normal radiograph of the thorax of a rabbit, lateral view. (B) Radiograph of the thorax of a rabbit demonstrates a slightly increased respiratory rate at initial presentation; and (C) the same rabbit in severe respiratory distress 2 months later. Note multiple mineralized densities throughout the caudal lung fields in B and C. Metastatic adenocarcinoma (origin: uterus) was confirmed at necropsy. (Used with permission from Vittorio Capello, DVM.)

manual restraint. Sedation reduces anxiety and stress, and many patients relax and demonstrate reduced dyspnea. Always use oxygen flow, administered by mask, during any restraint with a dyspneic animal, and place the rabbit in an oxygen cage during sedation and recovery.

Endoscopy

Endoscopy can be used in some cases to evaluate the nasal cavities, mouth, and trachea and to aid in collecting culture and biopsy samples (see Chapter 35). Rhinoscopy may allow direct visualization and examination of the nasal mucosa and help to identify granulomatous disease or nasal foreign bodies unlikely to respond to simple antibiotic therapy.[24] For rhinoscopy of rabbits weighing more than 2 kg, introduce a 1.9-mm rigid endoscope with diagnostic sheath through the nares of the anesthetized and intubated patient and carefully advance along the ventral and middle nasal meatus. The nasopharynx can also be evaluated by retrograde flexible endoscopy. Stomatoscopy can be helpful in evaluating the morphology and movement of the glottis and associated structures. Tracheoscopy, if indicated, can also be performed. Thoracoscopy has been done in rare cases to diagnose intrathoracic masses in the rabbit.

DISEASES OF THE UPPER RESPIRATORY TRACT

Infectious Diseases

Numerous infectious diseases are associated with disease of the upper respiratory tract; these are caused mainly by bacterial pathogens, but in rare cases, viral, fungal, or parasitic pathogens may be involved as well. The rabbit is a common

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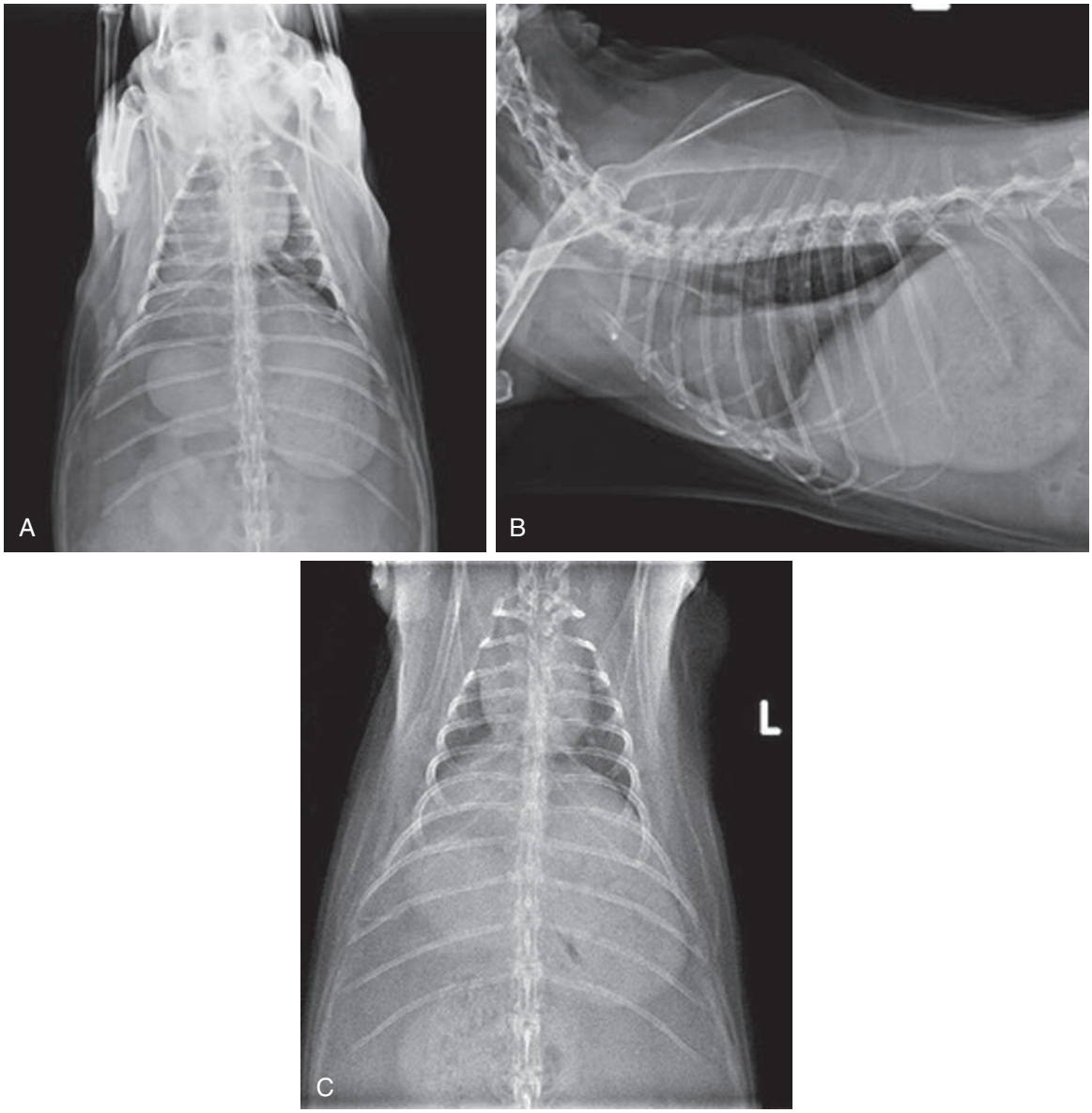


Fig. 15.5 (A) Ventrodorsal (VD) and (B) left lateral radiographic projections of the thorax of a rabbit. Alveolar lung pattern is present in the right middle and caudal lung lobes, silhouetting with the right lateral margin of the cardiac silhouette on the VD view and obscuring the margins of the caudal vena cava and caudal cardiac silhouette on the lateral view. The ventral distribution is most consistent with pneumonia. After antimicrobial therapy (C), the right lateral margin of the cardiac silhouette is now no longer obscured by a lung pattern. The right lung is now better aerated, consistent with positive response to therapy for pneumonia.

research model for rhinitis and sinusitis. Sinusitis is established after mechanical blockage of the ostium connecting the nasal and sinus cavities, resulting in impaired mucociliary function and clearance of organisms from the sinus cavity.[3] In laboratory models, dysfunction of the ostium resulting in occlusion appears to be an important requirement for the establishment of infection,[3] especially for organisms not considered as primary pathogens, and may have significance for naturally infected animals as well. Otitis media is associated with respiratory disease in rabbits because infection can spread via the eustachian tube to the tympanic bulla, middle, and possibly inner ear.[15,22]

Bacterial Pathogens

Although *P. multocida* is often implicated as an important cause of respiratory disease in rabbits, other pathogens must be considered. Results of an epidemiologic study of 121 rabbits with symptoms of upper respiratory tract disease (nasal discharge and sneezing) indicated that the most common bacterial isolates (deep nasal samples) were *P. multocida* (55%), *B. bronchiseptica* (52%), *Pseudomonas* species (28%), and *Staphylococcus* species (17%). Mixed infections were seen.[47] A similar report describing 171 rabbits with nasal discharge revealed the most common pathogens as *Pasteurella, Pseudomonas,* and *Moraxella* species and *E. coli*.[43] Results of bacterial culture and sensitivity

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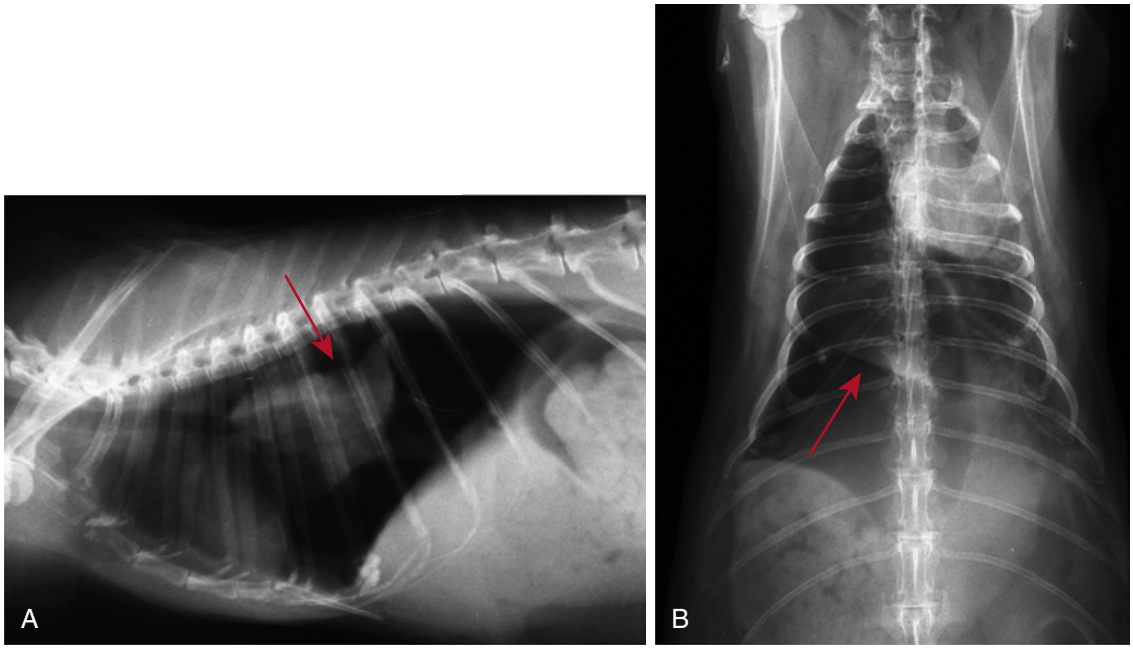


Fig. 15.6 Images of a rabbit with severe pneumothorax. (A) Right lateral projection. The caudal lung lobes are collapsed *(arrow)* and surrounded by free air in the pleural space. The cranial and middle lobes are also collapsed and retracted to the hilum and superimposed on the cardiac shadow. Notice that pulmonary vascular and bronchial markings do not extend to the periphery of the thoracic margins because of the accumulation of free air, a hallmark of pneumothorax. Pneumothorax is best detected on lateral radiographs, especially when smaller amounts of air are present in the pleural space. (B) Ventrodorsal projection. There is bilateral accumulation of free air, but the volume is greater in the right versus the left pleural cavity; therefore the heart is shifted to the left of midline. Collapsed lung lobes can be seen in the right pleural cavity *(arrow)*.

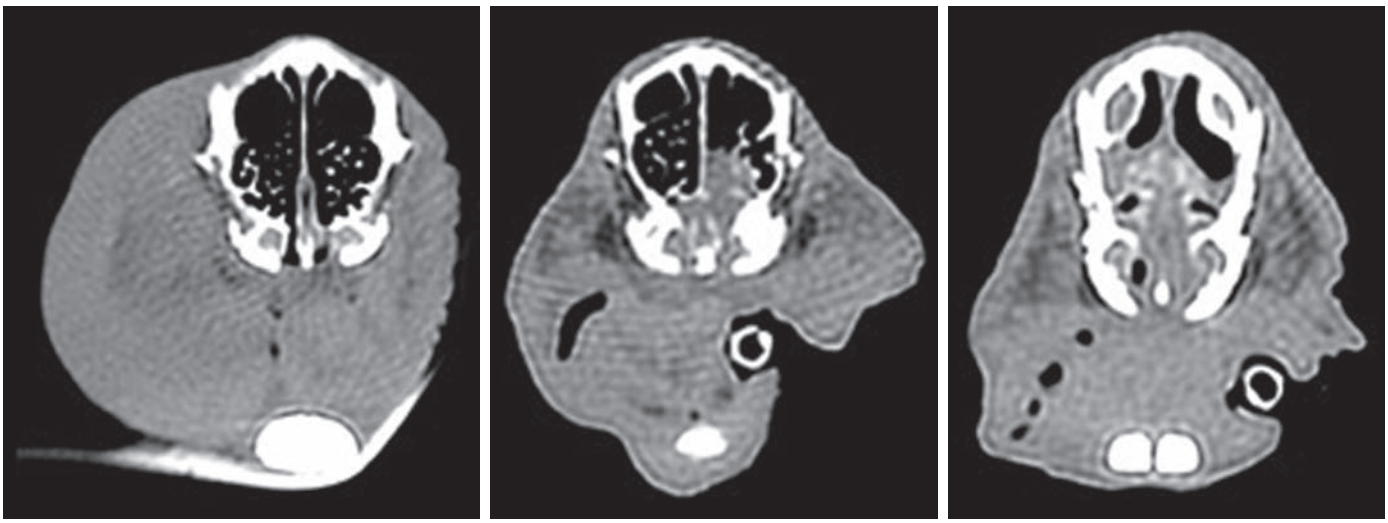


Fig. 15.7 Computed tomography axial slices through similar sections of three rabbits showing normal findings (left); moderate soft tissue/fluid filling of the airways (middle); and severe soft tissue/fluid filling with marked bony destruction (right). (Used with permission from Angela Lennox, DVM.)

testing of nasolacrimal duct fluid from 83 rabbits with signs of upper respiratory tract disease showed *P. multocida* as the most common pathogen isolated (29% of isolates).[46] However, 10% of 20 apparently healthy rabbits harbored this pathogen as well.

Pasteurellosis is associated with many disease processes in rabbits, including rhinitis, sinusitis, conjunctivitis, nasolacrimal duct infection, otitis, tracheitis, pneumonia, and abscesses (dental, skin, other). Although not identified as a pathogen in wild rabbit populations, *P. multocida* is a significant pathogen in laboratory animals, leading to the development of "*Pasteurella*-free" animals for research use. Because of its ubiquitous nature, *P. multocida* is prevalent in many pet rabbits. Many exhibit symptoms in response to stress, such as

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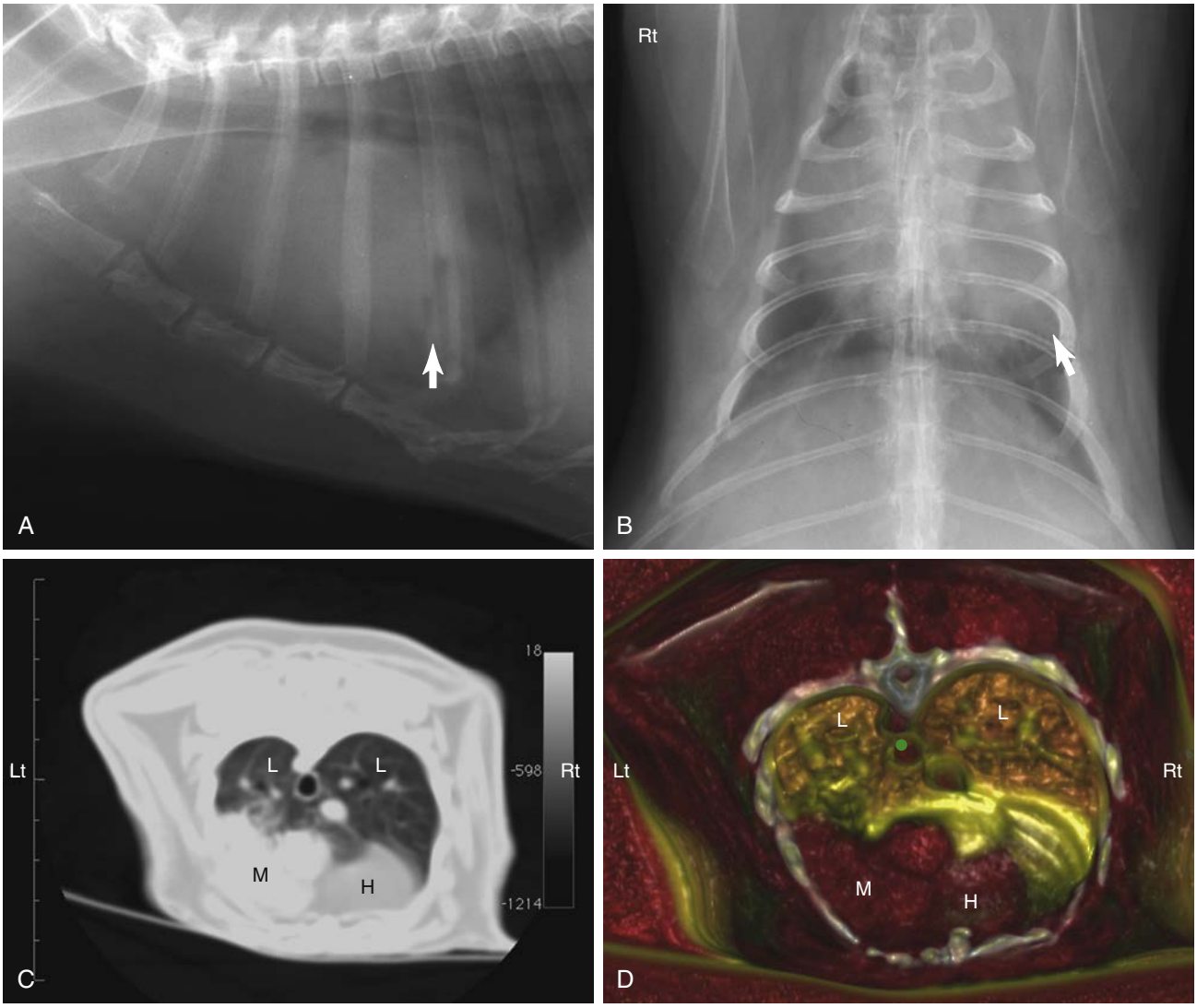


Fig. 15.8 (A) Lateral and (B) ventrodorsal radiographs of the thorax of a rabbit. A soft tissue opacity *(white arrows)* is present in the left thorax overlying the heart. Computed tomography scan; (C) axial view and (D) three-dimensional volume rendering reveal a soft tissue mass to the left of the heart. Ultrasound-guided fine-needle aspirate revealed =purulent material, suggesting the presence of an abscess. *H,* Heart; *L,* lungs; *M,* mass.

stress of weaning, transport, and purchase from the pet store, as well as poor sanitation and ventilation and concurrent illnesses.[15]

Strains of *Pasteurella* vary in pathogenicity,[41] with some being more likely to spread by the hematogenous route and causing acute septicemia, generalized disease, and death. The bacteria gain entry to the host primarily through the nares by aerosolization or by direct contact with infected rabbits or fomites. Does with venereal infections may pass the organism to their young, which may remain apparently healthy for several weeks until signs of infection develop. Infected rabbits can resist infection or become subclinical carriers, thus complicating determination of an incubation period. In experimental studies, rhinitis occurred 1 to 2 weeks after intranasal inoculation.[36] After infection, the organism spreads to the sinuses, nasolacrimal duct, eustachian tube and middle ear, trachea, and lungs. Factors facilitating disease expression are stress of concurrent disease, exposure to ammonia through improperly cleaned enclosures, and administration of corticosteroids.[14] Recent studies have indicated promise for the development of vaccines as an aid to management of this disease.[50]

Bordetella bronchiseptica is a common inhabitant of the rabbit respiratory tract, and disease incidence may increase with age.[15] Experimental inoculation of organisms may or may not produce disease. This organism is pathogenic in guinea pigs, dogs, cats, and pigs. *Bordetella* is suspected to be a copathogen or predispose to infection with *P. multocida.* However, severe infection in the absence of *P. multocida* has been documented in a colony of inbred laboratory rabbits, suggesting that more pathogenic strains may exist.[14]

Pseudomonas species infections in rabbits are common. Rabbits are used as a laboratory model for human *Pseudomonas* infections in multiple body systems, including the cardiovascular system.[25]

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Staphylococcus species are commonly isolated from the nares of rabbits and are considered to be secondary invaders. Pathogenicity depends on host susceptibility and the bacterial species and virulence. Disseminated staphylococcosis has been linked with fibrinous pneumonia and abscesses in the lung or heart.[14]

Although not a primary respiratory pathogen, *T. cuniculi* (rabbit syphilis) can produce crusting of the mucocutaneous borders of the nose, lips, and eyelids, in some cases resembling an upper respiratory infection (see Chapter 16). Marked crusting of the nares can produce mild to moderate respiratory distress.

Several other bacterial pathogens can produce upper respiratory disease in rabbits. *Pasteurella* species other than *P. multocida* can be cultured from rabbits but may be nonpathogenic. However, pure cultures associated with clinical disease should be treated as true pathogens. Other potential pathogens include *Moraxella* species, *Yersinia pestis*, and *Escherichia coli*. *Mycoplasma pulmonis* was isolated in the rhinopharynx of rabbits with evidence of upper respiratory disease. Infected rabbits were housed in close proximity to rats, which may have been the source of the infection.[14] Nasal granulomas caused by *Mycobacterium* species have been seen clinically (S. Kelleher, K. Quesenberry, personal communication, November 2019).

Viral Pathogens

Other than myxoma virus, viral pathogens that produce primary upper respiratory disease are uncommon. Myxoma virus can induce nasal and ocular disease, as well as dyspnea; it has also been associated with acute hemorrhagic pneumonia.[31,37] An outbreak of a herpes virus was reported in a commercial rabbitry in Alaska. Respiratory signs and symptoms were prominent features.[27]

Fungal Pathogens

Fungal granulomas of the sinuses have been described in pet rabbits and, as in other species, appear to require primary injury. Techniques used in rabbits to produce experimental models of fungal sinusitis include mucosal injury and blockage of the ostium.[17] Simple introduction of pathogenic fungi into the nasal cavity usually does not produce disease.

Noninfectious Disease

Trauma

Traumatic injury to the upper respiratory tract includes blunt force trauma, predator injury, and damage to the glottis and trachea after endotracheal intubation. Reports of inflammation of the glottis and stenosis of the trachea are numerous in laboratory animal literature.[20,44] In one report of three cases of tracheal stenosis caused by intubation, evidence of respiratory disease appeared within 17 to 21 days after intubation. Risk factors could not be identified.[44] One author (A.L.) has regularly performed endoscope-guided and blind endotracheal intubation in rabbits; the most severe complications have been rare cases of mild respiratory stridor that did not persist beyond 24 hours after the procedure. One author (E.M.) has encountered two cases of postintubation tracheal stricture in pet rabbits.[35] Successful intraluminal tracheal stent placment with a nitinol self-expanding stent has been described in a pet rabbit with a postintubation tracheal stenosis.[18] The rabbit remained healthy with no complications at the time of publication, almost 2 years after stent placement. Correct tube size (2- to 3-mm ID), gentle technique without the use of pressure, and avoiding damage to the glottis during placement are crucial to successful intubation. To prevent trauma to the trachea after intubation, avoid sudden or excessive movements of the head of intubated rabbits, do not overinflate the cuff if a cuffed tube is used, and always disconnect the tube from the anesthetic system when repositioning the animal.

All mammalian species are susceptible to airway irritation due to chemical exposure, and mucosal damage may predispose to infection. Numerous studies have demonstrated upper airway and lung damage secondary to irritants such as tobacco and dried dung smoke.[19] Other potential sources of respiratory irritants are household chemicals and ammonia from poorly cleaned enclosures.

Foreign materials in the nares, pharynx, or trachea have been reported. In one rabbit with chronic sneezing, clinical signs stopped after removal of hay from the nares.[49]

Dental Disease

Certain expressions of dental disease can produce symptoms of respiratory disease, including epiphora and nasal discharge.[7] The nasolacrimal duct in the rabbit courses close to the apex of first maxillary incisor tooth and the first maxillary cheek tooth (see Chapter 40). Therefore abnormalities or infections of the apices and reserve crowns of these teeth can affect the natural course of the duct, resulting in epiphora. More severe disease can produce infection or abscess of the duct and subsequent purulent nasal discharge. Elongation, deformation, and infection of the roots of maxillary cheek teeth (particularly the first two cheek teeth) can affect the maxillary sinus and nasal cavity, resulting in sinusitis and chronic nasal discharge.[7]

Neoplasia

Nasal mucosal adenocarcinoma has been reported. A single case presented as chronic rhinitis that did not respond to antimicrobial therapy. Diagnosis was suspected on the basis of severe changes seen on CT and confirmed after rhinotomy, biopsy, and histopathology (Fig. 15.9).[33]

Miscellaneous Conditions

Collapsing trachea was identified by tracheoscopy in a rabbit exhibiting dyspnea and an appreciable honking noise on inspiration.[13] A 3-year-old rabbit was diagnosed with laryngeal paralysis based on endoscopic identification of absence of motion of the glottis during breathing. The rabbit presented because of frequent bouts of food emerging from the nares and increasing respiratory distress. The rabbit was euthanized due to aspiration of food into the trachea and worsening pneumonia. Histopathologic examination of the glottis, trachea, and associated nerves revealed no lesions; therefore the condition was likely congenital.[34]

DISEASES OF THE LOWER RESPIRATORY TRACT

Infectious Diseases

Infectious agents, as described above, also produce lower respiratory disease, with the classic clinical signs and presentation of pneumonia. *Pasteurella multocida* and sometimes other organisms can also produce pleuritis and pericarditis. In a study of 66 rabbits with

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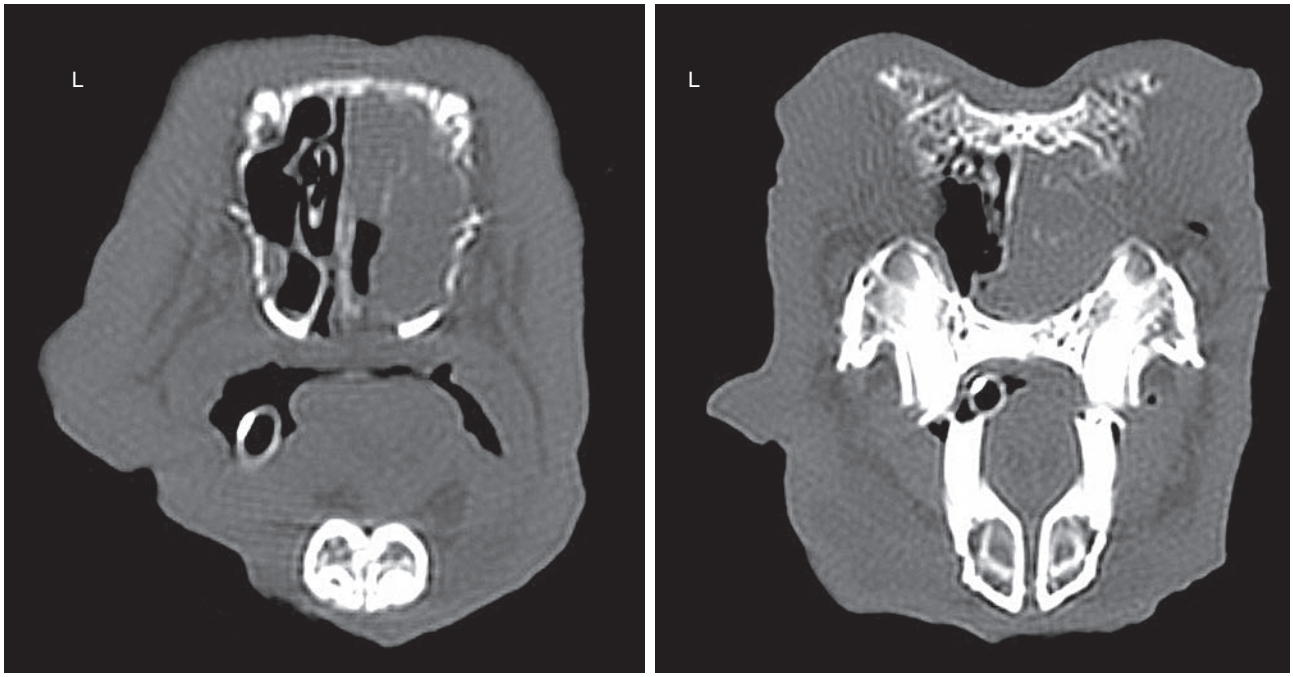


Fig. 15.9 Computed tomography axial slices of a rabbit with confirmed nasal adenocarcinoma, at the level just rostral to the premolars (left) and a more caudal slice at the level of the molars (right). Note filling of the right side of the nasal cavity with marked deviation of the nasal septum in both slices. Biopsy was obtained via dorsal nasal bone rhinostomy. (Used with permission from Angela Lennox, DVM.)

pulmonary lesions, the following pathogenic bacteria were isolated in order of frequency: *Pasteurella* species including *P. multocida, E. coli, B. bronchiseptica,* and *P. aeruginosa.*[37] *Chlamydia* species have been isolated from the lungs of domestic rabbits with pneumonia. A mild interstitial pneumonia occurred when the agent was inoculated into the trachea of laboratory rabbits.[14] *Pneumocystis oryctolagi* has been isolated from the lungs of newly weaned rabbits.[16] Myxoma virus has been associated with acute hemorrhagic pneumonia.[37]

Neoplasia

Several neoplasms can metastasize to the lungs or, in the case of thymoma or thymic lymphoma, indirectly affect the lower respiratory tract.[12,38,48] Neoplasms that more commonly metastasize are uterine adenocarcinoma, osteosarcoma, lymphoma, and mammary carcinoma.[54] Primary carcinoma of the lungs of a 7-year-old rabbit has also been reported.[23] Thymoma is discussed in more detail in Chapter 20.

DISEASES PRODUCING SECONDARY RESPIRATORY SYMPTOMS

Cardiovascular disease can produce signs that suggest respiratory disease, including increased respiratory rate and effort (see Chapter 19). As the life span of pet rabbits increases, it can be expected that the incidence of cardiac disease will increase as well.[22] Cardiomyopathy, endocardiosis, and congestive heart failure have been reported in rabbits.[42] Diaphragmatic herniation with entrapment of the stomach, parts of the intestinal tract, fat, and kidney has been identified, as well as pneumothorax resulting from trauma.[8,39]

TREATMENT OF RESPIRATORY DISEASE

Thoracocentesis Rabbits with respiratory disease may present in critical condition. Refer to Chapter 41 for more information on how to approach the rabbit in respiratory distress or provide emergency treatment for respiratory arrest. In brief, rabbits in respiratory distress benefit from the administration of oxygen in a quiet, low-light environment. As mentioned previously, mild sedation often benefits rabbits in respiratory distress by eliminating anxiety. Rabbits in acute respiratory arrest require intubation for positive-pressure ventilation, which is challenging to perform rapidly. Other options are the use of an epiglottal device (laryngeal mask) or a tight-fitting face mask for cardiopulmonary resuscitation.

Thoracocentesis

Rabbits with radiographic or clinical evidence of pneumothorax, hydrothorax, or hemothorax (dysynchronous breathing pattern) often require a chest tap, which, depending on the patient's condition, should be performed before diagnostic tests or treatments likely to produce respiratory compromise. Ideally, thoracentesis is done with ultrasound guidance to guide placing and advancing the needle. Perform the tap after preoxygenation and sedation by using a 22- to 25-gauge butterfly needle with syringe and three-way stopcock. Clip and prepare the area, then apply a topical anesthetic. Local infiltration of lidocaine into the muscle layers is also helpful. The technique is identical to that used in other pet species, and the patient is maintained in a normal upright position. The thoracic cavity of the rabbit is relatively small, and the heart occupies most of the entire length

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(second to fourth intercostal space). Therefore needle advancement is kept to a minimum. For thoracentesis in most cases of pleural effusion, insert the needle at the fifth to sixth intercostal space. For removing thoracic fluid in the cranial thorax associated with thymoma or other mediastinal masses, needle placement usually is at the second to third intercostal space.

Antibiotic Therapy

Antibiotic Therapy In treating rabbits with bacterial respiratory disease, accurate diagnosis, including identifying the pathogen, and localizing disease, will increase the chance of treatment success. In the case of bacterial pathogens, selecting an antibiotic on the basis of culture and sensitivity testing is ideal. In a study of 121 rabbits with evidence of nasal discharge and sneezing mentioned above, marbofloxacin was demonstrated as most likely to be effective against most identified bacterial strains with the exception of *B. bronchiseptica,* where other antimicrobials were slightly more effective.[47] In a recent report on bacterial sensitivity testing in rabbits with nasal discharge, enrofloxacin provided the broadest sensitivity ranges for identified pathogens.[43] Antibiotic selection, however, should be made with species-specific contraindications in mind. Enteric dysbiosis and potentially fatal enterocolitis or enterotoxemia are well-documented potential results of administration of inappropriate antibiotics such as oral penicillin, erythromycin, and similar drugs (see Chapter 14). Treponematosis (rabbit syphilis) responds well to once-weekly injections of procaine/benzathine penicillin over a three-week period (see Chapter 16).

Treatment and elimination of *P. multocida* has been the focus of much attention because of the economic impact of the disease on commercial and laboratory rabbit facilities. Treatment of acute cases is often associated with good outcomes, but numerous studies have demonstrated poor long-term prognosis for treatment of chronic infection, with high rates of recurrence after discontinuation of drug therapy.[14] Various treatment options are reported. Infection was eliminated in seven of eight rabbits treated with enrofloxacin (5 mg/kg subcutaneously every 12 hours) for 14 days.[4] Enrofloxacin given in the drinking water (50–100 mg/L) before and continuing for 48 hours after inoculation with a virulent strain of *P. multocida* protected rabbits against bacteremia, provided that daily intake of the drug was greater than 5 mg/kg.[14] Young from enrofloxacin-treated does were free of *P. multocida* infection, although the infection was not eliminated in the does.[51] Ciprofloxacin (20 mg/kg by mouth [PO] every 24 hours) for 5 days eliminated *P. multocida* infection in a group of diseased rabbits.[21] High tissue concentrations of ciprofloxacin were found in kidneys, lungs, liver, spleen, and muscle. Chronic cases of confirmed pasteurellosis have been controlled successfully by using enrofloxacin (5–10 mg/kg PO every 12 hours) or chloramphenicol (50 mg/kg PO every 12 hours) for up to 2 to 3 months.[14]

In an experimental study of rabbits with empyema caused by *P. multocida*, penicillin (24,000 U/kg IV) penetrated easily into the pleural space and remained at high levels after serum levels had decreased.[53] The length of time the tissue concentrations of penicillin remain at bactericidal level is also essential for the effective therapeutic use of the drug. There are, however, different minimal inhibitory concentrations (MIC) for different *Pasteurella* isolates/serotypes in rabbits. Therefore culture and sensitivity testing to determine the exact MIC for the specific pathogen isolated is warranted, because the dosing interval of penicillin G may vary between 8 to 14 hours based on the isolated bacteria. A dosing interval of 12 hours for penicillin G (60,000 IU/kg IM) may therefore not be sufficient against pathogen with a high MIC.[26]

Oral antibiotic therapy may be unrewarding. Treatment failure can result from misidentifying the underlying cause or because of the presence of foreign material, granulomas, or abscesses, where oral medications are often only partially to poorly effective. In some cases, treatment is enhanced with the addition of antibiotic therapy in the form of nebulization. Antibiotics and many other drugs, including mucolytics and bronchodilators, can be efficaciously delivered directly to the upper and lower part of the respiratory tract by nebulization for 15 minutes up to two to three times daily, along with systemic therapy. The use of nebulized saline solution alone can help in rehydrating the natural mucociliary escalator. Adequate drug and nebulizer (capable of producing particles <0.5 μm) choice is mandatory. The addition of mucolytic agents may be helpful as well.[22]

Flushing of the nasolacrimal duct and instilling antibiotics into the duct is also useful. Multiple flushing attempts may help resolve infection and occlusion of the duct with infectious/inflammatory debris (see Chapter 40). Long-term inflammation, rupture of the duct, or dental disease may result in permanent occlusion and failure to flush.[8,22]

Rhinotomy/Rhinostomy

Rhinotomy with surgical debridement and infusion of topical antibiotics may be an effective treatment option for granulomatous disease of the nasal cavity that is unresponsive to antibiotic therapy (see Chapter 32). In a laboratory rabbit model of *Pseudomonas* sinusitis, a decrease in bacterial count was achieved with a catheter embedded in the nasal cavity for irrigation with saline solution and tobramycin. However, although bacterial counts in the nasal cavity were decreased in experimental models, complete elimination of organisms in the mucosa was not achieved.[2] A dorsal surgical approach to the rabbit nasal cavity has been described in laboratory rabbits.[2a] For rhinotomy, a three-sided osteotomy technique (top, bottom, and one side) is used to gain access to the nasal fossae bilaterally while leaving a bone flap for closure. This technique was successful in optimizing postsurgical healing, airway patency, and airway dynamics but it does not provide a stoma for continued local treatment. One author (A.L.) has achieved significant improvement in rabbits with chronic nasal bacterial infection with rhinostomy of the nasal bone (unilateral or bilateral) for direct debridement and flushing of the nasal cavity.[32] The rabbits tolerated the procedure and postprocedural care well. For this procedure, the skin is incised over the nasal bones and the periosteum is retracted. The nasal bone is then perforated with a high-speed precision drill. The nasal cavity is debrided and flushed and the tissue is marsupialized to allow ongoing flushing and debridement until healed (Fig. 15.10). The nasal cavity is flushed daily with a small amount of sterile saline and antibiotics, based on culture and sensitivity test results. Once the infection has cleared, the skin heals over the rhinostomy site.

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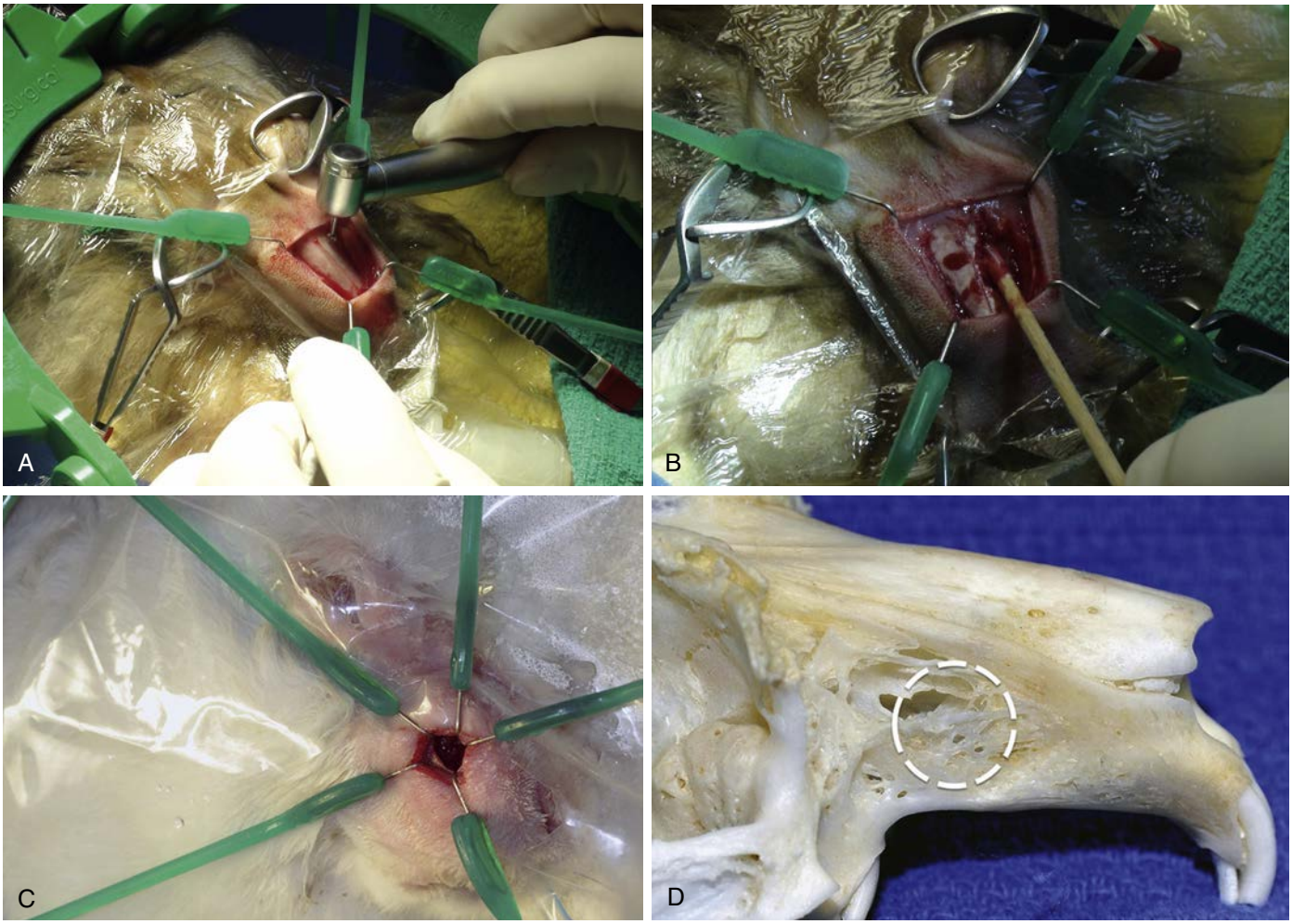


Fig. 15.10 Dorsal (A, B) and lateral (C, D) rhinostomy approaches in rabbits. Temporary dorsal rhinostomy in 9-month-old rabbit with severe rhinitis and osteomyelitis with loss of most normal structures of the nasal cavity. (A) Patient preparation demonstrating an incision over the skin of the nasal bone. The skin is retracted with the Lonestar retractor, and a dental burr is used to perforate the nasal bone. (B) Removal of purulent exudate and fluid through the initial rhinostomy site. (C) Lateral rhinostomy in a rabbit diagnosed with severe right-sided rhinosinusitis. (D) Skull of a rabbit showing the right maxillary bone and the facies cribrosa, which is the thinnest and perforated area of the maxillary bone used for approach to the nasal cavity. (A and B used with permission from Angela Lennox, DVM. C and D courtesy C. Mans, DVM.)

Reoccurrence of symptoms of rhinitis is treated with direct infusion of antibiotic flush into the nasal cavity through the skin and bone defect into the nasal cavity.[32] A less invasive technique of lateral rhinostomy can also be used for treatment of chronic sinusitis in rabbits.[52,55] For this technigue, access to the unilateral nasal cavity is made by an approach through the facies cribosa of the maxillary bone. In the described cases, after debriding and lavaging the sinus, the opening was marsupialized to create a stoma. The surgical site healed after one month with no recurrence of disease. Rhinotomy has also been used for successful treatment of odontogenic rhinitis in rabbits.[9]

Other Treatments

In one study, rabbits were used as an animal model to evaluate the use of therapeutic laser for acute bacterial rhinosinusitis. Bacterial counts were reduced by up to 99.9% after treatment with two different therapeutic lasers. This may represent an innovative method to destroy pathogenic bacteria without damaging host tissue in animals with chronic to severe upper respiratory tract disease.[30]

Otitis can contribute to respiratory disease via the spread of organisms through the eustachian tube. Therefore resolution of respiratory disease may rely on the management of otitis. In cases of inner- and middle-ear infection, lateral resection of the ear canal, ostectomy of the bulla, or both may be useful (see Chapter 32). Both procedures have been described and successfully used in pet rabbits.[5,10]

Treatment of pulmonary edema associated with cardiac disease in the rabbit is similar to that in traditional pet species. Drugs reported as useful for cardiac disease in the rabbit include furosemide, enalapril, digoxin, and pimobendam (see Chapter 19).[42]

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PREVENTION AND CONTROL OF INFECTIOUS RESPIRATORY DISEASE

A large part of prevention of infectious disease is optimal husbandry, including ideal diet, exercise, reduction of stress, and proper sanitation. Advise potential rabbit owners against purchasing rabbits from groups exhibiting nasal or ocular discharge, sneezing, or other signs or symptoms of respiratory disease. Quarantining new animals from existing pets is essential. Animals with evidence of respiratory disease should be housed away from other rabbits. Handwashing and disinfecting helps to prevent spread via fomites.

Pasteurella-free rabbits are available in the laboratory animal community through Webster's methods of barrier housing and testing, cesarean derivation, and fostering of kids onto *Pasteurella*-free does or possibly early weaning with or without antibiotic treatment of does. These animals are unlikely to be found in pet stores.[14] Examination of new rabbits immediately after purchase is beneficial, because early identification and treatment are more likely to result in cure.

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16

Disorders of the Urinary and Reproductive Systems

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DISORDERS OF THE REPRODUCTIVE SYSTEM

Rabbits reach sexual maturity by 4 to 6 months of age, are induced ovulators, and have serial cycles that last 7 to 14 days until conception. Receptivity is often accompanied by swelling and congestion of the vulva that should not be mistaken for vulvitis or vaginitis. Bucks are precocious and may attempt to breed as early as 3½ to 4 months of age. Spraying is a normal sexual behavior of intact bucks and sometimes of does, and it should not be confused with inappropriate elimination because of urinary tract infection or inflammation. The prevalence of naturally occurring reproductive disorders in rabbits is difficult to estimate. In wild European hares *(Lepus europaeus),* reproductive abnormalities were found in 21% (51 of 245) of the does examined.[98] Cystic endometrial hyperplasia was common and often accompanied by hydrosalpinx. Extrauterine fetuses, neoplasms, pseudopregnancies, and resorptions also were also found. Disorders of the reproductive tract in female pet rabbits are seen less commonly because educated owners typically elect to have their rabbits spayed to prevent uterine disease. Intact females must be carefully and regularly monitored for reproductive tract disease, especially neoplasia. Careful abdominal palpation allows for the detection of ovarian or uterine enlargement. Investigate any perceived abnormality fully and aggressively. The primary preventive measure for reproductive disorders, especially in female rabbits, is ovariohysterectomy/ovariohisterovaginectomy (referred now in the text as *ovariohysterectomy*). Currently, there is no ideal alternative to surgical gonadectomy in does or in bucks. The slow-release GnRH agonist implant deslorelin acetate (Suprelorin 4.7 mg, Virbac Corporation, Fort Worth, TX, USA) that is widely used in other species is not effective in male rabbits,[36] and although it effectively prevents ovarian activity in does,[33] it does not prevent development of uterine disorders.[34]

Uterine Adenocarcinoma

Uterine adenocarcinoma is the most common neoplasia of female rabbits.[112] Age is the most important factor in its

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development, and occurrence is independent of breeding history. Rabbits of certain breeds (tan, French silver, Havana, and Dutch) that are more than 4 years old have an incidence of 50% to 80%.[4,48,112] With age, the endometrium undergoes a progressive decrease in cellularity and an increase in collagen content. These changes are associated with the development of uterine cancer.[4] Adenocarcinoma of the uterus is a slowly developing tumor. Local invasion of the myometrium occurs early and may extend through the uterine wall to adjacent structures in the peritoneal cavity; hematogenous metastasis to the lungs, liver, brain, and bones may occur within 1 to 2 years.[112] Early clinical signs, such as decreased fertility, small litter size, and an increased incidence of fetal retention, fetal resorption, and stillbirths may be recognized in breeding does. The first sign observed in many pet rabbits is hematuria or a serosanguineous vaginal discharge. However, in one study, only 17% of rabbits with a uterine disorder presented with serosanguineous vaginal discharge.[109] Cystic mammary glands often develop concurrently with uterine hyperplasia or adenocarcinoma.[43,56] Clinical signs of late-stage adenocarcinoma are depression, anorexia, and dyspnea if pulmonary metastasis has occurred. Ascites may be present. Diagnosis relies on palpation of an enlarged uterus, uterine nodular masses (1–5 cm in diameter), or both in the caudal abdomen. Adenocarcinomas are often multicentric, involving both uterine horns (Fig. 16.1).[4,112] Other causes of uterine enlargement are pregnancy, pyometra, metritis, hydrometra or mucometra, endometrial venous aneurysms, endometrial hyperplasia, and other tumors such as leiomyosarcoma. In one pet rabbit, both a leiomyoma and an adenocarcinoma of the endometrium were found, with the latter extending into the leiomyoma.[59]

Immunohistochemistry was used in one study to evaluate the expression of estrogen receptor–α and progesterone receptors in normal, hyperplastic, and neoplastic endometrium of rabbits.[2] In this study, 16 of 27 (59%) cases of normal uteri and 13 of 19 (68%) cases of hyperplasia stained positive for both receptor types. Adenocarcinomas were subdivided into papillary and tubular/solid types. Papillary adenocarcinomas infiltrated and caused attenuation of the myometrium late in the disease, and 21 of 26 (81%) were receptor negative for both estrogen and progesterone. Tubular/solid adenocarcinomas invaded the deep myometrium early in the disease but did not cause thinning, and 15 of 16 (94%) were positive for one or both receptors. These results suggest that two different developmental pathways for uterine adenocarcinomas may be present in the rabbit.[2]

Abdominal radiography is an important diagnostic tool for rabbits in which uterine adenocarcinoma is suspected (Fig 16.2A). In one study, abdominal radiographs revealed an enlarged uterus in 32 of 39 (82%) of rabbits with uterine disorders.[109] Ultrasound imaging is more sensitive than abdominal radiography for diagnosis of uterine disorders, with sensitivity ranging from 87.5% to 100% depending on the study (Fig 16.2B).[88,109] Ultrasound imaging may also allow differentiation between potential causes of uterine enlargement, measurement of masses, and scanning for multiple nodules.[109] In rabbits with uterine enlargement, thoracic radiographs or computed tomography are used to rule out pulmonary metastasis (Fig 16.2C).

If uterine masses are identified in the early stages of disease before metastasis occurs, ovariohysterectomy is the treatment of choice. Ovariohysterectomy is curative if the tumor is contained within the uterus, with reported survival times of more than 22 months after surgery.[109] Metastatic disease or local invasion of peritoneal structures may not be apparent macroscopically at surgery; therefore, reexamine a rabbit with confirmed adenocarcinoma every 3 to 6 months for 1 to 2 years after surgery to detect pulmonary metastasis. Successful chemotherapy for metastasis of this tumor has not been reported.

Prevention is the key to management of this disease. Begin client education at the initial visit for routine health evaluation of the patient. The ideal age for ovariohysterectomy is undetermined, and uterine adenocarcinoma may occur in rabbits as young as 2 years of age.[109] Spaying rabbits between the ages of 8 and 12 months is generally preferred because the quantity of abdominal fat is limited and ovarian ligaments are easily distensible. Alternatively, discuss early clinical signs of the disease with the client and recommend semiannual health examinations including radiographs for intact female rabbits 3 years of age and older. Other reported uterine neoplasias in rabbits include spontaneous choriocarcinoma and a homologous malignant mixed Müllerian tumor (see Chapter 20).[37,54]

Endometrial Hyperplasia or Uterine Polyps

Endometrial changes can develop along a continuum—from polyp formation, to cystic hyperplasia, to adenomatous hyperplasia, to adenocarcinoma.[25,48,56] Uterine hyperplasia is associated with aging, as are cystic and hyperplastic changes in endometrial glands. Other reports, however, have found no association between cystic hyperplasia and uterine adenocarcinoma in rabbits because adenocarcinomas are associated with senile atrophy of the endometrium.[4] In one Australian study, wild hares were found to be particularly sensitive to the luteotrophic effect of exogenous estrogen, which can double the length of pseudopregnancy in that species; however, this was not found in sympatric wild *Oryctolagus* rabbits.[98] In a recent study, treatment of rabbits with a slow-release 4.7-mg deslorelin implant for reversible suppression of ovarian function did not prevent development of endometrial hyperplasia.[34]

Clinical signs of endometrial hyperplasia can mimic those associated with uterine adenocarcinoma, including intermittent hematuria, anemia, and decreased activity. A firm, irregular uterus is sometimes detected by palpation, and cystic mammary glands and cystic ovaries often occur concurrently.[43,56] Ultrasonography is the best technique to image soft tissue changes in the uterus. Ovariohysterectomy is the recommended treatment.

Pyometra and Endometritis

Vaginal discharge, anorexia, lethargy, weakness, and an enlarged abdomen are clinical signs that frequently accompany endometritis or pyometra. Clinical signs of mild endometritis can be subtle, making the condition difficult to diagnose. Rabbits with chronic disease may have no overt clinical signs. The history of an affected breeding doe often includes a recent parturition, pseudocyesis, or an inability to rebreed. Rabbits with mild

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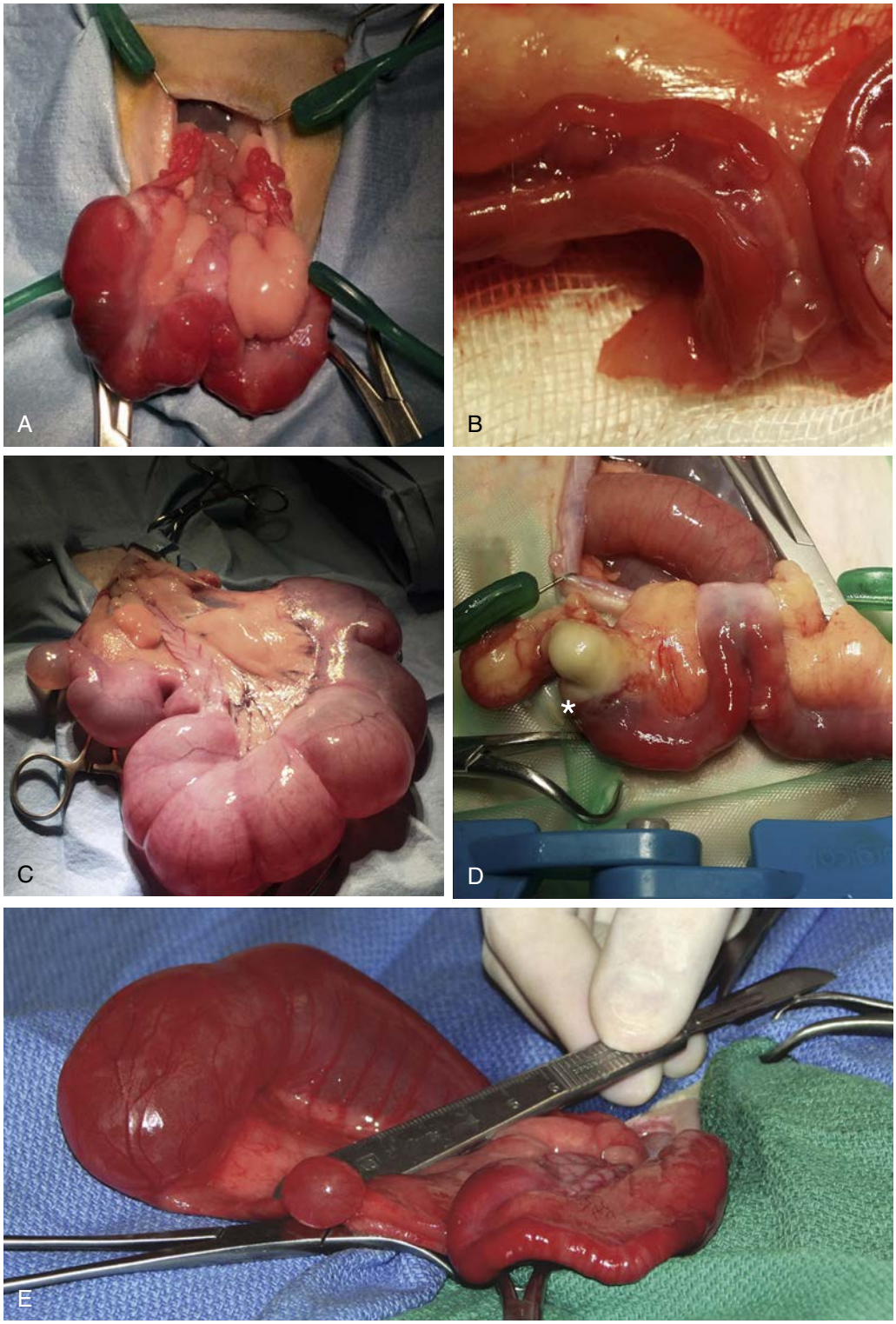


Fig. 16.1 Common uterine disorders in rabbits. (A) Uterine adenocarcinoma. (B) Uterine polyps and hyperplasia. (C) Hydrometra. (D) Unilateral uterine abscess (*asterisk*) in a hyperplastic uterus. E, Uterine atresia. The left uterine tube is normal, whereas the right side is engorged with fluid at the distal aspect with a blind proximal end because the right cervix is absent. (A, B, C, D, Courtesy Dr. Nicola Di Girolamo; E, Courtesy Dr. Matthew Johnston.)

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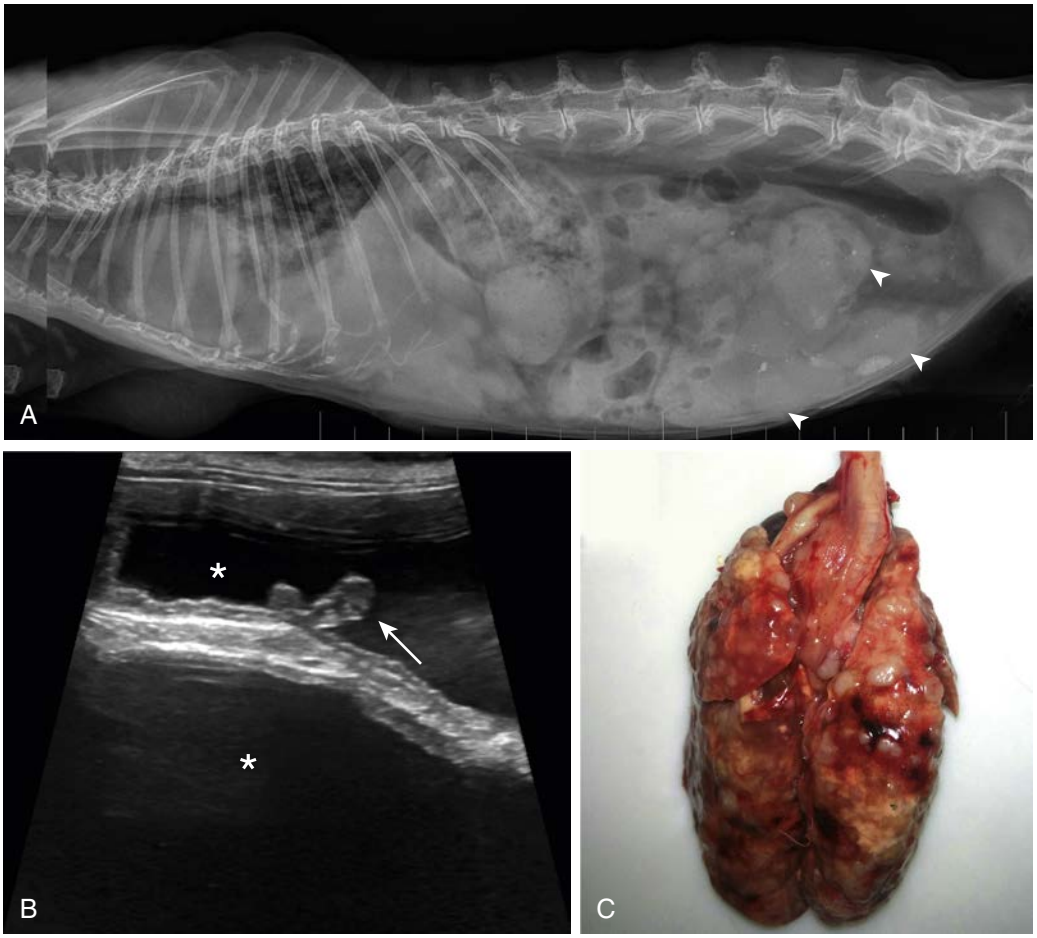


Fig. 16.2 (A) Radiographic evidence of advanced uterine adenocarcinoma in an intact doe. Multiple soft tissue opacities are present in the ventrocaudal abdomen *(arrowheads)*. Notice the pulmonary interstitial nodular pattern consistent with lung metastases. (B) Ultrasonographic features of the same doe. Notice presence of fluid in both uterine horns *(asterisks)* and of multiple polyps protruding into the uterine cavity *(arrow)*. (C) Macroscopic aspect of the lungs from the same doe showing metastatic dissemination. (Courtesy Dr. Nicola Di Girolamo.)

endometritis may kindle successfully or have fetal resorptions and stillbirths. Pyometra, endometritis, and uterine abscesses can also develop in nulliparous does (Fig. 16.1D). Pyometra can be secondary to uterine adenocarcinoma, indicating the importance of histopathology on all grossly abnormal uteruses. In does that were treated once or twice with a slow-release deslorelin implant to suppress ovarian function, 7 of 13 developed endometritis.[34]

Pasteurella multocida and *Staphylococcus aureus* are frequently isolated from rabbits with pyometra or metritis. Venereal transmission occurs when infected does breed with uninfected bucks or vice versa. Bacteria can localize in the genital tract by hematogenous spread from another location, or a retrograde infection can occur from vaginitis.[18] Ovarian abscesses may occur concurrently with *P. multocida* pyometra.[50] In one report, the 1-year incidence of pyometra in does culled on two industrial rabbit farms was 8.7%. *Pasteurella* species was the most prevalent bacterial species isolated in these cases, although *S. aureus* was also identified.[92] In another study, *S. aureus* was a prevalent cause.[105] Rare cases of metritis or pyometra have been associated with *Chlamydia* species, *Listeria monocytogenes, Moraxella bovis, Actinomyces pyogenes, Brucella melitensis,* and *Salmonella* species.[45,73,96,111] Postpartum metritis can occur in conjunction with hypervitaminosis A; the delivery of stillborn young and metritis have been associated with uterine torsion.[45]

Diagnosis relies on palpation of a doughy, enlarged uterus, best demonstrated on radiographs or ultrasonography. If the uterus is greatly enlarged, use caution in palpating the abdomen because the uterine wall becomes very thin and friable. Abdominal ultrasound scanning can rule out other uterine conditions such as polyps, masses, or cystic changes. Results of a complete blood count (CBC) may be normal or may show mild leukocytosis and heterophilia. Chronic inflammation of the uterus can induce amyloid deposition in the kidneys of affected rabbits[46]; therefore evaluate renal values in these animals. Cytologic assessment and a Gram stain of cervical discharge can assist diagnosis.

For a breeding rabbit with mild endometritis, treatment with appropriate antibiotics, nonsteroidal antiinflammatory drugs (NSAIDs), and fluids may be sufficient, but the tenacious and caseous nature of inflammatory exudates in rabbits precludes adequate drainage of the uterus. Ovariohysterectomy is

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the treatment of choice for pyometra. At surgery, uterine vessels may be engorged and prominent, and multiple adhesions to adjacent viscera often complicate the procedure. Obtain an intraoperative sample for bacterial culture. Preoperative antibiotics given immediately before surgery are indicated because of the risk of bacterial contamination from the uterus and surgical site infection. Intravenous fluids and pain management are important components of therapy. As for uterine adenocarcinoma, the most effective preventive measure against endometritis is ovariohysterectomy.

Hydrometra

Hydrometra is the accumulation of watery fluid in the uterus (Fig 16.1C). It has been described in four unbred half-lop rabbits from the same research colony[68] and in New Zealand white rabbits.[45] Clinical signs are an enlarged, fluid-filled uterus, increased respiratory rate, anorexia, and weight loss. Transabdominal uterocentesis yields clear fluid with a low specific gravity, a low cell count, and a moderate amount of protein.[45] Diagnosis is supported by radiography and ultrasonography. In described cases, rabbits were either euthanized or found dead. No anatomic abnormalities were correlated with this condition.[68] If diagnosed, ovariohysterectomy is indicated for treatment.

Uterine Torsion

Torsion of the uterus is rare in rabbits but has been associated with pregnancy, hydrometra, and endometritis.[45] Clinical signs of uterine torsion include shock, cachexia, and abdominal distention with hydrometra, or a bloody vaginal discharge when seen with endometritis.[45] The cause of uterine torsion is unknown, and the prognosis is grave. After stabilizing the doe with supportive care and pain management, ovariohysterectomy is the treatment of choice.

Uterus Unicornis and Uterine Atresia

Congenital anomalies of the female reproductive tract have been described in domestic rabbits.[95,104] Uterus unicornis with two ovaries but only one uterine horn, cervix, and oviduct was reported in a 4-year-old rex rabbit presenting with urinary and behavioral issues.[104] Uterine atresia was incidentally found in a 9-month-old female New Zealand white rabbit. The left portion of the uterus was normal, but the right lacked a cervix and the caudal portion of the right uterus. The right ovary was normal. A large and a second smaller cystic structure midway between the vagina and ovary in the mesometrium was noted (Fig. 16.1E).[104] Cervical and segmental uterine aplasia with mucometra were detected during elective ovariohysterectomy in an adult rabbit.[95] The right cervix was absent, and the right uterine horn was discontinuous with the vagina. The congenital cause of uterine anomalies makes it important to assess affected animals for renal and ureteral abnormalities.[104]

Endometrial Venous Aneurysms

Multiple endometrial venous aneurysms can cause hematuria because of episodic bleeding in the uterine lumen. Cylindrical blood clots molded within the uterine horns are typically passed with the urine and are highly suggestive of this condition. Affected does are at high risk for fatal exsanguination from uterine hemorrhage, and ovariohysterectomy should be performed as soon as the animal is stabilized. Endometrial venous aneurysms are most common in young does of larger breeds but can be seen in other breeds. The condition was first reported in three New Zealand white rabbits and was confirmed by exploratory laparotomy and histopathologic examination of the uterus.[9] In rabbits with this condition, the uterine horns have multiple blood-filled endometrial varices (veins) that periodically rupture into the uterine lumen, causing the clinical hematuria. Although the cause has not been elucidated, venous aneurysms in other species are related to congenital defects of the adventitia, increased intraluminal pressure, or trauma.[9]

Pseudopregnancy

Pseudopregnancy (pseudocyesis, false pregnancy) occurs in rabbits, even in pet does kept singly, and may be triggered by presence of aggressive conspecifics.[11] Pseudopregnancy typically lasts 16 to 17 days and may be followed by hair pulling and nesting behavior.[79] The corpus luteum secretes progesterone, causing uterine and mammary development.[74] Mammary development is most pronounced in the first 10 days of false pregnancy, after which mammary involution typically follows by day 16.[74,79] The condition resolves spontaneously but may recur or lead to hydrometra or pyometra. Pseudopregnancy depresses fertility, and its cause is still unknown.[103] A lower kindling rate was found in group-housed does with one buck versus does housed with bucks in a one-to-one ratio, with pseudopregnancies found in 23% of does in the group-housing system contrasted with 0% in does housed individually.[86] Ovariohysterectomy is the treatment of choice and ideally is performed once the mammary tissue has involuted.

Dystocia or Retained Fetuses

In rabbits, gestation averages 31 to 32 days but may vary from 28 to 36 days. Normal delivery usually is complete within 30 minutes after onset, although in rare cases young are delivered several hours apart. Litters range from 4 to 12 kits. Anterior and breech positions are normal for rabbits. Palpate does 24 hours after delivery to determine whether any fetuses have been retained.

Dystocia is rare in rabbits. A rabbit may be predisposed to dystocia by obesity, large fetuses, a small pelvic canal, or uterine inertia. Signs of dystocia are persistent contractions, straining, and bloody or greenish-brown vaginal discharge. In suspect does, obtain radiographs to determine abnormalities in the fetuses or in the width of the pelvic canal. Assistance in delivery usually requires analgesia, sedation, gentle manual removal of the fetuses, and rapid removal of fetal membranes. Oxytocin (1–3 units intramuscularly) can assist uterine contraction. If uterine inertia is suspected, give 5 to 10 mL of 10% calcium glubionate orally 30 minutes before administering the oxytocin. Place the doe in a quiet, dark room for 30 to 60 minutes after administration. Perform a cesarean section if there is no response to oxytocin injection. Prognosis is guarded. Focus should be placed on saving the doe unless adequate staff is present to try also to revive the kits.

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Pregnancy Toxemia

Pregnancy toxemia usually occurs during the last week of gestation, when nest-building behavior begins. Rabbit fetuses develop considerably during the second half of pregnancy.[28] Although the exact causes leading to metabolic disturbances and pregnancy toxemia are unknown, toxemia is more common in obese rabbits. Inadequate caloric is a predisposing factor, and environmental changes or stress can precipitate disease. Hair pulling for nesting can contribute to hair ingestion and inappetence.[78] Weakness, depression, incoordination, anorexia, abortion, convulsions, and coma are common clinical signs. Signs can progress over 1 to 5 days, or death may occur acutely. Some rabbits are dyspneic and may have ketotic breath. The urine becomes acidic and clear because the lower pH decreases the concentration of calcium carbonate crystals. Clinical pathologic findings include acidic urine (pH 5–6), proteinuria, ketonuria, hyperkalemia, ketonemia. hyperphosphatemia, and hypocalcemia. Hepatic enzyme values may be elevated, and lipidosis is commonly seen at necropsy.

There is no consistently effective treatment for pregnancy toxemia. Keep the animal warm and administer intravenous fluids. Calcium gluconate can be administered parenterally to treat hypocalcemia. Analgesics are indicated; however, concerns regarding the gastrointestinal effects of opioids and renal or hepatic effects of NSAIDs should be evaluated on a case-by-case basis. When the rabbit is stabilized, provide nutritional support, either by syringe feeding or nasogastric tube. Pregnancy toxemia carries a grave prognosis; treatment is usually unrewarding by the time it is recognized. The best approach is prevention. Avoid fasting or underfeeding does during late pregnancy and prevent obesity and sudden stress. If feeding timothy hay–based pellets, consider switching to alfalfa-based pellets until after weaning.

Abdominal Pregnancy

Abdominal pregnancy sometimes occurs in does and is usually subclinical.[1,6,7,17] Extrauterine implantation of fertilized ova, often on the parietal peritoneum, can lead to the development of near-term fetuses, with subsequent mummification.[7] Primary abdominal pregnancy is when there is no evidence of uterine rupture, with presumed regurgitation of early embryos from the uterine tube. In a study of 550 adult female New Zealand white rabbits culled from rabbit farms, 5% had abdominal pregnancies, with 25% of those having normal reproductive tracts.[35] Mummified fetuses were found free in the abdominal cavity of a healthy doe presented for a routine examination.[6] The uterus and ovaries appeared normal, and the rabbit recovered uneventfully after surgical removal of the fetuses. False abdominal pregnancy refers to cases in which fetal implantation occurs in the uterus and fetuses are expelled into the abdominal cavity as a result of a traumatic event.[7] One report describes a rabbit mortality associated with three partially mummified, full-sized fetuses free in the abdominal cavity 3 weeks after it delivered three kits.[1] At necropsy, one uterine horn showed evidence of a recent tear, suggesting that the uterine rupture had occurred at parturition. Primary or false abdominal pregnancy should be considered when palpable fetuses are present in does that have not undergone timely parturition.[35] Fetuses should be removed surgically, and ovariohysterectomy is indicated if the pregnancy is identified early. Euthanasia may be required in advanced cases.

Abortion and Resorption

Typically, fetal death before 21 days of gestation resolves as resorption, whereas after 21 days fetal death results in abortion. A critical period in gravid does occurs at 21 days because blood flow to the uterus is temporarily reduced with the changing size and shape of the fetuses. When abortion or fetal resorption is suspected, a thorough history is extremely important, including questions about previous abortions, environmental changes, or drug treatments. Always check the doe for remaining fetuses by obtaining radiographs or an abdominal ultrasound scan. Submit fetuses and placentas for histopathologic examination and anerobic and aerobic bacterial culture. Fetal resorption is not regarded as a disease condition in lagomorphs because it occurs in response to social or environmental stress.[98] Possible causes of fetal abortion are numerous and include infection, stress, genetic predisposition, trauma, adverse drug effects, and dietary imbalances (e.g., deficiencies of vitamin E, vitamin A, and protein). *Listeria* species have a predilection for the gravid uterus; this should be considered in rabbits with late-term abortion.[111] A herpesvirus infection affecting mini Rex and crossbred meat rabbits was identified in one rabbitry, with abortion as one symptom.[49] Abortion with fetal resorption may be induced with subcutaneous administration of 10 mg/kg aglepristone once daily on days 15 and 16 after mating.[76]

Reduced Fertility

Reduced fertility may result from multiple factors, such as malnutrition (e.g., excess vitamin A; deficiencies of vitamins A, D, or E), heat stress, systemic illness, nitrate contamination of food or water, environmental disturbances, a decrease in daylight, endometrial carcinoma, metritis, or pyometra. Old age, sexual exhaustion, or breeding of rabbits that are too young are additional causes of infertility. Vitamin E deficiency causes myodystrophy, which can lead to abortions, stillbirths, and neonatal deaths. An increased level of creatine phosphokinase occurs with hypovitaminosis E and indicates a need for diet supplementation.[73] Hypervitaminosis A can cause fetal resorptions, abortions, and stillbirths.[19,97] Hypovitaminosis A can cause similar reproductive disorders, resulting in poor fertility and weak, hydrocephalic young. The National Research Council recommends vitamin A levels of 1160 IU/kg of diet for gestation, or approximately 20 mg/kg of body weight per day.[71] Administration of vitamin E for 2 weeks lowers the serum vitamin A levels and increases the serum and liver vitamin E levels and appears to be an effective treatment for hypervitaminosis A.[97]

Uterine and Vaginal Prolapse

There are two distinct entities that may result in female genital organ prolapse in rabbits. One entity, which is presumed to be hormonal-dependent, is characterized by the prolapse of vulvar tissue, and can be defined vulvar prolapse or hyperplasia. A case series including eight closely related rabbits from a laboratory facility described the occurrence of vulvar hyperplasia and prolapse.[107] The prolapsed tissue consisted of overexpanded blood-sinuses, and all animals were in a period of increasing sexual activity when the prolapse developed.[107] The second entity, which is more likely associated with parturition, is the

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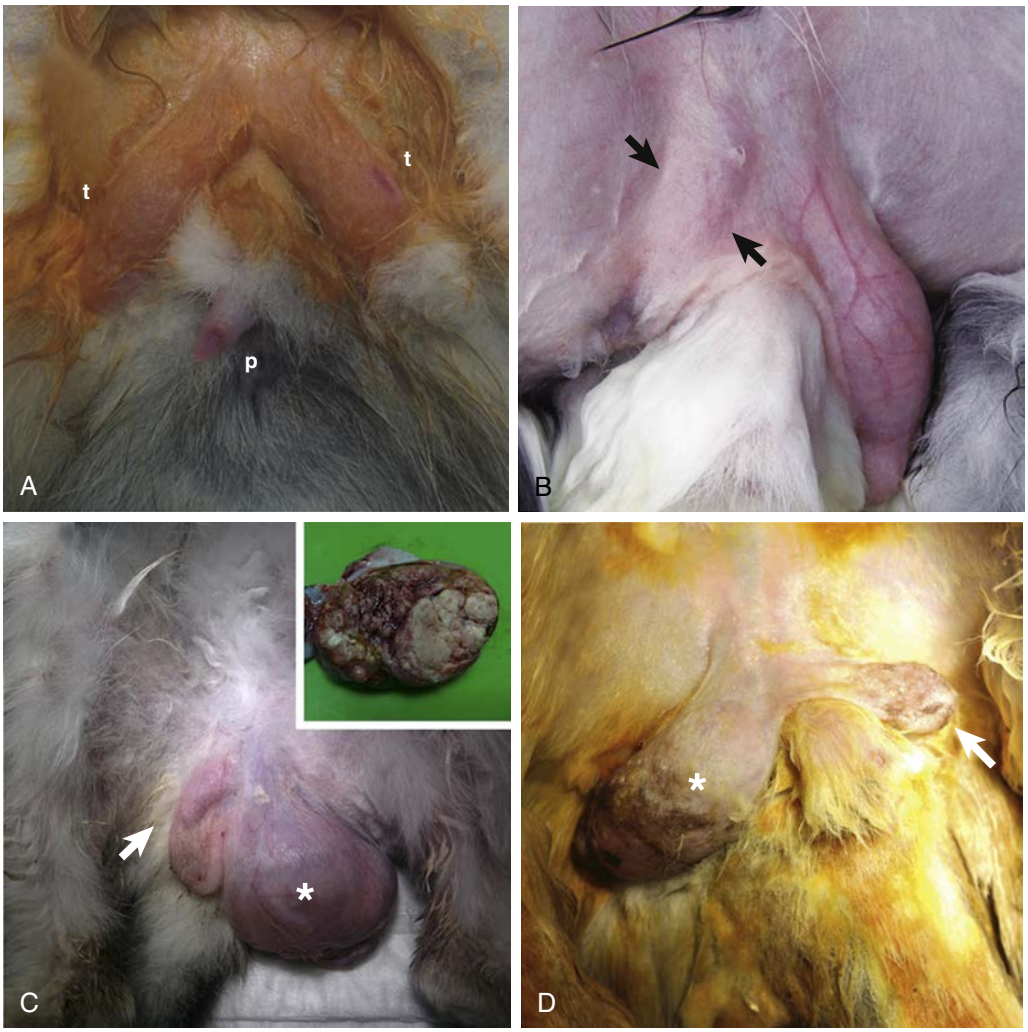


Fig. 16.3 (A) Normal male rabbit anatomy. Notice testicles (t) in two separates scrotal sacs, cranial to the penis (p). (B) Unilateral cryptorchid rabbit with lack of scrotal development *(arrows)*. (C and D) Unilateral testicular neoplasia (asterisk) in two adult rabbits. Notice the diminished size of the contralateral testes *(arrow)*. (A, C, D, Courtesy Dr. Nicola Di Girolamo; B, Courtesy Dr. Stephen Barten.)

true uterine prolapse. A case series described treatment of uterine prolapse in three < 2-year-old pet rabbits presented within 24 hours of parturition.[108] All the rabbits presented with a red mass protruding from the vagina. In some instances, the cervices were visible, and the uterine horns were prolapsed too. Resolution was achieved by performing a laparotomy to apply internal uterine traction while simultaneously using gentle external pressure with cotton-tip applicators. After reposition of the prolapse, an ovariohysterovaginectomy was performed in all the rabbits without further problems.[108]

Cryptorchidism

In bucks, the testicles usually descend by 12 weeks of age (Fig. 16.3A). Failure of one or both testicles to descend into the scrotal sacs by 16 weeks of age is defined as unilateral or bilateral cryptorchidism. Because rabbits can retract their testicles intraabdominally, cryptorchidism may be difficult to detect initially. In true cryptorchid bucks, the scrotal sac of the retained testicle does not develop (Fig. 16.3B). If the scrotal sac is present but the testicle cannot be palpated, it has most likely been retracted into the inguinal canal or the abdominal cavity. Cryptorchid rabbits retain their sexual drive but fertility is impaired. Neither the causes nor the medical implications of cryptorchidism for rabbits have been adequately investigated. Based on other species, a hereditary pattern for cryptorchidism in at least some rabbits is possible, as well as a potential for the development of testicular neoplasia in untreated animals. In cryptorchid rabbits, the testicle(s) should be localized by ultrasound scanning, and castration with a standard midline abdominal approach is advised. Incorrect age history may lead to unnecessary surgery, so waiting several more months beyond the estimated 16-week age estimate is prudent.

Orchitis and Epididymitis

Clinical signs of orchitis are fever, intermittent appetite, and weight loss. The testicles may be enlarged with obvious abscesses, or abscesses may be small and internal, with minimal swelling of the testicles. The epididymis rather than the

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testis may be infected. Affected breeding bucks have low conception rates. Treatment is castration, antibiotic therapy, and NSAIDs. *Pasteurella multocida* is often isolated from exudate or abscessed tissue on bacterial culture. Specific culture or testing for *Treponema* species should also be requested. House male rabbits separately to prevent bite wounds to the testes or scrotum and other fighting injuries that lead to abscesses. *Cuterebra* species larvae in the scrotum are also a cause of testicular abscesses (see Chapter 17).

Testicular Neoplasms

Testicular tumors are uncommon in rabbits and include seminomas, interstitial cell tumors, Sertoli cell tumors, and teratomas.[72,112] A tentative diagnosis is based on palpation of an enlarged, firm or nodular, nonpainful testicle (Fig. 16.3C and D). Definitive diagnosis is achieved by surgical castration and histopathologic examination. Rarely, tumors are incidentally found on the cut section of a normal-looking testicle.[117]

Collagenous hamartomas are benign proliferations of connective tissue that occur in rabbits in two forms: as a solitary nodule and as a disseminated form with multiple nodules. In one report, the average age of affected rabbits was 5.6 years, with nodules most commonly located on the abdomen or the thorax. These rabbits also had testicular tumors.[108a] The cause of collagenous hamartomas is unclear, but a hormonal cause or an X-linked recessive genetic disease may be involved. The disseminated form of this disease must be differentiated from malignant lymphoma.

Venereal Spirochetosis

Treponema paraluiscuniculi is the spirochete responsible for rabbit syphilis or vent disease. This is not a zoonotic disease. Transmission between rabbits is by direct and venereal contact. Bucks can spread the disease to several does, and young rabbits can be infected. The disease is self-limiting; carriers may be asymptomatic until stress occurs. Lesions first appear on the skin of the perineum and genitalia and begin as areas of redness that progress to edema, vesicle formation, ulcerations, and scabs. The lesions can be painful and can impair breeding activity. Autoinfection can lead to facial lesions around the chin, lips, nostrils, and eyelids. Inguinal lymph nodes may be enlarged. Colony epidemics result in a decreased rate of conception and an increased incidence of metritis, placental retention, and neonatal deaths.

Clinical signs and the distribution of lesions are often diagnostic. Few other skin problems resemble those of rabbit syphilis, but bacterial dermatitis, dermatophytosis, acariasis, and myxomatosis are possibilities. Lesions on the nose and lips are often proliferative and scaly and are commonly mistaken for dermatophyte lesions.

For a definitive diagnosis, submit a skin biopsy sample and request silver staining. Organisms also can be identified in wet mounts of fresh skin scrapings of the lesions examined by darkfield microscopy. Skin biopsy and cytologic samples, though, may not contain *Treponema* bacteria, leading to false-negative results. Large rabbitries can benefit from a serologic survey with the microhemagglutination test to screen and verify infected animals. Other serologic tests are available, such as the rapid plasma reagin card test, which is very specific.[20,89] Two nontreponemal serologic antigen tests are available: the venereal disease research laboratory test, which is more sensitive; and the rapid plasma reagin test, which is more specific.[20,89] Nontreponemal tests look for the presence of nonspecific reagin antibodies that appear and rise in titer after infection. The fluorescent treponemal antibody–absorption test is a serologic test used as a confirmatory treponemal antigen test. The rapid plasma reagin is the most common test, and many laboratories confirm with fluorescent treponemal antigen preparation. Serologic testing is considered more sensitive and less expensive than biopsy and is usually performed by specific diagnostic laboratories dealing with laboratory animals. Real-time polymerase reaction testing of genital swab or skin lesion samples for *T. parluiscuniculi* is available from some veterinary diagnostic laboratories.

In rabbitries, the prevalence of *T. paraluiscuniculi* infection increases with parity: often females that have had six or more litters are seropositive; bucks that have been in a breeding program for 6 to 12 months are also likely to be seropositive.[20] Bucks are often asymptomatic carriers and may have small, star-shaped scars on their scrotum.

Rabbits with venereal spirochetosis are effectively treated with parenteral (never oral) penicillin. Administer penicillin G benzathine-penicillin G procaine at 42,000 to 84,000 IU/kg subcutaneously at 7-day intervals for three injections[16] or penicillin G procaine at 40,000 to 60,000 IU/kg intramuscularly every 24 hours for 5 to 7 days. Tetracyclines and chloramphenicol can also be effective. Treat all exposed rabbits.

DISORDERS OF THE MAMMARY GLANDS

Does usually possess 8 but may have up to 12 mammary glands.[78] Disorders of the mammary glands are inflammatory, infectious, hormonal, or neoplastic and are often accompanied by ovarian or uterine abnormalities, or both.[7]

Septic Mastitis

Mastitis can occur in a lactating doe or in a rabbit in pseudocyesis. Abscesses can develop in the mammary glands independent of lactation, but mastitis is rare in ovariohysterectomized rabbits. Heavy lactation, poor sanitation, abrasive bedding or caging, or injury to the gland or teat predisposes the doe to mammary infection. Mastitis can occur in conjunction with metritis. Clinical signs are depression, fever, anorexia, polydipsia, septicemia, or death of the doe or the young. The mammary glands are firm, hot, and swollen, and the skin is discolored red to dark blue. Infection can begin in one gland and spread to others. Initially, discharge may not be purulent. *Staphylococcus aureus, Streptococcus* species, and *Pasteurella* species are most frequently isolated. Infections with *S. aureus* are associated with severe mastitis.[92] Suckling kits may die of peracute septicemia, particularly with *S. aureus* mastitis.[92,105]

Obtain cytologic and bacterial culture samples by expressing exudate from the gland. Start broad-spectrum systemic antibiotics initially, then modify antibiotic therapy based on results of aerobic and anaerobic culture and sensitivity

testing. Common antibiotic choices are enrofloxacin or trimethoprim-sulfa. Supportive care includes fluid therapy, pain management with NSAIDs or opioids, applying hot packs, and massaging the tissue to promote drainage if not caseous. Surgical excision or mastectomy is often necessary for severe infections. Force-feeding may be necessary if the doe is anorectic. Young rabbits should be removed, but fostering them to another doe may transmit infection; therefore they should be bottle-raised.

Cystic Mastitis, Mammary Dysplasia, and Mammary Tumors

Noninfectious cystic mastitis occurs in both breeding and nonbreeding does. The affected glands are swollen and firm, and a clear to serosanguineous discharge can be expressed from the distended nipples. The glands do not seem painful, and the doe is not depressed. Epithelial hyperplasia, adenosis, papillomatous changes, and cystic mammary glands have been associated with uterine hyperplasia and adenocarcinoma.[43,112] Cystic mammary glands may continue to progress and coalesce, with fibrous connective tissue accumulating around the cysts.[112] Eventually, malignant cellular changes may occur, leading to invasive mammary adenocarcinoma. Metastasis to regional lymph nodes, lungs, or other organs can occur with adenocarcinoma. Mammary adenocarcinomas are not uncommon in 3- to 4-year-old multiparous does.

Evaluate rabbits with clinical signs of cystic mastitis for infectious mastitis and uterine disease. Fine-needle aspiration and cytology of the gland or fluid will assist with the diagnosis of cystic mastitis versus neoplasia. The treatment for noninfectious cystic mastitis is ovariohysterectomy; clinical signs usually resolve within 3 or 4 weeks after surgery. Partial mastectomy or wide excision of mammary tumors is indicated if malignant changes have occurred. The correlation between mammary and uterine disorders suggests that routine ovariohysterectomy of young, healthy does may reduce the risk of mammary neoplasms at a later age.

Several cases of mammary dysplasia associated with pituitary adenomas have been described in older, primiparous New Zealand white rabbits.[80] One or more mammary glands were swollen and firm, with enlarged and discolored teats. Histologically, changes were dysplastic. At necropsy, prolactin-producing acidophil pituitary adenomas were found in affected does.[80] Hyperprolactinemia with mammary dysplasia (the first report of cystic mammary adenocarcinoma associated with a prolactin-secreting pituitary adenoma) in a rabbit was also reported.[94]

DISORDERS OF THE URINARY SYSTEM

Disorders of the urinary tract are common in rabbits. Incontinence, inappropriate elimination behavior, perineal urine scalding, hematuria, stranguria, and pollakiuria are common presenting complaints. In pet rabbits presented to the University of Wisconsin Veterinary Medical Teaching Hospital over a 5-year period, 10% were diagnosed with urinary tract disease.[77] Physical examination and careful abdominal palpation may reveal abnormalities in size, contour, and texture of the kidneys. Uroliths or excess granular material may be palpated within the urinary bladder. Results of a CBC and a serum biochemical profile may disclose changes consistent with acute or chronic renal insufficiency, but normal results do not rule this out. Creatinine is a more reliable test of renal function than blood urea nitrogen (BUN). Prerenal azotemia can be caused by dehydration, because rabbits have limited ability to concentrate urine. Lateral radiographs or ultrasound imaging may help to assess the contents of the urinary bladder and the bladder wall. Urinalysis is useful in assessing renal function and the presence of bacteria, proteinuria, glucosuria, ketonuria, and occult hematuria. Ideally, collect a urine sample by cystocentesis, taking care to avoid the voluminous intestinal tract. Alternatively, gentle manual pressure to the bladder often leads to micturition, and a midstream urine sample can be collected. Catheterization of the urethra is easily performed in male rabbits, whereas catheterization of female rabbits may require endoscopic assistance (Fig. 16.4). For catheterization, low-dose midazolam is recommended for sedation, and 2% sterile lidocaine gel may reduce pain associated with passing the catheter. Normal urine volume is approximately 130 mL/kg per day. Urine is the normal excretion route for calcium and magnesium.[74] The first urine of the morning is the best sample to assess. Clear urine indicates low calcium excretion and is physiologic in growing or lactating rabbits but may be pathologic if renal failure is present. Glucosuria can occur with stress hyperglycemia and should be interpreted with the stress level of the rabbit. Normal pH in rabbit urine is basic (pH 7.7–9.6). Normal rabbit urine has a specific gravity between 1.007 and 1.051.[84] Triple phosphate and calcium carbonate crystals can normally be found in large quantities.[74]

In one study, histologic lesions were observed in the kidneys of 77 of 237 (33%) rabbits that either died or were euthanized because of illness and in 19 of 75 (25%) apparently healthy adult rabbits.[44] This suggests that renal disease is likely underdiagnosed and underreported. Lesions associated with an infectious process such as renal abscesses, staphylococcal nephritis, pyelonephritis, and pyelitis were the principal findings in rabbits up to 5 months of age, whereas renal fibrosis with or without dystrophic calcification was the most common lesion observed in rabbits aged over 10 months.[44] Spontaneous amyloidosis was seen in rabbits, with amyloidosis being found only in the kidneys.[44]

Urolithiasis and Hypercalciuria

Urolithiasis refers to the presence of calculi in the urinary system. Rabbits can have any combination of cystic, urethral, renal, and ureteral calculi (Fig 16.5). The cause of urolithiasis in rabbits is not fully understood, but several factors are involved, including nutrition, anatomy, and, rarely, infection. Hypercalciuria is a clinical condition seen frequently in pet rabbits. Affected rabbits have a large amount of amorphous, pasty to slightly gritty calcium "sand" or "sludge" in their bladders, visible radiographically (Fig. 16.5A and B). A vaginal calculus has been described a rabbit, which may have developed in the bladder or in the vagina itself.[101]

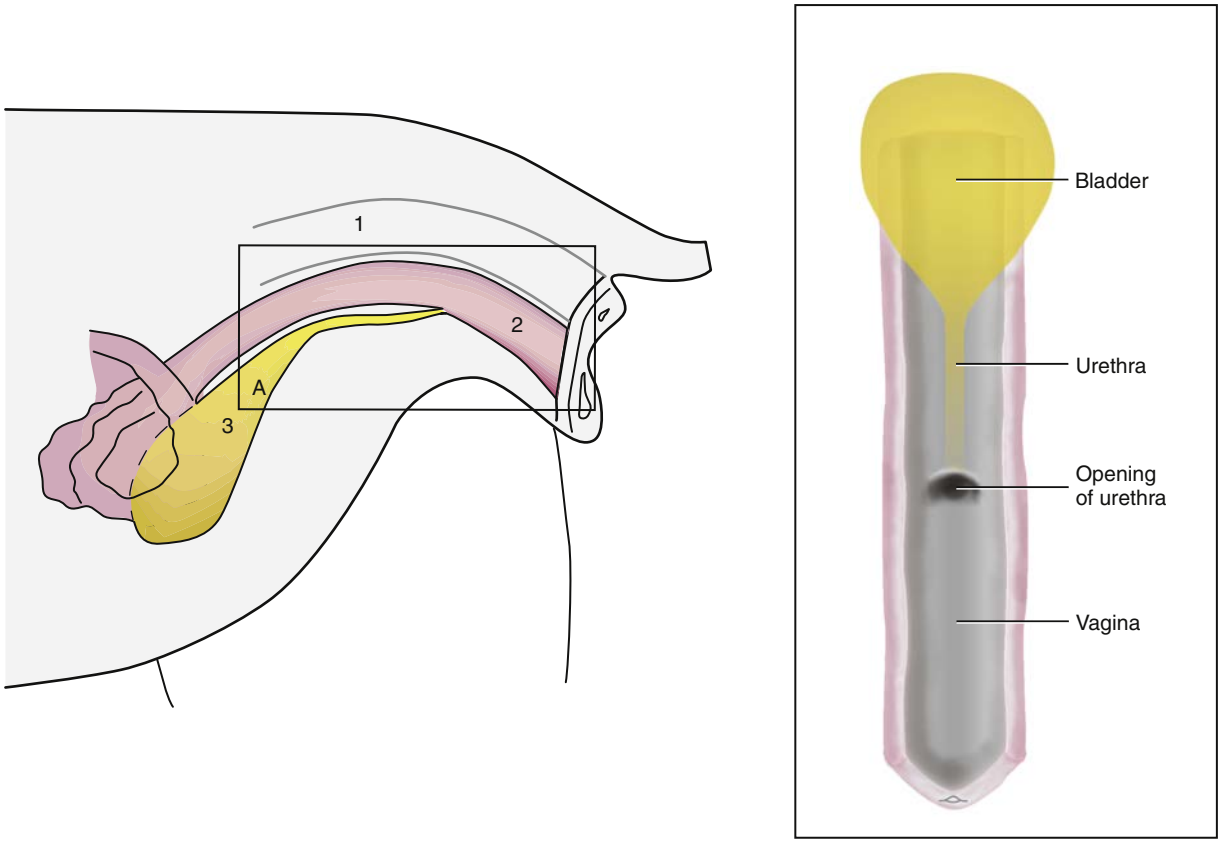


Fig. 16.4 Illustration of the anatomic location of the urethral opening in the female rabbit. The rabbit's vagina is long, and the urethral opening is located at about half the length. The insert illustrates that the opening lies along the midline of the ventral aspect of the vagina under a thin flap of tissue. A catheter must be advanced along the floor of the vagina.

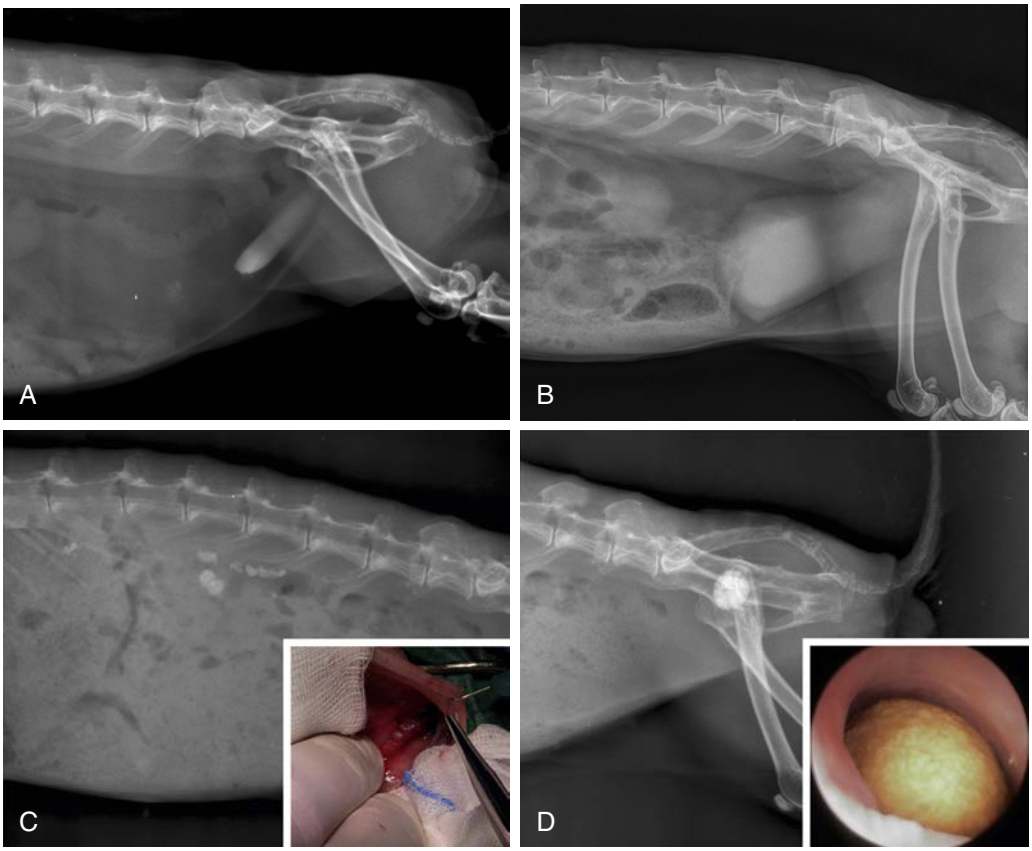


Fig. 16.5 Common presentations of urolithiasis and hypercalciuria in rabbits. (A) A small quantity of sludge is usually managed with diet and hydration. (B) Large quantities of sludge may require urinary bladder lavage. The rabbit in the radiograph suffered of atonic and extremely dilated bladder. (C) Radiographic evidence of multiple ureteral calculi. Ureteral calculi need to be surgically removed when medical therapy is ineffective (inset); (D) Radiographic evidence of a large urethral calculus. Urethral calculi may be endoscopically removed (inset) or retrohydropulsed in to the urinary bladder for later removal via cystotomy. (Courtesy Dr. Nicola Di Girolamo.)

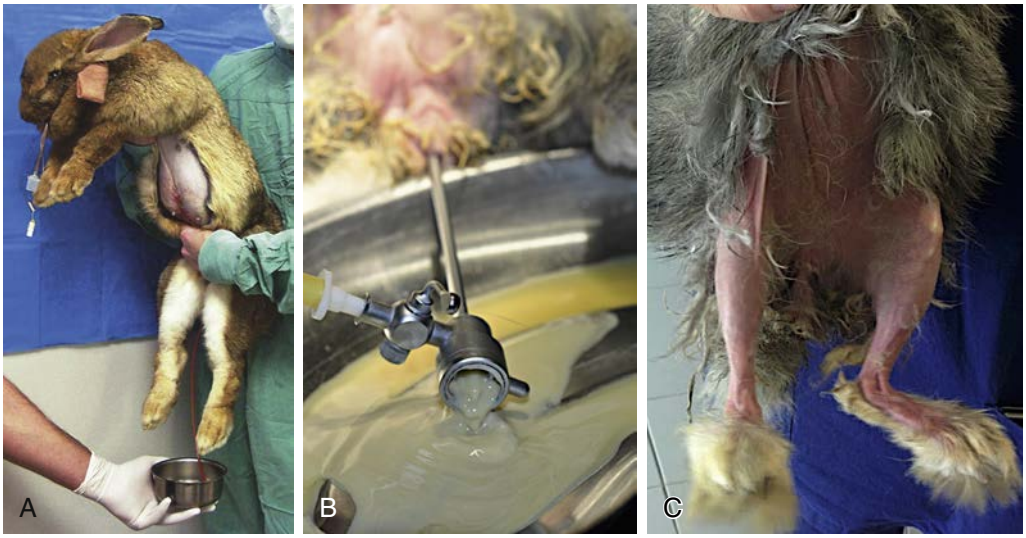


Fig. 16.6 Removal of urinary sludge in rabbits. (A) Manual expression with gentle caudal pressure on the bladder in a catheterized rabbit. The urinary bladder is catheterized and sterile saline is retropulsed into the urinary bladder, where it mixes with the calcium "sand." The bladder contents are then manually expressed to discharge the slurry. This procedure may have to be repeated several times. If the sandy urine flows around the catheter, administer a nonsteroidal antiinflammatory agent. (B) As an alternative, after cystoscopy, the protective sheath of the rigid endoscope is left inside the urinary bladder and sterile saline is flushed several times to completely void the sludge. Notice the thickness of the sludge. (C) Severe perineal scalding that often accompanies hypercalciuria.

Rabbits maximize absorption of dietary calcium, with the excess being normally excreted as calcium carbonate in the urine. Calcium metabolism in rabbits is unusual in that intestinal absorption of calcium is independent of vitamin D_3 levels. Although the fractional urinary excretion of calcium in most mammals is less than 2%, the range in rabbits is 45% to 60%. Increases in dietary calcium directly increase its urinary excretion.[10,14] This hypercalciuria also reflects the 30% to 50% higher blood calcium levels in rabbits compared with other mammals.[74] Phosphorus is excreted in the feces.[74]

Rabbits with either urolithiasis or hypercalciuria often have limited exercise, are fed a diet of free-choice of pellets, high-calcium greens, or alfalfa hay, and tend to be obese. Affected rabbits may have a history of vitamin or mineral dietary supplementation. Clinical signs of hypercalciuria or urolithiasis are depression, anorexia, weight loss, lethargy, hematuria, anuria, stranguria, a hunched posture, grinding of teeth, and urine scald of the perineum. Urolithiasis in rabbits also may be subclinical. Rabbits with hypercalciuria usually have thick, creamy urine and urine scald (Fig. 16.6). Often, voided urine appears only slightly turbid in these rabbits; however, with manual bladder expression, copious amounts of pasty urine are passed. In severe cases, a dough-like mass is palpated in the caudal abdomen, or a turgid bladder is evident if urethral obstruction is present. An enlarged kidney or ureter may be palpated and imaged with ultrasonography if hydroureter or hydronephrosis has occurred.[60] In one report describing a female rabbit, a large cystic calculus became wedged in the pelvic inlet and compressed and indirectly obstructed the bowel.[100]

Confirm the diagnosis of urolithiasis by diagnostic imaging. A discrete calculus or the presence of homogenous radiopacity can be seen in the dependent portion of the bladder or completely filling a distended bladder. A small amount of calcium sand in the bladder is a common incidental radiographic finding in normal rabbits, especially in older animals, because of the presence of amorphous calcium carbonate crystals. Close inspection may be needed to identify stones in the kidneys, ureters, or urethra. Perform an ultrasound examination to detect discrete calculi in a bladder that is distended and diffusely opaque radiographically. If renal calculi are present (Fig. 16.7A), intravenous pyelography or renal scintigraphy (Fig. 16.7B) may be performed to evaluate renal function. Intravenous contrast material can be given intravenously as a bolus to perform an intravenous pyelogram to evaluate renal structure and perfusion, ureteral size and patency, and bladder structure.[85] Glomerular filtration rate can be determined by dynamic computed tomography after infusion of intravenous contrast material.[116]

Urinalysis usually identifies crystalluria. Anhydrous calcium carbonate, ammonium magnesium phosphate (triple phosphate), and calcium carbonate monohydrate crystals are common.[67] Proteinuria and hematuria are usual additional findings. If bacteria are noted on urinalysis, submit a urine sample obtained by cystocentesis for culture. *Pseudomonas* species and *Escherichia coli* are bacteria known to cause cystitis. Results of a CBC and a serum biochemical profile assist in assessing renal function and in developing a prognosis.

Treatment of urolithiasis depends on the location and severity of the calculi, but minimally invasive, endoscopic techniques are increasingly being favored over standard surgical procedures. Uroliths obstructing the urethra may be endoscopically removed or dislodged by catheterizing the urethra, performed carefully with a 3.5- or 5.0-Fr soft catheter of sufficient length to pass the length of the vagina or penile urethra. As mentioned

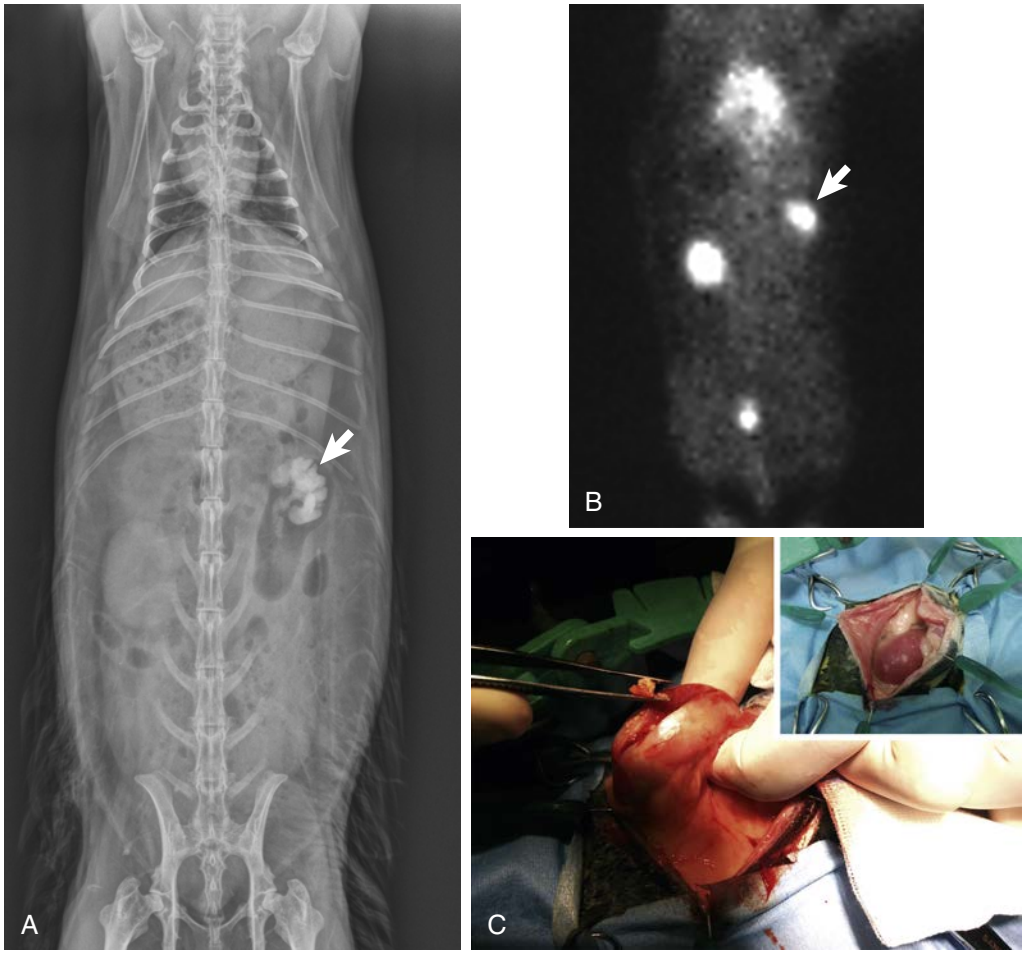


Fig. 16.7 (A) Ventrodorsal radiograph of a 2-year-old female spayed rabbit with a large left renal calculus *(arrow)* conforming to the contour of the dilated renal pelvis. The calculus extends down the proximal ureter on the left. There is evidence of thinning of the adjacent renal cortex due to chronic obstruction of the left ureter. (B) Scintigraphic image of the same rabbit. A photopenic area is visible in the caudal aspect of the left kidney—also cumulatively more radiopharmaceutical uptake in the right kidney than the left *(arrow)*. Relative filtrations were calculated. The left kidney contributed approximately 28% of total filtration and the right kidney approximately 72%. The rabbit underwent left nephrectomy based on the diagnostic information provided by radiology and nuclear imaging. (C) As an alternative to nephrectomy, nephrotomy and stone removal is feasible. The lateral flank approach avoids interaction with the gastrointestinal tract (inset). (C, Courtesy Dr. Nicola Di Girolamo.)

previously, catheterization is a painful procedure; therefore, use topical 2% lidocaine gel to reduce pain associated with passing the catheter. Midazolam provides sedation, as well as relaxation of the urethral sphincter. After catheterization and unblocking of the urethra, the critical supportive treatment for hypercalciuria is aggressive fluid therapy. In intact females, urethral calculi obstructing the distal urethra may be endoscopically retropulsed into the vagina and removed via ovariohysterovaginectomy.[22] Cystotomy is the treatment of choice for large cystic calculi. Preanesthetic benzodiazepines induce muscle relaxation and facilitate the passage of surprisingly large calculi into the urethra. The location of the calculus should therefore be ascertained immediately before surgery on radiographs. Attempts to force small stones out of the urethra during surgery may result in their becoming lodged within the neck of the bladder or in the urethra. Use a surgical spoon to retrieve small stones from the bladder. Flushing and gentle surgical suction can aid in removing fine granular sand. Submit the calculi for analysis and obtain a swab sample or biopsy of the bladder wall for bacterial culture. Perioperative support includes intravenous fluid diuresis, analgesia, and systemic antibiotics. Subsequent radiographic monitoring is helpful because this condition often recurs.

If hypercalciuria or nonobstructive calculi in the kidney or ureter are identified, consider a nonsurgical approach. Fluids administered either intravenously or subcutaneously are necessary to increase diuresis. Manually express the bladder daily for 2 to 4 days to encourage the passage of residual calcium sand that may not be voided during normal micturition. A technique like that used in dogs and cats, termed urohydropropulsion,[63] can be used in rabbits to remove fine granular or small, smooth cystic calculi without surgery. Rabbits must be heavily sedated or anesthetized for this procedure. Administer a preanesthetic benzodiazpine to help relax the urethralis muscle; additionally, opioids, such as butorphanol or buprenorphine,

are recommended because bladder expression is painful. Pass a sterile catheter to administer sterile saline solution into the bladder, then hold the rabbit in an upright position so that the vertebral column is vertical and apply steady pressure to the bladder (Fig. 16.6A). Hematuria is expected to occur for 1 to 2 days after urohydropropulsion.[63]

In cases of renal calculi not responsive to increased diuresis, lateral nephrotomy and manual removal has been successfully performed.[64] An incision is performed on the flank, over the affected kidney. The kidney is visualized and incised and the material removed (Fig. 16.7C). Extracorporeal shock wave lithotripsy has been experimentally applied to rabbit kidneys, but no information is available on a clinical application.[53] Nephrectomy is rarely required as a treatment of urolithiasis and is only indicated in case of severe hydronephrosis caused by chronic presence of an obstructive calculus.[85] Prognosis is guarded for rabbits with either unilateral or bilateral renal calculi.

Dietary changes are an important part of treatment and prevention. The alkaline pH of rabbit urine and the high concentration of calcium in the urine increase the risk of precipitation of solutes.[51] Decreasing dietary calcium levels directly lowers serum and urine calcium concentrations.[14,52] Increasing water intake will also lower calcium concentration in the urine.[106] To reduce calcium intake, feed grass hay (not alfalfa) and low amounts of timothy hay–based pellets. Increase dietary water intake by providing water in a bowl instead of nipple bottle and offering plenty of low-calcium fresh greens such as leaf lettuce. Discontinue any vitamin or mineral supplementation; such supplements are not recommended in rabbits at any time. One investigation determined that a level of 0.22 g of calcium per 100 g of food was necessary for maximal growth[13]; commercial alfalfa-based rabbit pellets contain 0.9 to 1.6 g of calcium per 100 g of food.[10] High-calcium greens such as kale and dandelion should be avoided. Consideration should be given to the hardness of drinking water, especially in polydipsic animals. Because many rabbits that develop urolithiasis are overweight, decreasing caloric intake and increasing exercise are helpful. Urinary acidifiers are ineffective because rabbits are herbivores with naturally alkaline urine.

Renal Failure

Both acute and chronic renal failure can occur in older rabbits. Clinical signs are lethargy, depression, anorexia, polyuria, polydipsia, and perineal urine scalding. Acute renal failure is characterized by a sudden onset of filtration failure by the kidneys, accumulation of uremic toxins, and dysregulation of fluid, electrolytes, and acid–base balance. It is potentially reversible if diagnosed quickly and treated aggressively. In chronic renal failure, there is a history of chronic loss of body condition, anemia, polydipsia, polyuria, and isosthenuria. One or both kidneys may be palpably small, with an irregular surface. Serum creatinine and BUN levels are altered in severe cases, as are serum concentrations of calcium, phosphorus, and potassium. Urine specific gravity can be isosthenuric, but isosthenuria can also be seen in normal rabbits. Urinalysis may show proteinuria, hematuria, pyuria, and cast formation. Urinary protein-to-creatinine ratio may be a further diagnostic test in rabbits with suspect renal failure. The upper limit of the reference range for urine protein: creatinine ratio in *E. cuniculi*–seronegative rabbits was 0.40,[84] with 85% of rabbits with confirmed renal alterations having values higher than 0.40.[93]

Pyelonephritis in rabbits is often caused by *P. multocida* or *Staphylococcus* species. *Encephalitozoon cuniculi* is a common cause of subclinical, chronic, interstitial nephritis. Noninfectious causes of chronic renal disease include hypercalcemia,[32] renal calcinosis or interstitial fibrosis resulting from hypervitaminosis D,[83,115] and fatty degeneration in overweight animals. Lymphosarcoma commonly involves the kidneys, often causing marked renomegaly and resulting in renal failure from infiltrative destruction of the cortices.[112] If an infectious cause is suspected, submit a urine sample for aerobic bacterial culture. Indicators of inflammation in the urine (pyuria, proteinuria, hematuria) occur more frequently with acute than with chronic renal failure.

Treatment focuses on diuresis and diminishing the consequences of uremia. Treatment of acute renal failure involves aggressive fluid therapy divided into three parts: (1) correcting perfusion, (2) correcting dehydration deficits, and (3) diuresis to correct azotemia, electrolyte, and acid–base status. The polyuric or diuresis phase of acute renal failure is after the animal is normotensive and rehydrated. Measure the urine volume produced every 4 hours by placing preweighed, absorptive pads in the cage, weighing the pad every 4 hours, and estimating urine voided by assuming that 1 g equals 1 mL. In acute renal failure, urine production can be as high as 5 to 10 mL/kg per hour. The volume of fluid to be administered in each 4-hour period is the sum of the calculated maintenance requirements (2 mL/kg per hour) and voided urine volume from the previous interval. Additional ongoing losses (such as diarrhea) are added to the volume of administered fluids. Most mammals with acute renal failure become 3% to 5% dehydrated each day because of ongoing losses. Discontinue fluids gradually when hydration and urine production are restored, BUN and creatinine concentrations are normal, and the rabbit is eating and drinking. Tapering fluids by 50% per day will prevent medullary washout. Acute renal failure has a better potential for response to treatment, but the prognosis remains guarded.

Chronic renal insufficiency requires long-term subcutaneous fluid support. Rabbits with chronic renal failure usually develop anemia; therefore frequent reevaluation of a complete blood count, renal values, and serum electrolytes is recommended. Dietary changes previously discussed for urolithiasis are also indicated.

The calcium and phosphorus content of diet markedly influences parathyroid hormone secretion in the uremic rabbit. When placed on a low-calcium, high-phosphorus diet, uremic rabbits develop secondary hyperparathyroidism.[5] Therefore ensure dietary calcium/phosphorus ratios are adequate. Oral phosphate binders may be necessary.

Masugi nephritis is an inflammatory nephritis seen in laboratory rabbits and induced by continuous immunization with large doses of antigen. Tea polyphenols were suggested to be an efficacious treatment for this induced condition.[29,114]

Hypervitaminosis D

Rabbits are sensitive to vitamin D toxicosis, and levels as low as five times normal may result in toxicosis. Adults are more sensitive, although clinical signs of toxicity may take weeks or longer to manifest. Pathologic changes consist of mineral deposition in various tissues, with arteries (especially the aorta) and kidneys being the most sensitive. Gross lesions in the kidneys consist of multifocal, tan-to-gray areas located throughout the cortices. The exact pathophysiology of the soft tissue mineralization is unknown. Clinical signs are nonspecific, making early clinical diagnosis difficult. Because rabbits normally have high serum calcium concentrations, radiographic evidence of soft tissue mineralization, especially of the aorta and kidneys, is most helpful in making the diagnosis.[29]

Nephrotoxicity

Several compounds are nephrotoxic in rabbits. Therapeutic use of gentamicin can result in acute tubular necrosis.[26,55] Diuresis and supplemental doses (10 mg/kg subcutaneously) of vitamin B_6 during aminoglycocide therapy may help protect the kidneys.[26] The tiletamine in the tiletamine/zolazepam anesthetic combination is nephrotoxic in rabbits, inducing nephrosis at low doses and severe irreversible nephrosis at high doses.[8,27] Long-term exposure to therapeutic doses of an NSAID (diclofenac) in experimental rabbits produced significant ultrastructural renal alterations.[99] In another study, increased renal artery vasoconstrictor activity was found after NSAID administration.[57] Rabbit studies support the premise that preexisting renal insufficiency increases the effect of NSAID-induced interstitial nephritis.[15]

Renal Adipose Deposition

Fatty infiltration of the kidney has been reported with pregnancy toxemia during the last week of pregnancy in primiparous, obese does that stop eating after being maintained on high planes of nutrition. Clinical pathologic abnormalities include ketosis, hypocalcemia, hyperphosphatemia, and fluctuating blood glucose levels. Fatty infiltration of the kidneys with subsequent acute renal failure may also occur in conjunction with anorexia and the development of hepatic lipidosis.[29,41]

Renal Cysts

Multiple small, subcapsular cysts in the kidneys occurs as an inherited condition in rabbits. Cysts are either of tubular origin or primitive ductules; the condition resembles renal cortical dysplasia in people.[61] Rabbits with renal cysts are usually asymptomatic, and cysts may be detected on imaging studies or at necropsy.

Of 203 records of New Zealand white rabbits with documented renal histopathology, seven cases of polycystic kidney syndrome were identified by three morphologic criteria: (1) cysts or microcysts derived from tubules, glomeruli, or both; (2) loose mesenchymal expansion of cortical or medullary interstitium; and (3) irregular thickening, thinning, and splitting of basement membranes.[65] This syndrome was associated with hypercalcemia, hypercreatinemia, and arterial mineralization. In the liver, mild chronic cholangitis with cholangiodysplasia and fibrosis was common. Anorexia and lethargy were the clinical signs most often reported.

Renal Agenesis

Renal agenesis, or congenital absence of one kidney, has been reported as an autosomal recessive mutation in one colony of laboratory rabbits.[70] Incidence is high in the Havana breed.[61] The condition is seen in both sexes. In males, the ipsilateral testicle is often missing as well.[61]

Encephalitozoonosis

Encephalitozoonosis, or nosematosis, is a common disease of rabbits. It is caused by *E. cuniculi,* a microsporidian obligate intracellular protozoan parasite (see Chapter 18). Transmission is by urine-oral passage, usually from doe to young. The organism is absorbed from the intestines into mononuclear cells and then distributed systemically. Spores have a predilection for kidneys, brain, and spinal tissue. After inoculation, spores appear in the kidney after 31 days and are excreted in the urine for up to 3 months.[80]

Infections typically result in nonsuppurative, granulomatous nephritis that may progress to interstitial fibrosis, but the disease is chronic and usually subclinical.[30] At necropsy, numerous small pits and stellate scars may be found on the cortical surface of the kidneys in rabbits with chronic encephalitozoonosis. Clinical signs of incontinence result from central nervous system infection rather than renal lesions. Diagnostic tests and therapeutic options for encephalitozoonosis are discussed in Chapter 18.

In a study of 184 rabbits with suspected encephalitozoonosis, 3.5% of 144 serologically positive rabbits had clinical signs of renal failure; 87.5% of these were moribund or euthanized.[58] Polymerase chain reaction did not detect parasite DNA in urine or cerebrospinal fluid.

Urinary Incontinence

Urinary incontinence can be caused by lumbosacral vertebral fractures or dislocations or by central nervous system lesions from *E. cuniculi* infection. Rabbits with urinary calculi or hypercalciuria often exhibit urinary incontinence and urine scalding (Fig. 16.6C). Clinical signs are a urine-soiled perineum, ulcerations of the vaginal mucosa and intertrigonal pouches, as well as sticky, strong-smelling urine. Urolithiasis or hypercalciuria can be identified radiographically. Vertebral fractures or luxations are determined by radiography. A positive titer to *E. cuniculi* and additional CNS signs may suggest a protozoal infection. Other neurologic diseases, such as toxoplasmosis and larva migrans, should also be considered. Additional differentials for urinary incontinence are ectopic ureter, urinary tract infection, neoplasia, and pyoderma.

Ovariohysterectomized rabbits can develop urinary incontinence; in some cases. this is responsive to diethylstilbestrol.[12] Estrogen supplementation mediates a functional hypertrophy characterized by increased contractile responses in rabbits that have undergone ovariohysterectomy. The increased contractile responses might be explained by the increases in vascular density and smooth muscle/collagen ratio.[75] A positive response to

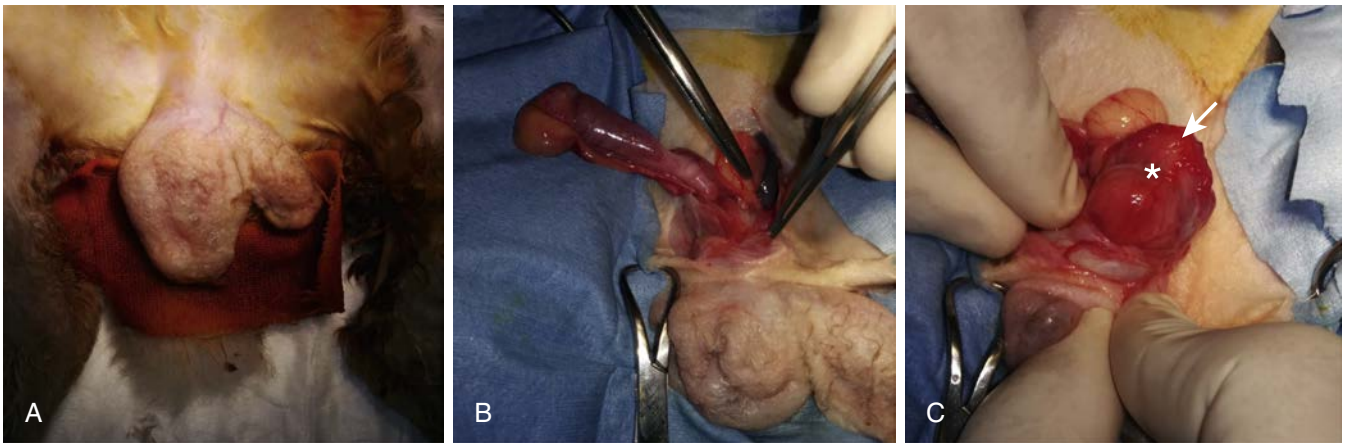


Fig. 16.8 Scrotal herniation of the urinary bladder in a rabbit. (A) The right scrotum is evidently distended. (B) A prescrotal incision is made over the inguinal ring on the herniated side and testicle, urinary bladder, and inguinal ring are visualized. (C) Notice the degree of fibrosis *(asterisk)* present between the urinary bladder *(arrow)* and surrounding tissues. (Courtesy Dr. Nicola Di Girolamo.)

0.5 mg of diethylstilbestrol given orally once or twice weekly to spayed females suggests a hormone-responsive urinary incontinence similar to that seen in dogs. However, treatment of rabbits with diethylstilbestrol or phenylpropanolamine is still under debate, with published results reflecting a scientific study not aimed at therapeutic relief.

Initial treatment includes daily cleaning of the perineum and topical treatment for dermatitis with a drying agent such as Domeboro's astringent solution or a topical hydrogel alternated with a topical silver sulfadiazine cream, in addition to treatment of the primary problem. If there is no evidence of renal insufficiency, NSAIDs can be used to decrease inflammation and provide analgesia. Older, obese, or arthritic rabbits may choose not to urinate in their litter box and appear suddenly "incontinent" to their owner. Using a litter box with easier access (low entry point) and keeping the box clean may be beneficial in these cases.

Psychogenic Polyuria and Polydipsia

Normal rabbits can drink less than 20 mL/kg to more than 130 mL/kg of water per day, depending on the feeding regimen. Urine output varies from approximately 20 mL/kg of body weight in rabbits fed dry concentrate diets (seed mix or pellets) to over 100 mL/kg in rabbits fed hay and greens.[106] Psychogenic polyuria/polydipsia of unknown cause has been reported in four laboratory New Zealand white rabbits.[82] In some affected rabbits, water consumption decreased after environmental enrichment measures were added, suggesting that boredom was a factor.[82]

Scrotal/Inguinal Herniation of Urinary Bladder

Inguinal herniation of urinary bladder has been described in three reports, including one female and seven male rabbits, and is seen frequently in clinical practice.[40,81,102] Male rabbits are likely predisposed to inguinal and scrotal hernias because their inguinal rings remain open throughout life.[81,102] In males, clinical presentation includes unilateral scrotal swelling (5/7 male rabbits), inguinal swelling (1/7), or both (1/7)[81,102]; in females, unilateral inguinal swelling is seen.[40] The swelling is typically fluctuant, and the urinary bladder is not palpated in the abdomen. Thick sludge or stones may be present in the herniated bladder.[40,81,102] Diagnosis is confirmed by radiographs and ultrasonography. Treatment is herniorrhaphy (see Chapter 32) (Fig. 16.8).

Urinary Bladder Rupture

Urinary bladder rupture in a rabbit has been observed by one author (N.D.) after trauma. Ultrasonography demonstrates a small bladder and presence of free fluid in the abdomen. Creatinine concentrations higher in abdominal fluid than in blood indicate uroabdomen.[113] Emergency treatment consists of abdominal lavage and surgical repair of the rupture.

Urinary Bladder Eversion

Transurethral eversion and prolapse of the urinary bladder has been documented in postparturient does shortly after kindling.[38] Multiple kindlings at a young age, along with other undetermined factors, may predispose to the occurrence of this condition.[38] Surgical reduction by laparotomy was successful in one Hotot doe.

Polypoid Cystitis

Polypoid cystitis, an inflammation of the bladder mucosa and development of single or multiple benign polypoid masses, has been described in rabbits.[21,69] The cause is unknown, but it is presumed to be an inflammatory and hyperplastic reaction to chronic irritation of the bladder mucosa.[24] In the two described cases, the rabbits had not been catheterized or had bladder surgery.[21] Both rabbits presented with urinary bladder sludge and calciuria. Large amounts of urine crystals have been associated with papillary hyperplasia of the urothelium in laboratory rabbits,[66] and chronic inflammation caused by stagnation of the sludgy urine may be a trigger for polypoid cystitis.[21] Diagnosis is made by ultrasonography, cystoscopy, and histologic examination of a biopsy sample. In people, treatment for polypoid cystitis is removing the source of irritation.[23] In the described rabbits, removal of the sludgy urine by cystoscopic-assisted

bladder lavage, reducing urinary calcium excretion by feeding a low-calcium diet, and treating with an antibiotic alleviated the clinical signs. However, at necropsy, incomplete remission of the polypoid cystitis was found in one case.

Tumors of the Urinary Tract

Various incidence of renal tumors in rabbits have been reported,[39,44] with an incidence of up to 1.7% (4 neoplasias of 237 rabbits examined).[44] Nephroblastomas are the most frequent neoplasm and may be associated with secondary polycythemia.[3,42,62,110] Other tumors involving the urinary tract are rarely reported (see Chapter 20).[77,87]

Red Urine

Rabbits can excrete porphyrin-pigmented urine that is dark brown, orange, or red and resembles hematuria. Determining pigmented urine from hematuria is fundamental, as porphyrinuria is a benign condition, whereas hematuria indicates a condition that needs to be addressed (e.g., uterine disorders and urolithiasis). Pigmented urine tends to be intermittent and lasts 3 or 4 days. Dietary compounds, ingestion of pine needles, or antibiotic administration may cause increased pigment levels in rabbit urine.

Macroscopic visualization of the urine may assist in the discriminating pigmented urine versus hematuria: typically, pigmented urine has a consistent, solid color, whereas hematuria contains multiple blood clots in a normal-colored urine. However, occasionally urine is diffusely hematuric. Spinning a urine sample in a centrifuge can help differentiate the cause of urine discoloration.[91] With true hematuria, centrifugation results in clear urine over a layer of red blood cells. With porphyrinuria, urine remains discolored after centrifugation. Porphyrin pigments, but not hemoglobin, fluoresce with a Wood's lamp. The presence of more than five red blood cells per high-power field also suggests true hematuria. A positive reaction for blood on a urine dipstick may also indicate hematuria or hemoglobinuria; however, dipstick results have not been validated in rabbits.

Hematuria can originate from the genital or the urinary tract. Blood from the reproductive tract can be associated with adenocarcinoma, polyps, abortion, or endometrial venous aneurysms. Blood originating from the urinary tract can result from cystitis, bladder polyps, pyelonephritis, renal infarcts, urolithiasis, or disseminated intravascular coagulation.[31] Lead toxicosis can cause hematuria and renal damage.[47] History, signalment, physical examination, laboratory tests, radiography, and ultrasound examination will help in determining the cause.

Pigmented urine has been associated with urobilinuria, which may resemble hematuria except that urine samples are negative for blood and positive for urobilinogen.[31] Porphyrias are inherited or acquired disorders of certain enzymes in the heme biosynthetic pathway. Porphyria was reported in an assymptomatic New Zealand white rabbit.[90] Necropsy findings included a pink tinge to the teeth, ultraviolet fluorescence of teeth and femurs, and increased uroporphyrin levels in the urine.[90]

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Dermatologic Diseases of Rabbits

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Skin disease is relatively common in pet rabbits and often is secondary to factors related to management, behavior, or environment.[30] Several factors may predispose pet rabbits to skin disease. Rabbits are social animals with mutual grooming as their natural behavior. However, many pet rabbits are single pets without a bonded companion to groom them. Rabbits can become obese because of diet and lack of exercise and may not be able to "reach" to groom all parts of their body. Decreased grooming may be one of the first signs of illness in asymptomatic rabbits in early stages of disease. Finally, domestic rabbits may be confined to small hutches or cages with inappropriate or soiled bedding and hard flooring, predisposing them to skin damage as a direct result of poor environmental conditions.

BACTERIAL DISEASES

Subcutaneous Abscesses

Subcutaneous abscesses are common in rabbits. Although these can result from obvious skin wounds (e.g., bite wounds) or related to dental disease, sometimes the cause is not apparent. Abscesses can develop as a result of bacteremia caused by infection in a distant location, such as respiratory tract infection caused by *Pasturella multocida*. Subcutaneous abscesses present as fluctuant to firm masses that may or may not be firmly attached to underlying tissues. Often abscesses are nonpainful, and the overlying skin appears normal. The rabbit may appear otherwise clinically normal, although functional disability such as lameness may be present, depending on abscess location. Abscesses in rabbits typically have very thick fibrous walls. Exudate is very viscous and tenacious because of the lack of the enzyme myeloperoxidase in rabbit heterophils, which liquifies pus.[30] Because of the thick fibrous walls and viscous exudate that does not drain, rabbit abscesses can be very difficult to treat both medically and surgically.

Diagnosis can be confirmed by aspiration of purulent material; a 22-gauge or larger needle is required for aspiration because of the viscosity of the exudate. Submit samples for bacterial culture and sensitivity testing to guide antibiotic choice. Because the center of an abscess is often sterile, a sample from

either a scraping or section of the abscess capsule is likely to yield more useful results.

Simple lancing and flushing of rabbit abscesses usually is not effective. Complete surgical excision is the best treatment option for a subcutaneous abscess. However, the feasibility of surgical removal depends on location, involvement of underlying tissue, and underlying disease conditions that might affect clinical outcome.[6] If the abscess cannot be completely excised, then remove as much of the abscess capsule as possible without damaging the structural integrity of underlying tissues. The remaining capsule can then be marsupialized to the surrounding skin and treated as an open wound.[3] Medical-grade honey or an antibiotic/antimicrobial topical cream is sometimes applied topically; however, most rabbits will groom this area, so choice of antibiotic is crucial to avoid dysbiosis. Alternatively, the skin defect/abscess cavity can be packed with an antibiotic-impregnated or antimicrobial packing material. Remove the packing every few days or according to the manufacturer's directions, flush and debride the wound, and then repack the wound on a regular basis until healthy granulation tissue fills in the cavity. Antibiotic-impregnated polymethylmethacrylate (PMMA) beads or calcium sulfate beads (Kerrier LLC, Palm Beach Gardens, FL; kerrier.com) are another therapeutic option for treatment of abscesses[4] (see also Chapter 36). Beads can be prepared incorporating various antibiotics. The beads placed in the debrided abscess cavity will elute antibiotics locally for days to weeks after placement. Beads are particularly useful where the position and depth of the abscess makes complete removal difficult and skin closure is desired, or if the abscess involves a bony cavity such as the mandibular ramus. Once the abscess has resolved, the PMMA beads may need to be surgically removed, whereas calcium sulfate beads will resorb. With any abscess, the success of the treatment also relies on identifying and treating predisposing conditions, such as dental disease. Continue systemic antibiotic treatment for at least 2 weeks or longer after surgery.

Cellulitis

Acute cellulitis is a bacterial infection of the dermis and subcutaneous fat that can develop as a result of distant bacterial infection (e.g., respiratory tract infection). Bacteria often implicated are *Staphylococcus aureus, P. multocida*, and *Bordetella bronchiseptica*.[45] Cellulitis often presents as a painful, erythematous, swollen area of the skin. Animals are often lethargic, inappetant, and pyrexic. Cytologic examination of touch preparations or lesion exudate can confirm the presence of infection, and bacterial culture of fine-needle aspirate samples will guide antibiotic choice. In cellulitis cases, treat with aggressive parenteral antibiotic therapy on the basis of sensitivity test results if possible. Administer nonsteroidal antiinflammatory drugs (e.g., meloxicam) to control pyrexia and provide analgesia. In severe cases, opiate analgesia may be necessary. Cellulitis may eventually result in abscess formation or skin necrosis and sloughing of a dry eschar.

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Reports of methicillin-resistant *S. aureus* (MRSA) in pets including rabbits are increasing. Research has shown that isolates from pets closely match those from human hospitals, and transmission between owners and pets is a risk factor of infection.[86] In one study, 39% of clinically normal rabbits in a rabbit colony were positive for MRSA.[1] Clinical signs are skin and particularly wound infections that are nonresponsive to normal antibiotic treatment. Cytologic examination of the lesions reveals cocci, and diagnosis is confirmed by bacterial culture and sensitivity test results.

Treatment can prove challenging because MRSA is commonly resistant to fluoroquinolones, penicillins, aminoglycosides, tetracyclines, and chloramphenicol. Treatment options are limited and often carry a higher risk of dysbiosis than would otherwise be acceptable. Many MRSA isolates are sensitive to potentiated sulphonamides and doxycycline.[66] However, antibiotics should be prescribed on the basis of the sensitivity test results. Treating with parenteral antibiotics at appropriate dosages carries the best prognosis; however, the outlook is generally guarded. Always ensure complete resolution of the infection before antibiotics are discontinued.

Moist Dermatitis

Moist dermatitis is a superficial colonization of the skin with bacteria often associated with skin maceration. *Pseudomonas aeruginosa* is often implicated; however, other bacteria, especially *S. aureus* and *P. multocida,* may be involved. Predisposing factors are obesity, unspayed females with a large dewlap, urine scalding, dental disease resulting in excessive salivation, or any other condition where an area of fur remains abnormally wet. The underlying skin is usually moist and erythematous. With *Pseudomonas* infection, the fur has a characteristic blue-green color associated with the pyocyanin pigment produced by the bacteria.[57] Cytologic examination of touch preparations reveals numerous bacteria. In suspect cases, submit swab samples of the skin for bacterial culture and sensitivity testing.

For treatment, clip the area and clean the skin with an antimicrobial cleanser such as chlorhexidine. Topical treatments are usually effective, such as astringents (Domeboro's solution) or silver sulfadiazine cream applied sparingly to lesions after cleaning. The underlying cause must be identified and treated for the condition to be resolved.

Ulcerative Pododermatitis

Ulcerative pododermatitis, also known as "sore hocks," is relatively common in pet rabbits. Unlike dogs and cats, rabbits do not have foot pads; instead the skin of the foot is firmly attached to the underlying structures and protected by thick fur. When this fur is damaged and the skin is unprotected, sores can develop. The primary pathologic lesion is avascular necrosis of the skin on the plantar and occasionally palmar surfaces of the feet. Risk factors are management factors, such as hard or rough flooring, inadequate bedding, or inability to move away from soiled bedding (due to hutch size), and physiologic factors, such obesity or poor mobility. Rex rabbits are overrepresented because of the absence of protective guard hairs on their foot pads.

Knowing the movement physiology of the rabbit foot is useful in understanding the pathogenesis of ulcerative pododermatitis.



Fig. 17.1 Alopecia and erythema of bilateral hocks in a rabbit with sore hocks. (Courtesy Katherine Quesenberry, DVM, MPH.)



Fig. 17.2 Nasal lesions and erosions in a rabbit infected with *Treponema cuniculi* (rabbit syphilis). (Courtesy Katherine Quesenberry, DVM, MPH.)

While standing, the rabbit distributes its weight evenly between the hock, metatarsus, and nails. The superficial digital flexor is under tension, allowing the rabbit to hop forward rapidly. Therefore the digits are always slightly flexed. The rabbit foot is mechanically designed such that, during forward motion, the digits press into the ground to lift the hock off the ground. On a hard substrate such as wood floors, weight distribution is altered because the nails are unable to dig into the ground, and digital flexion is prevented. This increases the tension in the superficial digital flexor tendon and consequently the pressure on the boney structures beneath. Rabbits kept on hard flooring find it more difficult to lift the hock clear of the ground, making damage to the hair cover and eventually the skin covering the calcaneus more likely.[30]

In early ulcerative dermatitis, the hair thins over the ventral aspect of the calcanean process and the central tarsal bone (Fig. 17.1). This progresses to hair loss, skin erythema, and then excoriation, ulceration, and infection that can extend into the underlying bone. As the disease progresses, the superficial digital flexor tendon can luxate medially, resulting in a rabbit that cannot flex its digits and is permanently disabled. Similar lesions can occur over the carpometacarpal joints as well. Various grading systems similar to those used in other species have been suggested, by either grade or type of lesion and ranging from mild to severe with bone involvement.[67] Early cases may respond well to treatment; however, in advanced cases, even aggressive treatment may not be successful, and prognosis is guarded.

Always inspect the hock skin and fur on clinical examination. Even mild changes in the skin should not be viewed as normal, and any husbandry and potential underlying management or physiological factors should be evaluated and corrected or addressed. In more severe cases, radiographs are indicated. If infection is present, submit appropriate samples for culture and sensitivity testing.

Treatment relies on a combination of topical preparations, bandaging the hocks, and systemic antibiotics. Avoid clipping fur on the hock if possible. For very mild lesions, topical preparations such as liquid bandages may be all that is required. With more severe lesions, thorough cleaning and appropriate wound care or even surgical debridement is necessary. For initial cleaning, use either dilute chlorhexidine or povidone iodine; subsequently, use a saline flush only so that developing granulation tissue is not disrupted. Debride infected skin and necrotic soft tissues. Primary closure of the skin defect may not be possible or even desirable. Whether the wound has been cleaned or debrided, the ongoing care is similar. Protect the tissue, keep the wound clean, and encourage tissue granulation. Wet-to-dry dressings, topical hydrogel wound dressings or gels, and padded bandages can be used. If the condition has progressed to skin ulceration, analgesia is needed. For mild pododermatitis, meloxicam may be sufficient; however, when underlying soft tissue and boney structures are involved, consider treating with opiates, tramadol, or gabapentin. Treat with systemic antibiotics on the basis of culture and sensitivity test results. In many cases, prolonged treatment with topical wound care, analgesia, and systemic antibiotics is required.

The end-stage of ulcerative pododermatitis is medial luxation of the superficial digital flexor tendon. When this happens, the digits cannot be flexed, the rabbit is forced into a plantigrade stance, and it becomes permanently disabled. At this stage, even aggressive treatment will be unsuccessful, and euthanasia should be considered.

Syphilis

Rabbit syphilis is caused by infection with the spirochete *Treponema paraluis cuniculi*. It is commonly seen in rabbit breeding colonies and occasionally in pet rabbits. Infection is generally sexually transmitted, transmission can also occur by direct contact or contact of the young with an infected dam at birth. Rabbit syphilis is not zoonotic. Rabbits with syphilis typically exhibit redness and swelling progressing to ulceration of the skin in the anogenital region. The skin around the nose, eyes, and commissures of the mouth is also commonly affected, caused by autoinfection during

cecotrophy and grooming (Fig. 17.2). Over 2 to 3 days, the ulcers progress to scabs, giving the characteristic appearance. Eventually the lesions may become proliferative. Some infected rabbits display no clinical signs but are contagious. Serologic screening results suggest that up to 25% of rabbits are infected or have been exposed.[45] Incubation periods may be up to 10 to 16 weeks.[15,20]

Serologic tests that demonstrate exposure to *Treponema* are available commercially; however, definitive diagnosis is by identifying the spirochetes in a lesion scraping by dark-field microscopy or on histologic examination. Serologic conversion takes 8 to 12 weeks in an exposed rabbit, whereas lesions will develop 3 to 6 weeks after infection. Therefore serologic testing is inaccurate in acute cases.

Benzathine penicillin G/procaine penicillin G (42,000–84,000 IU/kg SC every 7 days for 3 weeks) is the initial treatment of choice.[15] Fluoroquinolones are reputedly effective but, with some strains, may only suppress clinical signs rather than eliminate infection.[16,76] Increasingly, resistant infections are suspected, and treatment in these cases can be difficult or prolonged. Always make certain that all rabbits in contact are being treated.

Necrobacillosis

Necrobacillosis is a skin infection caused by the gram-negative anaerobic bacterium *Fusobacterium necrophorum*, which is a normal inhabitant of the rabbit intestinal tract. Disease occurs as a result of fecal contamination of wounds. Swelling, abscess formation, skin inflammation, ulceration, and necrosis may all occur, and underlying structures may also be involved. Cytologic examination of samples from the lesion reveals long, filamentous bacterial rods. Anaerobic culture of tissue samples will confirm the diagnosis. In rabbits with ulcerated wounds or abscesses, debride or surgically resect necrotic tissue, and administer antibiotics effective against anaerobic bacteria, such as penicillin G procaine or metronidazole. Placement of antibiotic-impregnated beads may be helpful in some cases.

FUNGAL DISEASES

Dermatophytosis

Dermatophytosis is common in rabbits.[47] Pet rabbits are most commonly infected with *Microsporum* species, usually *M. canis and M. gypseum,* whereas outdoor and laboratory rabbits are more commonly infected with *Trichophyton* species, usually *T. mentagrophytes*.[65,89] Other dermatophytes that have been isolated from rabbits are *M. gypseum, M. audouinii, M. cookie, T. verrucosum, T. ajelloi, T. terrestre,* and *T. schoenleinii*.[37,45,47,65] Rabbits become infected from contact with other infected animals or people or through fomites such as contaminated housing or grooming brushes. Young rabbits are predisposed to infection probably because of low levels of fungistatic fatty acids in their sebum.[47] An asymptomatic carrier state has been recognized in both laboratory and pet store rabbits, with prevalence ranging from 0.5% to 35%.[3,82] In wild rabbits, prevalence is as high as 26%.[27] Subclinical carriers can develop overt signs of disease in response to stress, such as overcrowding, malnutrition, or systemic disease. Early lesions are found on the head, especially the nasal planum, eyelids, and pinnae. Infection generally spreads by grooming to other areas of the body, typically the legs, feet, and occasionally the nail beds. Lesions appear as patchy areas of alopecia with varying degrees of erythema and dry, yellow crusting.

Diagnosis is based on clinical signs and results of specific testing, that is, typical apple-green fluorescence under Wood's lamp (isolates of *M. canis* only), examination of infected hair shafts, dermatophyte culture of fur samples, indirect enzyme-linked immunosorbent assay, and biopsy. Arthrospores can be seen on infected hair shafts in samples mounted in 10% potassium hydroxide or lactophenol cotton blue. An indirect enzyme-linked immunosorbent assay has been developed for the early diagnosis of *Trichophyton* infection in rabbits.[91,92] Although histopathology can be helpful in diagnosis, it is not the most sensitive method. Skin biopsy samples can be stained with special stains such as periodic-acid Schiff, Gridley, or Gomori's methenamine silver stain to identify fungal elements.

In many healthy rabbits, infection is self-limiting. However, treatment accelerates recovery and reduces the risk of transmission to other animals and people.[47] With focal lesions, clip the area to remove surrounding hair and treat with topical antifungal drugs such as clotrimazole or miconazole cream or lotion.[10,45] For more widespread lesions, other topical therapies are 2% chlorhexidine applied twice daily; antifungal shampoos such as 2% miconazole shampoo[37]; weekly lime sulfur dips (1:16 dilution)[10]; or 0.2% enilconazole twice weekly.[65] With lesions that are more generalized or have not responded to topical therapy, prescribe a systemic drug such as itraconazole (5–10 mg/kg orally [PO] every 24 hours),[28,50] terbinafine (10 mg/kg every 24 hours),[51] or griseofulvin (15–25 mg/kg PO every 24 hours or divided every 12 hours for 30 days)[7,38] (see also Appendix). Lufenuron (135 mg/kg PO every 4 weeks) is anecdotally effective in rabbits but not in cats; it is used mainly as adjunct treatment.[19,47] Treat with systemic therapy until two negative fungal cultures are obtained 7 days apart. Treat all in-contact animals. Environmental treatment includes thorough cleaning of the housing area to remove any organic material before disinfecting with either commercial disinfectants effective against fungi, bleach diluted 1:10 with water, or spray or foggers containing enilconazole.[47] In large rabbit colonies, use environmental treatment combined with topical treatment with lime sulfur and systemic itraconazole or griseofulvin to resolve infection. Griseofulvin can be added to food at a dose of 0.825 mg/kg of food until negative cultures are obtained as above.[2]

PARASITIC DISEASES

Ear Mites *(Psoroptes cuniculi)*

Psoroptes cuniculi is an eight-legged, obligate, psoroptiform mite that is large, oval, and 400 to 750 µm in length. It is differentiated from other psoroptiform mites by the presence of short, segmented stalks with a single bell-shaped structure on the end of each of the first two pairs of legs. Mites feed by piercing the skin and browsing on loose epidermal debris. Lesions in part may be caused by a hypersensitivity reaction to mite feces and saliva.[30,65] The 21-day life cycle is spent entirely on the animal, but mites can survive off the host for weeks in normal environmental temperatures.[65] *Psoroptes* mites are highly



Fig. 17.3 Severe ulcerative, scaling dermatitis of the ear, pinna, and surrounding skin in a rabbit with ear mites (*Psoroptes cuniculi*). (Courtesy Jan Declercq, DVM.)

contagious and spread by direct contact with infected rabbits and fomites (especially bedding material). Healthy rabbits may harbor low-grade subclinical infection for long periods and present with only mild pruritus.[45,89] In the early stages of infection, a dry grayish-white to tan crusty exudate is visible inside the ear canal.[47] As the disease becomes more chronic, the exudate becomes thicker, dark brown, and more extensive, often filling the ear canal and extending onto the pinna (Fig. 17.3).[30] Ears will often droop under the weight of the debris. In severe cases, the crusty material spreads to the head and neck and then to other areas of the body through grooming. Affected rabbits shake their heads and scratch at their ears, causing excoriation and fur loss around the pinna and neck. Secondary infection can occur, and the disease can spread to involve the middle and inner ears, leading to a head tilt and vestibular signs.[46,65,89] Mites can be seen with the naked eye, otoscope, or microscope. Microscopic examination of ear wax mounted in mineral oil or 10% potassium hydroxide reveals mites, mite feces, or eggs.

Ear mites can be treated with a range of parasiticides such as ivermectin (0.2–0.4 mg/kg subcutaneously [SC] or 0.45 mg/kg topically every 7–14 days for 3 treatments),[8,17,18,47,60,69] selamectin (6–15 mg/kg topically every 4 weeks for 2 to 3 treatments),[61,65,89] moxidectin (0.2–0.3 mg/kg PO; 2 doses 10 days apart),[65,85] moxedectin with imidocloprid (1 mg/kg and 10 mg/kg, respectively, topically every 4 weeks for 3 treatments),[29] eprinomectin (200–300 µg/kg SC)[68,81,88] and permethrin (2 mg of 2% permethrin spray applied to the ear canal on a single occasion)[62] (see also Appendix). Recently, fluralaner (25 mg/kg PO) administered as one dose has been shown to be effective in eliminating *Psoroptes* mites in 12 days.[77] Do not try to remove or soften crusts initially, because this is very painful and can cause bleeding. Administer meloxicam as needed for pain and irritation. After the mites have been treated and irritation is resolved, any residual crusts can be cleaned from the ear. Treat all in-contact animals, and clean the environment thoroughly to remove all organic material, including loose hair and crusts that will harbor mites. Disinfect or discard grooming equipment, and treat contaminated areas with flea products.



Fig. 17.4 White flaky debris and scaling ("walking dandruff") characteristic of fur mites (*Chyletiella parisitovorax*) on the dorsum of a rabbit. (Courtesy Katherine Quesenberry, DVM, MPH.)

Fur Mites

Cheyletiella parasitovorax

Cheyletiella parasitorvorax is a nonburrowing mite that is common in rabbits.[38,45,78] The mite lives on the superficial keratin layers of the epidermis, with a life cycle of 14 to 21 days. Eggs adhere to the hair shafts, and eggs and females can survive for at least 10 days off the host.[65] Although *Cheyletiella* can cause subclinical disease, severe infestations can be seen in rabbits that have grooming difficulties because of dental disease, obesity, or musculoskeletal disease or in young or immunosuppressed animals.[30,65] Mites are found predominantly on the dorsal neck and trunk, sometimes extending to the hindquarters and abdomen. Lesions consist of white, flaky, dry, dermatitis, which is often pruritic and associated with erythema and patchy alopecia (see Fig 17.4).[2,45,52,89] In severe disease, the mites can be seen with the naked eye as moving clear to white structures, leading to the term "walking dandruff."[45] Cheyletiella is transmissible to dogs and cats and zoonotic to people,[38,63] in whom it causes a mildly pruritic papular dermatitis.

Mites can be identified by microscopic examination of superficial skin scrapings, acetate tape preparations, or examination of dandruff collected by flea comb. If material is mounted in oil, the motility of the mites can be used to aid identification. If samples are not viewed immediately, the mites will curl up in oil, making identification difficult; in these cases, potassium hydroxide is a better mounting material, which also clears extraneous keratin and debris. *Cheyletiela* mites are saddle-shaped with inward curving claws, hook-like mouth parts, and short, hair-like setae at the distal end of their limbs.[37,45] Skin biopsy is not the best way to diagnose disease, but, when done, histopathologic examination reveals hyperkeratosis with a mixed inflammatory cell infiltrate.[45]

Treat affected rabbits with either ivermectin or selamectin at dosages used for ear mites, lime sulfur dips (1:32 to 1:16 dilution every 7 days for 4–6 treatments), or carbaryl flea powder (topically 2 times weekly for 6 weeks)[37,65] (see also Appendix). Treat all in-contact dogs, cats, and rabbits, and thoroughly clean

the environment before treating with flea products such as 5% carbaryl dust.[45] Address underlying predisposing factors such as obesity or musculoskeletal disease where possible.

Other Fur and Skin Mites

Leporacarus (Listrophorus) gibbus is a nonburrowing, nonpathogenic fur mite that affects both wild and domestic rabbits worldwide.[47] The mites browse on surface keratin and sebaceous secretions. The life cycle is completed on the host, and mites and eggs are found attached to hair shafts. The mite is usually nonpathogenic even if heavy infestations are present. Often it is present with other mites, especially *C. parasitovorax*. When clinical signs occur, they are usually associated with an underlying predisposing cause. Lesions consist of a pruritic, scaly, erythematous, alopecic dermatitis located at mite-feeding areas on the dorsum, ventral abdomen, and tail. Brown mites can be seen with the naked eye, attached to hair shafts.[47] *Leporacarus* mites can cause lesions in people.[21] Diagnostic tests are the same as described for *Cheyletiella*. *Leporacarus* mites are brown, laterally compressed with short legs and single projections extending from the head. Males have long clasping organs projecting caudally from their bodies. The eggs are smaller, stick more distally, and are less firmly attached to the hairs than those of *Cheyletiella*.[47] Drugs used for the treatment of *Cheyletiella* are suitable for *Leporacarus* infestations. In addition, treatment with imidocloprid with permethrin (0.1 mL/kg topically every 4 weeks)[5] and moxedectin with imidicloprid (1 mg/kg and 10 mg/kg, respectively, topical every 4 weeks for 3 treatments)[21] have been described. Empty mite cuticles will persist in the fur after the mites have been killed.

Sarcoptes scabiei var. cuniculi and *Notoedres cati var. cuniculi* are highly contagious burrowing mites that can be found in laboratory, commercial, and, less commonly, pet rabbits.[2,38] Both represent rare causes of skin disease in rabbits.[47] Female mites tunnel through the epidermis where they lay eggs, whereas males and older larvae live on the skin surface. The life cycle is 2 to 3 weeks. Lesions present as a highly pruritic, yellow, crusty dermatitis. With *Notoedres,* lesions are confined to the head, whereas with *Sarcoptes,* lesions occur on the head, neck, trunk, and external genitalia.[45,47] Severe infestations can cause anorexia, emaciation, and death.[47] Diagnosis and treatment are similar to those described for *Cheyletiella*. Ivermectin is an effective and safe therapy for both *Sarcoptes*[49,53] and *Notoedres* mites.[42,64,70] For *Sarcoptes* mites, selemectin[23,55,64] and doramectin (0.2 mg/kg of 1% solution given SC for two injections at 10-day intervals[84]; or 0.4 mg/kg of 1% solution for three injections at 80-hour intervals)[49] may be effective. Fluralaner is effective in dogs for *Sarcoptes* mites and may also be effective in rabbits, as it is for *Psoroptes* mites.[57,75]

Demodex cuniculi is a thin, elongated mite that is an obligate, host-specific parasite of rabbits. Although it can be a rare cause of dermatitis,[54] it is considered a normal resident of the epidermis and hair follicle in rabbits.[35] In clinical cases, alopecia, seborrhoea of the periocular skin with otitis externa, and crusting dermatosis of the face, head, and neck have been described.[54] Immunosuppression may result in clinical disease.[37] Diagnosis is made by identifying the mites, immature stages, and eggs from rabbits with clinical signs. Described treatments include ivermectin [64] or amitraz (diluted to 0.05% and treated weekly for six treatments[35]).

Ornithonyssus bacoti (tropical rat mite) is a blood-feeding ectoparasite with a worldwide distribution. Usually only the feeding stages, the protonymphs and adults, are found on the host. After feeding, mites drop off into the host's environment to moult or lay eggs. Clinical signs are usually associated with severe pruritus, generalized diffuse hair loss, crusts, and secondary infection. Anemia can develop with severe infestations or in young animals.

Isolating mites can be difficult because they are on the host only when they feed. Mites can be collected from the environment by using "sticky cards" (cardboard with a glue surface). Treatment of mites is as described for *Cheyletiella*, and environmental rather than animal treatment is more important. Pyrethrin dust has been described as an environmental treatment in a colony of rabbits infested with *O. bacoti*.[12]

Fleas

Fleas that infest rabbits are *Ctenocephalides felis* (cat flea), *Ctenocephalides canis* (dog flea), *Spilopsyllus cuniculi* (rabbit flea), *Cediopsylla* simplex (Eastern rabbit flea), *Odontopsyllus multispinosus* (giant Eastern rabbit flea), *Echidnophaga gallinacea* (stick tight flea), and *Hoplopsyllus* species.[37,45,65,89] Pet rabbits are most commonly affected by cat or dog fleas.[38,47] In rabbit colonies infested with *S. cuniculi*, the flea life cycle is affected by the hormonal cycle of the does. Outbreaks occur most commonly in pregnant does and in young animals.[87]

Rabbits with fleas usually have dull coats with patchy alopecia, pruritus, erythema, and variable degrees of crusting. Hair epilates easily. *Spilopsyllus* fleas commonly affect the face and pinnae, whereas *Ctenocephalides* fleas affect the dorsum and tail.[7,30,33] Severe infestations may cause anemia in young rabbits. Fleas also transmit myxoma virus. Fleas infestations can be diagnosed by finding fleas, flea feces, or eggs on the rabbit.

Effective treatments are topical application of imidacloprid/permethrin (0.1 mL/kg topically every 4 weeks) or selamectin, or oral lufenuron (30 mg/kg PO every 4 weeks).[30,39,64] Selamectin does not have prolonged residual activity in rabbits because of its very short half-life compared with that in cats and dogs.[11] Fipronil is not recommended for use in rabbits, because deaths have occurred after its use.[89] Treat in-contact animals and the environment to avoid reinfestation. Suitable products include insect growth regulators and insecticidal sprays. Remove rabbits from the environment during treatment.

Lice

Haemodipsus ventricosus (sucking rabbit louse) is rare in pet rabbits but common in wild lagomorphs in Europe.[47] Lice are host specific and spend their entire 14- to 21-day life cycle on the host, living only a few days in the environment. Pediculosis is commonly associated with poor husbandry. Rabbits with lice exhibit pruritus, erythema, papules, and alopecia because of self-inflicted trauma. In severe disease, rabbits may lose weight, become anemic and emaciated, and die.[37,89] Lice also may transmit tularemia.[30,89] Pediculosis is diagnosed by finding

lice and eggs. Lice are large insects, 1.5 to 2.5 mm long, and are commonly found on the dorsal and lateral body and around the perineum.[30] Eggs are larger than those of *Cheyletiella,* opeculate, and are firmly attached to hairs along their whole length. Ivermectin administered every 2 weeks for three doses is effective treatment.[47]

Black Flies

Black flies (*Simuliidae* species) are tiny biting flies that can spread myxoma virus. Flies reproduce in running water and are found seasonally in early spring and summer, feeding in sparsely haired areas of the body. Bite lesions are painful, pruritic papules with associated crust and scale, often with ulceration and hemorrhage, on the lips, ears, and nares. Fly avoidance and protective screens can help prevent fly feeding.

Ticks

Both ixodid (hard) ticks and argasid (soft) ticks are found primarily in wild rabbits. Ticks are rare in pet rabbits, primarily affecting rabbits housed outdoors. The most common hard tick in wild rabbits in the United States is the continental rabbit tick, *Haemaphysalis leporispalustris*.[13] Other ixodid ticks that affect rabbits are *Ixodes*, *Amblyomma, Boophilus, Rhipicephalus,* and *Dermacentor* species.[47] Argasid ticks found in rabbits include *Otobius lagophilus, Ornithodoros parkeri,* and *Ornithodoros turicata*.[47] Ticks are vectors of several diseases in rabbits, including myxomatosis, Lyme disease, Rocky Mountain spotted fever, and tularemia. Ticks attach around the ears, neck, and dewlap, causing local irritation from bites. Heavy infestations can cause anemia through blood loss. Remove visible ticks with forceps. Administer a single dose of ivermectin to kill remaining feeding ticks.

Myiasis (Flystrike, Blowfly Strike)

Myiasis is the parasitic infestation of the body of a live mammal by fly larvae. Myiasis is caused by host-specific obligate flies (*Cuterebra* species, *Wohlfahrtia vigil*) or faculative free living flies (*Lucilia* species). Botflies of the subgenus *Cuterebra* parasitize rabbits, especially wild rabbits.[43] Occurrence is highest in juvenile rabbits in late summer and fall. Female *Cuterebra* flies lay their eggs in rabbit runs and near burrows. As the rabbit brushes past, the eggs hatch and first-stage larvae crawl into the rabbit fur, entering the body through nasal or oral openings. Larval migration ensues, leading to the formation of cysts in subcutaneous tissue of preferred sites such as the ventral cervical region (*C. horripilum*) or axilla, rump and inguinal areas (*C. buccata*).[9] Aberrant larval migration can lead to neurologic signs.[37] As the larvae mature, a breathing hole or fistula develops, with discharge that mats the surrounding fur (Fig. 17.5). Each cyst contains a single larvae, 1 to 3 cm long. Secondary bacterial infection and local pain can lead to weakness, anorexia, and shock.[37,47]

Fly strike on living animals can be primary or secondary. With primary fly strike, usually involving *Calliphoridae* species, flies are attracted to soiled skin to lay eggs. The larvae that develop are capable of penetrating intact skin. In Europe, *Lucilia* species blowflies (greenbottle flies) are a common cause of primary myiasis in rabbits.[41,45,65] With secondary fly strike, larvae do not penetrate skin but attack an area of already damaged skin. The obligate secondary blowfly *Wohlfahrtia vigil* (gray flesh fly), common in the United States, lays eggs in wounds or body orifices of rabbits.[47] Myiasis occurs year round in warm climates and seasonally in summer and autumn in temperate areas. Predisposing factors are fecal or urine staining due to poor husbandry, debilitation due to obesity or neuroskeletal disease (especially spinal disease), inadequate grooming due to dental disease, and urinary incontinence.[65] Maggots cause moist dermatitis leading to erosions, ulcerations, and extensive tissue damage.[47] Hundreds of larvae may colonize a single skin area. Matted fur may conceal the extent of maggot damage, and rabbits may present initially with inappetance. Further tissue destruction can lead to shock and secondary bacterial infection.



Fig. 17.5 Swollen subcutaneous nodule with ulceration and fistula formation caused by *Cuterebra* larva in a rabbit. (Courtesy Katherine Quesenberry, DVM, MPH.)

Treatment involves removing the larvae, treating tissue damage, and managing any underlying disease process. To remove *Cuterebra* larvae, carefully extend the breathing hole to remove the larvae whole to avoid risk of anaphylaxis. If maggots are present, manually remove all larvae. Wound care includes clipping the fur around the area, debriding all necrotic tissue, and thoroughly flushing the wound, followed by continued application of topical silver sulphadiazine cream. Systemic antibiotic therapy and analgesics are indicated, and supportive care is essential.[37,65] Ivermectin can be administered for two treatments to kill any remaining or newly hatched larvae. Preventative treatment involves fly control and confinement of rabbits at risk to an indoor environment.

ENDOPARASITIC DISEASES INVOLVING THE SKIN

Oxyuriasis

The rabbit pinworm (*Passalurus ambiguus)* commonly inhabits the small intestine, cecum, and colon of both wild and domestic rabbits. Gravid females travel from the colon to the anus to lay eggs on the perineum. The worms are nonpathogenic, but the eggs can cause perianal pruritus. Diagnosis is based on clinical signs and identifying eggs on tape strips from perianal

skin or in fecal samples. Treatment includes cleaning pinworm eggs from the perianal area and administering anthelmintics (see Chapter 15).[22,32]

Tapeworms

Rabbits are the intermediate host of the several species of tapeworms that infect dogs and foxes (see Chapter 15). Ingested eggs hatch in the small intestine, then the larval tapeworms burrow through the small intestine and travel to the subcutaneous and intramuscular connective tissue. The coenurus develops in the connective tissue and presents as a swelling or space-occupying mass. Cysts up to 4 to 5 cm diameter occur in many different sites including the retrobulbar space, cheek, and axilla.[47] Diagnosis is based on clinical signs and ruling out other potential causes, such as abscesses or neoplasia. Surgical removal of the cyst is the treatment of choice.

VIRAL DISEASES

Myxomatosis

Myxoma virus is a poxvirus found naturally in *Sylvilagus brasiliensis* (jungle rabbits) in Central and South America and in *Sylvilagus bachmanni* (brush rabbits) in California. In *Sylvilagus* rabbits, infected animals develop cutaneous fibromas but do not develop systemic disease. However, *Oryctolagus* rabbits develop severe and generally fatal systemic disease. Since its first use in 1950 as a biologic means of controlling wild rabbits in Australia, both attenuated strains, as well as more resistant strains of myxoma virus, have evolved. The mortality rate is now lower, and successful treatment of selected cases has been reported.[24]

The incubation period of myxomatosis is 8 to 21 days. Infection can occur by either inoculation through biting arthropods (fleas and mosquitos) or by direct contact (uncommon). Clinical signs range from swelling of the eyelids and ear margins progressing to more generalized facial swelling; genital swelling and ocular discharge can also occur. Severely affected rabbits are pyrexic, lethargic, and systemically ill. Skin nodules up to 1 cm in diameter can develop. In severe cases, rabbits die from septicemia within 10 to 14 days of infection. Diagnosis can often be made on the basis of clinical signs alone; however, in less severe cases serologic testing and histopathologic examination of biopsy samples will confirm disease.

In the United Kingdom and Europe, vaccination against myxomatosis is recommended for all pet rabbits. Because infection is spread by insect vectors, even house rabbits should be vaccinated. In cases of infection with an attenuated virus strain or when rabbits exhibit disease resistance, treat supportively with nonsteroidal antiinflammatory drugs, fluid therapy, supported feeding, and antibiotics to prevent secondary infection. Rabbits that have been vaccinated may contract a less severe form of the disease, exhibiting scabbed lesions around the eyes, nasal planum, and bridge of the nose. In these cases, wound care of the scabbed lesions as they slough is often helpful.

An acute or peracute form of myxomatosis caused by a variant strain is seen in southern California.[72] Rabbits can die acutely within 5 to 7 days after infection. Unilateral or bilateral periocular swelling with injection of the conjunctiva can be seen in some individuals, and rabbits may exhibit perineal edema and skin hemorrhages shortly before death. There is no effective treatment.

Shope Fibroma Virus

Shope fibroma virus is a tumorigenic poxvirus that is endemic in *Sylvilagus* species in both North and South America. Biting insects such as mosquitos can inoculate the virus into domestic rabbits. Rabbits develop fibromatous skin lesions on the feet and legs, and occasionally face and back, that regress over time. Young or immunocompromised individuals can develop generalized disease that can be fatal. Definitive diagnosis is by histologic examination. Disease is often self-limiting; however, surgical resection of masses that impede mobility, cause discomfort, or become abraded or secondarily infected may be required.

Shope Papilloma Virus

Shope papilloma virus is a papovavirus that occurs naturally in *S. bachmani* and *S. floridanus*. Infection in domestic rabbits is rare and is likely due to viral inoculation by biting insects. Large keratinized papillomas develop around the face and ears that can restrict or prevent eating. Diagnosis is based on clinical signs, with histologic evaluation of the lesions if required. Papillomas can be manually or surgically removed. In *Sylvilagus* species, this results in healing of the area; however, in *Oryctolagus* species, experimental inoculation of the virus can result in malignant transformation to squamous cell carcinoma.[72] Insect vector control is the best prevention.

Oral Papillomatosis

Oral papillomatosis is caused by a distinct papillomavirus and is characterized by small, wart-like lesions that develop on the oral mucosa. Spread is by direct contact, and disease is most common in young or immunosuppressed animals. Clinical signs and histologic examination of biopsy samples are diagnostic. Oral papillomatosis is not known to undergo carcinomatous transformation. Treatment is not generally required; however, localized lesions that impede eating or are repeatedly traumatized may need to be removed.

Rabbit Pox

Rabbit pox was first recognized in laboratory rabbits in the 1930s.[79] Rabbits infected with this poxvirus exhibit eruptions over the skin and mucous membranes, lethargy, pyrexia, lymphadenitis, and, in some cases, orchitis, keratitis, and respiratory signs. Rabbit poxvirus has been reported only in laboratory colonies, and no commercial testing is available. Risk in pet rabbits is minimal.

NEOPLASIA

Skin neoplasia in rabbits can be of viral or nonviral origin (Table 17.1). Viral causes of skin neoplasia, including Shope fibroma virus and Shope papilloma virus, are discussed above. Primary skin neoplasms that are of nonviral origin are uncommon in rabbits,[83] with basal cell tumors being the most prevalent.[48] Spindle cell sarcomas, cutaneous hemangiomas, preputial

TABLE 17.1 A Summary of Observed Cutaneous Neoplasms Reported in Pet Rabbits

Tumor Origin	Tissue Type	Tumors Reported
Viral	—	Shope fibroma Shope papilloma
Nonviral	Epithelial	Apocrine carcinoma Trichoblastoma Basal cell tumors Meibomian adenoma Squamous cell carcinoma Trichoepithelioma Tricholemmoma Sebaceous gland carcinoma
Nonviral	Mesenchymal	Lipoma/liposarcoma Neurofibrosarcoma Haemangiosarcoma Myxosarcoma Malignant fibrous histiocytoma Extraskeletal osteosarcoma Fibrosarcoma Leiomyoma/leiomyosarcoma Rhabdomyosarcoma
Nonviral	Other	Malignant melanoma Lymphoma: epitheliotrophic and non-epitheliotrophic



Fig. 17.6 Subcutaneous nodular mass with erythema, alopecia, and ulceration in a rabbit with cutaneous lymphoma. (Photo courtesy Katherine Quesenberry, DVM, MPH.)

tumors, and cutaneous lymphoma are also diagnosed (Fig. 17.6). A variety of other malignant neoplasms can manifest as cutaneous or subcutaneous masses (see also Chapter 20).

The clinical signs of cutaneous neoplasia can vary from atypical or unusual skin lesions to cutaneous masses. Diagnosis generally relies on cytologic examination of touch preparations or fine needle aspirates or histologic examination of full-thickness biopsy samples. Once neoplasia is diagnosed, staging should be considered to determine the most appropriate treatment options. Surgical or medical therapy can be considered.

BEHAVIORS AFFECTING THE SKIN

Barbering

Barbering is caused by one animal (either a dominant or submissive animal) overgrooming another.[38,47] Self-barbering occurs primarily in does in estrus when they are nesting and in rabbits on a low-fiber diet. Barbering also may represent maladaptive behavior that develops as a result of environmental stress.[80] In affected animals, areas of fur appear chewed, leaving roughened edges and sometimes approaching baldness. Other causes of self-trauma and pruritis must be ruled out. Treatment depends on the initiating cause. Ensuring that the diet has adequate fiber, providing environmental enrichment, and noting the dynamics of the pair or group can be helpful. Spaying intact does will prevent hormonally stimulated barbering. Medical treatment is usually not required.

Self-Mutilation

Self-mutilation is a recognized disorder in pet rabbits that, like barbering, may represent a maladaptive behavior that develops secondary to environmental stress.[80] However, conditions leading to pruritus, dermal pain, or altered skin sensation should be ruled out. Self-mutilation has been observed after injection of irritant substances (e.g., intramuscular ketamine or enrofloxacin). It is a recognized genetic problem in laboratory rabbits.[40] Rabbits that are painful at an inaccessible location may self-mutilate as a displacement behavior, such as in a rabbit that obsessively licks or chews its dewlap. In rabbits that self-mutilate, the underlying cause must be identified simultaneously with treatment of the skin damage. Assess the environment, take a detailed behavioral history, and do diagnostic sampling and imaging to detect any underlying disease. Provide supportive care and analgesia and administer antibiotic therapy if the wounds appear infected. Prevention of self-mutilation by use of collars or bandages is controversial. Most rabbits do not tolerate collars well and find it difficult to eat and prehend cecotrophs with a collar. If a collar is necessary, use only soft collars. Although bandages can protect areas from self-mutilation, adjacent body areas may become the focus instead. Assess environmental factors such as environmental enrichment, interaction between bonded pairs, and the presence of (perceived) predators and correct these as needed.

DISEASES OF UNKNOWN ORIGIN

Sebaceous Adenitis

Sebaceous adenitis is postulated as a T-cell–mediated autoimmune reaction directed at the sebaceous glands and hair follicle. Lipid metabolism defects are also implicated. In rabbits, sebaceous adenitis has been linked to the presence of thymoma, and one case has been linked to autoimmune hepatitis.[25,26] Alternatively, exfoliative dermatitis associated with thymoma and autoimmune hepatitis may be unrelated to sebaceous adenitis.[56] Affected rabbits exhibit nonpruritic, chronic exfoliative dermatitis associated with areas of alopecia and are prone to secondary dermatitis (Fig. 17.7). Hair epilates easily and has characteristic keratin debris around the hair shafts called follicular casts.[44,90] Histopathologic examination demonstrates orthokeratotic



Fig. 17.7 Nonpruitic, chronic exfoliative dermatitis with alopecia in a rabbit with sebaceous adentitis. This rabbit had a thymoma, which has been associated with this condition in rabbits. (Photo courtesy Katherine Quesenberry, DVM, MPH.)

hyperkeratosis, absence of sebaceous glands, and lymphocytic folliculitis. Thoracic radiographs are indicated to screen for concurrent thymoma. Successful treatment with cyclosporin and miglyol has been reported.[44] Treatment with retinoids, glucocorticoids, and essential fatty acids is unsuccessful.[44,56]

Cutaneous Asthenia or Ehlers-Danlos–Like Syndrome

Ehlers-Danlos–like syndrome is a group of genetically distinct inherited diseases of connective tissue reported in rabbits that can result in joint laxity, skin hyperextensibility, and skin fragility leading to tearing during normal behavior or handling.[34] Diagnosis is based on clinical signs and histologic confirmation. No effective treatment is reported.

Dermal Fibrosis

Dermal fibrosis is a hormone-related, fibrous dermal thickening of the dorsum seen in intact male rabbits.[30] A defined edge of the fibrous tissue can be felt, which extends from the dorsal shoulder, laterally to midflank, and caudally over the tail base. The thickened skin is very difficult to penetrate when administering injections. There are no associated superficial skin changes, the condition is nonpruritic, and alopecia does not occur.[31,58] No treatment is required.

Eosinophilic Granuloma

Eosinophilic granuloma is a rare cutaneous reaction manifested as red, ulcerated skin lesions and associated with various underlying conditions such as ectoparasites or allergies. In one report, *Cheyletiella* mites were at the periphery of the lesion.[36] Diagnosis is based on histopathologic evaluation of lesions. Treatment of any potential underlying cause identified (e.g., ectoparasite infestation) is essential.

Contact /Allergic Dermatitis

Contact dermatitis is caused by direct contact with skin irritants such as cleaning agents. Atopy-type allergy is possible but has not been definitively diagnosed in rabbits. Suspect cases are rabbits exhibiting pruritus where alternate causes have been ruled out. Currently, intradermal skin testing and interpretation of test results has not been validated in rabbits. Both antihistamines and immune-modulating agents such as corticosteroids and cyclosporine have been suggested as potential treatments. However, cyclosporine is associated with toxicity in rabbits and should be used with caution.[28] In the case of suspected contact irritation, remove the inciting cause and use topical treatments such as antihistamine and steroid preparations as indicated.

DISEASES OF THE EXTERNAL EAR CANAL AND PINNA

The external ear canal of the rabbit is comprised of three interconnecting cartilaginous plates, the annular, auricular, and scutiform cartilages (see also Chapter 32). The canal is principally a vertical funnel containing a blind-ended diverticulum separated by a cartilaginous bridge of the auricular cartilage called the tragus. In lop-eared rabbits, a 3- to 5-mm gap exists between the tragus and the cartilaginous acoustic meatus, allowing the pinna to droop over and creating a stenotic fold in the nonrigid ear canal.[14]

The most common disease involving the external pinna is ear mites, *P. cuniculi* (see above). Generalized skin disease such as sebaceous adenitis[44] and thymoma-associated dermatitis,[25] other ectoparasites such as *Demodex cuniculi*,[35] and *Sarcoptes* infestations,[74] and dermatophytosis, especially *T. mentagrophytes*,[53] can also involve the pinna. Traumatic injury of the pinna can occur through fight or bite wounds and can progress to form abscesses. Actinic keratoses have been described on the ear pinna.[73] Numerous neoplastic conditions can involve the pinna, including Shope papilloma, Shope fibroma, trichoblastoma, squamous papilloma, sebaceous carcinoma, malignant melanoma, and trichoepithelioma.[83]

Many cases of otitis externa in the rabbit result from ascending infection from the middle ear through a ruptured tympanic membrane (see Chapter 18). Primary bacterial otitis externa, as it occurs in dogs, is uncommon. In lop-eared rabbits, however, ear cerumen can accumulate below the fold in the ear canal, allowing overgrowth of bacteria or, less commonly, yeast. The buildup of debris or exudate can escape through the gap in cartilage between the tragus and annular cartilage, resulting in a palpable swelling at the base of the ear. Uncommonly, otitis externa can affect the middle ear by extension after the membrane has ruptured. Histopathologic examination of sections of the external ear canal removed during surgical resection as part of the treatment for otitis externa/media rarely indicate more than minimal pathologic changes.[59] In a study of the normal flora of ear canals in clinically healthy lop and non-lop healthy, a wide range of commensal bacteria, as well as yeast, were identified.[71] The principal bacteria identified were *Staphylococcus aureus/xylosus/epidermidis*, *Bacillus* species, *Pantoea* species, *Enterococcus faecalis, P. multocida, Pseudomonas fluorescens, E.coli, Proteus* species, *Corynebacterium* species, and *Eikenella corrodens*. *Staphylococcus aureus* was more common in lop-eared rabbits, whereas *E. faecalis* and *P. multocida* were more common in non-lop rabbits. These findings highlight that caution is warranted in interpreting results of bacterial culture of discharge in the external ear canal that contains what may be a normal accumulation of wax, without also doing cytologic

examination to establish that an inflammatory process is present. In the cases where bacterial otitis externa is identified on cytologic examination and without middle ear involvement as evidenced by normal computed tomography scans, medical treatment is effective. Therapy for otitis externa involves gently flushing the canal with a mild cerumenolytic product. Where antibiotics are needed, use topical products based on culture and sensitivity test results if possible.

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18

Neurologic and Musculoskeletal Diseases

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Neurologic and musculoskeletal diseases are common in pet rabbits and are being recognized with increased frequency, reflecting both their increased longevity and the availability of improved diagnostic modalities. Causes of neurologic disorders in rabbits include infectious, traumatic, toxic, degenerative, nutritional, metabolic, vascular, neoplastic, and idiopathic causes.[31] Musculoskeletal disease is more commonly the result of traumatic, nutritional, developmental, or age-related degenerative disorders. Some neurologic diseases, particularly encephalitozoonosis, have zoonotic potential and therefore have been investigated more thoroughly in recent years, increasing our confidence in diagnosis and possible treatment.

Signs of musculoskeletal disease in rabbits may be associated with pain or decreased function and include diminished activity and varying degrees of limb weakness, gait and postural changes, and angular limb deformities. Signs of neurologic disease are head tilt (torticollis or wry neck), nystagmus, ataxia, tremors, paresis, paralysis, and seizures. Behavioral changes such as increased aggression, diminished socialization, and lack of normal grooming behavior reflected by poor coat condition and soiling may be seen with either disorder group. Head tilt, usually an indication of vestibular dysfunction, can be central (cerebellum, brain stem) or peripheral (inner ear) and was the most common clinical sign observed in a retrospective study of rabbits with neurologic disease.[31] Paresis was the second-most common clinical sign in this study, whereas seizures were uncommon.

Paresis and paralysis are most commonly associated with spinal cord disease, while seizures primarily indicate brain disease or toxicosis. Differentiating the causes of neurologic disease is challenging and may be complicated because more than one cause may be present in the same animal. Along with signalment, history, and physical examination findings, a thorough neurologic examination may help differentiate neurologic from musculoskeletal disease. The neuroanatomy of rabbits is comparable to that of dogs and cats; therefore the approach to a neurologic examination is similar, keeping in mind that rabbits can be very nervous and, as prey species, may mask signs of clinical illness. Based on observations of spontaneous or induced sensory or motor functions, the neurologic examination is used anatomically to localize the lesion and aids in forming a differential diagnosis and diagnostic plan. Detailed information on rabbit neuroanatomy, performing a rabbit neurologic examination, and neurodiagnostics in rabbits has been published.[49,71]

A neurologic examination helps to localize the lesion to a particular area of the nervous system but does not give a diagnosis. Observing the animal while it is ambulating may be challenging because many rabbits are nervous and will not move. If the rabbit hops, gait can be assessed and mentation, facial symmetry, and movement of the face can be evaluated. The cranial nerve examination is like that in other species. However, nervous rabbits do not blink when testing menace response. The gag reflex is difficult to assess, but a tongue depressor can be used to try to open the mouth. Among the postural reactions, hopping is the easiest to perform. While supporting the rabbit and keeping three legs off the ground, push the rabbit to the side with one limb on the ground and assess how fast the rabbit corrects its posture. Paw replacement (conscious proprioception) is less reliable because even normal rabbits may not replace their paw because of nervousness. Assess wheel barrowing of the thoracic limbs and extensor postural thrust of the pelvic limbs in the same way as for other animals; do this cautiously in nervous rabbits. For spinal reflexes, place the rabbit in lateral recumbency with good support of the back to prevent injury. If the rabbit does not allow this, the patella reflex and biceps reflex can be done while holding the rabbit in the assistant's arms in a more sternal position. The withdrawal reflex is more difficult to assess when the rabbit is held by an assistant in sternal position but can be done. Palpating the vertebral column and muscles is done last.

Diagnostic procedures used to help narrow the differential diagnoses for neurologic and musculoskeletal disease include clinical pathology, diagnostic imaging, and serologic testing. A complete blood count, biochemical analysis, and urinalysis may help identify systemic diseases that may manifest with neurologic signs. Radiology is useful in cases of lameness, gait abnormalities, head tilt, and spinal abnormalities. Magnetic resonance imaging is invaluable in looking for fine detail, including soft tissue of the central nervous system (CNS), and computed tomography (CT) scanning is preferred to evaluate the inner ear, skull, and vertebral column. Antibody titers may support or rule out a diagnosis of an underlying infectious cause such as encephalitozoonosis or toxoplasmosis.

FUNGAL DISEASES

Encephalitozoonosis

In rabbits, *Encephalitozoon cuniculi* infections are commonly chronic and subclinical. However, *E. cuniculi* is often associated with neurologic disease in pet rabbits, and encephalitozoonosis seems to be a widespread disease, with reports of infection found in 50% to 75% of conventional rabbit colonies.[47] Signs of neurologic disease caused by *E. cuniculi* mainly include vestibular signs such as head tilt, nystagmus, ataxia, circling, and rolling. This organism has shown zoonotic potential, primarily in persons who are immunocompromised.[21] It may therefore be important to know the serologic status of pet rabbits.

Transmission and Pathobiology

Encephalitozoan cuniculi is a microsporidium, obligate intracellular pathogen. Although eukaryotic, microsporidia lack most cytoplasmic organelles found in nucleated cells; most significantly, instead of mitochondria, they posess enzymes with mitochondrial function.[41] The phylum Microsporidia is now classified within the fungal kingdom[31a]; however, the relationship of microsporidia as a basal branch of the fungal kingdom is not fully understood.

Postnatal transmission often occurs within 6 weeks from an infected dam or contact with other infected animals[47]; however, vertical transmission is possible.[20,73] Spores, measuring 1.5 × 2.5 μm (Fig. 18.1), are either ingested or inhaled as the infectious stage of *E. cuniculi,* with oral ingestion from the urine of infected rabbits being the most common source of infection. Spores can be found in the urine 1 month after infection and are excreted in large numbers for up to 2.5 months after infection, after which they are eliminated intermittently in low concentrations.[9,33] Spores can survive outside the host for up to 6 weeks at 72°F (22°C). Spores possess a polar filament that is extruded into host intestinal mucosa cells, injecting sporoplasm into the target cell (reticuloendothelial cells), thus initiating infection. Multiplication of the organism takes place in host alimentary cell vacuoles (parasitophorous vacuoles) by ordinary fission (merogony). Subsequently, meronts differentiate via sporonts into environmentally resistant, infective spores by acquiring the polar filament and developing a thick spore wall (sporogony). With time, the pseudocyst becomes overcrowded, with eventual cell rupture and spore invasion of the reticuloendothelial system and systemic circulation by infected macrophages. Initial target organs are those with high blood flow such as the lungs, liver, and kidneys,[60] with infection of nervous tissue occurring later (see Fig. 18.2 for complete life cycle). Cell rupture is associated with an inflammatory response, and most immunocompetent rabbits develop chronic, subclinical infections in a balanced host/parasite relationship associated with granulomatous lesions primarily affecting the brain, kidneys, or eyes. A wide range of tissues may show morphologic lesions; however, in general, these histologic alterations are not associated with clinical disease.

The most commonly recognized neurologic sign in rabbits with encephalitozoonosis is vestibular disease (Fig. 18.3). However, the underlying pathology of the vestibular dysfunction attributable to *E. cuniculi* has not been fully investigated. In addition, *E. cuniculi* has repeatedly been reported as a cause of paresis and paralysis; one author (F.K.) believes that these neurologic signs are often falsely attributed to the organism.[43] Typically, vestibular signs have a sudden onset after a stressful event. Vestibular disorders can range from subtle evidence of swaying at rest or nystagmus to a state of severe head tilt with intermittent rolling, resulting in lateral recumbency exacerbated by handling. Occasionally, rolling may be misinterpreted as seizure activity by the animal owner. However, even in the case of extreme vestibular dysfunction, immobilized rabbits may eat spontaneously as long as food is within reach.[34] Although accurate neurologic assessment is strongly recommended in rabbits with vestibular disorders, often it may not be helpful to differentiate central from peripheral disease as a result of otitis interna, because central vestibular dysfunction caused by *E. cuniculi*

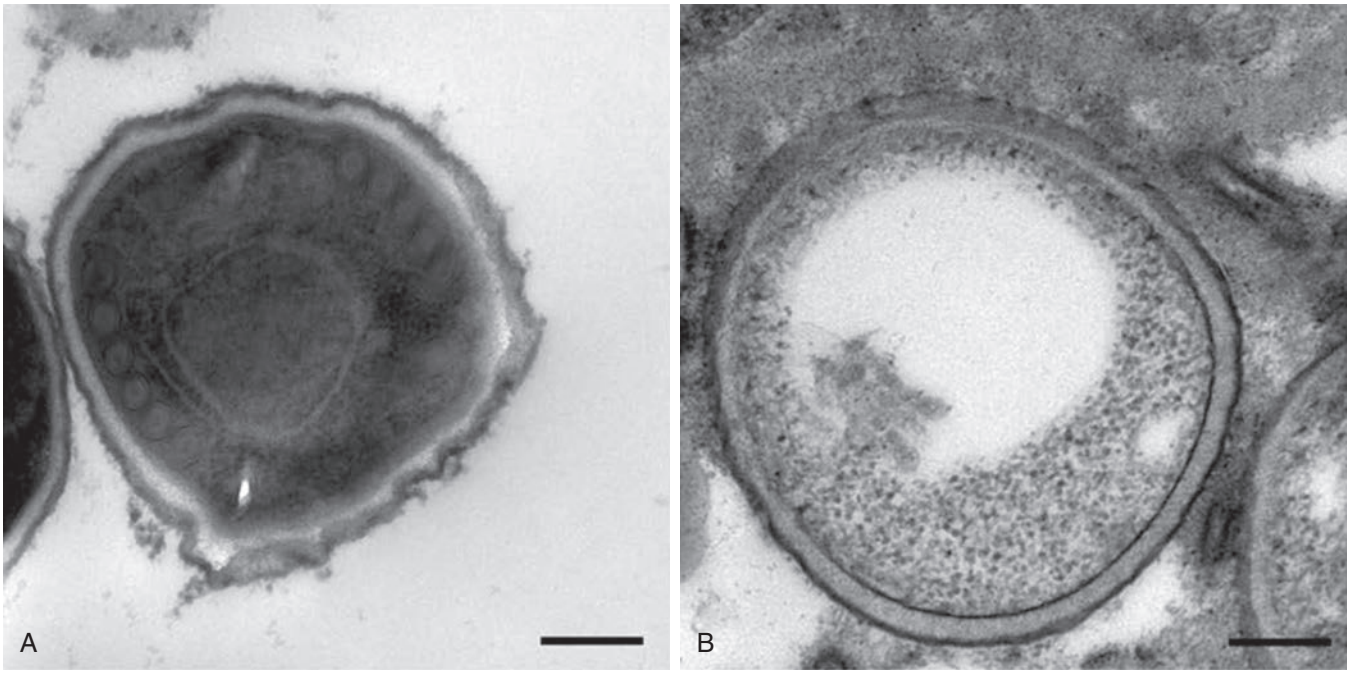


Fig. 18.1 Electron microscopic image of *Encephalitozoon cuniculi* spores. (A) Electron micrograph of an intact *E. cuniculi* spore containing cross-sections of the polar filament, the nucleus, and electron-dense sporoplasm. Three layers of the spore wall, an outer electrondense exospore, an intermediate electron-lucent endospore, and a plasma membrane are visible. Bar = 250 nm. (B) Partially empty spore after having discharged the polar tube and released most of the sporoplasm. A retained irregular layer of granular material lining the inner spore wall can be observed. Bar = 250 nm. From: Habenbacher B, Klang A, Fragner K, et al. Comparative evaluation of specific methods for labeling of *E. cuniculi* in paraffin wax-embedded tissue samples. *J Vet Dig Invest* 2012;24:370-375.

frequently mimics the condition of a peripheral disorder.[43,44] Signs of central vestibular dysfunction are mentation change, other cranial nerve signs, poor gag reflex or poor tongue movement, and postural reaction deficits. Despite a central vestibular disorder, often these signs are not present in rabbits with encephalitozoonosis. Neurologic examination of rabbits may be even more problematic if animals are anxious or rolling. In addition, changes in mentation are often subtle and therefore difficult to identify. In contrast to rabbits with encephalitozoonosis, rabbits with otitis interna, the primary differential diagnosis, sometimes have signs of upper respiratory disease.[44] Another differentiating clinical sign is unilateral facial spasm or hemifacial dysfunction that may accompany otitis interna and is not present in rabbits with encephalitozoonosis.

In one study determining the extent of histologic lesions in the brain of naturally infected rabbits, the cerebrum was most frequently affected, followed by the leptomeninges (Fig. 18.4).[13] The vestibular cores, cerebellum, and spinal cord were less commonly affected, despite vestibular dysfunction being the most frequently manifested clinical sign. Animals were considered infected with *E. cuniculi* if spores were present, and the use of Ziehl-Neelsen stain was slightly more sensitive for spore detection than acid-fast trichome stain.[13] On histopathologic examination, most rabbits showed perivascular inflammatory infiltrates and, less frequently, granulomas. In this study, no significant difference was found in the presence of CNS granulomas in rabbits with or without neurologic signs. The conclusion of the study was that histologic findings of inflammatory lesions are not always indicative of overt encephalitozoonosis as the cause of neurologic signs.

As *E. cuniculi* organisms spread to various organs, antibodies develop and encapsulation occurs, thus limiting tissue damage and spore excretion. Antibodies become detectable 3 to 4 weeks after infection, with maximum titers occurring 6 to 9 weeks after infection. A healthy immune system prevents the organisms from multiplying, but the spores remain viable. A decline in immune function associated with illness or stress may result in overt disease many years after initial infection. Interestingly, the reported median age of rabbits with suspected clinical encephalitozoonosis is 2.4 years.[43]

Diagnosis

Definitive antemortem diagnosis of encephalitozoonosis continues to be a challenge. Encephalitozoonosis often is diagnosed by using a combination of physical examination (neurologic and ophthalmologic findings) and serologic test results and by ruling out other differential diagnoses, such as otitis interna, suppurative meningoencephalitis, trauma, or brain tumor. Serologic testing is the most reliable diagnostic tool for verifying *E. cuniculi* infection in clinical cases. However, many rabbits are chronically infected but remain asymptomatic, and seropositivity only indicates previous exposure to the pathogen and does not confirm that infection is the underlying cause of current clinical signs. Because *E. cuniculi* infection is persistent, antibodies continue to be produced, and, as a general rule, the validity of serologic testing compares favorably

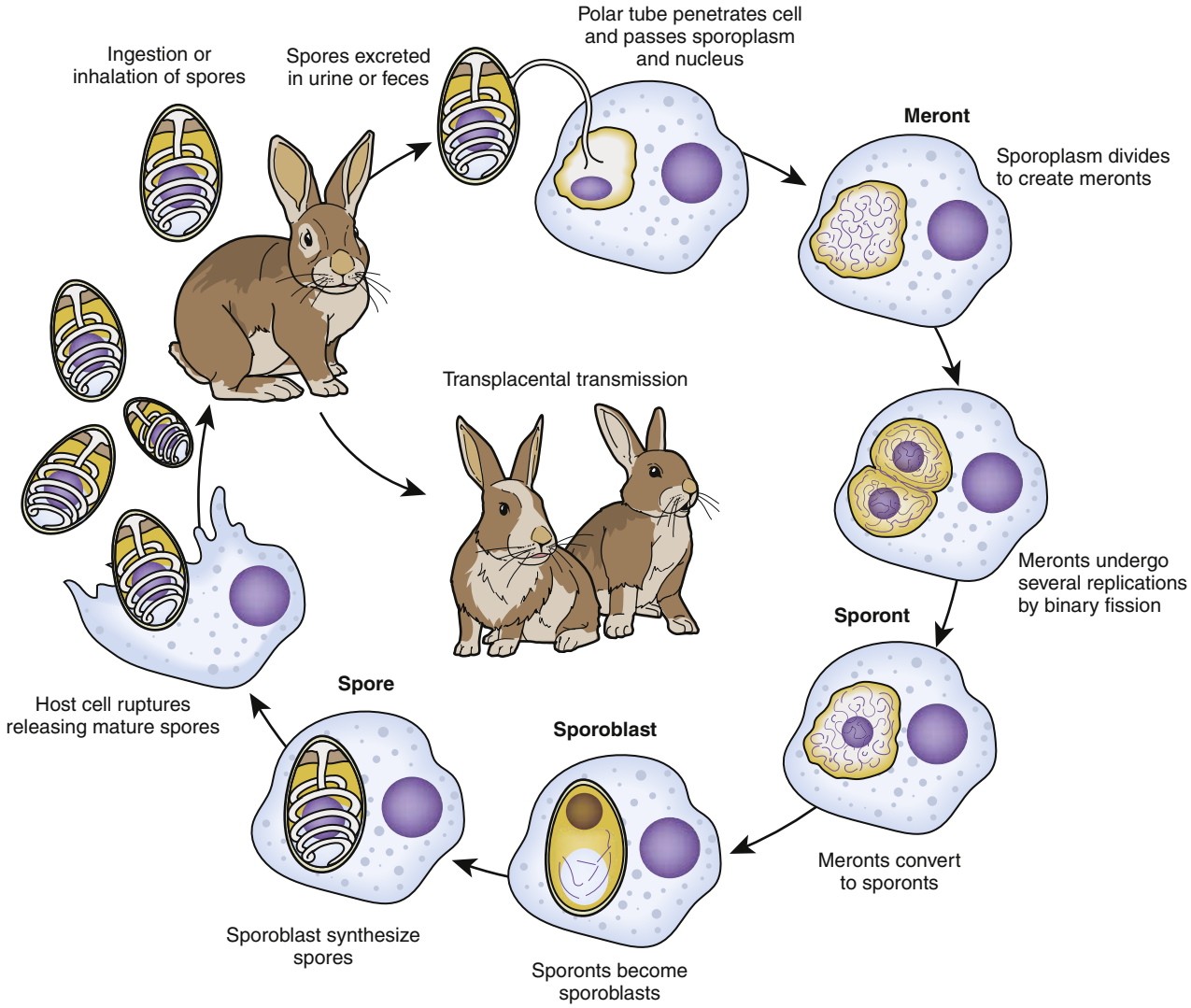


Fig. 18.2 General life cycle of microsporidia. (From Jordon CN. *Encephalitozoon cuniculi:* diagnostic test and methods of inactivation. Masters thesis. Virginia Polytechnic Institute, Blacksburg, VA. 2005; p 23. [https://vtechworks.lib.vt.edu/handle/10919/34162].)

with histologic results to detect *E. cuniculi* in rabbits.[59,72] Results of a study comparing two indirect immunofluorescence assays, two enzyme-linked immunosorbent assays (ELISA), and the carbon immunoassay (or India-ink assay) to determine antibodies to *E. cuniculi* showed that any of the assays would be suitable for monitoring rabbits for evidence of infection.[3]

A positive antibody titer indicates exposure to the organism and does not differentiate between rabbits with an active versus a latent infection. With the exception of results of one study, which showed a 1.7 times higher antibody titer in rabbits with suspected encephalitozooonosis compared with titers in normal animals, antibody titers in rabbits with encephalitozoonosis generally do not differ significantly from titers in rabbits with latent infection.[10,43] Seroconversion typically occurs as early as several weeks before the organism or pathogen-associated tissue alterations can be demonstrated in the CNS.[8,9,32,43] Therefore a negative immunoglobulin G (IgG) antibody titer generally excludes *E. cuniculi* as the cause of current neurologic signs.

Experimentally, it has been shown that immunoglobulin M (IgM)–specific antibodies are an indicator of early stages of infection, because IgM levels decrease to 0 by day 35 after infection.[9] Subsequently, simultaneous determination of IgM and IgG antibodies was hypothesized to be an aid in the diagnosis of encephalitozoonosis because evaluating both titers gives evidence of the infection status (acute, reactivated infection or reinfection) of the animal.[38] However, detection of IgM-specific antibodies may be misleading because antibodies often can be detected even in asymptomatic rabbits.[38] Moreover, determining IgM antibody titers seems to have minor importance as a diagnostic tool in rabbits with suspected disease because antibody titers (no matter of IgM or IgG antibodies) in general precede the presence of the organism in the brain.[8] Further research is needed to evaluate the significance of the simultaneous determination of specific IgM and IgG antibody titers for antemortem diagnosis of encephalitozoonosis.

Other methods advocated for antemortem diagnosis of *E. cuniculi* are measurement of urine antibody levels, plasma or serum protein electrophoresis, C-reactive protein assessment, and cerebrospinal fluid (CSF) analysis (Fig. 18.5). One study demonstrated an increase in anti-*E. cuniculi* IgG antibodies in urine samples from asymptomatic seropositive rabbits.[26]

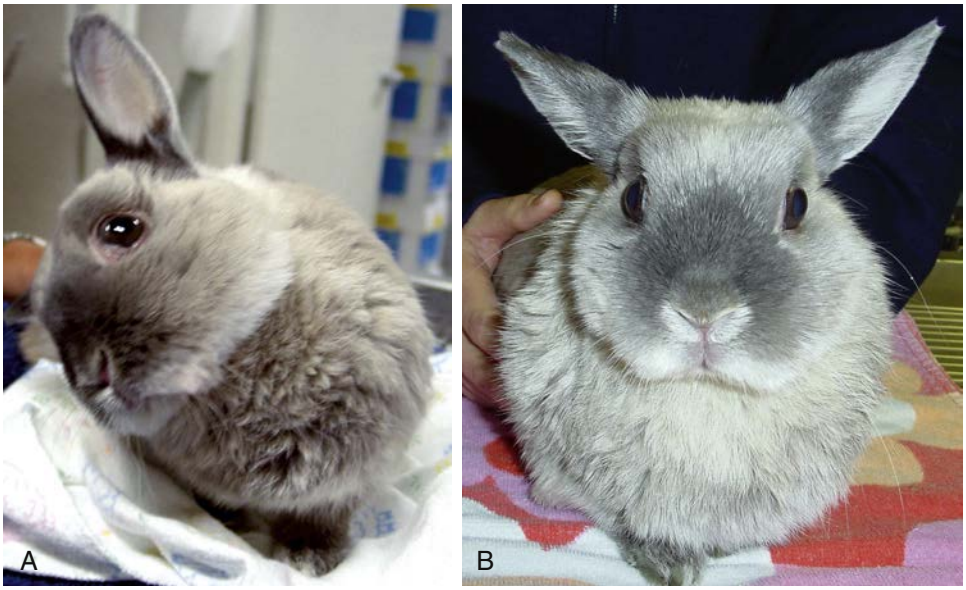


Fig. 18.3 (A) This 8-year-old female rabbit was presented with signs of vestibular disease, including a right head tilt and nystagmus. No evidence of tympanic bulla disease was visible on skull radiographs. Result of an enzyme-linked immunosorbent assay for *Encephalitozoon cuniculi* was positive, and the rabbit was treated with fenbendazole (20 mg/kg by mouth every 24 hours × 28 days). (B) The vestibular signs resolved with time. With encephalitozoonosis in rabbits, it is difficult to determine whether resolution of clinical signs is the result of specific medical therapy or spontaneous recovery.

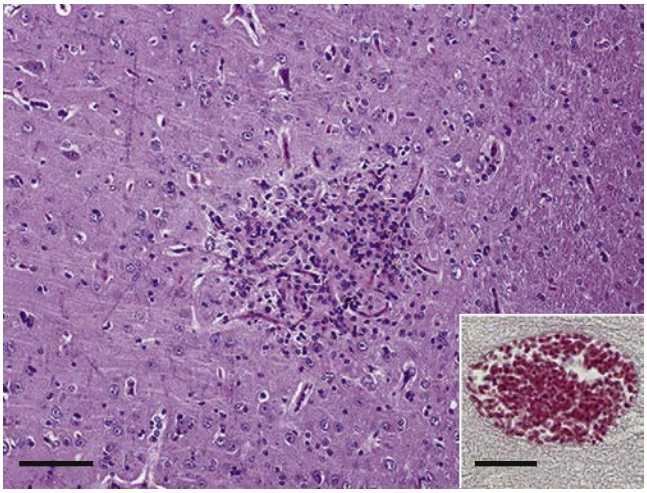


Fig. 18.4 Section of cerebrum from a rabbit with encephalitozoonosis. A granulomatous inflammatory focus is shown. Hematoxylin and eosin stain; bar, 100 μm. The inset shows a parasitophorous vacuole located within the parenchyma without any associated inflammatory reaction. Acid-fast trichrome stain, bar, 17.7 μm. (From Gruber A, Pakozdy A, Weissenböck H, et al. A retrospective study of neurological disease in 118 rabbits. *J Comp Pathol.* 2009;140:31-37.)

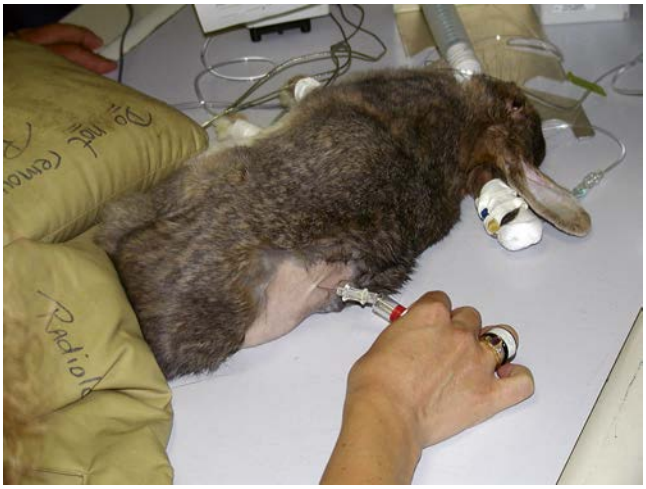


Fig. 18.5 A lumbar cerebrospinal fluid tap is performed in a rabbit with neurologic disease to collect a sample for cytologic examination and bacterial culture.

However, antibodies were only detected in strongly seroreactive rabbits. Further research is needed regarding the usefulness of urine as a noninvasive sample matrix to detect IgG antibodies in rabbits.[26] The results of another study, in which the diagnostic value of protein electrophoresis was assessed, indeed showed significant abnormalities in serum or plasma concentrations of proteins in rabbits with suspected encephalitozoonosis compared with healthy rabbits. However, although protein electrophoresis may aid as an accessory tool in diagnosis, electrophoresis alone currently appears unreliable in the diagnostic process because clinically abnormal rabbits that are not suspected to have an *E. cuniculi* infection can have similar changes in protein concentrations.[10] The presence of increased concentrations of C-reactive protein has been reported in rabbits with a suspected encephalitozoonosis. However, acute-phase proteins are not specific for any single infectious process. Even so, especially when determined in combination with increased IgM or IgG antibody titers or both, C-reactive protein can provide a high specificity and positive predictive value (95% to 100%).[11,12] One study showed that CSF of rabbits with suspected encephalitozoonosis was characterized by nonspecific changes (lymphomonocytic pleocytosis and increased protein concentrations) compared with changes in healthy rabbits. Although these changes may be seen with other viral, protozoal, or immune-mediated encephalopathies in

rabbits, CSF analysis may be helpful as a supportive test for clinical diagnosis of encephalitozoonosis in rabbits.[37]

In human medicine, *E. cuniculi* is an opportunistic pathogen in immunocompromised patients, such as transplant recipients or those infected with human immunodeficiency virus or who have developed acquired immunodeficiency syndrome. Polymerase chain reaction (PCR)–based studies have been very successful in identifying *E. cuniculi* DNA in stool specimens of infected persons with clinical diarrhea.[55] Several attempts have been made to evaluate PCR analysis for a faster and more accurate diagnosis of encephalitozoonosis in rabbits. However, only PCR testing of liquefied lens material has been demonstrated as an excellent diagnostic tool for antemortem diagnosis of phacoclastic uveitis.[14,44] In contrast, because of a very low sensitivity, PCR of CSF is not recommended for diagnostic purposes in rabbits with neurologic disorders attributable to encephalitozoonosis. Moreover, PCR testing of urine has been recognized as an unreliable diagnostic tool for in vivo diagnosis because spores are only sporadically excreted in clinically affected as well as latently infected rabbits.[8,14,37,43]

Treatment and Control

In the absence of controlled studies, assessing the efficacy of therapeutic agents against *E. cuniculi* is difficult because latent infections occur, and some clinical cases may improve spontaneously without treatment, presumably because of the host's immune response.[33] In addition, clinical signs may not be associated with presence of the organism itself, but rather with the inflammatory response that persists after the organism has been eliminated.[32,67]

So far, treatment protocols for rabbits showing neurologic signs suspicious for *E. cuniculi* infection have been primarily based on fundamental principles of therapy for granulomatous inflammation, results of studies demonstrating efficacy against human encephalitozoon infections, and results of in vitro susceptibility studies of *E. cuniculi* organisms to various pharmacologic agents. However, there is still no universal agreement on how to effectively treat encephalitozoonosis in rabbits. Numerous drugs have been tested regarding in vitro drug susceptibility of *E. cuniculi,* and several antimicrobial agents (e.g., fumagillin, oxytetracycline), and benzimidazole derivatives, including albendazole, oxibendazole, and fenbendazole, are effective.[24] However, with most of the suggested drugs, susceptibility of the pathogen has not been assessed in clinical settings. Antibiotic treatment is no longer advocated; however, benzimidazole derivatives continue to be the drug of choice for treatment of presumptive *E. cuniculi* infections in rabbits because of their antiinflammatory actions and in vitro activity, including bioenergetic disruptions of membranes and microtubular (tubulin) inhibition of *E. cuniculi*.[24,52] The use of albendazole is partially based on its effectiveness in treating and eliminating *Encephalitozoon* species in infected human patients. In one treatment trial, fenbendazole was shown to prevent and treat naturally acquired and experimentally induced *E. cunciuli* infections in rabbits.[66] Based on this study, fenbendazole (20 mg/kg orally, once a day over a period of 28 days) is commonly used for the causative treatment of encephalitozoonosis in rabbits (Fig. 18.3). However, because of reported toxicosis associated with the use of benzimidazoles in rabbits (mainly bone marrow aplasia and intestinal tract crypt epithelial necrosis), always adhere to recommended dosages, educate rabbit owners about potential health risks, and consider assessing a complete blood count before and during treatment.[17,24,28]

The systemic use of (short-acting) glucocorticoids has been anecdotally advocated to control inflammation associated with the organism when neurologic signs appear acutely. However, results of a recent study did not provide any evidence that dexamethasone has a therapeutic effect in rabbits with neurologic disorders caused by suspected encephalitozoonosis.[63] Results of one study showed that rabbits experimentally infected with *E. cuniculi* that were treated with immunosuppressive doses of dexamethasone before and after infection responded poorly to treatment with fenbendazole administered for 4 weeks beginning at 28 days after infection. Weight loss, hematologic changes, and severity of histopathologic lesions did not differ significantly between post-infection treated and untreated rabbits. However, immunosuppressed rabbits that were treated prophylactically with fenbendazole for 7 days before infection showed improvement in these parameters compared with untreated and post-infection treated rabbits.[1a] Also, vestibular dysfunction in rabbits is most probably not associated with nausea, because they usually will eat spontaneously, even with severe torticollis.[33,44] Therefore, in contrast to dogs and cats, antiemetic drugs are not indicated in rabbits with vestibular disease. In cases of severe vestibular disease (e.g., rolling), rabbits may benefit from benzodiazepines (diazepam, midazolam) to suppress neurologic signs associated with acute vestibular lesions.[34,44]

The nervous system of rabbits with encephalitozoonosis apparently has a high ability to compensate for vestibular dysfunction, as morphologic CNS alterations attributable to *E. cuniculi* progress relatively slowly.[34] Therefore supportive therapy in terms of enforced activity has been advocated to adequately challenge the vestibular system and to improve the rate of compensation in rabbits with vestibular disorders.[34,44] In contrast, a longer time of immobilization after an acute onset of vestibular disorders may limit the improvement of clinical signs.[34,44] Although restricting mobility may be required short term to avoid trauma, therapeutic exercise under medical supervision should be initiated as early as possible. Because episodes of rolling may be triggered by excitation, a quiet environment is recommended, and unnecessary manipulations should be avoided.

Control of encephalitozoonosis may be most effective when applied to rabbitries where transmission has been reported. The acute phase of infection usually occurs in very young rabbits, and spores are shed in urine until antibodies establish a balance between host and pathogen. A simple test to determine whether rabbits are shedding spores in the urine is needed to clarify duration of potential transmission. This information could then guide quarantine recommendations when new rabbits are introduced. Selecting *E. cuniculi* antibody–negative breeders and developing encephalitozoon-free rabbit colonies may then be possible. In addition, cleaning and sanitation are essential to limit transmission. Most disinfectants are effective at inactivating spores, including quaternary ammonium compounds, amphoteric surfactants, phenolic derivatives, alcohols, iodophors, and hydrogen peroxide.

PARASITIC DISEASES

Neural Larva Migrans

Neural larva migrans due to *Baylisascaris* species has been reported in rabbits. The history includes an outdoor environment with possible exposure to eggs of *Baylisascaris procyonis* or *Baylisascaris columnaris*, the roundworms carried, respectively, by raccoons and skunks. The parasite *B. procyonis* is more pathogenic with respect to aberrant host larva migrans and, like other ascarids, produces large numbers of eggs that are very resistant to the environment. An important cause of neural larva migrans and ocular larva migrans in people, the disease has been reported from areas of North America where indigenous raccoons thrive, most notably northeastern, midwestern, and West Coast regions of the United States, but also from areas of the world where raccoons have been purposely or inadvertently released into the wild, most notably Japan.[27] Larva migrans due to *B. procyonis* has also been reported in small animals kept in close proximity to raccoons in zoo collections in Germany, Ireland, and Japan.[25] Paratenic hosts, such as rabbits, are exposed when they ingest vegetation, hay, or bedding contaminated with raccoon feces carrying *Baylisascaris* eggs. After eggs are ingested, larvae (L3) penetrate the intestinal wall and migrate through the bloodstream to reach other organs and tissues, where they have a predilection for the CNS, particularly the cerebral cortex, midbrain, and brain stem, causing encephalomalacia. Invasion and mechanical damage by larvae are key pathogenic factors and often result in necrotic "track-like" linear areas (malacic tracks) in affected CNS tissues.[27] In addition, migrating larvae produce abundant excretory-secretory antigens, including migratory enzymes, shed cuticular proteins, and metabolic waste products, which are highly antigenic and stimulate host inflammatory reactions, most notably eosinophilic and granulomatous responses.[27]

Signs of disease associated with neural larva migrans are tremors, ataxia, head tilt, circling, and vertical nystagmus, progressing to falling, rolling, paralysis, seizures, and recumbency. Swaying and falling are usually pronounced with cerebral larva migrans, whereas this degree of neurologic deficit is seen less often with encephalitozoonosis or otitis interna. An affected rabbit may show intermittent improvement, followed by more severe signs, or the disease may be rapidly progressive.

Antemortem diagnosis is difficult, but treatment is based on a history of potential exposure and clinical signs. In the United States, the Veterinary Parasitology Laboratory at the College of Veterinary Medicine, Purdue University (West Lafayette, IN) is the primary reference laboratory for updates on serologic testing and molecular tests.[27] In people, significantly increased eosinophils levels, both peripheral and in CSF, have been reported, and current treatment recommendations in suspect cases are to start albendazole and corticosteroids while diagnostic tests are being pursued.[27] Corticosteroid treatment for suspect cerebral larva migrans is controversial in rabbits, but many believe the disease-associated eosinophilic and antigenic inflammation warrant their use in a disease that may be rapidly progressive and carries a grave prognosis. In rabbits, slowing the progression of presumptive cerebral larva migrans by treatment with oxibendazole (60 mg/kg by mouth every 24 hours) indefinitely has shown some success.[16] Signs may recur and progress when the drug is discontinued. Rabbits that are severely affected are probably best euthanized. Information about the various successful anthelmintic treatments has been published.[4]

Advise rabbit owners to prevent neural larva migrans by eliminating access to feed and bedding that is potentially contaminated by raccoon feces. In zoos where wild raccoons are present, in addition to removal and translocation, anthelmintic baiting of raccoons is gaining attention as an effective measure to lower risk of infection.[27]

Cuterebra Species

Larvae of *Cuterebra* species, or bot flies, commonly pupate in the rabbit subcutis but have also been reported to migrate through the ear canals and CNS, causing neurologic signs.[35] This aberrant migration has been reported more commonly in cats where clinical abnormalities tend to be progressive and include blindness, depression, and behavioral changes.[75] No specific clinical or clinicopathologic test is diagnostic for cuterebriasis in rabbits (see Chapter 17).

Toxoplasmosis

Although toxoplasmosis is a very rare cause of neurologic disorder in rabbits, it is considered a differential diagnosis for encephalitozoonosis.[38,43] Infection with CNS involvement may include various nonspecific neurologic signs such as ataxia, tremors, posterior paresis, paralysis, and tetraplegia. However, most *Toxoplasma gondii* infections are subclinical in rabbits,[31,43] with positive serologic tests indicating exposure. Studies looking at the seroprevalence of *T. gondii* in populations of rabbits have demonstrated varying results. A 2006 study measured serum antibodies to *T. gondii* by indirect ELISA assay in domestic rabbits from three rabbit farms in Mexico and demonstrated a seroprevalence in 27% of animals tested.[23] A 2008 Austrian study tested for the presence of antibodies against *T. gondii* by an indirect immunofluoresecent antibody test and found 8 positive out of 157 (5%).[43] In a 2010 study in the Czech Republic, IgG levels to *T. gondii* were measured in parallel with IgM and IgG levels for *E. cuniculi*; specific anti-*T. gondii* IgG antibodies were detected in 19% of 500 rabbits.[38] In these studies, most positive rabbits were asymptomatic, reinforcing that detection of specific anti-*T. gondii* IgG antibodies indicates only exposure to the infective agent. In rabbits with neurologic signs consistent with toxoplasmosis, serologic testing may aid in the differentiation of toxoplasmosis and encephalitozoonosis. On postmortem examination, *T. gondii* may induce granulomatous meningoencephalitis similar to that seen with encephalitozoonosis, but foci of necrosis, as well as tachyzoites, may be found in many organs, including skeletal muscle, spleen, heart, lungs, and lymph nodes.[31]

If toxoplasmosis is diagnosed, treat with trimethoprim-sulfa and pyrimethamine or doxycycline. Clindamycin, which is used for treatment in cats, should not be used because it causes gastrointestinal dysbiosis and death in rabbits. Herbivores may acquire *T. gondii* via congenital transmission or by ingesting oocysts from infected cat feces. Prevent toxoplasmosis in rabbits by avoiding exposure to outdoor grazing areas, feed, or bedding contaminated by cat feces.

BACTERIAL DISEASES

Otitis Media-Interna

Vestibular signs resulting from otitis interna include nystagmus and a head tilt of varying severity, with loss of balance and rolling in severe cases. Otitis media, or inflammatory disease of the middle ear, is commonly reported in rabbits but can be difficult to definitively diagnose antemortem because many infected animals are asymptomatic unless disease is concurrently associated with otitis externa or interna.[18] As a result, reports vary with respect to the prevalence of concurrent bacterial otitis media in rabbits with otitis interna–associated vestibular dysfunction.[5,18] Stenosis and anatomic folding of the deep ear canal in lop rabbits predispose this breed to otitis.[5] Bacterial otitis interna or media historically have been associated with *Pasteurella multocida* infection in rabbits; however, other causative bacterial agents are *Staphylococcus aureus, Streptococcus* species, *Bordetella bronchiseptica, Pseudomonas aeruginosa, Escherischia coli,* and *Proteus mirabilis.* For further discussion of pasteurellosis, see Chapter 15.

Primary otitis media may be associated with upper respiratory tract infection that has migrated to the middle ear via the auditory or Eustachian tubes. A concurrent sinusitis or rhinitis is suggestive of this pathogenesis. Infection may also spread from the middle ear to the external ear canal (if the tympanic membrane ruptures) (see also Chapter 17), or to the inner ear, causing vestibular dysfunction due to labyrinthitis. Spread of infection through the internal acoustic meatus and along the vestibulocochlear nerve to the brain has also been associated with severe neurologic signs, including seizures, resulting from encephalomyelitis.[18] Facial nerve damage is often observed in rabbits with otitis media-interna due to the involvement of the facial nerve that runs in close proximity to the vestibulocochlear nerve through the internal acoustic meatus. As a result, facial nerve deficits in rabbits may manifest as a hemifacial paresis or a hemifacial spasm (Fig. 18.6) with chronic infection of the inner ear, frequently representing the only clinical sign associated with otitis interna in this species.[22]

Diagnosis of otitis media/interna is based on clinical signs, aural examination, and diagnostic imaging, including skull radiography or CT scanning (See Chapter 38). Computed tomography allows cross-sectional evaluation of the entire head without superimposing structures and is an excellent technique to identify early otitis media as well as specific lesions, such as soft tissue filling of the tympanic bulla and osteolysis scans of the bulla wall (Fig. 18.7).[5,18] One publication[68] provides an excellent review of CT scans and cross-sectional head anatomy in healthy rabbits. Because of the association of otitis media/interna with concurrent rhinitis and otitis externa, bacterial culture and sensitivity testing of deep aural and nasal swab samples collected in an anesthetized patient are indicated when physical examination findings support infection. However, bacterial culture results often reveal false-positive or false-negative results. Endoscopic examination (otoscopy), preferably performed with the animal under general anesthesia, aids in visualizing the distal ear canal and tympanic membrane (Fig. 18.8). However, neither an apparently normal external ear canal nor tympanic membrane excludes the presence of otitis media.[18] Otoscopy may also be used therapeutically to flush out debris. In some cases, rabbits with severe otitis media have a soft tissue swelling at the base of the ear canal resulting from the buildup of purulent material within the ear.

In cases with concurrent bacterial otitis media, surgical intervention is often indicated to remove the thick, purulent debris that may fill the tympanic bulla and diseased ear canal tissue. Various surgical approaches to the external ear canal and tympanic bulla have been described (see also Chapter 32).[5,15] With or without surgery, antimicrobial treatment of otitis interna should be long term, at least 4 to 8 weeks, because antibiotics do not penetrate well into pus-filled tympanic bullae. Systemic antibiotics, preferably based on results of a bacterial culture results and their ability to penetrate the CNS, are recommended. Fluoroquinolones, such as enrofloxacin, ciprofloxacin, and marbofloxacin, are common choices. Provide rabbits with otitis interna with nutritional supplementation and environmental support to minimize the rolling and severe ataxia associated with this disease.

Bacterial Infections of the CNS

Primary bacterial suppurative encephalomyelitis has been reported in rabbits, with various bacterial species including *Staphylococcus* species[31] and *P. multocida*[54] being cultured as causative agents. Bacteria may reach the CNS by hematogenous extension or some other focus of infection, such as the nasal cavity. However, otogenic intracranial infection as an extension of otitis media has been reported with relative frequency in rabbits[18,31] compared with other species, and in those cases, clinical signs of central vestibular dysfunction may be preceded by peripheral vestibular signs, making the distinction between two vestibular syndromes difficult.[18,31] In most cases, encephalitis related to bacterial extension from the middle ear is diagnosed histologically on postmortem examination.

VIRAL DISEASES

Rabies

Rabies has been reported in rabbits, albeit rarely. Between 1971 and 1997, 30 cases of rabies in rabbits were reported in the United States to the Centers for Disease Control and Prevention.[40] Most cases were in pet rabbits located in states in which the raccoon variant of rabies was enzootic or epizootic. Infected rabbits usually develop varying degrees of paralysis or paresis in one or more limbs but may also develop head tremors. Early signs of rabies in rabbits may be nonspecific and include anorexia, fever, and lethargy.[40] No rabies vaccine is approved for use in rabbits in the United States; therefore pet rabbits housed outdoors should be protected from contact with wildlife, especially in areas where rabies is endemic or epizootic.

Herpes Simplex Virus

Herpes simplex virus (HSV) encephalitis is rare but has been reported in rabbits. In reported cases, rabbits with spontaneous

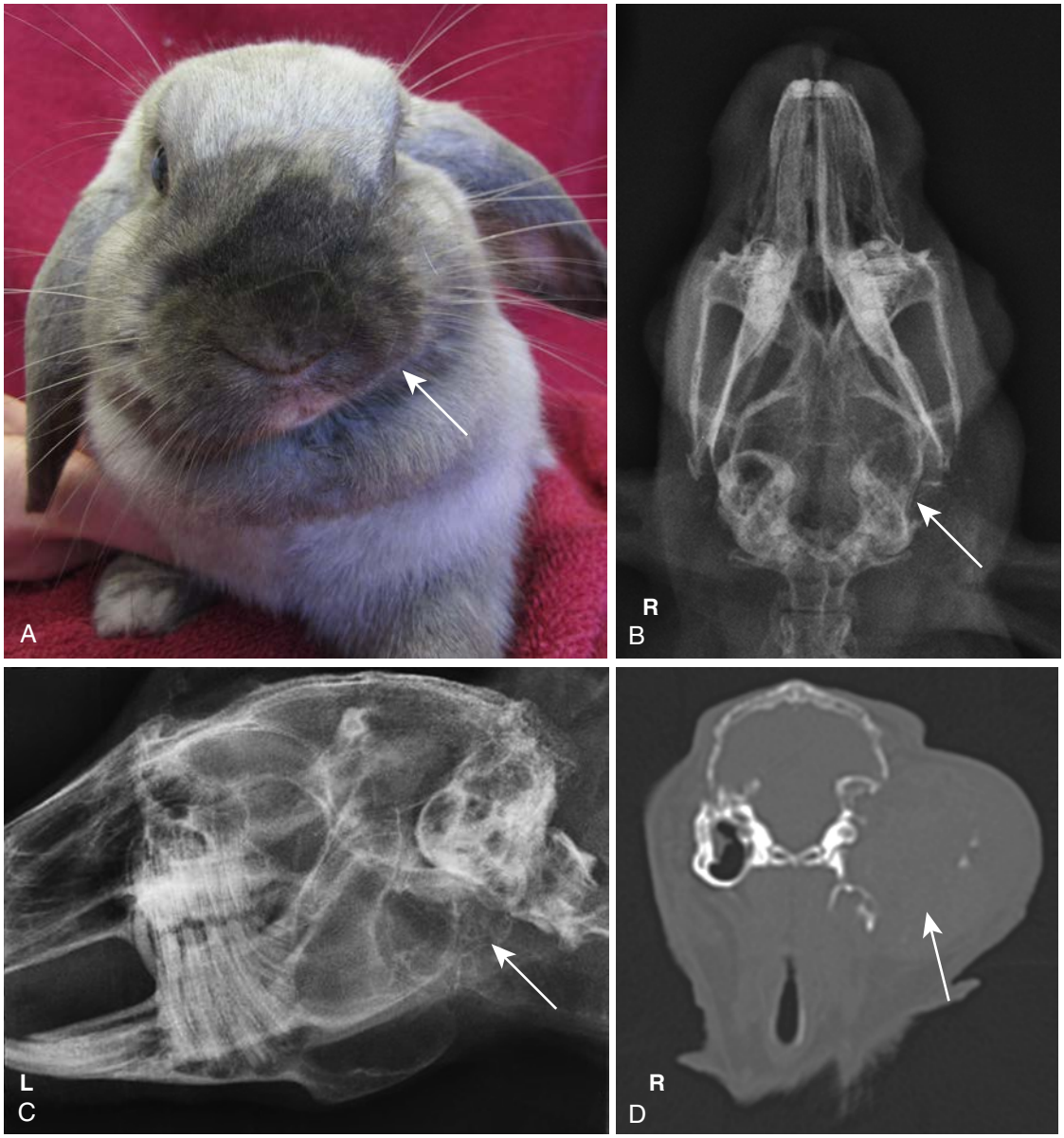


Fig. 18.6 (A) A female lop-eared rabbit with visible left-sided facial spasm. (B) Ventrodorsal radiograph of the head of this rabbit showing severe, irregular, lytic changes of the left bulla wall *(arrow)* and regional soft tissue swelling. (C) Oblique view of the left lytic bulla with expansile irregular thinning and lytic changes of the bulla wall *(arrow)*. (D) Transverse computed tomography image in a bone window performed 1 year later shows lytic destruction of the left osseus bulla with massive soft tissue swelling *(arrow)*. The final diagnosis was a bacterial otitis media resulting in abscessation and lysis of the osseous bulla. (Images B-D with permission from the Clinic for Diagnostic Imaging, University of Veterinary Medicine, Vienna, Austria.)

infection often have been associated with close contact with people with herpes labialis,[30,31,53] suggesting that transmission from people to rabbits is the likely source of infection. The disease is characterized by nonsuppurative meningoencephalitis, mainly located in the gray matter of the cerebral hemispheres. Clinical signs are circling and spinning, hypersalivation, and seizures.[19,31,53] The diagnosis is confirmed by the histologic presence of numerous intranuclear inclusions in neurons and glial cells. Immunohistochemistry and in situ hybridization performed in these case reports found the virus to be consistent with human HSV, and in one case HSV-1 infection was proven by PCR analysis.[31]

TRAUMA

Vertebral Fracture or Luxation

The most common cause of acute posterior paralysis is vertebral fracture or luxation (Fig. 18.9A). Fractures are more common than dislocations. The most common site of fracture (or luxation) is the lumbosacral region (L6-L7); however, fractures can occur at any site, including the thoracic vertebrate. This injury can occur in rabbits that are startled or frightened. In attempting to escape, the heavily muscled hindquarters of the rabbit twist about the lumbosacral junction, which acts as a fulcrum in applying leverage to the vertebral column. This

traumatic injury often is associated with inappropriate handling, but even properly restrained rabbits can suddenly flinch and fracture their lumbar vertebrae. In addition to paraplegia, neurologic signs may include loss of deep pain perception, skin sensation, and motor control of the urinary bladder and anal sphincter, depending on the amount of compromise to the spinal cord.

The clinical diagnosis of pelvic limb paresis or paralysis due to vertebral trauma is confirmed radiographically. Prognosis depends on the site and severity of the lesion and clinical signs. If the spinal cord is not transected, moderately affected rabbits may respond to conservative medical management, including very strict cage rest for several weeks to months. Medical therapy depends on the severity of the condition and usually includes administration of analgesics and nonsteroidal antiinflammatory drugs. Other treatment options for disc disease and spinal cord trauma are discussed below. The use of appropriate sedatives before performing procedures requiring restraint may help prevent this injury.

In rabbits with back injuries, always assess bladder function and control and institute manual bladder expression if indicated. Decubitus ulcers often develop, and the perineum may become soiled with urine and feces. Many rabbit owners are very dedicated to their rabbits, and if quality-of-life issues are addressed, some animals with severe posterior paresis can be fitted with a cart to permit movement, similar to carts used in paraplegic dogs. In rabbits with paralysis and lack of bladder function, euthanasia may be necessary.

DEGENERATIVE/ DEVELOPMENTAL DISORDERS

Osteoarthritis, Spondylosis, and Intervertebral Disc Disease

Age-related osteoarthritis (degenerative joint disease) and spondylosis deformans (degenerative spinal disease resulting in vertebral joint ankylosis) (Fig. 18.9B) are commonly encountered because improved husbandry and nutrition have extended the lives of pet rabbits. Additional risk factors for both osteoarthritis and spondylosis deformans are trauma, genetic predispositions, and obesity. Osteoarthritis may be associated with any joint but is most frequently seen in the stifles and elbows of aged rabbits. Spondylosis may occur anywhere along the length

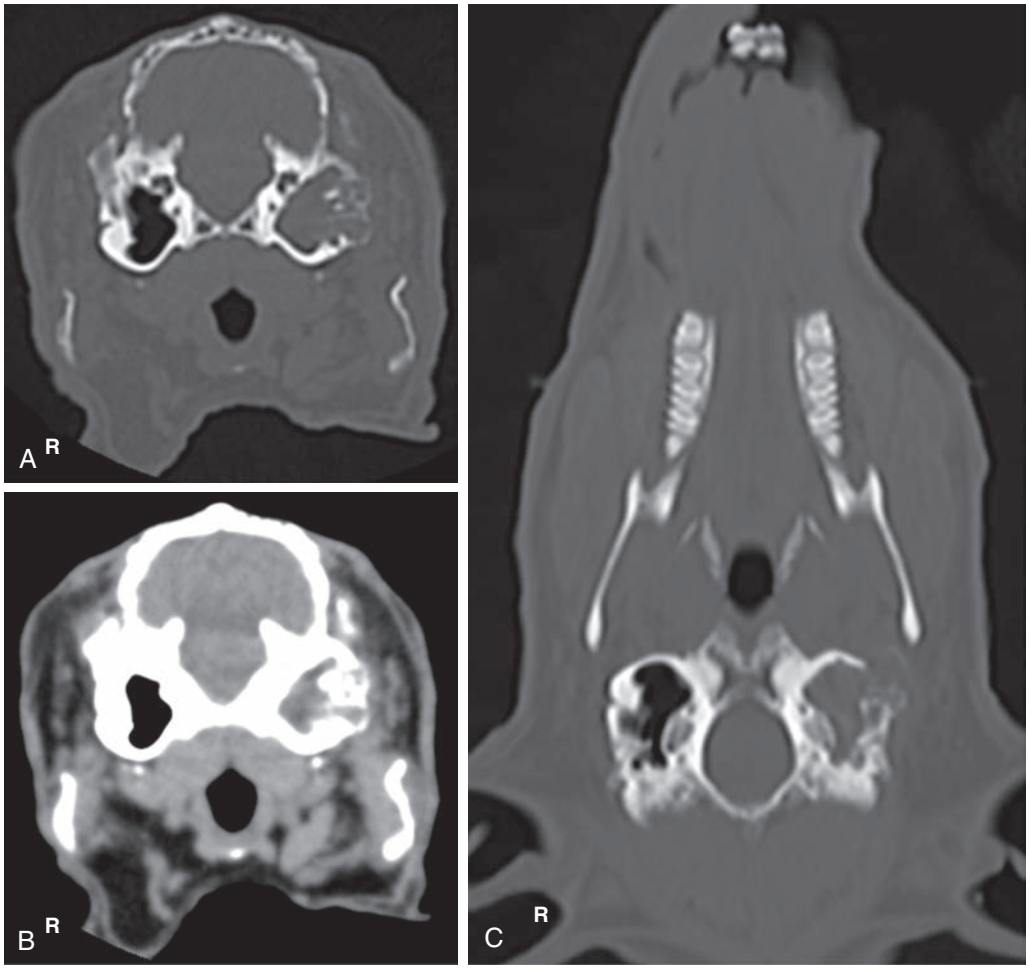


Fig. 18.7 Transverse (A, B) and dorsal (C) computed tomography images at the level of the tympanic bulla of a 5-year-old male rabbit with left facial nerve paralysis and no head tilt. The images are displayed using a bone (A, C) or soft tissue (B) algorithm/window and in 1-mm contiguous slices. There is increased attenuation within both external ear canals, and the left ear canal is mineralized with a mild mass effect and thickened wall (A). The left tympanic bulla is subjectively thickened along the ventral aspect and is occupied by a fluid/soft tissue attenuating material. Lysis is present on the lateral aspect of the left tympanic bulla. The right tympanic bulla has no abnormalities. The inner ears appear intact (A-C). Images courtesy Ricardo de Matos.

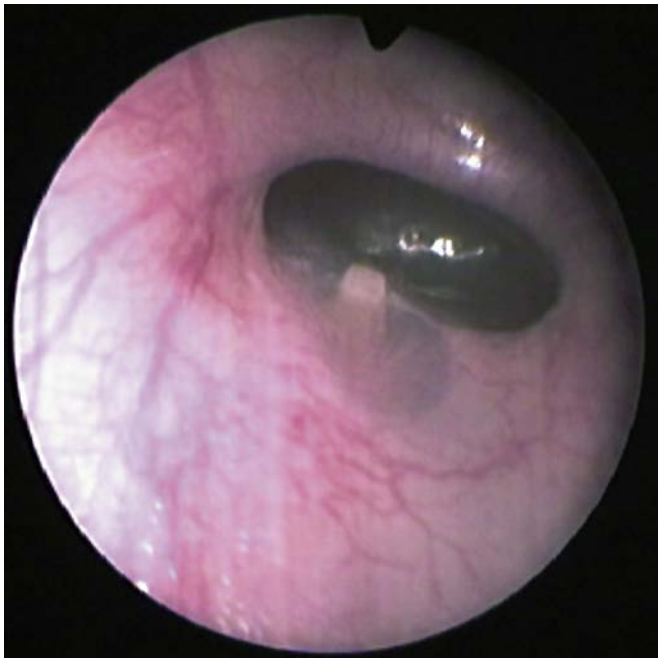


Fig. 18.8 Normal endoscopic appearance of the tympanic membrane in a 1.5-kg dwarf rabbit. (With permission from Vittorio Capello, DVM.)

of the spinal column but is frequently seen in the cervical vertebrae.[29] Kyphosis, lordosis, scoliosis, and hemivertebrae are common in pet rabbits, and although these are often incidental findings, they also may be associated with significant disease.[36]

Spontaneous degenerative spinal disease has been studied in laboratory rabbits.[29] Postmortem examinations of the spines of 32 New Zealand white and 3 AC/J rabbits, ranging in age from 3 months to 8½ years, were investigated systematically for degenerative changes. Three spontaneous degenerative changes were observed: chondroid metaplasia of the nucleus pulposus throughout the vertebral column by the age of 2 years; calcification of nucleus pulposus principally in the caudal thoracic spine; and spondylosis, especially in the cervicothoracic region. Disc protrusion and extrusion of nuclear material, associated with hind limb paralysis and urinary and fecal incontinence and confirmed at necropsy, are reported in rabbits.[65,70] Forceful movements and hyperflexion of the spine resulting in compression of the spinal cord is a likely cause. The clinical signs associated with extrusion of intervertebral disc material into the vertebral canal, particularly of the lumbar spine, can mimic spinal fractures.

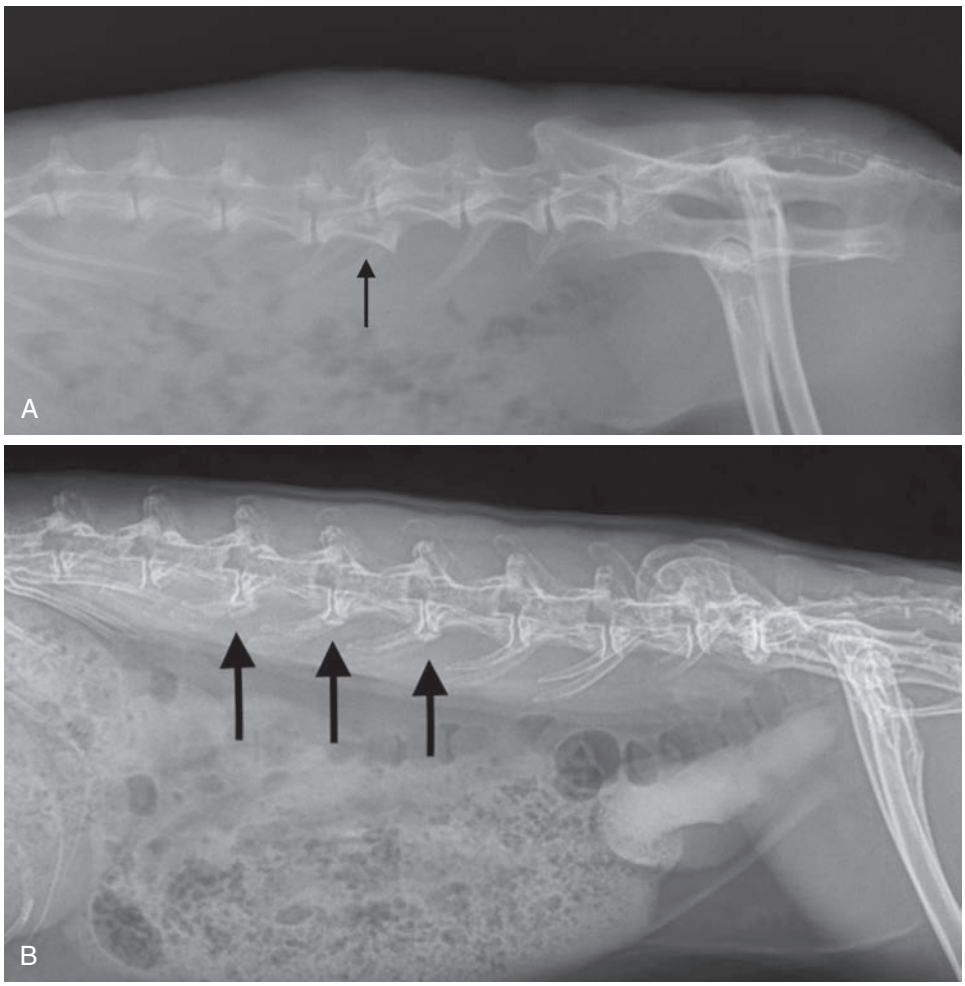


Fig. 18.9 (A) Lateral radiograph of the lumbar spine of a rabbit show a compression fracture and luxation of the L4-L5 vertebrae *(arrow)*. (B) Lateral radiograph of the lumbar spine of a from a 10-year-old male rabbit with a history of rear limb weakness and back pain. Radiographic evidence of spondylosis *(arrows)* can be seen between multiple lumbar vetebrae, as well as at the lumbosacral junction. The rabbit's clinical signs improved with a combination of oral antiinflammatory (meloxicam) and acupuncture therapy.

Clinical signs of musculoskeletal pain are often subtle, and many times owners associate the quiet and immobile nature of affected rabbits with aging alone. Pain associated with degenerative musculoskeletal diseases may result in an abnormal gait, lameness, or immobility, as well as decreased grooming behavior manifest as an unkempt coat, perineal soiling and dermatitis, or uneaten cecotrophs. Although spondylosis deformans per se does not cause clinical signs, neurologic signs may be secondary to trauma or disc herniation that has resulted in the spondylosis deformans. Spinal cord compression may cause neurologic deficits such as ataxia, proprioceptive deficits, paresis, paralysis, and fecal or urinary incontinence, or both. Spinal pain has also been associated with aggression and reduced gut mobility, leading to recurrent episodes of gastrointestinal disorders. Behavioral signs of pain are summarized in Table 18.1.

Radiographs of joints with degenerative disease may show capsular distension, osteophytosis, narrowing joint spaces, or surrounding soft tissue thickening or mineralization. Spondylosis deformans is identified radiographically mainly by spinal exostoses but also by other degenerative changes. With intervertebral disc degeneration, narrow disc spaces and calcification of the nucleus pulposus may be seen along with other degenerative spinal changes. However, these changes can be seen without the spinal cord being affected. Advanced imaging such as myelography, CT scanning, or magnetic resonance imaging is necessary to confirm spinal cord compression.

Multimodal therapy is often needed to improve the physical well-being of rabbits with degenerative diseases. Rabbits with pain and inflammation due to degenerative musculoskeletal conditions often show remarkable improvement when treated with analgesics including nonsteroidal antiinflammatory drugs, such as meloxicam, or centrally acting opiate-like agonists, such as tramadol. Gabapentin, a neuropathic pain analgesic, and polysulfated glycosaminoglycan (Adequan; American Regent Animal Health, Shirley, NY), a chondroprotectant and proteolytic enzyme inhibitor, have also been advocated for control of musculoskeletal pain. Some veterinarians also use nutraceuticals such as glucosamine and sodium chondroitin sulfate because of their reported beneficial effects on the healing of joint cartilage. Physical therapy to improve joint motion and function, as well as therapeutic laser therapy to improve blood supply and reduce inflammation, often play a role in improving the physical well-being of these patients. Lifestyle changes such as maintaining optimum body condition to prevent excessive weight loading on joints, adjusting housing to reduce the need to climb stairs or ramps, and providing nonslip, soft surfaces all help in reducing the difficulties associated with osteoarthritis and aging. Perineal scald treatment involves routinely cleaning the affected areas with a nonirritating cleanser, as well as using local antimicrobial creams (e.g., Silvadene cream) or systemic antibiotics as needed to control infection.

Some practitioners are using traditional Chinese veterinary medicine (TCVM) and chiropractic therapy in rabbits to address geriatric conditions such as osteoarthritis, degenerative joint disease, or disc herniation, as well as neurologic disease resulting in torticollis, pelvic limb paresis, or paralysis. The core of TCVM is the balance of Yin and Yang, and knowing species energetics and TCVM patterns to treat as noninvasively as possible is important. The rabbit is a Yin species compared with most mammals. *Yin* refers to the parasympathetic system such as resting, storage of energy, decreased heart rate, vasodilation, etc.[77] In Yin species, a gentle and quiet approach is required, and warm foods and herbs may be used to balance the Yin constitution.[77] In TCVM treatment, rabbit acupuncture points and herbal treatment can be extrapolated from canine transpositional points.[77] Currently, 51 acupoints have been described in the rabbit. Acupuncture treatment is generally more successful when beginning with simple point combinations (3-6 acupoints). Use the acupoints that are acceptable to the patient and avoid distal acupoints on the paws or toes that are considered "no-touch" zones in many species.[77] In general, use needle or acupressure Bai-hui or GV-20 first if available, and then start with acupoints around the neck, shoulders, and back.[77] Keep the first acupuncture treatments relatively short (5-10 minutes) and offer favorite foods to calm the patient. Aquapuncture with vitamin B_{12} and laser acustimulation may be used in patients that are less tolerant of traditional needling (L. Alvarez, personal communication, October 2017).

The following acupoints have also been described in the rabbit[76]:

Seizure: *Da-feng-men, Nao-shu*, LIV-3
Coma: GV-26, PC-6/TH-5, KID-1, PC-8, HT-9
General weakness: LI-10, ST-36

In herbal medicine, the dosage depends on different herbal formulas, severity of disease, size of animal, and individual variation.[76] Universal guidelines are difficult; however, in rabbits a dosage of 0.3 to 0.6 g/kg by mouth every 12 hours has been advocated as a baseline.[76] Most rabbits will readily accept herbal medications if mixed with a sweet liquid and offered by syringe (Table 18.2).

TABLE 18.1 Clinical Signs and Behavioral Changes Used to Assess Pain in Rabbits

Clinical Signs	Behavioral Changes
Change of body posture; tensing of abdominal muscles, pressing abdomen onto ground	Decreased grooming activity, piloerection; unkempt and ruffled fur coat
Change of body posture; tucking of abdomen, hunched body. Splinting on palpation	Decreased interest in food or cessation of food intake
Eyelids squinted, lack of focus, orbit may be retracted or bulging	Decreased frequency and duration of exploring/searching
Muzzle and nares contracture; increased intensity associated with level of pain	Decreased frequency and duration of movement or response to stimuli
Increased teeth grinding (bruxism)	Decreased conspecific interaction
Ears pinned back, held close to head	Irritable or aggressive temperament
Increased heart rate, frequency and depth of respirations	Stiff gait, lameness, staggering. Difficulty finding comfortable resting position

TABLE 18.2 Herbal Formulas in TCVM Suggested for Treatment of Musculoskeletal and Neurologic Disorders in Rabbits[76]

Clinical Condition	TCVM Pattern	Herbal Formula
General pain management	*Qi*- blood stagnation	Body sore[a] or *Shen Tong Zhu Yu*
Pelvic limb weakness	*Qi*- deficiency with stagnation	*Bu Yang Huan Wu*
Pelvic limb weakness	*Qi* + *Yin* deficiency	Hindquarter weakness[a]

[a]Manufactured and distributed by Jing-tang Herbal Inc., Reddick, FL.
TCVM, traditional Chinese veterinary medicine.

Veterinary chiropractic has been advocated as a treatment modality in exotic species and is a skill that must be taught in a comprehensive and logical manner, using both didactic and practical hands-on training.[48] For more introductory information, readers are referred to an overview of veterinary chiropractic in exotic species[48] and a case study demonstrating the use of TCVM in a rabbit with chronic pelvic limb weakness.[77]

Splay Leg

Splay leg, a developmental musculoskeletal condition, occurs in young rabbits or in sedentary senior rabbits. The condition may be related to housing on smooth, slippery flooring that results in the inability to adduct one or more limbs and the subsequent inability to ambulate effectively. The condition may be relatively mild, allowing some clumsy movement, or so severe that the animal cannot ambulate. The hind limbs are commonly affected in juvenile rabbits, resulting in various degrees of flattening and reduction of the femoral head, subluxation of the hip, valgus deformity, and patellar luxation.[59] If diagnosed early in young growing rabbits, splay deformities may be reversed by splinting and hobbling of affected limbs into a more appropriate anatomic position. Success requires frequent splint changes and anatomic assessment along with improved traction of bedding or flooring. Because this condition may also have a genetic component in a simple autosomal recessive pattern, breeding from the affected animal and its parents is discouraged.

Abduction or splaying of the front limbs may also be seen in sedentary senior rabbits. Long-term inactivity and associated muscle wasting may lead to abduction of the shoulder joints and splaying of the front limbs. Obesity and osteoarthritis may contribute to this condition, and, once developed, it is hard to treat effectively. Prevention or slowing progression involves trying to improve muscle tone through increased activity, housing on a surface that allows for firm footing, and treating any predisposing conditions.

Hereditary Cerebellar Degenerative Disease

Cerebellar cortical abiotrophy, a degenerative disease of the cerebellum, has been reported as a repeatable hereditary disease in offspring from a single breeding pair of rabbits.[62] This condition was described in littermates soon after birth and was reproduced in a subsequent litter. All affected rabbits were euthanized, and results of histopathologic, immunohistochemical, and electron microscopy investigations supported a diagnosis of cerebellar degenerative disease.

Radial Hemimelia

Hemimelia is a congenital bone dysmorphology characterized by a complete or partial absence of one or more bones of the limbs, usually present at birth. Radial hemimelia was been reported in a 1.5-month-old rabbit that presented for acute lameness after a fall.[50] Examination revealed antebrachial shortening, varus deformity of the carpal joint, and elbow joint luxation, and radiographs confirmed the diagnosis of radial hemimelia, lateral elbow luxation, first digit agenesis, and carpal bone malformations. The pathogenesis may involve abnormal embryonic development in the medial limb ray.

TOXICOSES

Lead Toxicosis

Lead toxicosis may cause neurologic signs in rabbits, including seizures, torticollis, and blindness,[39] although anemia, anorexia, depression, loss of body condition, and gastrointestinal stasis are more characteristic. Signs result from oxygen deprivation and CNS edema. Potential sources of lead contamination are household paint (structures built before 1978 in the United States), old glazed ceramic dishes, old linoleum, stained glass solder, and lead weights in curtain hems. Lead poisoning should be suspected in rabbits that have the tendency to chew at baseboards, flooring, plasterboard, or metallic objects. Plasma biochemical test results are usually unremarkable in rabbits with lead toxicosis; however, nonspecific hematologic changes such as anemia with reticulocytosis, presence of nucleated erythrocytes, hypochromasia, and basophilic stippling may be present.[39] When lead toxicosis is suspected, obtain abdominal radiographs to assess for gastrointestinal metallic densities that may represent the source of lead. Definitive diagnosis of lead toxicosis is based on measuring blood lead concentrations; however, lead levels can fluctuate based on chronicity of exposure and the form of lead ingested.[39] In general, treatment is indicated for any rabbit that has a blood lead concentration of >10 µg/dL. The recommended treatment is chelation with calcium disodium ethylenediamine tetraacetate (calcium versenate, 30 mg/kg subcutaneously every 12 hours for 5-7 days). Repeat measurement of blood lead levels after treatment because two courses of treatment 1 week apart may be required. Adjustable dog fencing works as a portable barrier in which to exercise house rabbits when not supervised and thereby prevent exposure to lead-containing objects in the home.

Fipronil Toxicosis

Fipronil is a topical ectoparasiticide approved for use in dogs and cats. Multiple reports exist of rabbits being intentionally dosed with fipronil and, within 24 hours, showing signs of anorexia, lethargy, and potentially fatal seizures.[7] The prognosis for recovery is guarded in rabbits already showing clinical signs. In cases of acute, known application of topical fipronil, gently bathe the rabbit with a mild shampoo and use precautions to

prevent subsequent hypothermia. Rabbits normally will groom any foreign substance off their fur coat; therefore be aware of oral ingestion of topical toxicants and consider treating with activated charcoal administered by an orogastric tube to adsorb toxicants from the stomach. Use injectable midazolam or diazepam as needed to control seizures. Additional supportive care including intravenous (IV) fluids and assist feeding may also be indicated.

Pyrethrin/Permethrin Toxicosis

Pyrethrin-containing ectoparasiticides are widely available, and some may cause anorexia, lethargy, muscle twitching, and seizures when applied to rabbits. Control of toxicosis and treatment of clinical signs are similar to protocols outlined for fipronil toxicosis.

METABOLIC DISORDERS

Pregnancy Toxemia

Pregnancy toxemia is rare in rabbits but, when seen, may produce neurologic signs. Toxemia primarily develops in late gestation in obese, multiparous does. Clinical signs vary from mild or nearly asymptomatic to severe, rapidly progressive, fatal disease. In severe cases, neurologic signs may be seen, including generalized weakness, depression, incoordination, convulsions, and coma. Death can occur within a few hours. Obesity and diminished dietary intake are predisposing factors. Postmortem and histopathologic findings often show fatty changes in the kidneys, heart, adrenal glands, and liver, with hepatic lipidosis and necrosis being severe. If diagnosed early, treatment may be successful and involves monitoring and treating electrolyte disturbances as well as associated ketosis with IV administration of crystalloid fluids with 5% glucose. Prevention involves maintaining the body condition of pregnant does, monitoring for anorexia, and providing a high-energy, palatable diet during late gestation.

Heat Stroke/Stress

Rabbits prefer environmental temperatures <80°F (27°C) and are particularly susceptible to heat stroke or stress. Rabbits dissipate heat to the environment from hairless areas of the body such as the feet and ear pinnas. With elevated body temperatures, whether physiologic or environmental, cutaneous vasodilation enhances heat dissipation from the skin as part of the heat-defense response. Cutaneous blood flow is controlled by the centrally regulated sympathetic nervous system.[56] As exposure to high levels of environmental heat and humidity continue, or if the rabbit exerts itself or is stressed, sympathetic nerve terminals release norepinephrine and subsequent vasoconstriction inhibits the physiologic cooling from the skin, exacerbating the potential for pathologic hyperthermia. Prolonged hyperthermia may eventually lead to damage or death of cerebellar Purkinje cells.[1] Decreased cerebral blood flow and perfusion pressure are seen during the onset of heat stroke and may result in cerebral ischemia and edema.[45] Depending on severity and duration of the hyperthermic episode, neurologic signs may include weakness, depression, incoordination, seizures, and coma and are accompanied by an increase in rectal temperature greater than 105°F (40.5°C). Treatment includes slowly reducing the body temperature by spraying the rabbit with tepid water or wrapping it in cool, wet towels and using fans, being careful to monitor body temperature and discontinue cooling as the rectal temperature approaches 102°F (38.9°C). Depending on clinical signs, benzodiazepines or other appropriate anesthetics can be administered to stimulate vasodilation and subsequent heat dissipation or to control seizures, if necessary. Intravenous hypertonic saline solution may be used to reduce cerebral edema. Resuscitation may involve a combination of crystalloid and colloid IV fluids. The primary goal is to give the least amount of fluids possible to reach the desired endpoints of resuscitation based on correction of the clinical signs, with special attention being given to monitoring for secondary gastrointestinal stasis, metabolic abnormalities, or renal failure. Pet rabbits housed outdoors during the summer, when the ambient temperature can exceed 85°F (29.4°C), require shade, good ventilation, and an adequate supply of cool drinking water.

NUTRITIONAL DISORDERS

With the current rigid quality-control standards for commercial feed production, confirmed nutritional problems are rare. However, the following nutritionally related neurologic or musculoskeletal problems occur in rabbits:

- **Vitamin E.** Nutritional muscular dystrophy, characterized by degeneration and necrosis of skeletal muscle myofibers and manifesting as clinical paresis, has been associated with hypovitaminosis E. Rabbits with vitamin E deficiency have increased plasma concentrations of creatine kinase and cholesterol. Prolonged storage of feed adversely affects the vitamin E content. Therefore feeding pet rabbits fresh pellets or supplementing the diet with an alternative vitamin E source such as wheat germ or leafy green vegetables should prevent this problem.
- **Vitamin A.** Hydrocephalus resulting from defective bone growth with stenosis of the cerebral aqueduct leading to increased cerebrospinal fluid pressure has been observed in young rabbits born to does with hypovitaminosis A.[51] In young, growing rabbits this syndrome is vitamin A responsive.
- **Vitamin D.** Excess vitamin D may cause resorption of bones and calcification of soft tissues such as arteries, liver, and kidneys.[51] Vitamin D deficiency has been associated with ataxia, paralysis, and death.[51]
- **Calcium.** Dietary calcium or vitamin D levels below established nutritional requirements may result in nutritional hyperparathyroidism and its related deleterious effects on the skeletons both of young, growing rabbits and of adult females. Young rabbits exhibit enlarged joints, crooked legs, arched backs, and enlarged rib costochondral junctions. Adults may experience demineralization of the bones, resulting in fragile bones and pathologic fractures. Hypocalcemia in lactating does has been associated with generalized

musculoskeletal weakness, paresis, and lateral recumbency. Adequate calcium supplementation rapidly reverses these problems.

- **Manganese.** Manganese acts as a coenzyme in amino acid metabolism and in the formation of cartilage matrix. Deficiency may result in poor bone consistency leading to brittle bones and limb problems.[51]
- **Magnesium.** Magnesium is a major component of bones and acts as a cofactor in many energy metabolism reactions.[51] Seizures may occur in rabbits maintained on diets deficient in magnesium.
- **Potassium.** Potassium plays a key role in the regulation of acid–base balance and is a cofactor of numerous enzymes. Deficiencies of dietary potassium may result in muscle weakness and paralysis.[51]

OTHER/MISCELLANEOUS DISEASES

Neoplastic

Lymphoma is reported to be the most common cause of CNS neoplasia in rabbits (see also Chapter 20).[74] Other tumors reported within the CNS of rabbits include several teratomas,[2,31,64] ependymoma,[42] plasma cell myeloma,[58] and a neuroblastoma.[61]

Both skeletal (axial and appendicular) and extraskeletal osteosarcomas have been reported in rabbits, and in most cases are associated with the facial bones (mandible, frontal bones).[69] Metastatic disease in the lungs, parietal pleura and peritoneum, heart, liver, kidneys, and pericardium have been reported. The biologic behavior of osteosarcoma and survival times after limb amputation have not been well defined in rabbits, but, like disease in dogs, tumors seem to readily metastasize.

Vascular

Neurologic signs in rabbits may be secondary to CNS hypoxia resulting from primary disease of the vascular system or heart. Cerebrovascular accidents have not been documented but have been suspected in older rabbits that develop sudden, unilateral loss of motor function. If other causes of neurologic disease have been ruled out, a diagnosis of cerebral thromboembolism may be considered. Supportive care allows recovery of function in many cases.

Idiopathic

In a study of 118 rabbits with varying signs of neurologic disease,[31] including vestibular signs, paresis, and seizures, a cause was not identified in 16 rabbits. A characteristic clinical phenomenon of tetraplegia, colloquially named "floppy rabbit syndrome," has been documented.[34] Several cases of this syndrome, representing a generalized lower motor neuron lesion, have been observed by one author (F.K.). Typically, acute tetraplegia is observed in young rabbits, but it is occasionally recognized in older animals (Fig. 18.10). Apart from paralysis, rabbits are clinically normal, will eat and drink spontaneously, and are able to urinate and defecate. The most prominent plasma biochemical change is increased creatine kinase activity, indicating possible myopathy as an underlying cause. Affected rabbits have no serologic evidence of *E. cuniculi* or *T. gondii* infection. Thus far, the cause is unknown, and primary metabolic, toxic, and neoplastic causes should be included as differential diagnoses. Usually, the prognosis is good, and rabbits spontaneously recover within 2 to 3 days.[34]



Fig. 18.10 (A) This 7-month-old male rabbit was presented showing sudden onset of tetraplegia. However, the rabbit was eating and drinking spontaneously when food and water were supplied within reach and could urinate and defecate normally. Neurologic examination revealed generalized lower motor neuron lesion indicating "floppy rabbit syndrome." The rabbit otherwise was clinically unremarkable. Results of serum biochemical analysis revealed high level of creatine kinase activity, and serologic testing was negative for *Encephalitozoon cuniculi*. (B) As in most cases of rabbits with this syndrome, the animal recovered spontaneously within 2 days without any treatment.

Miscellaneous

Various other conditions can cause generalized muscular weakness, incoordination, and other neuromusculoskeletal signs in rabbits. Neurologic signs in rabbits have been associated with listeriosis. Seizures also may be caused by hypoxia secondary to empyema, pneumonia, terminal stages of hepatic lipidosis, or metastatic tumors or associated with the azotemia and electrolyte disturbances of renal disease.[6,31] In addition, various hereditary disorders causing neuromuscular or skeletal diseases in rabbits have been reported.[46]

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19

Cardiovascular Disease

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OUTLINE

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Cardiac disease has become increasingly recognized in pet rabbits, presumably because pet rabbits are living longer and increasingly sophisticated diagnostic and therapeutic modalities are used for their care. However, despite their frequent use as laboratory models for cardiac disease in people, reports of spontaneous heart disease in rabbits are sporadic, and case numbers are often low. As a result, relatively little is known about the pathogenesis and treatment of naturally occurring heart disease in pet rabbits.

NORMAL CARDIOVASCULAR STRUCTURE AND RELATED ANATOMY

The rabbit heart is unique in several ways: the tricuspid valve is composed of two rather than three cusps, the aortic nerve is not associated with chemoreceptors but only with baroreceptors, the pulmonary artery and its branches are heavily muscular, and a persistent left cranial vena cava is normally present and drains into the coronary sinus.[4,15,17] In addition, the right and left auricles are relatively large compared with the rest of the atria, and the ostium of the coronary sinus is quite large.[15,27] Important clinically is the fact that the rabbit's myocardium has limited collateral circulation and is therefore predisposed to ischemia mediated by coronary vasoconstriction.[22]

The rabbit's thoracic cavity is extremely small compared to the rest of its body, and its heart occupies more of the thoracic area relative to other animals.[25] The mediastinum and pericardium of the rabbit normally contain fat, which can mimic cardiomegaly in obese animals.[26,27]

EXAMINATION OF THE RABBIT WITH CARDIOVASCULAR DISEASE

History

A thorough general history, including husbandry, diet, and past or present illnesses, should be obtained for rabbits suspected of having cardiac disease. Tachypnea, dyspnea, syncope, anorexia, weight loss, and malaise may be signs of heart disease in rabbits.[26]

Physical Examination

Take care to minimize the handling of a rabbit in cardiac distress; a complete physical examination and further diagnostic testing must sometimes be delayed until the rabbit is clinically stable. Stress can be minimized by examining the rabbit in a quiet room and moving slowly. Rabbits are a prey species and therefore very sensitive to external stimuli. If necessary, the rabbit may be sedated to minimize the risk of self-injury. Sedation can be achieved with midazolam (0.5–1 mg/kg intramuscularly [IM] or intravenously [IV]) (see also Chapter 37).[26,27,29] Provide flow-by oxygen as needed if the rabbit is dyspneic or becomes tachypneic with handling. In rabbits suspected of having cardiac disease or respiratory distress, focus the initial examination on observing the respiratory rate and pattern, obtaining the heart rate and rhythm, auscultating the thorax, examining the mucous membranes, and palpating the pulses. The normal heart rate is 200–300 beats/min, and the normal respiratory rate is 30–60 breaths/min[26,27]; however, the respiratory rate can approximate the heart rate in stressed animals. Rabbits are obligate nasal breathers; therefore, do

not occlude the nares during restraint. Peripheral pulses can often be palpated at the central artery of the ear and should be strong and synchronous with the heartbeat.[27] Two heart sounds (S_1 and S_2) are normally ausculted.[27] Referred upper airway sounds often overlie heart sounds and can mimic a murmur; therefore perform auscultation until the respiratory and heart sounds can be resolved.[26] Auscultation of any murmur should be followed by echocardiography.[27]

Rabbits with heart disease may have cyanotic or pale mucous membranes, arrhythmias, or heart murmurs. Rabbits in congestive heart failure often have tachycardia, tachypnea, and labored breathing; however, coughing is uncommon in the authors' experience. Pulses may be irregular or weak. The entire thorax should be auscultated to localize heart murmurs and detect extra heart sounds (gallop sounds), arrhythmias, and abnormal lung sounds. A pediatric stethoscope allows better localization of heart sounds in rabbits and is preferred for cardiac auscultation, whereas a stethoscope with a larger diaphragm enhances auscultation of the lungs. Auscultatory findings vary among rabbits with congestive heart failure, and these findings are not pathognomonic. The clinician may hear muffled heart and lung sounds with pleural effusion and increased bronchial sounds or crackles with pulmonary edema. However, the absence of crackles should not be used to rule out pulmonary edema in this species. Most rabbits in congestive heart failure have an increased, superficial respiratory pattern. In addition, although heart and lung sounds can be muffled in rabbits with pleural effusion, similar findings can be detected in obese rabbits with significant subcutaneous and intrathoracic fat deposits.[27]

DIAGNOSTIC METHODS

Diagnosis of cardiovascular disease is based on a complete history and physical examination, as well as findings of diagnostic tests. Thoracic radiographs, electrocardiography, echocardiography, and routine blood tests are useful in reaching a definitive diagnosis and developing a treatment plan.

Radiography

Thoracic radiography provides critical information in the patient with cardiopulmonary disease—namely, cardiac shape and size, pulmonary pattern, vascular pattern, and other thoracic lesions. The vertebral heart score has been determined for New Zealand white rabbits (n = 50), and for cross, lop, and dwarf breeds (n = 27) by using the method described by Buchanan et al. for dogs.[2,9,25] However, this measurement in rabbits is not commonly used in clinical practice in the United States.

Congestive heart failure and respiratory disease can be differentiated by evaluating thoracic radiographs. Radiographic findings supporting a diagnosis of cardiac disease are similar to those in other species: cardiac enlargement, pulmonary vascular enlargement, a pulmonary interstitial and alveolar pattern of pulmonary edema, and pleural effusion. However, in the normal rabbit, the cranial heart border is usually difficult to distinguish from the cranial mediastinum.[9] Figs. 19.1 and 19.2 show thoracic radiographs of a normal adult rabbit and a rabbit with congestive heart failure, respectively.

Electrocardiography

Electrocardiography is a simple and practical diagnostic test in rabbits with suspected or confirmed cardiac disease. An electrocardiogram (ECG) is critical to diagnosing and managing arrhythmias or syncope. The ECG may also be a helpful addition to the cardiac database. However, one should not use an ECG to assess or detect chamber enlargement or hypertrophy. In most rabbits, the ECG can be recorded with the rabbit awake and under only minimal restraint.[9] Record the ECG with the rabbit in sternal recumbency. Use toothless alligator-style electrodes to minimize skin trauma; then place medical-grade alcohol or electrode gel on the clips to enhance conduction. Record tracings with a vertical calibration of 2 cm/mV and a horizontal paper speed of 50 mm/s. Normal rabbit rhythm is sinus and does not include respiratory sinus arrhythmia.[26] Spontaneous changes in the QRS complex have been observed in normal rabbits in serial ECG recordings.

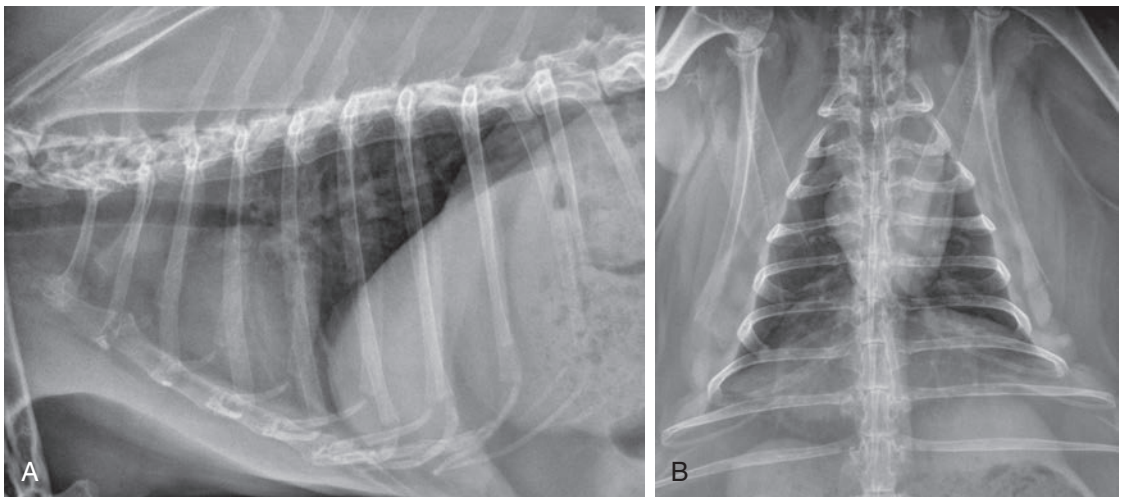


Fig. 19.1 Normal thoracic radiographs of a 6-year-old rabbit. (A) Right lateral projection. (B) Ventrodorsal projection.

Normal ECG values for a variety of pet rabbit breeds have been reported.[20,27] Reference ranges for ECGs are summarized in Table 19.1.

Echocardiography

Echocardiography provides a sensitive, accurate, noninvasive means of assessing cardiac structure and function. Most rabbits tolerate echocardiography without sedation, making it a practical diagnostic tool. However, in rabbits that are tachypneic or dyspneic, administer oxygen by face mask during restraint. The echocardiographic exam may be performed with the rabbit in lateral or sternal recumbency. Standard views used to evaluate dogs and cats can also be obtained with the rabbit. Because of the rabbit's rapid heart rate and small size, optimal evaluation requires a high-frequency transducer (e.g., 7.5 MHz) and a high frame-rate ultrasound machine. Two-dimensional and M-mode echocardiography assess cardiac structure, chamber size, wall thickness, and motion as well as extracardiac structures, masses, and pleural effusion. Color-flow, spectral, and tissue Doppler echocardiography assess direction and velocity of blood flow, further defining cardiac conditions with more insight on systolic and diastolic function.

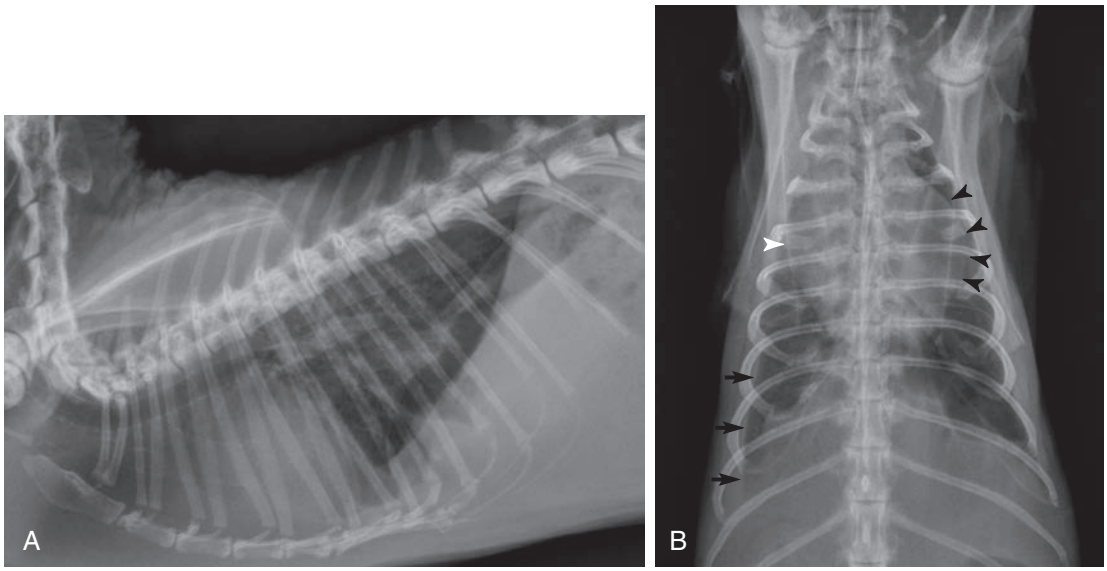


Fig. 19.2 Severe generalized cardiomegaly with congestive heart failure in a 5-year-old male castrated Angora rabbit. (A) In the right lateral projection, the cardiac silhouette is generally enlarged. The carina is elevated owing to left atrial and ventricular enlargement. A marked bronchointerstitial pattern is present in the caudal dorsal lung lobes, which is compatible with pulmonary edema. The lung lobes are mildly retracted and the ventral border of the cardiac silhouette is obscured, indicating mild pleural effusion. (B) In the ventrodorsal projection, a markedly enlarged left auricle is present *(black arrowheads).* An enlarged right atrium is also present *(white arrowhead).* An increased bronchointerstitial pattern is evident in the caudal lung lobes, which is more pronounced on the right than the left. Retraction of the lung lobe indicates pleural effusion *(black arrows).*

TABLE 19.1 Electrocardiographic Values (Lead II) in Clinically Normal Rabbits

	New Zealand White Rabbits (awake)[9] (N = 100: 44 M; 56 F)		Client-Owned Fancy, Fur, and Cross Breeds (awake)[20] (N = 46: 24 M [8 intact]; 22 F [8 intact])	
Parameter	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
Age, mo	—	6 (all)	—	2–84
Body weight, kg	2.62 ± 0.20	2.1–3.0	—	1.1–7.9
Heart rate, beats/min	243 ± 34	154– 330	264 ± 34	198–330
P wave amplitude, mV	0.05 ± 0.02	0.01–0.13	0.08 ± 0.02	0.04–0.12
P wave duration, s	0.032 ± 0.004	0.021–0.045	0.03 ± 0.01	0.01–0.05
P-R interval, s	0.050 ± 0.006	0.036–0.072	0.06 ± 0.01	0.04–0.08
R wave amplitude, mV	0.18 ± 0.09	0.04–0.42	0.21 ± 0.09	0.03–0.39
QRS duration, s	0.056 ± 0.004	0.043–0.066	0.04 ± 0.01	0.02–0.06
Q-T interval, s	0.143 ± 0.012	0.115–0.173	0.12 ± 0.02	0.08–0.16
T wave amplitude, mV	0.16 ± 0.07	0.01–0.51	0.11 ± 0.03	0.05–0.17
Mean electrical axis	—	–60° to 180°[a]	19° ± 31°	–43° to 80°

[a]In 85% of the rabbits, the mean electrical axis was –30° to 90°.

Relative structural measurements are similar to those in other mammalian species—e.g., the diameter of the left atrium is 1 to 1.5 times that of the aorta, the left and right atria are similar in size, and the diameter of the aorta and the pulmonary artery are equivalent.[27] In addition, the thickness of the left ventricular free wall approximates that of the interventricular septum and is 2 to 3 times thicker than the right ventricular free wall.[27] The coronary sinus, which encircles the atrioventricular junction, is normally quite large in the rabbit and should not be inadvertently interpreted as a congenital anomaly or a structural sign of right heart failure.[27]

Note that sedative drugs used for restraint, especially alpha-2 agonists such as dexmedetomidine and xylazine, may affect cardiac measurements. Reduced percent fractional shortening, reversal of the E/A ratio (peak velocity blood flow from gravity in early diastole [E wave] to peak velocity flow in late diastole due to atrial contraction [A wave]), decreased heart rate, and other changes have been documented with ketamine at a dose of 50 mg/kg IM and xylazine at 4 mg/kg IM.[34] Sedation with ketamine (20 mg/kg) and midazolam (2 mg/kg) given subcutaneously has been shown to be less cardiodepressive.[7] Normal echocardiographic values have been published for several breeds of rabbits (Tables 19.2 and 19.3).

Blood Pressure Measurement

Hypotension is not uncommon in rabbits anesthetized with inhalant agents.[11] Doppler-measured arterial blood pressure reportedly correlates well with direct peripheral (auricular artery) blood pressure measurement in the rabbit.[11] Using the technique described for a dog or a cat, place a 8.2-MHz frequency ultrasonic Doppler flow detector transducer over a branch of the radial artery on the medial aspect of the carpus, and use a pediatric blood pressure cuff with a width 40%–50% of the circumference of the limb.[11] The systolic blood pressure in the clinic is generally 120–180 mmHg.[27] Indirect blood pressure measurements <80 mmHg indicate hypotension.[11] Rabbits demonstrate circadian patterns in heart rate, as well as both systolic and diastolic blood pressure, with all three parameters being higher at night.[31]

DISEASES AND MANAGEMENT

Although the prevalence of cardiovascular disease in rabbits is unknown, the incidence generally increases with age—for example, over 4 years of age.[27,38] Large breeds, such as New Zealand white rabbits, may be overrepresented.[38]

To date, there are no cardiac drugs approved by the U.S. Food and Drug Administration for use in rabbits. Recommended dosages published in the literature are primarily based on extrapolation from dogs and cats, the authors' clinical experience, or both.[27] Drugs should always be dosed on a milligram-per-kilogram basis, and oral drugs should be given in liquid, not tablet, form.

Congestive Heart Failure

Congestive heart failure is the clinical condition in which pulmonary edema, pleural effusion, hepatomegaly, or all three

TABLE 19.2 M-mode and 2-dimensional Echocardiographic Measurements in Clinically Normal New Zealand White Rabbits[a,b]

Parameter	Awake (N = 100)[9]	Sedated[c] (N = 26)[7]
Body weight, kg	2.6 ± 0.2	2.3 ± 0.4
Age, mo	6 (all)	4 - 5
Sex	44 M; 56 F	26 M; 0 F
Heart rate, beats/min	227 ± 36	263 ± 37 (Doppler)
IVSd, mm	2.74 ± 0.51	2.65 ± 0.31
IVSs, mm	4.01 ± 0.70	3.63 ± 0.34
LVIDd, mm	13.28 ± 1.91	13.51 ± 1.05
LVIDs, mm	8.32 ± 1.47	8.64 ± 0.82
LVFWd, mm	2.78 ± 0.54	2.25 ± 0.29
LVFWs, mm	3.56 ± 0.52	3.15 ± 0.38
FS, %	37.17 ± 4.99	36.01 ± 4.31
EF, %	71.12 ± 6.32	69.58 ± 5.33
LA, mm	8.62 ± 1.02 (2D)	7.49 ± 1.14
Ao, mm	7.90 ± 0.77 (2D)	6.57 ± 0.46
LA/Ao	1.09 ± 0.10 (2D)	1.15 ± 0.19
EPSS, mm	—	1.41 ± 0.25

[a]Values are mean ± standard deviation except for age and sex.
[b]All values are M-mode derived unless indicated otherwise (2D).
[c]Sedated with ketamine (20 mg/kg SC) and midazolam (2 mg/kg SC).
Ao, aorta diameter; *EF,* ejection fraction; *EPSS,* E-point to septal separation; *FS,* fractional shortening; *IM,* intramuscularly; *IVSd,* interventricular septum in diastole; *IVSs* interventricular septum in systole; *LA,* left atrial diameter; *LVIDd,* left ventricular internal diameter in diastole; *LVIDs,* left ventricular internal diameter in systole; *LVFWd,* left ventricular free wall in diastole; *LVFWs,* left ventricular free wall in systole; *SC,* subcutaneously.

TABLE 19.3 Doppler Echocardiographic Measurements, Including Tissue Doppler Imaging (TDI) Derived Values, in Clinically Normal New Zealand White Rabbits[a]

Parameter	Awake (N = 100)[9]	Awake (N = 20)[34]	Sedated[7] (N = 26)
Body weight, kg	2.62 ± 0.20	2.92	2.3 ± 0.4
Age, mos	6 (all)	4	4 – 5
Sex	44 M; 56 F	10 M; 10 F	26 M; 0 F
Heart rate, beats/min	227 ± 36	234 ± 26	263 ± 37 (Doppler)
$Ao_{max,}$ m/s	0.75 ± 0.14	0.75 ± 0.20	0.86 ± 0.12
$PA_{max,}$ m/s	0.79 ± 0.16	—	0.78 ± 0.12
Mitral *E*-wave, m/s	0.64 ± 0.13	0.72 ± 0.14	0.78 ± 0.15
Mitral *A*-wave, m/s	0.52 ± 0.10	0.51 ± 0.15	0.55 ± 0.11
Mitral E/A	1.23 ± 0.25	1.44 ± 0.28	1.44 ± 0.16
IVRT, ms	36.29 ± 12.77	38 ± 5	31.42 ± 6.19
DT E, ms	64.95 ± 17.67	—	—
IVCT, ms	—	24 ± 11	25.00 ± 3.68
LVET, ms	—	126 ± 14	95.72 ± 10.21
Tei index	—	0.57 ± 0.20	0.60 ± 0.10
TDI Lat E′, m/s	—	0.067 ± 0.019	0.16 ± 0.05
TDI Sep E′, m/s	—	0.050 ± 0.017	0.11 ± 0.04
TDI Lat A′, m/s	—	0.039 ± 0.007	0.09 ± 0.03
TDI Sep A′, m/s	—	0.032 ± 0.009	0.08 ± 0.02
TDI Lat S′, m/s	—	0.055 ± 0.013	0.11 ± 0.02
TDI Sep S′, m/s	—	0.053 ± 0.010	0.10 ± 0.02
TDI Lat E′/A′	—	—	1.83 ± 0.43
TDI Sep E′/A′	—	—	1.55 ± 0.44
Mitral E/TDI Lat E′ (E/E′ lateral)	—	—	5.24 ± 1.55
Mitral E/TDI Sep E′ (E/E′ septal)	—	—	7.75 ± 2.69

[a]Values are mean ± standard deviation except age and sex.
[b]Sedated with ketamine (20 mg/kg SC) and midazolam (2 mg/kg SC).
[c]Sedated with ketamine (2 mg/kg IM) and medetomidine (0.15 mg/kg IM).
Aomax, maximal aortic outflow velocity; *DT E,* E-wave deceleration time; *IM,* intramuscularly; *IVCT,* isovolumetric contraction time; *IVRT,* isovolumetric relaxation time; *LVET,* left ventricular ejection time; *Mitral A,* peak transmitral late diastolic (atrial contraction) velocity; *Mitral E,* peak transmitral early diastolic velocity; *PAmax,* maximal pulmonary artery outflow velocity; *SC,* subcutaneously; *TDI Lat A′,* peak late diastolic mitral annular velocity from lateral wall; *TDI Lat E′,* peak early diastolic mitral annular velocity from lateral wall; *TDI Lat S′,* peak systolic mitral annular velocity from lateral wall; *TDI Sep A′,* peak late diastolic mitral annular velocity from septal wall; *TDI Sep E′,* peak early diastolic mitral annular velocity from septal wall; *TDI Sep S′,* peak systolic mitral annular velocity from septal wall.

develop as a result of structural or functional cardiac disease. As a prey species, rabbits may hide signs of illness or debilitation; thus, rabbits with congestive heart failure may be presented after heart disease has become advanced.[27] Any rabbit with respiratory abnormalities, particularly in the absence of upper respiratory signs, should be evaluated for heart disease. In some instances, aggressive fluid therapy for treatment of ileus or other abnormalities may result in abnormal breathing and radiographic signs of congestive heart failure.[26]

The goal of therapy for congestive heart failure is to relieve congestion, control future retention of sodium and fluids, and improve cardiac performance. Various management strategies are used during the acute stage. A common initial treatment protocol is to place the patient in a quiet cage with supplemental oxygen and administer parenteral furosemide (1–4 mg/kg IV or IM every 4–12 hours); nitroglycerin 2% ointment (1/8 inch applied transdermally every 6–12 hours) can be applied to the inner pinna for vasodilation to reduce preload. In a rabbit with pleural effusion, perform therapeutic pleurocentesis if the rabbit is dyspneic.

Long-term therapy of congestive heart failure should include a diuretic (furosemide 1–3 mg/kg by mouth [PO] every 8–24 hours) combined with treatment directed at the underlying precipitating cause.[27] Knowledge of the cardiac disease process is the basis of specific treatment of the underlying condition. An angiotensin-converting enzyme (ACE) inhibitor, such as enalapril maleate (0.25–0.5 mg/kg PO every 24–48 hours, begun every 24 hours), is often added to furosemide for the treatment of rabbits with congestive heart failure. Pimobendan (0.1–0.3 mg/kg PO every 12–24 hours), which has both inotropic and vasodilatory properties as well as antiinflammatory effects, may also be used for treatment of systolic dysfunction and myocardial failure.[27] During acute and chronic management, it is

critical that clinical and radiographic signs, hydration status, appetite, and body weight, as well as serum or plasma blood urea nitrogen, creatinine, and electrolyte concentrations be monitored.

Congenital Heart Disease

Congenital heart disease is rarely reported in rabbits. A ventricular septal defect in an unnamed breed and suspected cor triatriatum dexter in a dwarf lop were both diagnosed with echocardiography.[28,38] A ventricular septal defect, pulmonary hypertension, and a valvular cyst identified at necropsy have been described in a New Zealand white rabbit.[18]

Arrhythmias

Although relatively rare, arrhythmias such as atrial fibrillation and ventricular premature complexes have been identified in pet rabbits with underlying cardiomyopathies and congestive heart failure.[21,26,27] In a rabbit with a clinically relevant arrhythmia, the treatment protocol should be based on ECG findings and clinical signs.

For anesthesia-induced bradycardia, glycopyrrolate may be more effective than atropine sulfate in increasing heart rate, in large part because some rabbits produce atropinesterases.[24,38] For syncope associated with bradycardia, oral theophylline or pacemaker implantation may be indicated. Although wireless-powered microimplant pacemakers have been used experimentally in New Zealand white rabbits,[13] clinical use of a pacemaker has not yet been reported in a pet rabbit.

Supraventricular tachycardias may be treated with oral digoxin or diltiazem. If digoxin is used, monitor the rabbit's appetite as well as stool production and measure blood levels by ≤8 hours after the last dose.[27] The dose may need to be reduced or digoxin discontinued if the rabbit becomes anorexic or develops ileus.[38] Use of diltiazem can result in hypotension, so closely monitor rabbits treated with this agent. Ventricular tachyarrhythmias may respond to boluses of intravenous lidocaine.[27,38] Using dosages determined for dogs, sotalol and mexiletine have also been used anecdotally in rabbits.[38]

Empirical dosages are published for lidocaine, atropine, and glycopyrrolate (see the Appendix). Other antiarrhythmic drugs have been used at dosages published for cats or ferrets.

Myocardial Disease

Numerous myocardial diseases have been reported in rabbits, and cardiomyopathy is a common postmortem finding in older rabbits.[28] Giants breeds may be most susceptible.[38] Hypertrophic, restrictive, and dilated forms of cardiomyopathy have all been reported,[38] and anecdotally, dilated cardiomyopathy appears to be the form of cardiomyopathy diagnosed most frequently in rabbits.[23,26]

The primary causes of cardiomyopathy in rabbits are generally unknown.[38] Vitamin E deficiency produces a muscular dystrophy in which the myocardium may be affected.[3] Taurine deficiency has not been reported in rabbits.[26] However, in a study of 5-month-old albino rabbits with experimentally induced aortic regurgitation and subsequent congestive heart failure, daily supplementation with taurine dosed at 100 mg/kg significantly improved myocardial contractility and decreased mortality.[35] There are no published reports of pet rabbits being supplemented with taurine.[26]

Although infectious myocarditis is rare in pet rabbits, organisms reported to be associated with myocarditis in this species include *Pasteurella multocida, Salmonella* species, *Clostridium piliforme*, *Encephalitozoon cuniculi,* and coronavirus.[1,5,6,16]Although infection with a coronavirus is used to create a rabbit model of dilated cardiomyopathy, no naturally occurring cases have been reported.[1,4] In experimental studies, myocardial disease has also been induced by inoculation of *Trypanosoma cruzi*[30] and administration of doxorubicin.[37]

The alpha-agonist drug detomidine has been associated with myocardial necrosis and fibrosis in New Zealand white rabbits.[14] A similar ischemia-mediated process is suggested in association with ketamine/xylazine administration in Dutch belted rabbits.[22] Rabbits subjected to intermittent crowding developed an apparent stress-induced cardiomyopathy, which was fatal in 34 of 44 experimental animals.[39]

Valvular Disease

Mitral and tricuspid insufficiencies are not uncommon and have been identified in pet rabbits, particularly as animals age.[23,25,38] Valvular insufficiencies may be associated with primary valve degeneration, cardiomyopathy, or infection. Progression of the condition leads to volume overload and potential congestive heart failure. A focal murmur is the most common clinical finding. Valvular disease is diagnosed with two-dimensional and Doppler echocardiography (Fig. 19.3). Echocardiographic findings most often include thickening of one or both atrioventricular valves, dilation of cardiac chambers, and turbulent regurgitation of blood detected by Doppler scanning.

Dental Disease and Abscessation

Vegetative endocarditis due to *Haemophilus parainfluenzae was* diagnosed post mortem in a 4-year-old rabbit that had presented with a 2-week history of progressive lethargy and weight loss.[22a] A continuous IV/VI parasternal murmur and an arrhythmia had been ausculted on physical examination. The ECG findings revealed atrial fibrillation conducted with a left bundle branch morphology, and echocardiography showed vegetative and aortic endocarditis and a secondary aortocavitary fistula. Bacteremia was suspected secondary to severe dental disease.

Vascular Disease

Spontaneous arteriosclerosis of the aorta and other arteries has been observed in nearly all rabbit breeds, with historical incidence ranging from 13% in Dutch breeds to 40% or greater in Flemish giant, chinchilla, New Zealand white, and English spot breeds.[8,19] Arterial walls and other soft tissues mineralize; the aortic arch and descending thoracic aorta are most commonly affected. Radiopaque vessels, caused by calcification, may be visible on radiographs.[19,32] Clinical signs, if present, may include lethargy, anorexia, and weight loss. The cause is unknown; however, such variation of incidence by breed suggests a genetic predisposition.[8,19]

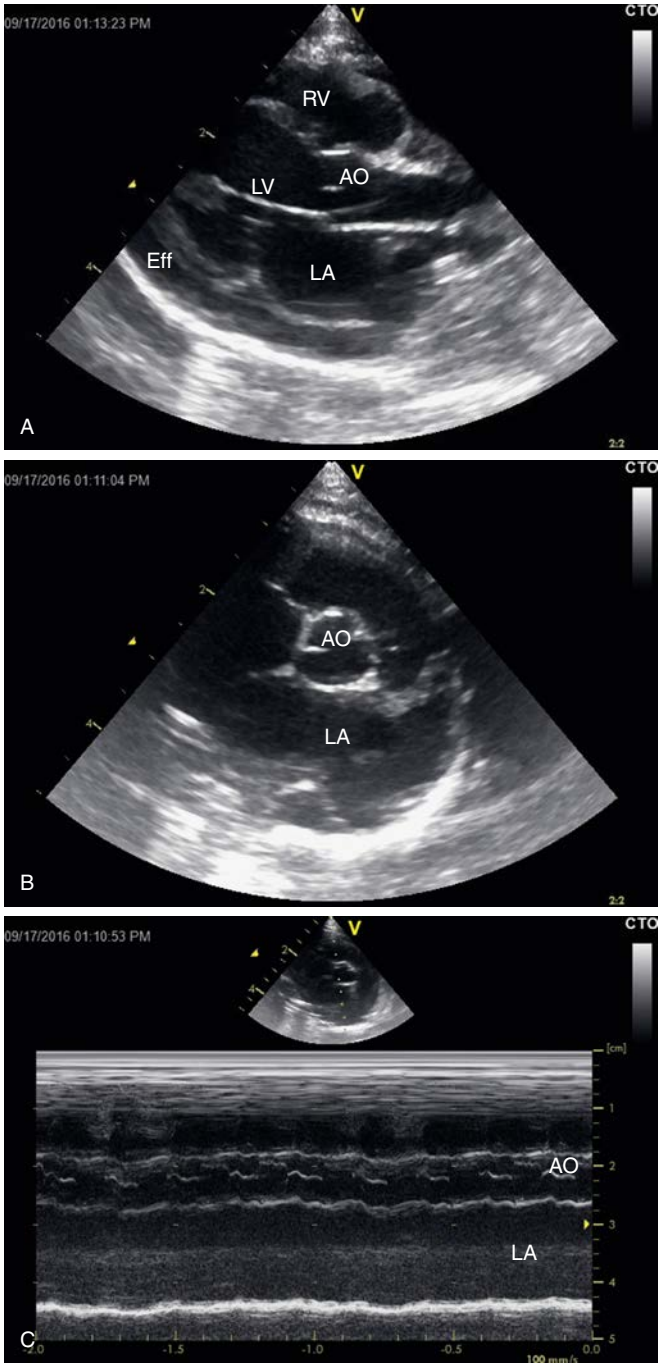


Fig. 19.3 Standard echocardiographic views in rabbits with cardiac disease. (A) Right parasternal long-axis view of a rabbit with dilated cardiomyopathy and pericardial effusion, which is a manifestation of congestive heart failure. Note the dilated left atrium and left ventricle, and the thin left ventricular walls. (B) Right parasternal short-axis view at the level of the heart base in a rabbit with dilated cardiomyopathy. Note the dilated left atrium and auricle. (C) M-mode derived from a right parasternal short-axis view of a rabbit with dilated cardiomyopathy, showing aortic root and left atrial dimensions. *LV,* Left ventricle; *LA,* left atrium; *RV,* right ventricle; *RA,* right atrium; *Ao,* aorta; eff, pericardial effusion.

Hypervitaminosis D, resulting from errors in feed formulation, can result in excessive absorption of dietary calcium and subsequent calcification of blood vessel walls and other soft tissues.[10,33] It has also been suggested that aortic mineralization can occur in hypercalcemic rabbits secondary to renal disease and compromised calcium excretion.[10]

Pulmonary hypertension associated with high altitude has been reported in a rabbit.[12] Lesions included right ventricular hypertrophy and pulmonary artery proliferation from hypoxia. Based on research, rabbits with pulmonary hypertension may respond to phosphodiesterase type-5 inhibitors, particularly vardenafil.[36] Systemic hypertension is reportedly rare but may occur with renal failure.[27] Rabbits tolerate enalapril well; however, anecdotal reports suggest that they are particularly susceptible to the hypotensive effects of benazepril.[29]

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Lymphoreticular Disorders, Thymoma, and Other Neoplastic Diseases

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Much of the early data and what we understand about neoplasia in domestic rabbits originated from laboratory rabbits used as models in biomedical research. However, the popularity of pet rabbits in recent years, combined with their better care and longer natural life span, has broadened our knowledge base.[38] Numerous case reports, as well as research studies related to experimentally induced tumors, have contributed to our understanding of cancer in pet rabbits and provide current descriptions of biological behavior.

The rabbit's physiology can present its own unique challenges, but the approach to diagnosis, staging, and treatment of the rabbit cancer patient is similar to that of other small animals. A histopathologic diagnosis from tissue biopsy is needed to make diagnostic and therapeutic decisions for the patient. Cytologic results of a fine-needle aspirate may be sufficient when an accurate diagnosis is possible. Access to diagnostic imaging modalities such as radiography, ultrasonography, and often computed tomography (CT) scans or magnetic resonance imaging is needed, as well as the ability to consult with a veterinary oncologist for advice in diagnosis and treatment. Prognosis for rabbit cancer patients depends on many variables, including tumor type, grade, and staging, patient health and concurrent disease, patient tolerance, and owner willingness to undertake the financial obligations and known risks of therapy.

Once a diagnosis is made and the patient has been evaluated, treatment options can be offered.[94] For locally aggressive tumors, surgical resection and/or radiation therapy is indicated, depending on tumor type, location, and ability to obtain clean margins. For systemic neoplasia, chemotherapy is indicated, although effective protocols in rabbits are lacking. In many cases, a combination of surgery, chemotherapy, and radiation treatment may be required, but the sensitive and even fractious nature of rabbits limits treatment options. Depending on the type of cancer, extending the quality of life is often the goal rather than aggressive treatment, which can carry significant risks. Discussion of euthanasia as an option is sensible depending on the particular prognosis.

LYMPHORETICULAR NEOPLASIA

Neoplasia of the lymphoreticular system is common in domestic rabbits. Before the 1960s, only rare cases of lymphoid neoplasia were reported.[32,92] Most cases of lymphoreticular neoplasia reported in both laboratory and pet rabbits have been diagnosed as generalized or multicentric lymphoma; however, cutaneous lymphoma, lymphoid leukemia, thymic lymphoma, and thymomas are described with varying incidence. Since the 1990s, thymic neoplasias in rabbits have been reported commonly.

Etiology

The cause of lymphoreticular neoplasia in rabbits is largely unknown and likely multifactorial. Owing to their use in biomedical research, disease pathogenesis of experimentally induced lymphoid neoplasia in rabbits is well described; however, few studies have investigated the cause of naturally occurring lymphoid disorders. In an early report, multiple

cases of naturally occurring lymphoma were described in rabbits from a breeding farm,[62] leading to speculation that a breed or strain susceptibility exists or that disease is associated with an infectious agent.[26,62,92] A strain susceptibility associated with a single autosomal recessive gene, termed *Is*, was shown in wirehair rabbits, where affected rabbits typically die at 5 to 13 months of age, usually with generalized lymphoma involving visceral organs and lymph nodes.[26] Generalized lymphoma in rabbits has been speculated as compatible with vertical transmission of an oncogenic virus, as occurs with feline leukemia virus[26] or murine C-type retrovirus.[91] Virus-like particles were demonstrated by electron microscopy in the kidneys of a 7-month-old New Zealand white rabbit with generalized lymphoma; however, the significance of these particles was not determined.[33] In a study of cutaneous lymphoma in rabbits, no evidence of a retrovirus or a herpes virus was detected by polymerase chain reaction testing.[80] To date, the hypothesis that an oncogenic virus may be involved in the pathogenesis of lymphoid disease in rabbits has not been confirmed.

Types of Lymphoreticular Neoplasia

Multicentric Lymphoma

Multicentric lymphoma is the most common type of lymphoproliferative disease in rabbits and has been reported in several breeds, including New Zealand white, Japanese white, Dutch, and Netherland dwarf rabbits.[12,37,84,90,91] Clinically, lymphoma has been observed in a variety of rabbit breeds, including satin, mini lop, and tan breeds. Lymphoma can occur in rabbits of all ages, from animals less than 1 year of age to geriatric animals.[12,26-28,33,37,67,84,90-92,96,103]

Multicentric lymphomas of both T-cell and B-cell origin are documented in rabbits; however, B-cell lymphomas appear more common.[28,44,77,90,96] Neoplasia determined as of T-cell origin was reported in a rabbit with multicentric lymphoma and lymphocytic leukemia.[90] Multicentric T-cell rich, B-cell lymphoma was described in a dwarf Dutch rabbit, involving the skin, lungs, kidneys, liver, intestines, and lymph nodes.[28] B-cell lymphoma has been described involving the Harder's gland in a young rabbit with acute unilateral exophthalmos,[96] the cecum of a 6-year-old rabbit,[44] and the lumbar vertebrae of a rabbit with pelvic paralysis.[77] Rabbits with multicentric lymphoma may exhibit nonspecific general signs such as anorexia, lethargy, emaciation, pallor, diarrhea, exophthalmos, upper respiratory stridor, and rhinitis, depending on organ involvement and location.

Laboratory findings depend on the organs involved. Results of plasma biochemical analysis may be unremarkable or reveal increases in concentrations of aspartate aminotransferase, creatine phosphokinase, blood urea nitrogen, and creatinine. Rabbits may be moderately to severely anemic[26,103]; in young rabbits, fluctuating and depressed hematocrit values may be the best diagnostic tool for early identification of lymphoma.[26] The white blood cell count is often within reference intervals; however, rabbits with lymphoma may show a leukemic phase. In young rabbits with multicentric lymphoma, high white blood cell counts were less frequent than a relative predominance of lymphoid cells, including immature and atypical cells, representing 80% to 90% of total white cells.[26] At necropsy, neoplastic lesions are commonly found in the lymph nodes, gastrointestinal tract, kidneys, liver, spleen, adrenal glands, gonads, and bone marrow.[12,33,44,91,92,103] Less-common sites of neoplastic infiltrates are the auditory meatus, vertebrae, eyes, and heart.[12,77]

Cutaneous Lymphoma

Cutaneous lymphoma is usually primary but can be secondary to multicentric involvement. Two main forms are distinguished histologically and immunohistochemically: the epitheliotrophic form (a subtype of which is *mycosis fungoides)*, in which T-cell lymphocytes infiltrate the epidermis and adnexal structures, and the nonepitheliotropic form, in which B-cell lymphocytes infiltrate the middle and deep portions of the dermis. Both types of cutaneous lymphoma have been reported in rabbits.[80,103] Cutaneous B-cell lymphomas in rabbits have been further divided into two subtypes: a large cell, centroblastic/centrocytic subtype, and a T-cell–rich B-cell subtype, which is rare in species other than horses.[80] Cutaneous lymphomas have the potential to metastasize to visceral organs, or cases may be diagnosed as visceral lymphomas with cutaneous involvement. Cutaneous lymphoma has been more commonly reported in pet rabbits in Europe than in North America.[80,97] Although no evidence of a virus has been found, other risk factors such as genetic or extrinsic factors may play a role.[80] In a large retrospective study of cutaneous neoplasms in pet rabbits in the United States over 16 years, a single case of lymphoma in the flank of a 4-year-old female rabbit was reported. In this case, epitheliotropism was not noted.[97]

Cutaneous lymphoma can develop in rabbits of all ages, and reported cases involve rabbits from 7 months to 9 years of age.[39,46,80,97,103] Affected rabbits can present with solitary or multiple subcutaneous nodules in various locations, erythematous alopecia and hemorrhagic crusts involving the chin and neck, blepharitis, or nonpruitic alopecia. [39,80,103] In three cases seen by one author (K.Q.), rabbits presented because of one or more subcutaneous masses. In a 7-year-old rabbit, cutaneous lymphoblastic lymphoma was diagnosed by excisional biopsy of a subcutaneous nodule on its dorsal neck. Three more masses developed within 1 month and were excised, but the rabbit died 2 months after the first biopsy. At necropsy, lymphoma was found in the cervical, mesenteric, and thoracic nodes. A rabbit that presented with a large, hemorrhagic mass on the ventral thorax was diagnosed with lymphoma involving the skin mass and spleen at necropsy. In a 9-year-old rabbit that presented with multifocal subcutaneous masses on the dorsum and ventral abdomen, lymphoma was found to be widely disseminated to the skin and subcutis, all abdominal organs, lungs, diaphragm, heart, adipose tissues, lymph nodes, mandible, and incisor pulp cavity at necropsy (Fig. 20.1). Because of the extensive involvement of multiple sites, the primary source of lymphoma was unclear.

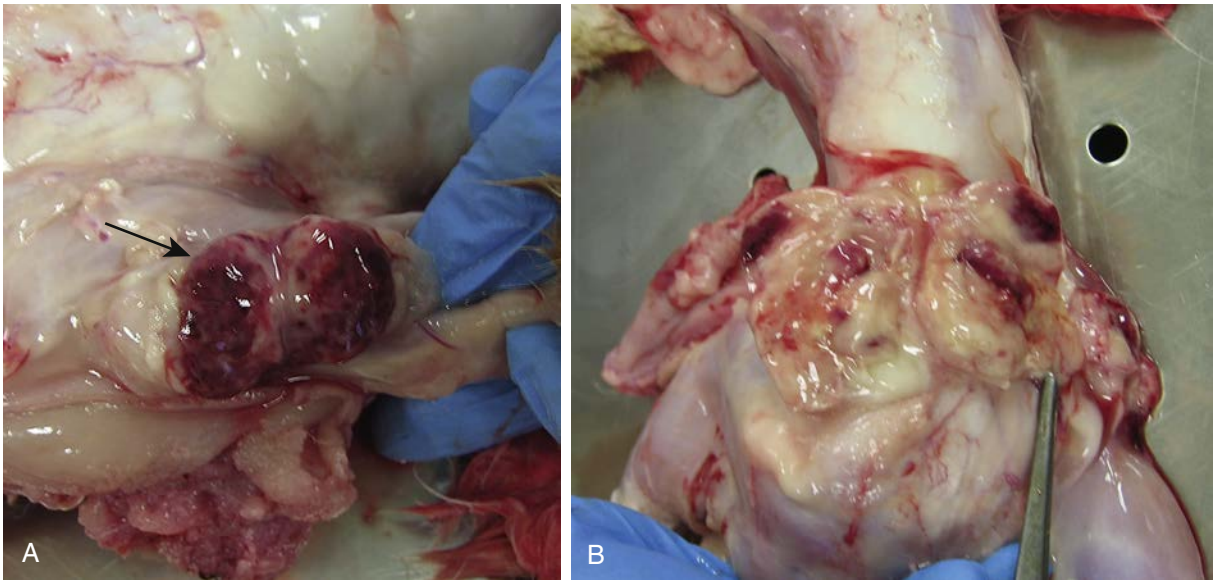


Fig. 20.1 Multicentric large cell lymphoma in a rabbit at necropsy. (A) Enlarged and hemorrhagic lymph nodes *(arrow)*. (B). Lymphoma of the subcutis over the back.

Leukemia

Lymphoid leukemia is the proliferation of neoplastic lymphocytes that typically originate in the bone marrow and occasionally in the spleen. The neoplastic cells may or may not be found circulating in peripheral blood. Lymphoblastic leukemia and myeloid leukemia have been documented in rabbits.[12,22,66,90] In rabbits with lymphoid leukemia, white blood cell counts have ranged from 30,000 to more than 100,000 cells/μL. In all reports of rabbits with lymphoblastic leukemia, neoplastic cells were present in bone marrow, lymph nodes, and other organs typical of stage IV lymphoma.

Thymic Lymphoma

Thymic lymphoma is a neoplasm of T-lymphocytic origin, possibly with other organ and systemic involvement. The clinical presentation of thymic lymphoma is similar to that of thymoma (see below). Paraneoplastic syndromes of chylothorax and exfoliative dermatitis have been reported in rabbits with thymic lymphoma.[76,82]

Thymoma/ Thymic Carcinoma

Normal rabbits have a persistent large thymus that lies craniventral to the heart and extends into the thoracic inlet (Fig. 20.2).[53] In adult rabbits, the thymus can become hyperplastic and enlarge up to three or four times normal size, grossly resembling a tumor but with no neoplastic characteristics on histologic examination.[101] Thymomas and thymic carcinomas are tumors derived from the epithelial components of the thymus. These tumors differ in that thymomas are generally slow growing and benign and may feature a mix of lymphoid and epithelial cells, whereas thymic carcinomas have malignant cytologic features and are more likely to spread.[21] Differentiating the tumor types histologically can be difficult and is based on the morphologic and histologic features.[21] Thymomas in rabbits have been graded as lymphocyte predominant, mixed lymphoepithelial, and epithelial predominant types.[55]

Thymomas are more common in rabbits than thymic lymphoma or thymic carcinoma.[55] The incidence of thymomas is higher in older rabbits but does not appear to differ by sex, and no breed predilection has been found.[4,55] The first report of a thymic tumor in a rabbit in 1939 described a 4-year-old laboratory rabbit that was euthanized because of weight loss and weakness.[75] At necropsy, a large thymic mass was identified with metastasis to the heart, lungs, and abdominal lymph nodes. In an early study of female laboratory rabbits with two or more primary tumors, 4 of 55 (7%) had thymomas, all of which occurred in rabbits with uterine adenocarcinoma.[32] In two case series of 13 and 19 rabbits with thymoma, mean age at presentation was 6.1 and 6.7 years, respectively.[4,55]

The presence of the mediastinal mass usually causes difficulty breathing (hyperpnea, open-mouth breathing), which is one of most common presenting complaints.[4,55] Physical examination findings typically relate to respiratory symptoms with nasal flaring evident, secondary to increased respiratory rate and effort.[52,76] Auscultation of the thoracic cavity may reveal decreased or muffled lung sounds over the anterior mediastinum or ventral or dorsal lung lobes, depending on the size and extent of the thymoma. Although subjective, decreased compressibility of the thoracic cavity in smaller breeds of rabbits may be appreciated. On thoracic radiographs, a mediastinal mass often displacing the trachea may be identified (Fig. 20.3).

Uniquely, rabbits with thymic masses may have exophthalmos or present with prolapse of the third eyelids.[4,52,55,98] In affected rabbits with exophthalmos, the eyes can be retropulsed, suggesting that the exophthalmos is not caused by a retrobulbar mass. These signs are consistent with a diagnosis of cranial vena

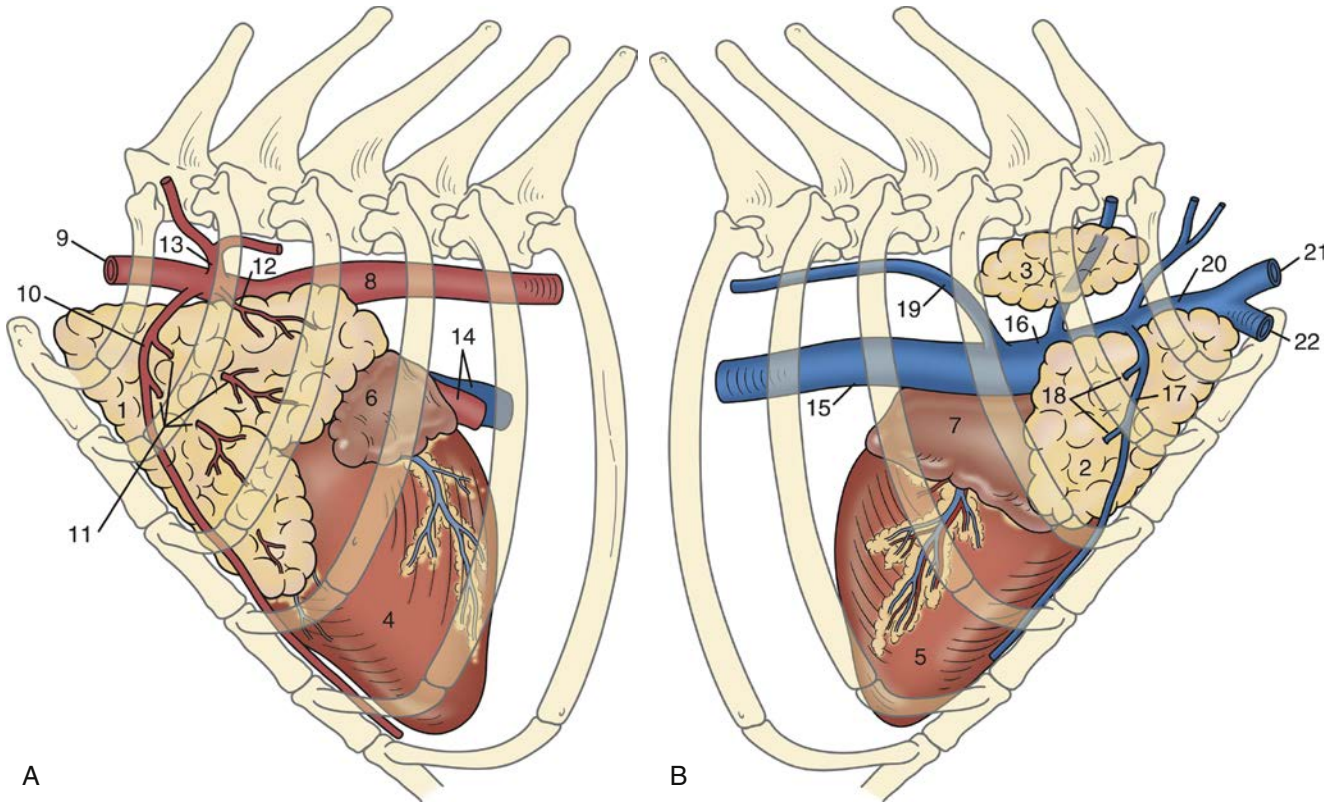


Fig. 20.2 Anatomy of the thymus of a normal adult rabbit. (A) Left lateral view; (B) right lateral view. The thymus remains large in adult rabbits and is located cranioventral to the heart and extending into the thoracic inlet. *1,* Left thoracic lobe, thymus; *2,* right ventral thoracic lobe, thymus; *3,* right dorsal thoracic lobe, thymus; *4,* left ventricle, heart; *5,* right ventricle, heart; *6,* left auricle, heart; *7,* right auricle, heart; *8,* thoracic aorta; *9,* left subclavian artery; *10,* left internal thoracic artery; *11,* thymic branches; *12,* thymic branch of the left subclavian artery; *13,* costocervical trunk; *14,* left pulmonary artery, pulmonary vein; *15,* caudal vena cava; *16,* right cranial vena cava; *17,* right internal thoracic vein; *18,* thymic veins; *19,* right azygos vein; *20,* right subclavian vein; *21,* right external jugular vein; *22,* right axillary vein. (Adapted from Popesko P, Rajtova V, Horak J, eds. *Colour Atlas of the Anatomy of Small Laboratory Animals. Vol I: Rabbit and Guinea Pig.* St. Louis: Elsevier; 1990/1992.)

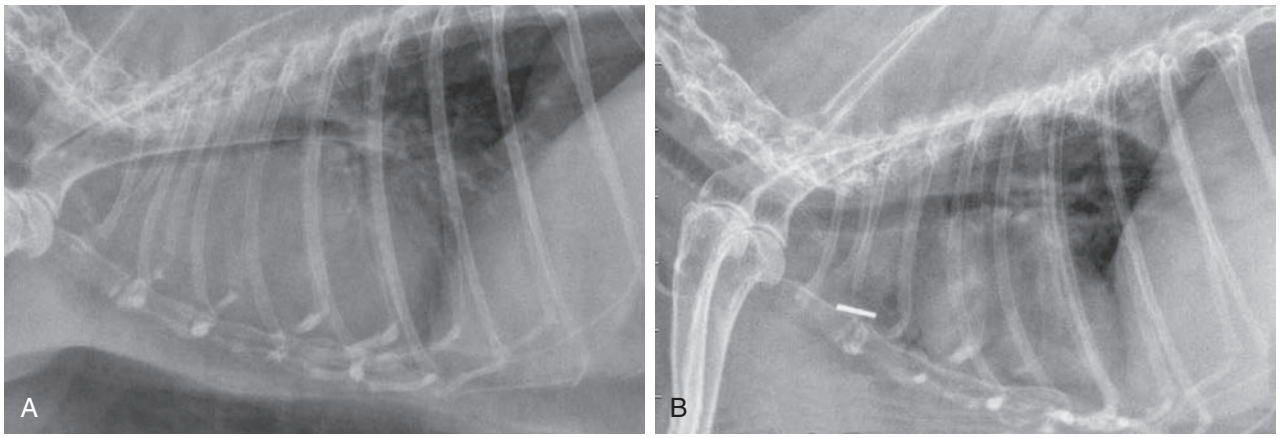


Fig. 20.3 (A) Right lateral thoracic radiographs of a lop rabbit with a thymic mass. Ultrasound-guided fine-needle aspirates were diagnostic of thymoma. At presentation, preoperative radiographs show loss of cardiac silhouette, with tracheal elevation on the lateral radiograph. (B) Postoperative lateral radiograph with surgical staple present show a more defined cardiac silhouette and return of the trachea to its normal anatomic position.

caval syndrome *(precaval syndrome)* caused by a space-occupying mass compressing the vessels of the anterior thorax, causing changes in blood pressure and impeding vascular return to the heart.[11] In rabbits, the orbital venous sinus involves most of the back of the eye, and changes in blood pressure can directly affect orbital venous pressure.[78]

Evidence of paraneoplastic syndromes have been described in rabbits with thymoma.[25,45,95] Hypercalcemia (14.7 mg/dL) was described in one report,[95] but this conclusion likely was erroneous because the unique calcium metabolism of rabbits and the influence of diet on the plasma calcium levels were not considered. Rabbits with thymoma may present with

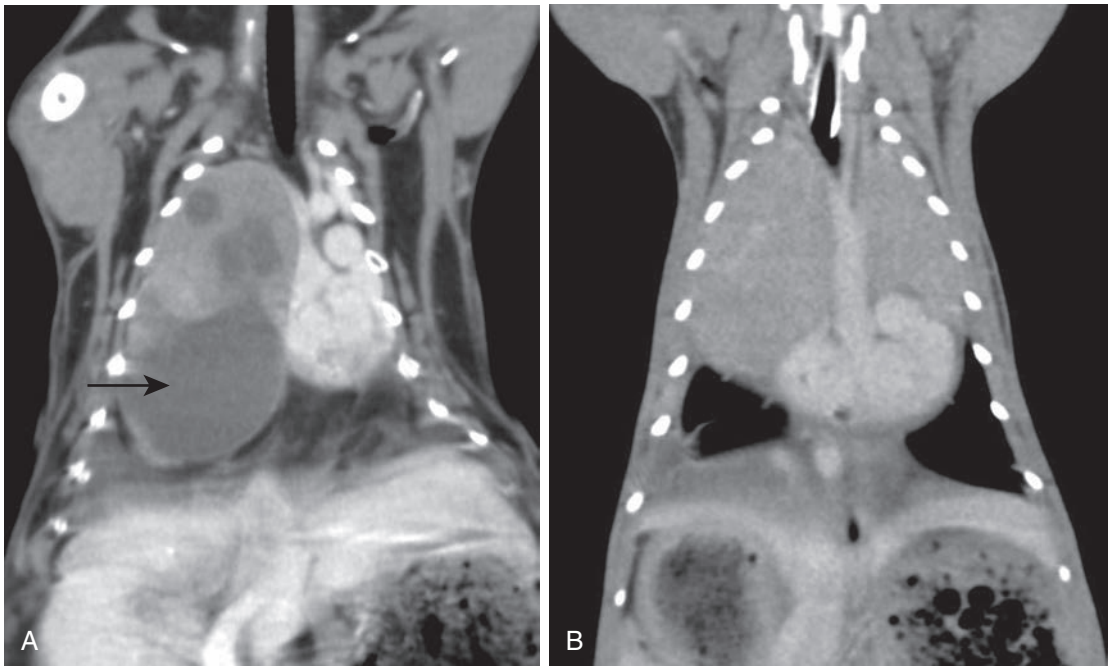


Fig. 20.4 Contrast computed tomography studies of two rabbits with thymoma, showing different composition (A) Cystic thymoma with a large multilocular fluid component *(arrow)* and heart displaced to the left. (B) Solid thymoma with the heart displaced caudally.

generalized scaling, dermatitis, or sebaceous adenitis. A paraneoplastic syndrome of thymoma-associated exfoliative dermatitis in rabbits similar to the syndrome in cats has been described.[25,82] Sebaceous adenitis, characterized as an autoimmune reaction directed at the sebaceous glands and a defect in lipid metabolism, is also described as associated with thymoma; one rabbit responded to treatment with cyclosporine and oral triglycerides.[45] Metastasis of thymic carcinoma and thymoma in rabbits has been reported.[75,98]

Rabbits with thymic masses may have a normal complete blood count (CBC), moderate to severe leukocytosis, or anemia. Lymphocytosis with more than 70% small lymphocytes can be present. Heterophilia with monocytosis, eosinophilia, basophilia, and thrombocytosis was described in one rabbit.[4]

Diagnosis of Lymphoproliferative Disorders and Thymic Masses

The basic diagnostic workup of a rabbit with a suspected lymphoproliferative disease should include hematologic testing, plasma biochemical analysis, and thoracic and abdominal radiographs. Additional diagnostic tests depend on the results of the preliminary findings. If the CBC results reflect either a leukocytosis with mature lymphocytosis or a normal white blood cell count with an inverse lymphocyte/heterophil ratio, repeat the test to confirm the findings. If anemia is found on a routine CBC, consider a bone marrow aspirate. Perform abdominal ultrasound scanning to identify abdominal masses or enlarged lymph nodes. Obtain a fine-needle aspirate or biopsy sample of any subcutaneous mass or enlarged peripheral lymph node. Submit full-thickness skin biopsy samples if cutaneous lymphoma is suspected.

If a thoracic mass is suspected or identified on radiographs, a CT scan with contrast is the imaging method of choice to determine the location and extent of the mass, particularly if surgery or radiation therapy are treatment options (Fig. 20.4). If CT is not available, perform an ultrasound examination to determine the architecture of the mass, if it is primarily cystic or solid, or aspirate the mass with ultrasound guidance for cytologic examination. Cytologic results may vary because of the usually poor exfoliation of epithelial cells compared with lymphocytes, the variable amounts of lymphocytic proliferation, or nondiagnostic results of the cystic fluid in the neoplasm.[4] Results may show a mixed population of small to intermediate mature lymphocytes and varying numbers of epithelial cells with thymomas, whereas a finding of primarily intermediate to large lymphoblasts would support a diagnosis of lymphoma.[4,55] Tissue biopsy samples are often needed for definitive diagnosis, because thymomas are classified based on the cell type that is undergoing neoplastic transformation (epithelial, lymphocytic, or both). Thoracic needle core biopsy can be a diagnostic option but may yield necrotic or cystic material that precludes a definitive diagnosis, and the procedure is much riskier than ultrasound-guided fine-needle aspiration in these compromised animals.

Treatment of Lymphoproliferative Disorders

In general, little information is available on treating rabbits with lymphoproliferative diseases. Much information is anecdotal, with protocols based on those used in other small animals. At best, the long-term prognosis of lymphoma and other lymphoid disorders with treatment is guarded to poor. Always consult with an oncologist when clients are interested in pursuing chemotherapy. Advise clients of the risks, benefits, and potential adverse effects of treatment options.

Chemotherapy

Although extensive information has been published in experimental studies about chemotherapeutic agents in rabbits, few reports describe the use of chemotherapy in clinical cases of lymphoproliferative neoplasia, and much information is anecdotal. The CVP/COP (cyclophosphamide, vincristine, prednisolone) protocol, with or without doxorubicin and L-asparaginase, and other chemotherapeutic agents have been recommended in individual cases, with limited success.[19] Because of the lack of data available on efficacy of chemotherapy in rabbits, potential risks must be considered before treatment. One rabbit with mediastinal lymphoma that did not respond to prednisone therapy was treated with lomustine, an alkylating agent related to streptozotocin, at a dosage of 50 mg/m^2 at 21-day intervals for two treatments.[74] Although the authors described remission in this rabbit, it died of renal failure 21 days after the second treatment. In an experimental study, rabbits that were intraperitoneally infected with spores of *Encephalitozoon cuniculi* were treated with cyclophosphamide (50 mg/kg first dose, then 15 mg/kg weekly during the 12-week experimental period).[41] In these rabbits, clinical signs of encephalitozoonosis developed between weeks 4 and 6, and all died during week 6. These results indicate that immunosuppression induced by chemotherapy can give rise to lethal encephalitozoonosis in rabbits that are subclinically infected. Therefore consider serologic testing to determine whether a rabbit is seropositive for *E. cuniculi* before beginning treatment with immunosuppressive drugs (see below).

Other adverse effects of chemotherapy include severe anemia, enteritis, typhlitis, and nephrotoxicity.[93] In an experimental study of rabbits given daunorubicin or doxorubicin at 3 mg/kg weekly for 10 weeks, cardiotoxicity was documented with daunorubicin but not with doxorubicin.[51] However, both drugs produced hemotoxicosis manifesting as aplastic anemia, and evidence of higher general toxicity with doxorubicin in rabbits was reflected by higher mortality rates. A single dose of L-asparaginase at 10,000 IU/kg when given intravenously can induce a hyperinsulinemic, insulin-resistant, diabetic syndrome in rabbits.[57] However, in small animals, L-asparaginase is given intramuscularly or subcutaneously; therefore route of administration may be a factor in toxicity. The neurotoxic effects of vincristine have been well studied in rabbits.[23,72,73]

Rabbits with thymomas have been treated with immunosuppressive therapy.[4,70] Prednisone (0.5-2.0 mg/kg every 12 hours) has been used successfully as adjuvant therapy in rabbits with thymoma undergoing radiation therapy.[70] Prednisone is used both for its antineoplastic and antiinflammatory effects, potentially helping to ameliorate the adverse effects of radiation treatment to thoracic structures, in particular radiation pneumonitis.[70] In rabbits treated for thymoma with radiation therapy, survival time did not differ between rabbits treated additionally with prednisone and those that received radiation alone.[4] In one rabbit treated with radiation therapy and cyclophosphamide (50 mg m^{-2} every 4 weeks for 7 treatments until death), severe bilateral renal fibrosis was found at necropsy, with death attributed to renal failure. The renal changes were attributed to repeated cyclophosphamide administration.[4] Similar to risks of encephalitozoonosis associated with cyclophosphamide treatment, emergence of subclinical encephalitozoonosis in infected rabbits is a potential adverse effect of steroid therapy.

Treatment Options for Thymomas

Radiation

Unlike the wide variation in chemotherapy metabolism from one species to another, the interaction of radiation with normal tissues, as well as malignant tissues, is remarkably similar in all species. Protocols that can be administered safely to people can, for the most part, also be safely administered to any species, with the important procedural difference that chemical immobilization is required in veterinary patients. Radiation therapy on exotic companion mammals has been practiced for decades. A good introduction to radiation therapy's basic principles as applied in exotic pet medicine is available.[50]

Although ultrasonography and standard two-dimensional radiography may be sufficient for the initial diagnostic workup, neither is sufficient for the detailed evaluation of tumor extent and stage essential for radiation therapy recommendations as well as surgical guidance. For this reason, three-dimensional (3D) imaging involving CT, with or without magnetic resonance imaging, is considered vital when radiation therapy, surgery, or both are considered as possible treatment options.[4,18]

In general, radiation therapy has played three different roles in veterinary therapy for the treatment of thymomas: before surgery, after surgery, and occasionally without surgical intervention. In people, cats, and dogs, surgery is the treatment of choice for thymomas. For large tumors that complicate surgery, one low dose of preoperative radiation may reduce the mass sufficiently to render it more feasible to remove surgically and to better stabilize the patient before surgery. Radiation of lymphocytes results in their fast depletion via an apoptotic death. Unlike radiation-induced mitotic cell death, radiation induced apoptosis occurs very quickly because it does not depend on the cell cycle phase of each cell at the time of radiation.[35] Therefore tumors with a high lymphocyte population are expected to shrink down more quickly and to a more dramatic extent. However, because microscopic invasion of the capsule is not evident on 3D imaging studies and early macroscopic invasion into the mediastinum may only be obvious when significantly advanced, complete resection may not be feasible in some surgical patients. Therefore follow-up radiation therapy of residual disease may be recommended to further extend tumor control time.

For rabbits diagnosed with thymoma, it is questionable whether surgery should be recommended as the treatment of choice because of the high perioperative complication rate that can occur in rabbit thoracotomies.[52,55] If rabbits are assessed as being nonsurgical candidates, then radiation alone may be recommended. Although radiation therapy does require a higher number of anesthetic sessions than does surgery, the procedure is much less invasive and is expected to result in a lower overall risk of early complications and, it is hoped, a higher survival rate. The reported success rate so far in rabbits treated with multiple-dose radiation therapy protocols does

seem to favor it over surgery, and radiation therapy should be considered as a first treatment of choice wherever it is available.

Technology in veterinary radiation oncology has advanced significantly in recent decades. Although manual and 3D planning are still being used, intensity modulated radiation therapy (IMRT) is quickly becoming the method of choice in facilities offering this technology, especially for more challenging cases where critical organs surround the tumor. The IMRT technology can help achieve a better dose distribution to the tumor while significantly reducing the dose to adjacent organs that may be at risk. This is particularly beneficial for patients being treated for thymoma because of the tumor's frequent close proximity to the heart, lungs, esophagus, and spine. That said, the most common detrimental adverse effects reported from radiation of thymomas are cardiac and pulmonary toxicities.[4,70] The successful sparing of these organs will depend on the tumor's degree of invasion and the experience and conscientiousness of the radiation oncologist, as well as the available technology.

Two recent studies have specifically described the response of thymomas to radiation therapy in rabbits. One retrospective study included rabbits at multiple institutions treated with variable protocols and variable treatment planning methods and technology,[4] whereas the second was a prospective study that utilized one single protocol, taking full advantage of the advanced technology of volumetric modulated arc therapy (VMAT) intensity modulation to achieve good tumor dose coverage and greatly reduce incidence of adverse effects.[18] In the retrospective study, the reported mean survival time of 19 rabbits was 313 days.[4] When three rabbits that died acutely after extubation on the day of radiation were excluded from the initial data, survival time increased to 727 days. Because no necropsies were performed, causes of death were unknown. Both palliative protocols (fraction doses of more than 4 Gy) and definitive protocols (fraction doses of less than 4 Gy) were used in these cases, and total cumulative doses varied from 24 Gy to 48 Gy. The treatment planning methods used in the 19 cases also varied greatly and included manual planning, 3D computer planning, and one IMRT planning. In seven rabbits, documented response time varied from 4 to 42 days. In six rabbits, the total decrease in tumor size ranged from 30% to 86% of the presenting volume, based on follow-up CT imaging performed midtreatment.[4] As mentioned above, lymphocytes tend to die an apoptotic death in the face of radiation, resulting in a rapid depletion of the lymphocytic cells.[35] The epithelial cell population, however, is expected to shrink down much more gradually and may not show significant reduction in size at all, such as seen in stable disease responses. In this study, the individual cytologic descriptions of tumors were not available, and therefore whether the speed of response and degree of tumor volume decrease were associated with the proportion of lymphocyte population could not be determined.[4] Radiation-induced adverse effects affected 3 of 19 rabbits and included alopecia in the radiation site, presumed radiation-induced pneumonitis based on thoracic radiographs 3 months after-treatment, and radiation-induced myocardial failure 12 months after treatment.[4]

In the prospective study of the stereotactic VMAT protocol, mean survival of 15 rabbits was 777 days, with ⅔ of the patients still alive at the time of publication.[18] All live patients showed no evidence of recurrence on CT scans at their 2-year posttreatment follow-up visits. The same protocol, cumulative dose, and planning method were administered in all patients. All rabbits were treated with six treatments administered every other day over a period of 11 days and received a total dose of 40 Gy planned with VMAT technology. Evidence of >30% reduction of the original mean tumor volume occurred during the course of radiotherapy. Of 15 rabbits, 14 showed a complete response by the 40-day evaluation, and one achieved complete response within 6 months. Unfortunately, this protocol and planning technology is more costly, and its availability in veterinary medicine presently is still very limited. This more advanced technology allowed much better sparing of the organs at risk and resulted in 100% complete response within 6 months and 0% recurrence within 2 years in all patients not lost to follow-up. No clinically evident acute or late adverse effects were reported.[18]

Understanding the cancer biology and behavior of this tumor type is important to minimize the risk of adverse effects. Because early marked reduction in tumor size resulting from lymphocytic cell apoptotic death allows adjacent organs at risk to displace into the treatment planning target, unintended dosing to these organs can occur if the plan is not adjusted accordingly. Frequent imaging is therefore beneficial during the course of treatment, especially if a high lymphocytic cell population is noted on biopsy or cytology. Therefore, midtreatment plan adjustment is beneficial. In the retrospective study, a follow-up CT to assess change in tumor size was performed approximately ⅓ to ¾ of the way into the course of treatment in six of the computer-planned patients; in all rabbits, the plan was modified to account for the significant early decrease in tumor size.[4] In the prospective study, follow-up CTs were performed in all patients on the fifth and ninth day of treatment, and plans were adjusted as needed.[18] Plan adjustments performed in all patients as needed in this study may be a major reason why no adverse effects were observed.[18] However, additional CT studies performed during treatment, together with plan adjustments, may be cost-prohibitive for some owners, thus increasing the risk of adverse effects. Fortunately, the newer linear accelerators available in some facilities have advanced digital imaging technology and CT imaging capability that allow easy daily reimaging for the close monitoring required for treatment. In making a final treatment decision or protocol recommendation for radiation therapy, many factors must be weighed carefully, including the particular technology that may be available, the cost of treatment, the radiation oncologist's expertise, and more importantly, the overall risk of anesthesia, the stress level and general health status, along with the severity of clinical signs of each individual patient.

Surgical Excision

In most other species, surgery is the treatment of choice for thymic neoplasia when there is a solitary mass because it provides the best chance of a cure by removal of the entire tumor

(Fig. 20.3). Although surgical excision of thymic masses is done successfully in rabbits, the risk of surgical or anesthesia-related complications and death is high. In one report describing seven rabbits that underwent thoracotomy for thymoma excision, five rabbits died within 3 days after surgery.[55] Two rabbits survived longer than 6 months (180 days and 955 days), but both were euthanized because of mass recurrence. In a case series of 14 rabbits with mediastinal masses treated surgically by median sternotomy and mass excision, seven (50%) rabbits survived 6 months or longer (F. Harcourt-Brown, personal communication, 2010). Of the 14 rabbits, 1 rabbit died during surgery, 6 died within 10 days after surgery, 1 survived 6 to 12 months, 4 survived 12 to 24 months, and 2 survived more than 24 months. In a clinical report describing a thymoma excised through a right fourth intercostal thoracotomy with placement of a chest drain, pneumothorax persisted after surgery and the rabbit was euthanized.[95] In another rabbit, the mass was removed by median sternotomy.[11] A chest drain was kept in place for 24 hours, after which it was removed and the rabbit recovered uneventfully. At the time of euthanasia 9 months later because of recurrent appendicular neurofibrosarcoma, no evidence of thymoma recurrence was present. In a study of radiation therapy, two rabbits treated with radiation therapy were also treated with surgical cytoreduction after completion of radiation, but the effect on survival was unknown.[4]

Acute perioperative death is the most common risk associated with surgical excision of thymic masses.[70] Tumor-related cardiac dysfunction, anesthesia-related perfusion abnormalities, stress, and analgesia are important considerations in these cases. When a rabbit is positioned in dorsal recumbency for surgery, the mass may impinge on normal lung tissue and decrease ventilation and perfusion. Therefore intubation is mandatory, and a short anesthesia time is extremely important.

Therapeutic Aspiration of Cystic Thymomas

Thymomas can be primarily cystic or solid (Fig 20.4). In rabbits with thymomas that have large cystic components confirmed by CT or ultrasonography, removal of cystic fluid by ultrasound-guided aspiration may alleviate dyspnea and improve quality of life by decreasing compression on the lungs. This is a palliative option if radiation or surgery is not feasible for financial or clinical reasons. In one report, two rabbits that were treated with aspiration of cystic fluid survived 150 and 270 days after diagnosis.[55] The procedure is repeated at varying intervals, usually every 3 to 6 months, as clinical signs of dyspnea or tachypnea recur. In cases seen by one author (K.Q.), ultrasound-guided aspiration of cystic fluid as needed generally provides symptomatic relief for 8 to 12 months. These rabbits generally are euthanized after this time because of worsening of clinical signs.

OTHER NEOPLASTIC DISEASES

Many types of primary tumors have been described in rabbits. The most common organ systems involved are the reproductive system and the skin and subcutaneous tissues. Reported primary tumors in rabbits are described in other chapters related to diseases of particular organ systems, and some are briefly described below.

Primary Tumors Affecting the Reproductive System

Uterine adenocarcinoma remains the most common neoplasia seen in the doe (see Chapter 16); however, other uterine tumors, including leiomyosarcoma and leiomyoma, choriocarcinoma, hemangiosarcoma, deciduosarcoma, and mixed Mullerian tumors, can occur.[13,29,48] In one report, both leiomyoma and adenocarcinoma of the endometrium were identified, with invasion of the adenocarcinoma into the leiomyoma.[56] Hypertrophic osteopathy associated with pulmonary metastasis from a uterine adenocarcinoma in a rabbit that was spayed 9 months earlier has been reported.[15] Squamous cell carcinoma in the vaginal junction is considered a rare tumor in the doe, as is hemangioma of the ovary.[31]

Although relatively uncommon, mammary gland adenocarcinomas in does is often associated with concurrent uterine disease. In a report on 109 mammary tumors in rabbits, frequency of lesions did not differ between the left and right mammary chains or cranial and caudal mammary glands.[7] Studies suggest that tumors arise from hyperplastic lesions and transition to invasive carcinoma over 12 to 24 months.[30] Mammary carcinomas can be histologically classified as tubular, papillary, solid, comedo, adenosquamous, complex, cribiform, ductal, and anaplastic, with benign tumors classified as papillary adenoma, simple tubular, or complex adenoma.[32,83] A breed predisposition has been reported in older literature, but most pet rabbits are now mixed breeds, so a genetic link is indeterminable. Metastatic mammary adenocarcinoma has also been reported in an intact male rabbit.[88] Additionally, cystic mammary dysplasia and adenocarcinoma have been associated with high serum prolactin levels from prolactin-secreting pituitary adenomas.[61,85]

Spontaneous testicular neoplasia is uncommon, but interstitial cell tumors (Leydig cell), seminomas, Sertoli cell tumors, granular cell tumors, and teratomas can occur, with interstitial cell tumors occurring most frequently.[6,24,43] Most tumors are benign, and rabbits are cured by castration, but metastasis has been reported.[1,3] An interstitial cell tumor with concurrent gynecomastia was described in an adult rabbit, which was also the first description of gynecomastia in this species.[63]

Primary Tumors Affecting the Skin and Subcutis

Skin tumors are uncommon in rabbits but easily recognized (see Chapter 16). Trichoblastomas (previously basal cell tumors) are the most common cutaneous neoplasm in rabbits; other common skin tumors are collagenous hamartomas, Shope and non-Shope fibromas, spindle cell sarcomas, squamous cell sarcoma, squamous papillomas, and lipomas, whereas myxosarcomas are the most common mesenchymal tumors reported (Fig. 20.5).[64,97] Other nonviral skin tumors occurring in rabbits include sebaceous cell and apocrine carcinoma, rhabdomyosarcoma, meibomian adenoma, anaplastic sarcoma, leiomyosarcoma, and leiomyoma. A cutaneous histiocytic sarcoma was diagnosed on the lip of a geriatric dwarf rabbit and metastasis to the cervical lymph nodes was diagnosed 6 months later.[47]



Fig. 20.5 Tumors of the skin and subcutis in rabbits. (A) Squamous cell carcinoma presenting as a proliferative mass arising from the base of the inner ear pinna. (B) Squamous cell carcinoma of the calcaneus in a rabbit. Surgical resection in this location is very difficult. These tumors can result from neoplastic changes of the epithelium in areas of repeated trauma. (C) Myxosarcoma on the lateral tarsus of a rabbit.

Melanomas are uncommon tumors that can involve a variety of sites in rabbits, including the ear pinna, eyelid, head, peri-vulvar area, thigh, stifle, and scrotum. [46,64,97] Melanomas usually contain abundant melanin with a high mitotic index and exhibit marked anisocytosis and anisokaryosis. A melanoma of the upper eyelid of an 8-year-old rabbit regressed after treatment with radioactive gold-198 seeds.[86]

Miscellaneous Primary Tumors of Other Organ Systems

Primary tumors of the gastrointestinal tract are rare and usually involve the liver (see Chapter 14). Bile duct adenomas, malignant variant adenocarcinomas, and a single report of a biliary hamartoma have been found incidentally at necropsy in older rabbits.[16,34,87] Hemangiosarcoma of the liver with pulmonary metastasis and hemoperitoneum was described in a rabbit that died unexpectedly. The endothelial cell marker CD-31 was identified in neoplastic cells by immunohistochemistry.[34] No primary splenic tumors have been reported.

Primary lung carcinoma has both been reported and seen by one author (A.P.).[38] A review of spontaneous age-related lung lesions found at necropsy (laboratory rabbits > 2 years of age) identified 5 of 36 rabbits with fibropapillomas, which are benign primary lung tumors.[14] A pulmonary histiocytic sarcoma was described in an 8-year-old rabbit that presented with respiratory symptoms and anorexia.[58] Nasal mucosal adenocarcinoma was diagnosed after CT scanning and exploratory rhinostomy in a rabbit with refractory upper respiratory disease.[59]

Musculoskeletal neoplasms in rabbits act like those of other mammals. Osteosarcoma is the most frequently diagnosed bone tumor in rabbits, with tumors developing in the skull, facial bones, or limbs (see Chapter 18).[2,99,102] Rhabdomyosarcomas are also reported.[10]

Neoplasia of the oral cavity is rare, but osteosarcomas, ameloblastic fibroma and ameloblastoma, fibrosarcoma, cementoma, ossifying fibroma, chondrosarcoma and salivary gland adenocarcinoma have been reported.[8,9,20,40,69,79,89,99,102] Bony

changes seen on radiographs of the mandible or maxilla often represent osteomyelitis related to dental disease (e.g., mandibular abscess); therefore be cautious to avoid misdiagnoses of these lesions as neoplastic changes.

Nephroblastoma, or embryonal nephroma, is a benign tumor in rabbits that has been associated with polycythemia.[36,38,54,60,100] Tumors can be seen in young rabbits and increase in size with age. These are common incidental findings at necropsy and appear as solitary or multiple sharply circumscribed nodules projecting from the cortical surface of the kidney. Renal carcinoma, transitional cell carcinoma of the kidney and ureter, and leiomyoma of the rabbit urinary bladder have been rarely reported.[49,81]

Other than pituitary adenomas, endocrine tumors are rare in rabbits.[5,42] Carcinoma of the adrenal cortex has been reported as an incidental finding at necropsy in a rabbit with increased serum concentrations of testosterone and progestin.[5] The neoplastic lesion is distinguishable from nodular hyperplasia, which is considered common in *Oryctolagus*, by the lack of capsular demarcation in the adrenal gland. Nonneoplastic adrenomegaly is a common finding on abdominal ultrasonography. Although uncommon, intraocular sarcomas diagnosed after enucleation are suspected to result from long-term inflammation and chronic eye disease or traumatic insults, as reported in three rabbits.[17,65]

Teratomas are rare and are usually incidental findings at necropsy. Pituitary gland teratoma, an intracranial teratoma causing central nervous system signs, as well as gonadal teratomas are reported.[68,71] A retroperitoneal teratoma was found incidentally connected to the parietal wall cranial to the kidney in a 4-month-old domestic rabbit.[68]

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21

Guinea Pigs

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BIOLOGY AND ANATOMY

Taxonomy and Natural History

Guinea pigs (*Cavia porcellus*), also known as cavies, were domesticated in South America between CE 500 and 1000 and possibly as early as 1000 BCE.[92] Guinea pigs were raised by the Incas for food and for use in religious ceremonies.[92] Guinea pigs were brought to Europe about 500 years ago. Although they never became popular as a food source outside of South America, in Europe and North America they have been raised as pets and laboratory animals ever since. Domestic guinea pigs remain a food source in the Andean mountains, and they are raised by families and often left uncaged to forage for food about the dwellings.[92]

Breed and Fancy Standards

The cavy fancy and breed standards arose in Britain well over 100 years ago. Today, the fancy is worldwide with clubs in most countries. The leading standards are the American (American Cavy Breeders Association, www.acbaonline.com) and the British (British Cavy Council, http://www.britishcavycouncil.org.uk/). Examples of several breeds are shown in Figure 21.1. Short and smooth-haired varieties, such as the American shorthair, are bred in solid colors (English self) (e.g., black, chocolate, cream, golden, white, etc) and the marked and ticked/agouti variants. The agouti is the original color pattern seen in wild guinea pigs. Other smooth-haired variants are the crested, with a rosette on the forehead and the satin, with hollow hair shafts giving the coat a sheen and sparkle. The Abyssinian cavy has 10 rosettes in a well-defined pattern. Different rexoid breeds have a short, frizzy coat; the two most recognized are the rex and the teddy.

Several long-haired variants are the original smooth-coated Peruvian, with two rosettes over the rump making the coat grow forward covering the head; the silkie (United States) or sheltie (Europe), similar to the Peruvian but with the head uncovered; and the coronet, with a crest on its forehead. Additionally, some hairless breeds are popular. The skinnies are hairless except for the head and the lower legs. Baldwins are born with hair but lose all fur at a young age. Unlike in other species, a true albino gene does not exist in the guinea pig. Genetically, the pink-eyed whites, mainly used as laboratory animals, are Himalayans with homozygous recessive genes suppressing black and chocolate colors.

Anatomy and Physiology

General Characteristics

Guinea pigs have stocky bodies, delicate short limbs, rounded hairless pinnae, and no tails. Males are larger than females, weighing 900 to 1200 g compared with 700 to 900 g for females (Table 21.1). Obesity is relatively common in pet animals. The normal life span of pet guinea pigs can be up to 8 years, whereas in the wild they typically live 4 to 5 years.

The hair coat is composed of large guard hairs surrounded by an undercoat of fine hairs. Guinea pigs have areas of physiologic alopecia caudal to their ears. Androgen-dependent sebaceous glands are abundant along the dorsum and around the anus and are important for marking. The caudal gland, also known as *grease* or *coccygeal gland*, is a focal accumulation of sebaceous glands and is located 1 cm dorsal to the anus at the base of the spine. It is more developed in males, and in older males excessive accumulation of sebaceous secretions from this gland results in thick, matted, greasy fur (Fig. 21.2A), predisposing to infection (Fig. 21.2B).[12] Both male and female guinea pigs have one pair of inguinal nipples. Guinea pigs have 32 to 36 vertebrae; the vertebral formula is C7, T13(14), L6, S2(3), Cd4(6). There are 13 to 14 pairs of ribs, of which the last one or two are cartilaginous. The small cylindrical clavicle attaches laterally to the coracoid process of the scapula and medially to the manubrium. The pelvic symphysis generally remains fibrocartilaginous,[91] and a gap in the symphysis can be palpated at the time of impending parturition. Guinea pigs have four digits on the front feet and three on the rear; each has a short claw that may require periodic clipping. They have large tympanic bullae.

In immature animals, the thymus is located within the ventral cervical area and the cranial mediastinum; in adults, a thymic remnant may be present in the cranial mediastinum.[91] Guinea pigs, like New World monkeys, ferrets, and people, are considered to be corticosteroid-resistant species because steroid administration is not associated with marked changes in thymic physiology or peripheral lymphocyte counts.[25]

Guinea pigs have no laryngeal ventricles, and their vocal folds are small; nonetheless, they command a wide range of vocalizations. The right lung comprises four lobes (cranial, middle, caudal, and accessory), whereas the left lung has three lobes (cranial, middle, and caudal).

Gastrointestinal System

The dental formula of guinea pigs is 2 (I1/1, C0/0, PM1/1, M3/3) = 20. All teeth are elodont and grow throughout life. The upper and lower cheek teeth form an occlusal line that is at about a 30-degree angle from the horizonal plane. In animals with dental malocclusion, the maxillary cheek teeth tend to overgrow laterally into the buccal mucosa, and the mandibular cheek teeth tend to overgrow medially, entrapping the tongue. The incisors are white, unlike those of many other rodents.

Guinea pigs have large tongues and relatively small, narrow oral cavities. The soft palate is continuous with the base of the tongue. The oropharynx communicates with the remainder of the pharynx through a hole in the soft palate called the palatal ostium.

Guinea pigs have four pairs of salivary glands—parotid, mandibular, sublingual, and molar—the ducts of which empty into the oral cavity near the molars. The entire alimentary tract measures approximately 2.3 m (7.5 ft) from pharynx to anus.[41] The stomach is lined with glandular epithelium; unlike the stomachs of rats, mice, and hamsters, there is no nonglandular portion.[91] The small intestine is on the right side of the abdominal cavity, and the cecum occupies the central and left portions. The cecum contains 65% of the gastrointestinal (GI) content and is a large (15-20 cm long), thin-walled sac with many lateral pouches formed by the action of three taeniae coli.[91] The liver has six lobes—right, medial, left lateral, left medial, caudate, and quadrate. The gallbladder is well developed.



Fig. 21.1 Guinea pig breeds. (A) Golden agouti/golden crested. (B) Clipped coronet. (C) Self black. (D) Abyssinian/rosetted crossbred. (E) Skinny, hairless except for the head and the lower legs. (Courtesy Pouline Grosboel.)

The normal gastric emptying time in guinea pigs is approximately 2 hours. Total GI transit time is approximately 20 hours (range 8–30 hours); however, when coprophagy is factored in, the total GI transit time is 66 hours.[41] In laboratory guinea pigs, the mean gastric pH is 2.9, whereas the small intestinal pH ranges from 6.4 to 7.4.

As herbivorous hindgut fermenters, guinea pigs are coprophagic and may ingest feces from the anus many times per day.[18] Obese or pregnant animals may eat fecal pellets from the floor, and young, unweaned guinea pigs can be seen eating the dam's droppings. Coprophagy appears to be an important function, although its contribution to the nutritional needs of guinea pigs has not been fully characterized. As in rabbits, coprophagy may be a source of B vitamins and a means of optimizing protein utilization. However, unlike rabbits, guinea are not cecotrophic; whereas cecotrophs provide a rich source of B vitamins for rabbits, guinea pigs require a dietary source of 7 of 10 B vitamins, whereas rabbits require a dietary source for only

TABLE 21.1 Physiologic Values for Domestic Guinea Pigs[59,65]

Average life span as pet	5–7 years
Adult weight	Males, 900–1200 g; females 700–900 g
Heart rate	240–310 beats/min
Respiratory rate	40–120 breaths/min
Rectal temperature	37.2–39.5°C (99.0°F–103.1°F)
Average blood volume	70 mL/kg
Type of estrous cycle	Nonseasonally polyestrous
Length of estrous cycle	15–17 days
Ovulation	Spontaneous
Gestation period	68 days (59–72 days)
Litter size	2–4 (1–13 possible)
Normal birth weight	70–110 g (45–115 g)
Weaning age	21 days (or at 180 g body weight)
Sexual maturity	Males, 3 months; females, 2 months



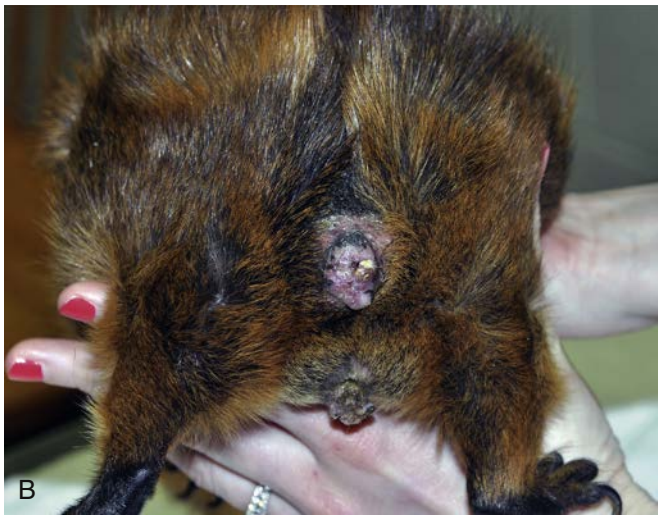


Fig. 21.2 The coccygeal (grease) gland is about 1 cm dorsal to the anus and is more developed in males. The fur surrounding it can appear matted and greasy (A). The gland can also come impacted and infected (B). (Courtesy C. Mans)

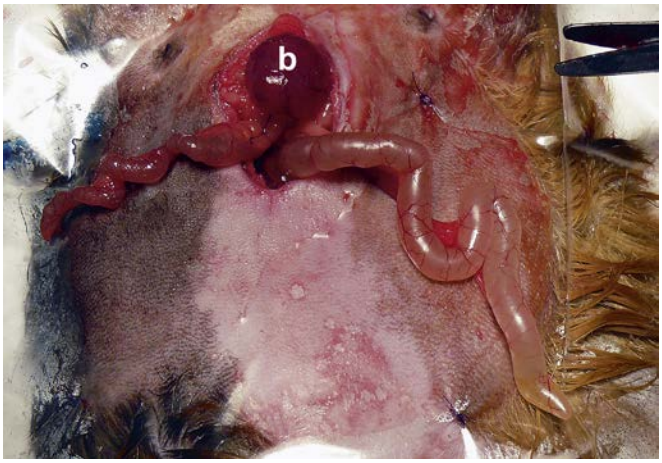


Fig. 21.3 Vesicular glands in a male guinea pig during laparotomy. These accessory sex glands are blind-ending sacs up to 10 cm in length and are frequently mistaken for uterine horns. *b,* Urinary bladder. (Courtesy Exotics Medicine Service, Alfort National Veterinary School).

three.[85] If coprophagy is prevented, guinea pigs lose weight, digest less fiber, and excrete more minerals in the feces.[18] Guinea pigs exhibit a "mucus trap" strategy, in which bacteria from the cecum are trapped in mucus in the colon with few to no food particles and returned to the cecum by antiperistalsis. Rabbits and other lagomorphs exhibit a "wash-back" strategy, in which bacteria, solutes, and small food particles are returned to the cecum by antiperistalsis in a stream of water from the proximal colon. The mucus-trap strategy is less efficient than the wash-back strategy in extracting bacteria from the colonic digesta.[24] Therefore the colon of guinea pigs is comparatively larger and heavier than that of rabbits.[24] Guinea pigs have a colonic furrow in the ascending colon, in which the concentration of bacteria and nitrogen is twice as high as in the lumen. Bacteria in the proximal colon are transported in the furrow into the cecum as part of the separation mechanism.[37] Like the GI flora of rabbits, that of guinea pigs is primarily gram-positive and anaerobic.[91]

Urogenital System

The accessory sex glands of male guinea pigs (boars) are the vesicular glands, prostate gland, coagulating glands, and bulbourethral glands. The vesicular glands are long, coiled, blind sacs that lie ventral to the ureters and extend 10 cm into the abdominal cavity (Fig. 21.3).[91] They can be mistaken for uterine horns. The testes are located in the open inguinal canals and in the scrotum, which is not well developed in this species (Fig 21.4). Guinea pigs have an os penis. A pouch, called the intromittent sac, is located caudoventral to the urethral opening (Fig 21.5A). During erection, the pouch is everted and two horny styles project externally (Fig 21.5B). Do not mistake the opening of the intromittent sac with the external urethral opening during urinary catheterization.

Females (sows) have a bicornuate uterus characterized by a short uterine body (12 mm long) with paired uterine horns, with a single cervix opening into the vagina. A vaginal closure membrane opens at estrus, at parturition, and, in many animals, at around day 26 of gestation.[92]



Fig. 21.4 (A) Normal genitalia of an adult male guinea pig. (B) The penis has been everted from the prepuce, and the testicles can be palpated in the scrotal pouches. (Courtesy Exotics Medicine Service, Alfort National Veterinary School)

The renal pelvis is relatively large and has a single longitudinal renal papilla. As in other rodents, the urethra in female guinea pigs exists outside the vagina on the urinary papilla, which is cranial to the vaginal opening (Fig 21.6). The urine is usually opaque and yellow amber, with a pH of 8 to 9, a specific gravity of 1.005 to 1.050, and predominately amorphous crystals.

HUSBANDRY

Housing

Guinea pigs are social animals and should not be housed alone. They require relatively simple housing with good ventilation. If a solid-sided cage, such as an open glass aquarium, is used, change the bedding frequently to minimize ammonia levels in the cage. Guinea pigs do not jump or climb; therefore the top of the cage can be open. Solid flooring is preferred to wire mesh: foot and leg injuries are more common in guinea pigs that are kept on wire. Bedding made of recycled paper products rather than wood chips is recommended; cedar chips could be associated with respiratory disease. A small upside-down cardboard box or plastic hide box provides shelter within the cage. The recommended temperature range for guinea pigs is 65° to 79°F (18°C to 26°C), and humidity should be around 30% to 60%.[31]

For breeding purposes, harem-style housing is common, with a single boar and 1 to 10 sows in a pen. They can also be housed in pairs. In intensive breeding systems, the sow and young are left in the pen so that the sow can be rebred at the postpartum estrus. However, removing the sow and young to a nursery area shortly after parturition minimizes trampling and ear chewing of the young by other adults.

Nutrition and Feeding

Wild cavies eat many different types of vegetation. Domestic guinea pigs are also completely herbivorous. A crude protein level of 18% to 20% is adequate for growth and lactation, and the recommended minimum level of crude fiber is 10%.[8] The recommended diet for pet guinea pigs consists of guinea pig pellets and good-quality grass hay, supplemented with fresh vegetables. Commercial guinea pig pellets usually contain 18% to 20% crude protein and 10% to 16% fiber. Good-quality grass hay should be available at all times. Guinea pigs enjoy a variety of leafy greens, and these can be offered in handfuls. Fruits and treats should be offered rarely, if at all. Any additions or changes to the diet should be made gradually.

Guinea pigs require a dietary source of vitamin C (ascorbic acid) because they lack L-gulonolactone oxidase, an enzyme involved in the synthesis of ascorbic acid from glucose. Nonbreeding adults require 10–25 mg/kg daily of ascorbic acid; 30 mg/kg per day should be provided for growing and pregnant animals. Approximately half of initial naturally occurring vitamin C content in foods may be oxidized and lost within 90 days. Because vitamin C oxidizes readily once exposed to air, heat, and light, commercial food sources must contain the stabilized form of vitamin C (L-ascorbyl-2-polyphosphate), which is heat and shelf stable. Feeds with the stabilized form, L-ascorbyl-2-polyphosphate, maintain adequate vitamin C levels for 6 months or longer when stored in dry conditions at room temperature (70°F/21°C). Using a liquid vitamin C supplement in the drinking water (1 g/L) is not recommended because it can change the taste of the water, which might decrease water consumption. Fresh foods that contain high levels of ascorbic acid are red and green peppers, broccoli, tomatoes, kiwi fruit, and oranges. Many types of leafy greens (kale, parsley, beet greens, chicory, spinach) are high in vitamin C, but some contain high levels of calcium or oxalates, which may be contribute to other disease problems such as urinary calculi; these should be offered in only small amounts.

Guinea pigs favor nipple drinkers over open dishes, and water intake is generally higher with the nipple drinkers.[1] Nipple drinkers are therefore recommended for guinea pigs because these can be considered as behavioral enrichment and a tool to potentially increase water consumption.[1]

Behavior

Wild cavies live in small groups (5 to 10 individuals) in burrows or crevices and feed at dawn and dusk.[96] Pet guinea pigs seek

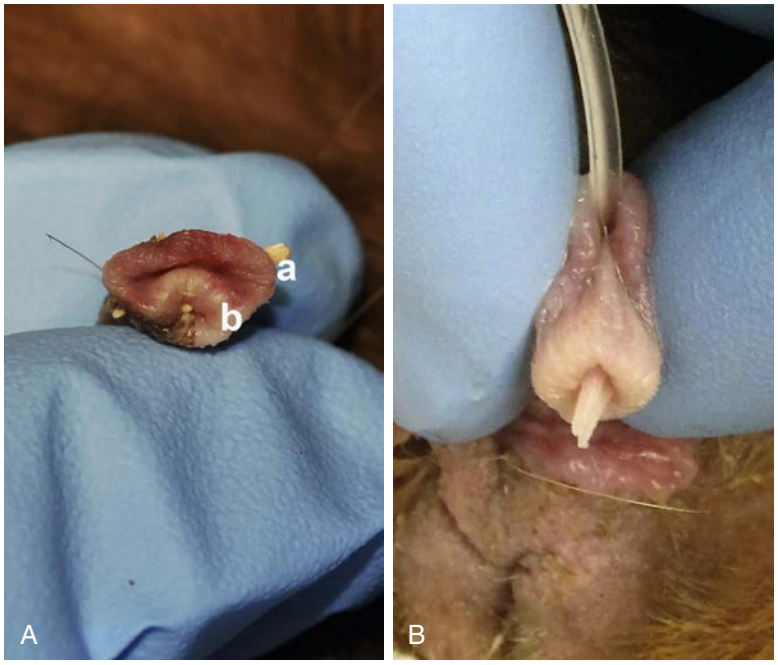


Fig. 21.5 Appearance of the glans penis in a guinea pig. A) Note the two separate openings: the external urethral opening *(a)* and the opening of the intromittent sac *(b)*. (B) Catheterization of the urethra and eversion of the intromittent sac with the two stylets visible. (Courtesy C. Mans)

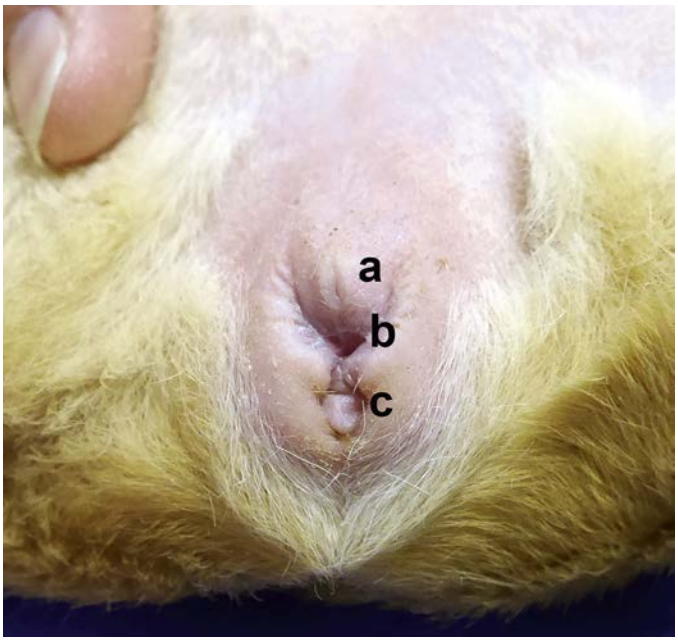


Fig. 21.6 Normal genitalia of an adult female guinea pig. External urethral opening located on the urinary papilla *(a)*, vaginal orifice *(b)*, and anus *(c)*. (Courtesy Exotics Medicine Service, Alfort National Veterinary School.)

physical contact with other guinea pigs when housed together. They often stand side by side when resting and crowd together at feeders. However, there is little mutual grooming. Hair pulling can be a form of aggression, and hair pulling and ear nibbling of subordinate animals is seen in crowded or stressful environments.[91]

The vocalizations of guinea pigs are well characterized. Recognized call types include the chutt, chutter, whine, tweet, whistle (single or in long bouts), purr, drr, scream, squeal, chirp, and grunt.[91] Many owners are familiar with the excited squeals emitted by their pets when a refrigerator door is opened or feeding is imminent. When the guinea pig is jumping from excitement, the owners often refer to this as "pop corning."

Breeding and Neonatal Care

Reproductive values for guinea pigs are summarized in Table 21.1. Puberty, defined as age at first conception, occurs at 2 months of age in females and at 3 months in males. Males begin to mount at 1 month of age, and ejaculation is evident by the time they are 2 months old. Sows are polyestrous and breed year-round in captive settings. The peak reproductive period for females is from 3 or 4 months to 20 months of age; pet animals may reproduce until they are 4 or 5 years old.[23] The estrous cycle in most females is 15 to 17 days (range 13–21 days), and ovulation is spontaneous. Fertile postpartum estrus occurs in most females from 2 to 10 hours after parturition.[91] Females show distinct signs of proestrus and estrus. During proestrus, they become more active and may chase their cage mates; they may sway their hindquarters and utter a distinct guttural sound. Estrus lasts 6 to 11 hours, during which time females show lordosis, or the copulatory reflex—an arching and straightening of the back with elevation of the rump and dilation of the vulva. In mature sows, the vaginal membrane is open for approximately 2 days during estrus; it closes after ovulation. Copulation in guinea pigs can be confirmed by finding the vaginal (copulatory) plug, a solid mass of coagulated ejaculate that falls out of the vagina several hours after mating. Rodent copulatory plugs are typically hard and rubbery or waxy in consistency and are the exclusive product of male secretions.

The duration of gestation is 65 to 71 days (average 68 days). Impending parturition is signaled by separation of the pubic

symphysis; a gap of 15 mm is palpable about 2 days before parturition and increases in width (up to 25 mm or more) at the time of parturition. This separation may be inadequate in sows that are bred for the first time after 7 or 8 months of age, and dystocia may result. Normal parturition is typically rapid, with only a few minutes between births. Guinea pigs do not build nests. The average litter size varies according to guinea pig strain and management practices but is typically 2 to 4,[80,91] with a range of 1 to 13 young reported.[80] Birth weights range from 45 to 150 g and are inversely related to litter size[91]; young weighing between 100 to 120 g have better growth and survival rate.

Newborn guinea pigs (typically called pups or youngs but not piglets) are precocious.[80] The pups ideally should receive sow's milk for a minimum of 5 days, and the normal lactation period is 3 weeks.[80] Pups often do not survive if they fail to receive sow's milk for the first 3 to 4 days of life. Guinea pig sows are not very "motherly." They passively allow nursing to occur rather than seeking out the young. Lactating sows permit the young of other females to nurse. Because voluntary micturition does not occur until the second week of life, the sow must lick the pup's anogenital region to stimulate urination and defecation. The young are weaned at 21 days (15–28 days of age) or at a weight of 180 g.

Orphaned guinea pigs should be fostered to a lactating sow if feasible. If there is no suitable foster mother, the young can be fed from a dropper or pet nurser beginning at 12 to 24 hours after birth. Feeding the pups every 2 hours until 5 days of age, after which feeding every 4 hours becomes sufficient. The hand-rearing formula should approximate guinea pig milk, which contains 4% fat, 8% protein, and 3% lactose. Evaporated milk mixed with an equal amount of water can be used. Guinea pigs begin nibbling on solid food at 2 days of age, and guinea pig pellets moistened with water or formula can be offered at that time.

BASIC PROCEDURES AND PREVENTIVE MEDICINE

Handling and Restraint

Guinea pigs are docile animals that usually need minimal restraint during a physical examination. Most will sit quietly on the examination table while the owner or an assistant places a hand on the rump so that the animal does not back away. Carry a guinea pig by supporting its weight in one hand and cupping its dorsum with the other. Avoid excessive handling if the guinea pig is nervous or not tolerant to handling.

Physical Examination

The initial examination should involve observing the guinea pig in its cage. Focus on the animal's movement, mentation, and rate and rhythm of breathing. Healthy guinea pigs have an alert demeanor with clear eyes. The animal should react to stimuli by moving or vocalizing; some animals will move very quickly. Healthy guinea pigs usually eat readily when offered treats or greens.

Begin the physical examination by measuring body weight; this is also a good time to obtain the animal's temperature, if indicated, before it becomes excited or stressed. Check the rectal area for impaction of feces, especially older boars, as this can artificially lower the "rectal" temperature. Palpate the ventral neck area for an enlarged thyroid gland, and the peripheral lymph nodes, particularly the submandibular nodes, for enlargement. Overgrown nails are common in guinea pigs. Often a horny growth is present and extends from the footpads, especially in older animals. Trim the nails of guinea pigs with fingernail clippers or cat claw clippers. The horny overgrowth can be trimmed back carefully, but avoid causing bleeding.



Fig. 21.7 Blood collection from the gingival vein located below the lower incisors in an anesthetized guinea pig. (Courtesy C. Mans.)

Blood Collection

The blood volume in guinea pigs averages 70 mL/kg body weight.[91] Approximately 7% to 10% of the blood volume (5–7 mL/kg) can be safely collected from a healthy, nonanemic guinea pig. Venipuncture in guinea pigs can be difficult. The lateral saphenous and cephalic veins are accessible, but they are very small, and only small amounts of blood can be collected from each vein. Shave the fur from the area and wet the skin with alcohol to enhance visibility of the vein. Use an insulin or tuberculin syringe and a small (25- to 28-gauge) needle to prevent collapse of the vein. Venipuncture of multiple peripheral veins is often necessary to collect an adequate volume of blood for analysis. The jugular vein can be used to collect large blood samples; however, manually restraining a guinea pig for jugular venipuncture can be very stressful, and therefore sedation or anesthesia may be required. Guinea pigs have short, thick, compact necks, and it is often difficult to locate the jugular vein. Another suitable blood collection site, which allows for repeated and reliable collection of blood samples, is the gingival vein (labialis mandibularis vein) located subgingivally in front of the mandibular incisors (Fig 21.7). Anesthesia or deep sedation is required, and the use of 25- to 28-gauge needles and 0.5- to 1-mL syringes is recommended. No adverse effects after repeated venipuncture from this site have been reported.[79]

Venipuncture of the cranial vena cava in guinea pigs carries an increased risk of hemorrhage because of the close proximity of the cranial vena cava to the major vessels of the thoracic cavity and the heart. Complications such as traumatic bleeding into the thoracic cavity or pericardial sac and death after vena cava venipuncture can occur, and therefore this technique should only be used as the

last resort. For this technique, anesthesia or deep sedation of the animal is mandatory. Use a small (25-gauge) needle attached to a 1-mL syringe. Palpate the manubrium and insert the needle lateral to the manubrium under the first right rib at an approximate 30-degree angle to the horizontal axis of the body. Insert the needle about 1 cm (½ in.), then withdraw slowly with negative pressure until blood starts to fill the syringe. If venipuncture is unsuccessful, do not redirect the needle because of the risk of lacerating surrounding vessels. Instead, withdraw the needle and try again.

Urethral Catheterization and Cystocentesis

Guinea pigs have a relatively wide urethra, measuring 3 to 4 mm in diameter. Catheterization of male guinea pigs is sometimes necessary to retropulse urethral calculi into the bladder. Be careful if a urolith is lodged in the urethra, because these are often deeply embedded in the mucosa, and forcing them back can be traumatic or nonproductive. For catheterization, a 5- to 8-Fr red rubber catheter or a clear nasogastric feeding tube can be used. Extrude the penis by placing gentle pressure on the scrotum at the base of the penis (Fig. 21.5). Ensure that the catheter is placed into the urethra and not the intromittent sac. Minimize handling of the penis itself to prevent irritation and trauma, which can lead to temporary partial prolapse.

Cystocentesis is sometimes necessary in animals with urethral obstruction or to obtain a sample for urinalysis. The method is similar to that used with other small animals, and a small (25-gauge) needle is used. Use ultrasonography to visualize the bladder and orientate the insertion of the needle if possible. Anesthesia or sedation is necessary for catheterization and cystocentesis.

Clinical Laboratory Findings

Representative hematologic, biochemical, and hormonal values are listed in Tables 21.2 and 21.3. Clinical laboratory values can vary according to the physiologic state of the animal, sex, and the laboratory techniques used (see Chapter 39). In guinea pigs, alanine aminotransferase activity is low in hepatocytes; therefore it is not sensitive or specific as a marker of hepatocellular injury. Hypercholesterolemia is common in guinea pigs, often in conjunction with fatty infiltration of many tissues, including the liver.

A unique leukocyte of the guinea pig is the Kurloff cell (see Chapter 39). This mononuclear cell resembles a lymphocyte but contains round or ovoid inclusions termed *Kurloff bodies*.[91] This cell is believed to be a modified natural killer cell and is a special aid to the immune system with possible antileukemia activity. The cellular distribution of bone marrow in the guinea pig is 26.7% erythroblasts, 63.3% myeloid cells, 4.6% lymphocytes, and 5.4% reticulum cells.[16] The myeloid/erythroid ratio is 1.2 and 1.6:1.

Diagnostic Imaging

In many cases guinea pigs should be sedated or anesthetized to allow proper radiographic positioning. Radiographs of the skull, the thoracic cavity, the abdominal cavity, and the limbs are routinely performed. Whole body radiographs including the thorax and abdomen are often done to decrease restraint stress on the animal. Ultrasound can be performed in guinea pigs without sedation, unless needle aspirates are to be done. Computed tomography (CT) scanning is increasingly used in guinea pigs and frequently can be performed in sedated animals, without the need for general anesthesia.

TABLE 21.2 Hematologic Reference Values for Guinea Pigs[34]

Analyte	Values
Hematocrit/PCV, %	39–55
Hemoglobin, g/dL	11.6–16.9
Red blood cells, $\times 10^6/\mu L$	4.5–6.4
Mean corpuscular volume, fL	80–89
Mean corpuscular hemoglobin, pg	24–27
Mean corpuscular hemoglobin concentration, g/dL	29–32
White blood cells, $\times 10^3/\mu L$	2.9–14.4
Lymphocytes, %	28–84
Neutrophils, segmented, %	12–63
Monocytes, %	0–9
Eosinophils, %	0–14
Basophils, %	0–2
Platelets, $\times 10^3/\mu L$	273–745

TABLE 21.3 Biochemical and Hormonal Reference Values for Guinea Pigs.[34,59,66]

Analyte	Values
Alanine aminotransferase, U/L	0–61
Albumin, g/dL	2.6–4.1
Alkaline phosphatase, U/L	0–418
Amylase, U/L	0–3159
Aspartate aminotransferase, U/L	0–90
Bile acids, μmol/L	0–84.5
Bilirubin, mg/dL	0.3–0.9
Blood urea nitrogen, mg/dL	9–62
Calcium, mg/dL	9.6–12
Chloride, mEq/L	94–111
Cholesterol, mg/dL	12–65
Creatine kinase, U/L	0–2143
Creatinine, mg/dL	0.6–2.2
Fructosamine, μmol/L	134–271
γ-Glutamyl transferase, U/L	0–13
Globulin, g/dL	2–4
Glucose, mg/dL	89–287
Glutamate dehydrogenase, U/L	0–17
Lactate dehydrogenase, U/L	0–515
Lipase, U/L	0–152
Magnesium, mg/dL	3.5–4.1
Potassium, mEq/L	4.5–8.8
Phosphorous, mg/dL	3.2–21.6
Protein, total, g/dL	4.4–6.6
Sodium, mEq/L	130–150
Triglycerides, mg/dL	29–206
Total bilirubin, mg/dL	0–1
Cortisol, μg/dL	5–30
Thyroxine, μg/dL	1.1–5.2

Treatment Techniques

Intravenous and Intraosseous Catheters

Peripheral intravenous (IV) catheters can be placed in the cephalic and the medial saphenous veins in guinea pigs but can be difficult to place because of the small size and fragility of the veins. Use a small (26-gauge) indwelling catheter. Intraosseous catheters can be placed in the cranial tibia under general anesthesia.

Fluid Therapy

Normal daily water intake in the guinea pig is estimated to be approximately 100 mL/kg. Calculate supplemental fluid requirements based on this estimation plus additional fluids to compensate for dehydration or fluid loss. Supplemental fluids are commonly given subcutaneously into the loose skin of the dorsal neck and upper back areas. The total volume can be divided into two to three daily treatments. Volumes of 25 to 35 mL can be given into each subcutaneous injection site with a 22-gauge to 25-gauge butterfly catheter. Many guinea pigs react to the pain caused by subcutaneous fluid administration and become very stressed. In animals with IV catheters, give fluids by continuous-rate infusion if possible, or divide total daily fluids into two or three IV administrations. To avoid unnecessary stress, animals that are drinking water can be given oral fluids unless they are azotemic or moderately to severely dehydrated.

Antibiotic Therapy

Because guinea pigs are hindgut fermenters that depend on the bacterial production of volatile fatty acids for energy, they are very susceptible to changes in enteric microbial flora.[85] Although all administered antibiotics have the potential to affect normal gut microflora, drug classes such as sulfonamide/trimethoprim, fluoroquinolones, tetracyclines, chloramphenicol, and aminoglycosides have less impact than penicillins, cephalosporins, lincosamides, and older macrolides. Therefore choose antibiotic therapy cautiously, especially oral antibiotics, to lessen the risk of enteric dysbiosis and antibiotic-associated enterotoxemia.

Administration of Medications

Give parenteral medications by subcutaneous or intramuscular injection. The upper back is a common site for subcutaneous injection. The skin in this area is thick in guinea pigs, especially in intact males, and is sometimes difficult to penetrate with a 25-gauge or smaller needle. Give intramuscular injections in the lumbar muscles. Give oral medications and nutritional supplements by syringe into the side of the mouth. Oral medications in tablet form must be compounded into liquid formulations so that they can be easily administered by owners. Force-feed guinea pigs that are partially or fully anorectic with commercially available critical care diets or softened guinea pig pellets.

DISEASES OF GUINEA PIGS

Gastrointestinal and Hepatic Diseases

Dental Disease

Dental disease is common in guinea pigs (see Chapter 36).[64] Diets deficient in fiber or vitamin C, infection, and trauma are common reasons for malocclusion; genetic predisposition while not proven, is also possible. A thorough oral examination in an awake guinea pig in not possible because of their small mouth opening, and abnormalities of the cheek teeth are easily overlooked. Therefore, a complete intraoral examination requires sedation or general anesthesia and magnification or oral endoscopy (Fig. 21.8). The cheek teeth have a sloped angel and the occlusal surface angle is approximately 30º (Fig 21.8A–B). Tongue entrapment by the overgrown crowns of the mandibular cheek teeth is the most common dental abnormality (Fig 21.8C–D). Radiographs or preferably a CT scan of the skull are required to assess the reserve crowns and bones of the skull. Because guinea pigs with dental disease often have concurrent disease processes, a thorough systemic evaluation is indicated before dental treatment is initiated. Perioperative supportive care is equally critical to a good outcome as the dental treatment itself; consider pain, hydration, nutrition (including vitamin C supplementation), and secondary infection. Prevention is aimed at ensuring an appropriate high-fiber diet and vitamin C support.

Gastrointestinal Hypomotility

Gastrointestinal (GI) hypomotility or stasis occurs as a primary process or as a sequel to virtually any other disease process in guinea pigs. Inadequate dietary fiber is a significant predisposing factor, but any disease process causing pain or anorexia can lead to GI hypomotility and dehydration of GI contents. A thorough history is invaluable in determining the inciting cause and should include complete dietary and husbandry information, duration of clinical signs (specifically anorexia), health status, and any recent antibiotic use. Dental disease is commonly identified in guinea pigs presenting with signs of GI stasis. Hepatic lipidosis can occur secondary to anorexia, especially in obese guinea pigs.

Clinical signs of GI stasis include decreased/absent fecal material, anorexia, bruxism, gas-or fluid-distended stomach, cecum, and bowel loops, pain on abdominal palpation, and decreased gastrointestinal sounds. The GI contents become dehydrated during stasis, exacerbating GI pain and anorexia. Stasis can also result in gas accumulation within the intestinal tract ("bloat"), which can become life threatening. Differential diagnosis for gastric dilatation and volvulus includes intestinal obstruction due to intussusception or omental torsion.[22,84] Abdominal radiographs (Fig. 21.9) and ultrasound evaluate GI anatomy and motility. Submit blood tests to evaluate for evidence of inflammation, infection, and organ dysfunction.

Regardless of the cause or severity, medical management of GI stasis consists of aggressive supportive care with replacement fluid therapy, pain management, and, after stabilizing the animal, assisted nutrition if the animal is still anorectic. Pain management is an essential component of therapy. Pain is visceral and often too severe to respond to nonsteroidal antiinflammatory drugs (NSAIDs) alone, which can potentially induce gastric ulceration. The risks and benefits of using opioids are considered for each case, but guinea pigs with GI stasis usually respond well to buprenorphine (0.2 mg/kg oral-transmucosal every 4 hours), morphine (1–2 mg/kg every 4 hours subcutaneously [SC]), methadone (1–2 mg/kg every 4 hours SC), oxymorphone (0.2–0.5 mg/kg every 4 hours SC), or fentanyl

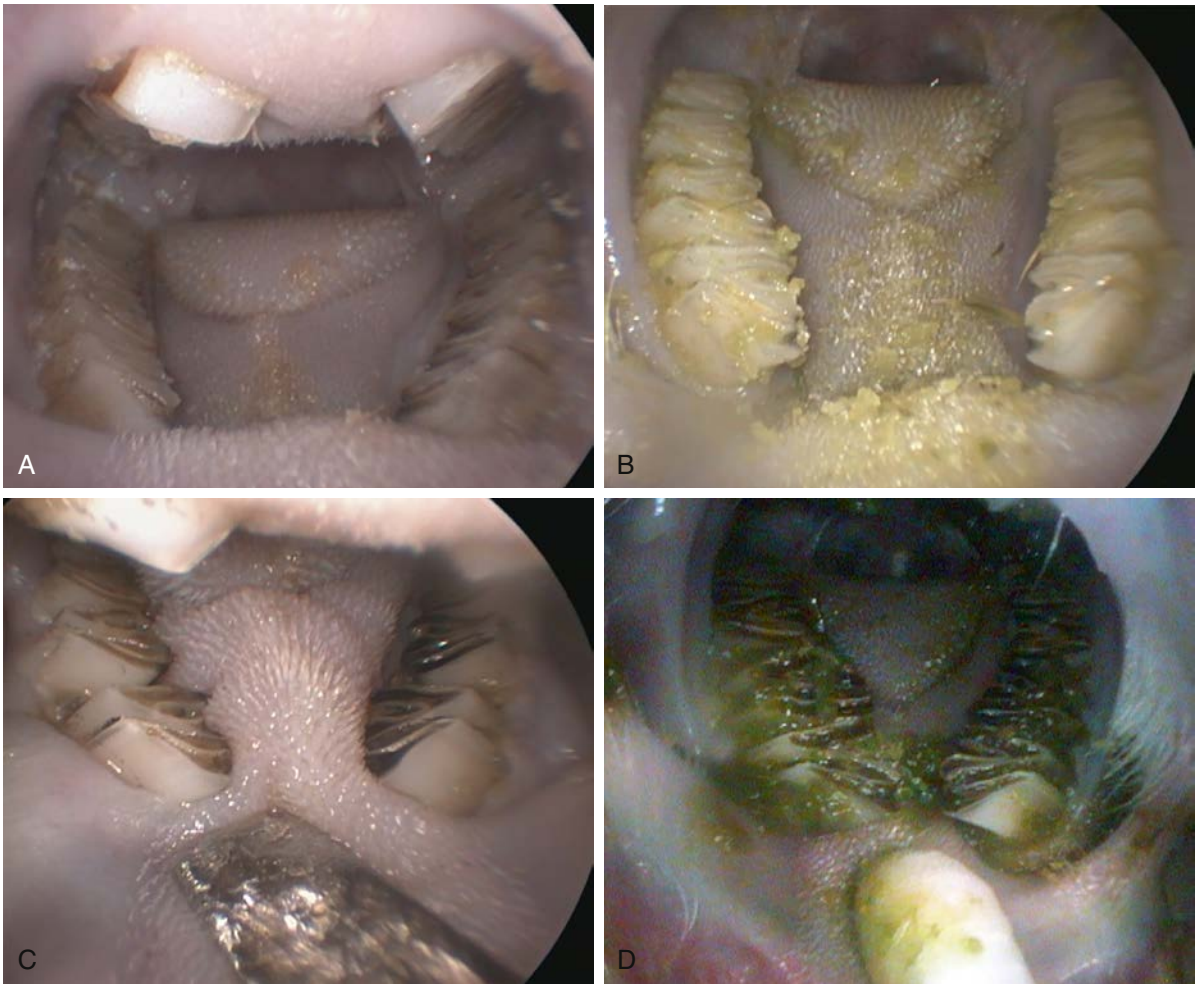


Fig. 21.8 Oral endoscopy in guinea pigs. (A and B) Appearance of normal cheek teeth. Note that the retention of food in the oral cavity is a normal finding in guinea pigs. (C) Malocclusion of the lower cheek teeth. Note the coronal elongation, discoloration of the occlusal surfaces, and partial entrapment of the tongue. (D) Severe tongue entrapment due to coronal elongation of the first cheek teeth of both mandibular quadrants. (Courtesy Exotics Medicine Service, Alfort National Veterinary School.)



Fig. 21.9 (A) Lateral and (B) ventrodorsal whole-body radiographs of a guinea pig with gastrointestinal stasis. Note the large amount of gas filling the stomach and the cecum.

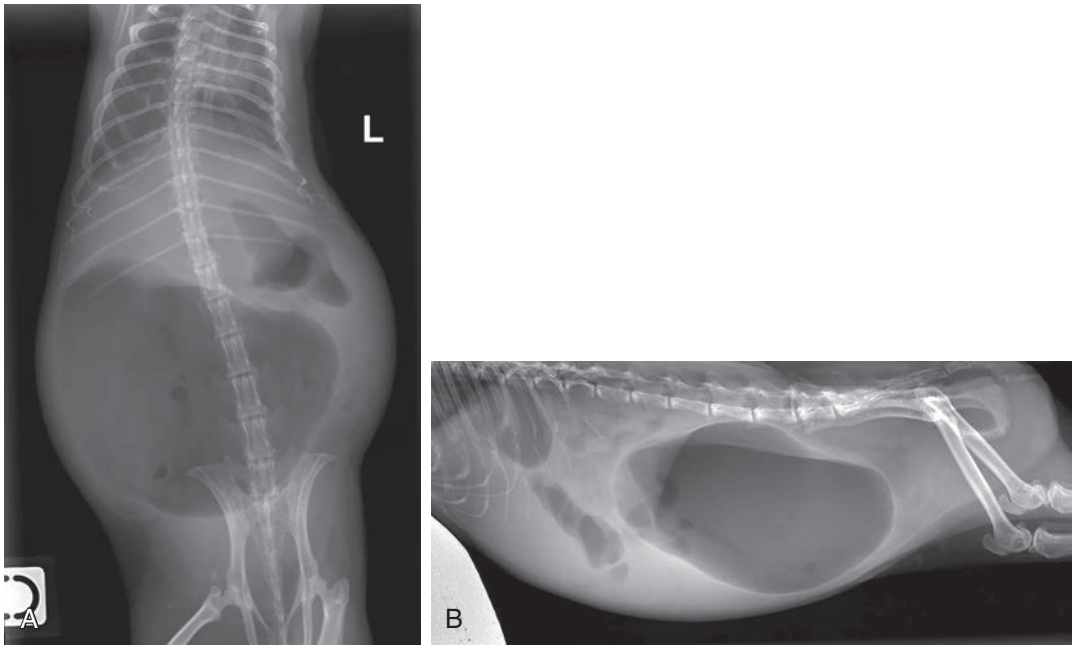


Fig. 21.10 Radiographs of a guinea pig diagnosed with a gastric dilatation and volvulus. (A) On the ventrodorsal view, the stomach is positioned on the right side of the abdomen. (B) On the laterolateral view, the stomach is distended with gas, and intestines are positioned between the stomach and the liver. (Courtesy Imaging Service, Alfort National Veterinary School.)

(2–7 µg/kg/h CRI). Gastric decompression carries a high risk in the already debilitated patient, and often the volume of gas yielded is disappointing. Gastric decompression is performed on an emergency basis in cases of gastric tympany and is accomplished by passing a large-bore red rubber tube into the stomach through the oral cavity, being careful to not obstruct the glottis; however, gas lower in the GI system will not be affected. Before any decompression attempt, a gastric torsion, which is not uncommon in guinea pigs, should be ruled out.

Gastric Dilation and Volvulus

Gastric dilation and volvulus (GDV) is an acute and generally fatal syndrome in guinea pigs, in which the stomach fills with gas and fluid, followed by rotation on its mesenteric axis.[17,19,69,74,75] It is more common in animals older than 2 years.[64] Guinea pigs, like other rodents, cannot vomit owing to reduced muscularity of the diaphragm and stomach geometry that is not well structured for moving contents toward the esophagus.[38] Differentials for gastric dilatation without volvulus include severe dysbiosis and small intestinal intussusception.[22]

Clinical signs are characterized by an acute onset of depression, reluctance to move, abdominal distention, inappetence, and sometimes sudden death. Physical examination shows severe depression, painful body posture, tachypnea, and gas-filled tympanic cranial abdomen, and pain may be noted on abdominal palpation. Signs consistent with hypovolemic shock (e.g., nonresponsive, tachycardia, weak pulses, pale mucous membranes, dyspnea, hypothermia) will be seen in advanced cases.

Abdominal radiographs are the first recommended diagnostic test. In case of a GDV, usually a large, gas-filled stomach silhouette is positioned on the right side of the cranial abdomen (Fig. 21.10). In some cases, the stomach may be displaced caudally with intestines visible cranial to the stomach. In contrast to dogs, the dilation of the stomach does not induce a fold of the stomach along the *incisura angularis*. Gastric rotation between 180 and 540 degrees has been reported in guinea pigs.

The prognosis for guinea pigs with GDV is poor, and reported survival rate after surgical intervention is 25% or less.[17,19,69,74] If treatment for GDV is pursued, stabilize the animal and correct hypovolemia by intravenous or intraosseous fluid administration. Opioids are recommended analgesia *(see Gastrointestinal Hypomotility above)*; provide oxygen. After stabilizing the patient, decompression can be attempted in sedated patients using either orogastric or nasogastric tube placement. As soon as the patient is stabilized and the stomach decompressed, surgical intervention is indicated. During surgery, the volvulus is reduced, and the integrity of the stomach is assessed. In cases of necrosis of the stomach, a gastrectomy can be attempted. To prevent recurrence, perform a gastropexy by suturing the serosa of the stomach to the abdominal wall with a continuous pattern during closure of the abdominal wall.

Dysbiosis and Antibiotic-Associated Enterotoxemia

Guinea pigs possess a predominantly gram-positive and anaerobic GI flora and are very susceptible to oral administration of antibiotics that specifically target these bacteria, permitting overgrowth of gram-negative bacteria as well as *Clostridium difficile*. Clostridial enterotoxin production results in secretory diarrhea and hemorrhagic typhlitis. Nonantibiotic-induced dysbiosis also occurs and is generally associated with abrupt dietary changes, ingestion of contaminated foods, and stress. Anorexia, dehydration, tympany, and hypothermia are the most common clinical signs; diarrhea may or may not be present.

Diagnosis is usually based on history, clinical signs, and histopathologic lesions. Although *C. difficile* is difficult to isolate, polymerase chain reaction (PCR) testing and enzyme immunoassay for its toxin are commercially available. Treat animals with antibiotic-associated enterotoxemia symptomatically. Provide thermal support and administer intravenous or subcutaneous crystalloid fluids as needed. Commercially available probiotics containing *Lactobacillus* species[46] or transfaunation can be used to try to reestablish normal microflora. Chloramphenicol, florfenicol, or metronidazole may be somewhat effective in suppressing further clostridial overgrowth.

Enteritis and Diarrhea

Diarrhea is uncommon in adult animals, but soft stools frequently develop because of excess dietary simple carbohydrates or inadequate dietary fiber. Some animals have intermittent soft stools without an identified cause. Bacterial enteritis can also cause soft stools and diarrhea. Tyzzer's disease, caused by *Clostridium piliforme*, is transmitted by the fecal-oral route. Young, stressed, or immune-compromised animals are particularly affected. Clinical signs include lethargy or anorexia, diarrhea, unthrifty appearance, and acute death. Lesions observed at necropsy include intestinal inflammation and focal hepatic necrosis. Treatment is generally unrewarding. The disease can be prevented by good husbandry practices and reducing stress, particularly at weaning.

Salmonella typhimurium and *Salmonella enteritidis* are less frequently reported causes of bacterial enteritis in pet guinea pigs, but mortality can be high during outbreaks. Transmission is usually by fecal contamination of feed or water. Weanlings, pregnant sows, aged animals, and those with nutritional deficiencies are particularly susceptible. Signs include scruffy hair coat, weight loss, weakness, conjunctivitis, and abortion. Diarrhea may or may not be present. At necropsy, the spleen and liver are often enlarged, and yellow necrotic foci may be present in the viscera.[73] Diagnosis is by fecal or intestinal culture and sensitivity testing. Treatment is usually not recommended because affected animals can become asymptomatic carriers and salmonellosis can be zoonotic. Prevention is aimed at proper disinfection/sanitization of the environment, storing food in airtight containers, and thorough washing of all fresh fruits and vegetables offered.

Other causes of bacterial diarrhea include *Yersinia pseudotuberculosis, Clostridium perfringens, Escherichia coli, Pseudomonas aeruginosa, Citrobacter freundii,* and *Listeria monocytogenes*.[73] Like *Salmonella* species, these organisms are usually contracted through food contamination. *Yersinia* infection can cause abscesses of the intestine, liver, and regional lymph nodes.[73] In weanlings, *E. coli* causes wasting, depression, and death. Intestines may contain yellow fluid.

Guinea pigs are host to gastrointestinal parasites including *Eimeria caviae*, *Balantidium caviae*, and *Paraspidodera uncinata*. In juvenile animals, *E. caviae* causes diarrhea, but this is much less common in adults. Cryptosporidia such as *Cryptosporidium wrairi* can infect guinea pigs and cause failure to gain weight, weight loss, and diarrhea, more commonly in weanlings and immunosuppressed animals; however, animals usually recover spontaneously.[13] Regardless of the underlying cause, diarrhea is a serious problem because hypoglycemia, dehydration, hypothermia, and electrolyte imbalances quickly develop and should therefore be addressed accordingly.

Fecal Impaction

Fecal impaction is most commonly identified in older intact boars. Soiled bedding combined with inguinal sebaceous secretions can become adhered, potentially resulting in inguinal sebaceous gland infections and fecal impaction. The guinea pig is usually presented for straining to defecate, constipation, or passing large amounts of foul-smelling soft stool. Often the only physical abnormalities detected will be an enlarged and flaccid anus impacted with normal, soft feces. Suggested therapy includes a dietary change to increase fiber and manual evacuation of stools using a cotton-tipped applicator and is frequently long term.

Respiratory Diseases

Guinea pigs have a relatively small thoracic cavity compared with body mass. They seem particularly sensitive to airborne pollutants and respiratory infections; thus husbandry plays an important role in disease risk. Insufficient airflow in combination with ammonia buildup from soiled cages can predispose to respiratory disease. Bedding made of nonshredded paper products is recommended, rather than wood shavings; cedar chips in particular should be avoided.

Pneumonia

Bacterial pneumonia is common in guinea pigs. Poor husbandry conditions predispose to pneumonia. Common causative agents are *Bordetella bronchiseptica*, *Streptococcus pneumoniae*, *Streptococcus equi* subsp. *zooepidemicus*, and *Pseudomonas aeruginosa,* among others. *Bordetella bronchiseptica* is a gram-negative rod that is an important cause of respiratory disease in guinea pigs. The disease is characterized by purulent bronchopneumonia often involving consolidated lung lobes and fibrinosuppurative pleuritis (Fig. 21.11). Infection may also cause otitis media, encephalitis, metritis, abortions, and death. Clinical signs can develop within 4 to 6 days of exposure. Although antiobiotic treatment should be based on culture and sensitivity results, trimethoprim/sulfamethoxazole and florfenicol are suggested as first-line antibiotics. Prevent exposure of guinea pigs to rabbits and dogs that might be asymptomatic carriers of *Bordetella*.

Streptococcus pneumoniae is transmitted by asymptomatic carriers of many species, including guinea pigs. Serotypes III, IV, and XIX cause disease in guinea pigs. Infection is predisposed by poor husbandry and is most common in young animals. Bronchopneumonia, fibrinopurulent pleuritis, and pericarditis are common manifestations of this infection. Viral pathogens have not been reported to induce pneumonia in pet guinea pigs, but adenoviral pneumonia has been described in laboratory animals.[19a]

Regardless of the cause, the general progression of clinical signs may include tachypnea, dyspnea, increased respiratory



Fig. 21.11 Bronchopneumonia and fibrinosuppurative pleuritis *(arrow)* in a guinea pig with *Bordetella bronchiseptica*.

sounds, sneezing, coughing, depression, anorexia, weight loss, and unthrifty coat.[61] Thoracic auscultation findings include crackles, rales, and wheezing or minimal air movement, depending on the severity of the disease. Thoracic radiographs or preferably CT scan are recommended. Treat with systemic antibiotic therapy, covering against commonly involved pathogens and supportive care (fluid and nutritional support); consider nebulized antibiotics (e.g., gentamicin in saline solution 5 mg/mL) as well.

Cardiovascular Disease

Cardiac disease is not uncommon in guinea pigs, and the most common clinical signs are dyspnea, lethargy, and anorexia. In a retrospective study, a heart murmur was present in 8% of guinea pigs diagnosed with cardiac disease.[14]

Thoracic radiographs often reveal cardiomegaly, pleural effusion, and pulmonary cardiogenic edema (Fig. 21.12). Although a vertebral heart score has not been published in guinea pigs, tracheal elevation sometimes may be present with cardiac enlargement. Electrocardiographic and echocardiographic parameters of normal guinea pigs are listed in Tables 21.4 and 21.5. Common echocardiographic findings in guinea pigs with heart disease include pericardial effusion (63%), dilated cardiomyopathy (61%), pleural effusion (24.%), hypertrophic cardiomyopathy (16%), and valvular heart disease (8.0%).[14] Pericardiocentesis should be performed if pericardial effusion has been identified, for diagnostic and therapeutic reasons. Because of the lack of published pharmacological data treatment of heart disease is extrapolated from other species. Drugs commonly used in guinea pigs with cardiac disease are enalapril (0.5–1 mg/kg orally [PO] every 12–24 hours), pimobendan (0.2–0.4 mg/kg), and furosemide (1–4 mg/kg intramuscularly [IM], subcutaneously, PO every 4–12 hours).[33] The prognosis for cardiomyopathy in guinea pigs is poor. Guinea pigs may survive 3 months but typically not more than 6 months with treatment after diagnosis (K. Quesenberry, unpublished data, 2019).

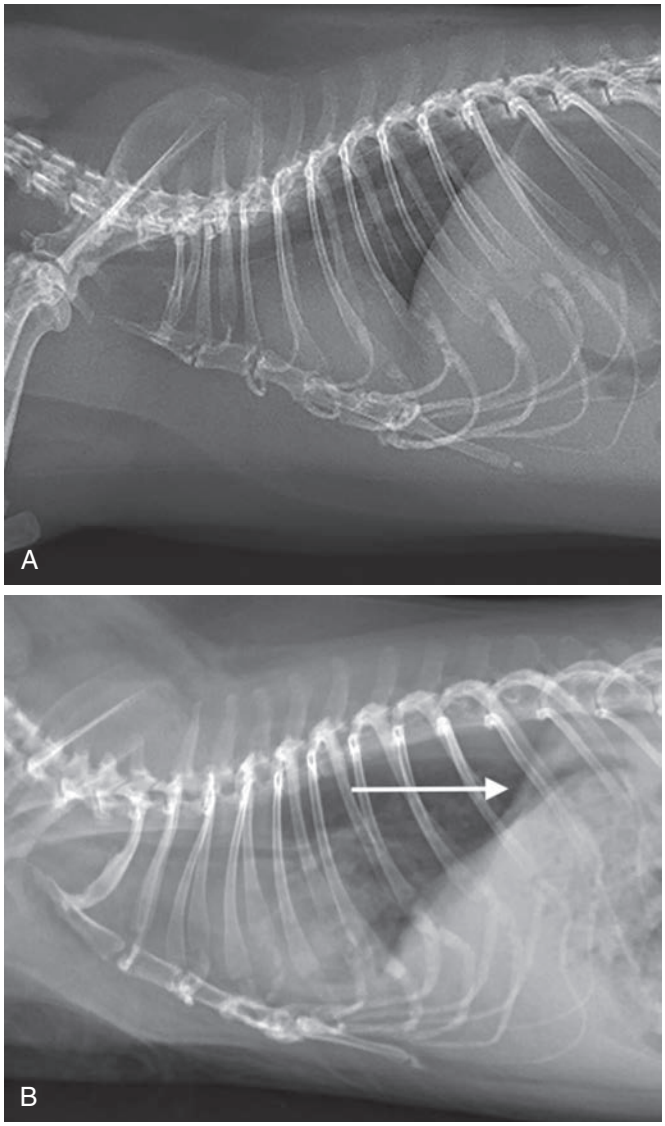


Fig. 21.12 (A) Normal lateral thoracic radiograph in a guinea pig. (Courtesy Imaging Service, Alfort National Veterinary School). (B) Lateral radiograph of a guinea pig with pleural effusion *(white arrow)*. The lungs are pulled away from the thoracic wall, and the cardiac silhouette is difficult to assess but appears enlarged. (Courtesy K. Quesenberry, The Animal Medical Center, New York, NY.)

TABLE 21.4 Reference Values for Electrocardiographic Parameters in Guinea Pigs[91]

Parameters	Values
P-wave duration, sec	0.015–0.035
P-wave amplitude, mV	0.01
P-R interval, sec	0.048–0.060
QRS duration, sec	0.008–0.046
R wave amplitude, mV	1.1–1.9
QT interval, sec	0.106–0.144
T wave amplitude, mV	0.062
Mean electrical axis, degrees	+20 to +80

TABLE 21.5 Echocardiographic Measurements in Anesthetized Guinea Pigs (n = 12)[11]

Parameter	Mean ± SD	Range
LVIDd, mm	6.8 ±0.4	6.30–7.50
LVIDs, mm	4.4 ± 0.2	4.20–4.60
LVPWd, mm	2.3 ± 0.4	1.30–2.10
LVPWs, mm	2.8 ± 0.6	1.70–2.70
IVSd, mm	1.8 ± 0.3	1.50–2.70
IVSs, mm	2.3 ± 0.4	1.90–3.50
LA, mm	5.0 ± 0.3	4.40–5.00
AO, mm	4.7 ± 0.3	4.60–5.40
FS, %	35.6 ±2.6	67.00–78.00
EF, %	70.9 ± 3.0	32.00–41.00
BW, g	570.13 ± 31.09	500.00–650.00

AO, aortic root diameter; *EF,* left ventricular ejection fraction; *FS,* fractional shortening; *IVSd,* interventricular septum thickness in diastole; *IVSs,* interventricular septum thickness in systole; LA, left atrial diameter; *LVIDd,* left ventricular internal diameter in diastole; *LVIDs,* left ventricular internal diameter in systole; LVPWd, left ventricular posterior wall thickness in diastole; *LVPWs,* left ventricular posterior wall thickness in systole.

Urinary Diseases

Urolithiasis

Urolithiasis is a common problem in guinea pigs, and the etiopathogenesis is unclear. Calculi are found in animals of both sexes and usually in animals more than 2 years old.[32] More than 90% of urinary calculi in guinea pigs are composed of calcium carbonate.[32] Most calculi are located in the bladder, urethra (commonly at the urethral orifice in sows), or ureters, but calculi are also found in the kidneys and occasionally in the seminal vesicles or vagina. In males, calculi often lodge at the bladder neck at the seminal colliculus, which is the narrowing at the urethral mound where the seminal vesicles and prostate gland open into the urethra. Clinical signs are commonly associated with the size and location of the calculi. Bladder or urethral calculi are often associated with micturition abnormalities such as hematuria, stranguria, or dysuria and vague clinical signs such as lethargy, reluctance to move, and anorexia. If the calculus is located higher in the urinary tract, micturition abnormalities may still be present, but lethargy, anorexia, weight loss, and a hunched posture may be the only clinical signs. Concurrent urinary tract infections involving *Corynebacterium renale* and other bacteria may be associated with urolithiasis.[70,71]

Diagnosis is based on clinical signs, physical examination findings, and results of diagnostic imaging and urinalysis. Calcium carbonate uroliths are radiopaque, allowing for ease of identification on survey radiographs (Fig. 21.13). Ultrasonography is useful for anatomic location of the calculi and for evaluating anatomic changes in the kidneys or ureters, such as hydronephrosis or hydroureter, ureteral mucosal inflammation, or perforation. A contrast urethrogram may be useful in male guinea pigs to determine the location of the stone. Excretory intravenous pyelograms or contrast CT are useful to further elucidate relative functional abnormalities in the kidneys or ureters. In suspect cases of urolithiasis, perform a urinalysis, including both a standard dipstick and microscopic examination of the sediment. Hematuria is the most commonly reported abnormality on urine sediment.[32]

Medical treatment of urolithiasis has been unrewarding to date. Uroliths smaller than 5 mm in diameter may pass unaided

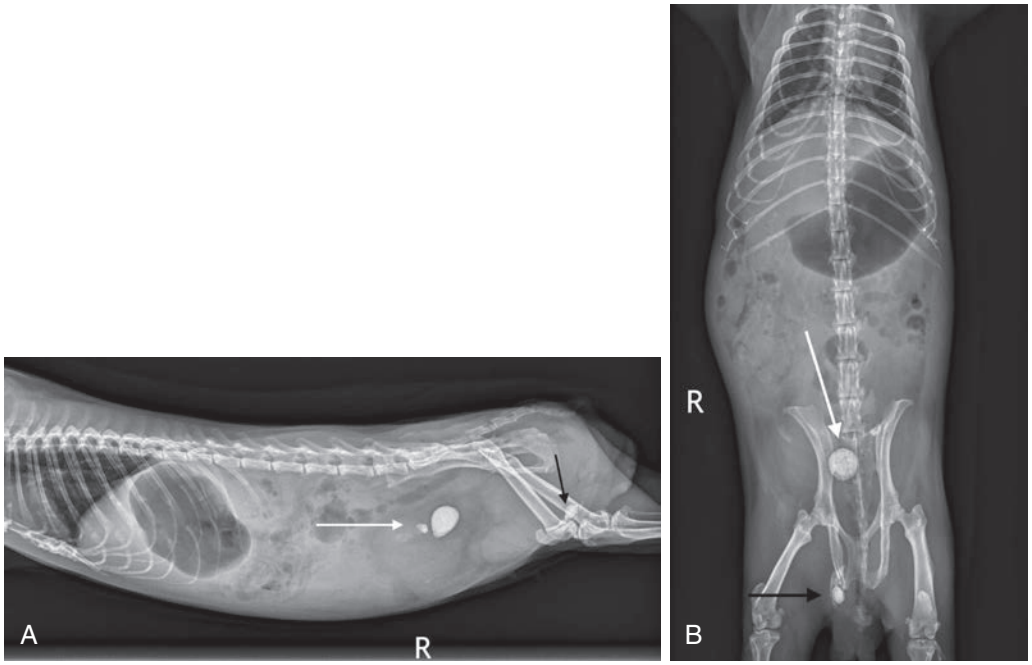


Fig. 21.13 Lateral (A) and ventrodorsal (B) radiographs of a male guinea pig with multiple radiopaque calculi in the bladder *(white arrow)* and urethra *(black arrow)*. Orthogonal views are necessary to determine the location of the calculi. The entire caudal body of the guinea pig must be included so that urethral calculi are not missed. (Courtesy K. Quesenberry, The Animal Medical Center, New York, NY.)

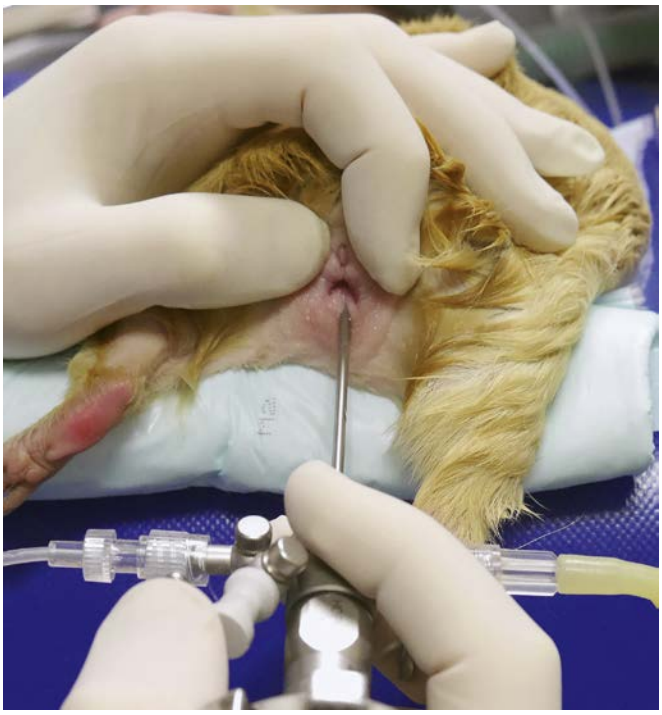


Fig. 21.14 Removal of a urinary calculus in a female guinea pig by using a 1.9-mm–diameter rigid endoscope passed through the urethra. (Courtesy Exotics Medicine Service, Alfort National Veterinary School)

because of the large diameter of the urethra in both male and female guinea pigs. Surgical or cystoscopic (Fig. 21.14) removal of larger stones is necessary (see Chapter 33). Rigid endoscopes can be used in female guinea pigs for cystoscopy and stone removal.[76,92] Smaller urethral calculi located at the urethral orifice in sows can be expelled manually under general anesthesia.

Recurrence of urolithiasis is common in guinea pigs. Prevention is targeted at increasing water intake and reducing (but not eliminating) dietary calcium. When given the choice between a dish and a water bottle, guinea pigs prefer to drink from a nipple drinker[1]; therefore all guinea pigs should have access to a minimum of one nipple drinker. For most animals, water is the cornerstone of any prevention protocol. Diets should contain a high percentage of timothy, oat, or grass hays, a lower overall percentage of pellets, and a wide variety of low calcium vegetables; alfalfa hay and pellets and high calcium greens should be avoided. Potassium citrate (30–75 mg/kg PO every 12 hours) binds intestinal and urinary calcium, decreases urinary calcium excretion, and alkalinizes the urine. Because guinea pigs have alkaline urine even with disease, the efficacy of this treatment is unclear. Potassium citrate at a high dose (150 mg/kg divided every 24 hours) has been used by one author (J.M.) in repeat cases of urolith formation without any evidence of adverse effects and stone formation did not recur. In rats, potassium citrate reduced urinary calcium levels but had no effect on calcium phosphate stone formation and size.[52] Hyperkalemia occurs with potassium citrate, and therefore blood potassium levels should be monitored.

Cystitis and Urinary Tract Infections

Bacterial cystitis is frequently identified concurrently with urolithiasis, and *Corynebacterium renale*, *E. coli*, *Enterococcus* species and others have been reported. Clinical signs mimic those of urolithiasis, with vocalizing/straining during urination, pollakiuria, dysuria, hematuria, anorexia, and depression. Base diagnosis and treatment on results of urinalysis, urine culture and sensitivity testing, and diagnostic imaging to rule out urolithiasis.

Anecdotal reports have described cases of recurring cystitis where no clear cause was discovered and treatment was challenging.[94] In these reported cases, it appears that there is a predilection toward females because all cases described have been in intact females. Some of these cases appear to have been managed with long-term treatment of NSAIDS (meloxicam or carprofen) but the exact mechanism or the disease dynamics in unknown at the time of writing.

Other Uropathies

Chronic interstitial nephritis occurs most commonly in guinea pigs more than 3 years of age. Guinea pigs more than 1 year of age can develop some degree of renal segmental fibrosis, progressing in the aged animal to chronic renal failure. The pathogenesis of this disease is unclear. However, because guinea pigs do not show particular adaptations to water scarcity, inadequate water on a dry food diet may be a risk factor, and constant adequate water provision is imperative.[1] In advanced cases, guinea pigs can be presented with polyuria/polydipsia, chronic weight loss, cardiac compromise, and other vague clinical signs such as anorexia or diarrhea and loose stool. Increases in blood urea nitrogen, creatinine, and electrolyte levels, isosthenuria, and nonregenerative anemia can be present.[61] Ultrasonography may be more sensitive than blood test results and urinalysis to diagnose renal disease in guinea pigs.[80] Typical histopathologic changes include interstitial fibrosis, glomerular ectasia, and sclerosis with variable numbers of mononuclear inflammatory cells.

Renal cysts are sometimes identified incidentally at necropsy (J.M., personal observation, August 2017). One report describes renal failure in a guinea pig after ingestion of peace lily. Laboratory findings were suggestive of renal failure and included increased blood urea nitrogen and creatinine levels with concurrent isosthenuria. The guinea pig was euthanized 1 month later because of worsening clinical signs.[36]

Female Reproductive Diseases

Ovarian Cysts

Ovarian cysts are common in guinea pigs, and older animals are more frequently affected.[6,63] Two types of ovarian cysts occur: serous cysts (cystic *rete ovarii,* nonfunctional cysts) and hormone-producing follicular cysts. No significant correlation has been identified between reproductive history and the prevalence of cysts,[67] but other problems reported concurrently with ovarian cysts include leiomyomas of the uterine structures, granulosa cell tumors,[9] cystic endometrial hyperplasia, and endometritis.

Serous cysts develop spontaneously throughout the estrous cycle (Fig 21.15A), do not respond to surges of luteinizing hormone, and are not hormone-producing. They may be single or multilocular and are usually filled with clear fluid. Serous cysts

range in diameter from 0.5 to 7 cm and increase in size and prevalence as the animal ages.[67] Serous cysts frequently do not cause clinical signs, unless they are large and compress abdominal organs. With very large cysts, animals may present with abdominal distention and sometimes with anorexia, weakness, depression, and hunching in pain. However, other disease processes can be responsible for these clinical signs, and ovarian cysts could be an incidental finding. Diagnosis of serous cysts is best done by ultrasound (Fig. 21.15B). The treatment of choice for serous ovarian cysts that are associated with clinical signs is ovariohysterectomy, which is challenging in the presence of large cysts. Palliative therapy for serous cysts includes ultrasound-guided percutaneous drainage of the fluid, but cysts commonly return, sometimes within days. Unlike follicular cysts, serous cysts do not respond to hormone treatment.

Follicular cysts usually coincide with serous cysts and are derived from preovulatory follicles that fail to ovulate.[82] The aberrant follicular structure reaches ovulatory size, fails to ovulate, and alters normal ovarian cyclicity. Follicular cysts are associated with bilaterally symmetric nonpruritic flank alopecia and mammary hyperkeratosis (Fig. 21.16A). Follicular cysts may respond to gonadotropin-releasing hormone (GnRH) and human chorionic gonadotropin (hCG) by inducing a surge of luteinizing homone (LH), resulting in luteinization of cysts, and these drugs are an option in medical treatment (Fig. 21.16B). Good results have been achieved by two injections of short-acting GNrH agonist (25 µg/animal every 14 days for two injections; Cystorelin, Merial, Duluth, GA). No adverse effects from the use of GnRH in guinea pigs have been reported. Injection of hCG will stimulate an antibody response, making the second or third doses potentially less effective and possibly stimulating an allergic reaction after subsequent injections. Sustained-release GnRH formulations (e.g., deslorelin implants) have not been shown to

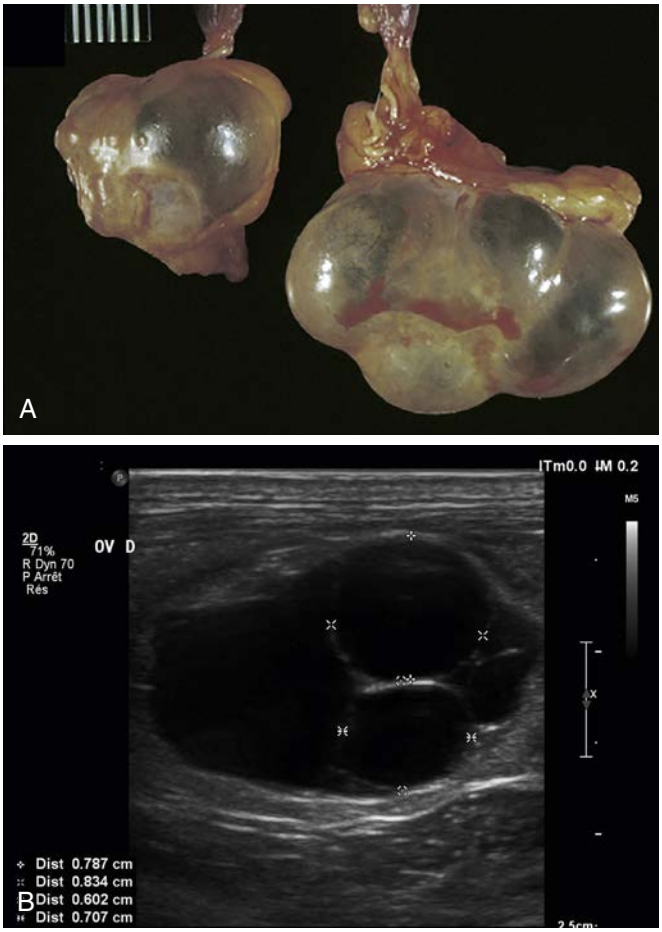


Fig. 21.15 (A) Voluminous ovarian cysts removed by ovariohysterectomy in a guinea pig. (B) Ultrasound scan of the right ovary in a guinea pig. Four cysts can be seen, characterized by their anechoic structure. (Courtesy Imaging Service, Alfort National Veterinary School.)



Fig. 21.16 (A) Bilateral symmetric nonpruritic alopecia in a female guinea pig diagnosed with ovarian follicular cysts. (B) Treatment with short-acting gonadotropin-releasing hormone agonists results in luteinization of the follicular cyst and resolution of alopecia. (Courtesy J. Mayer.)

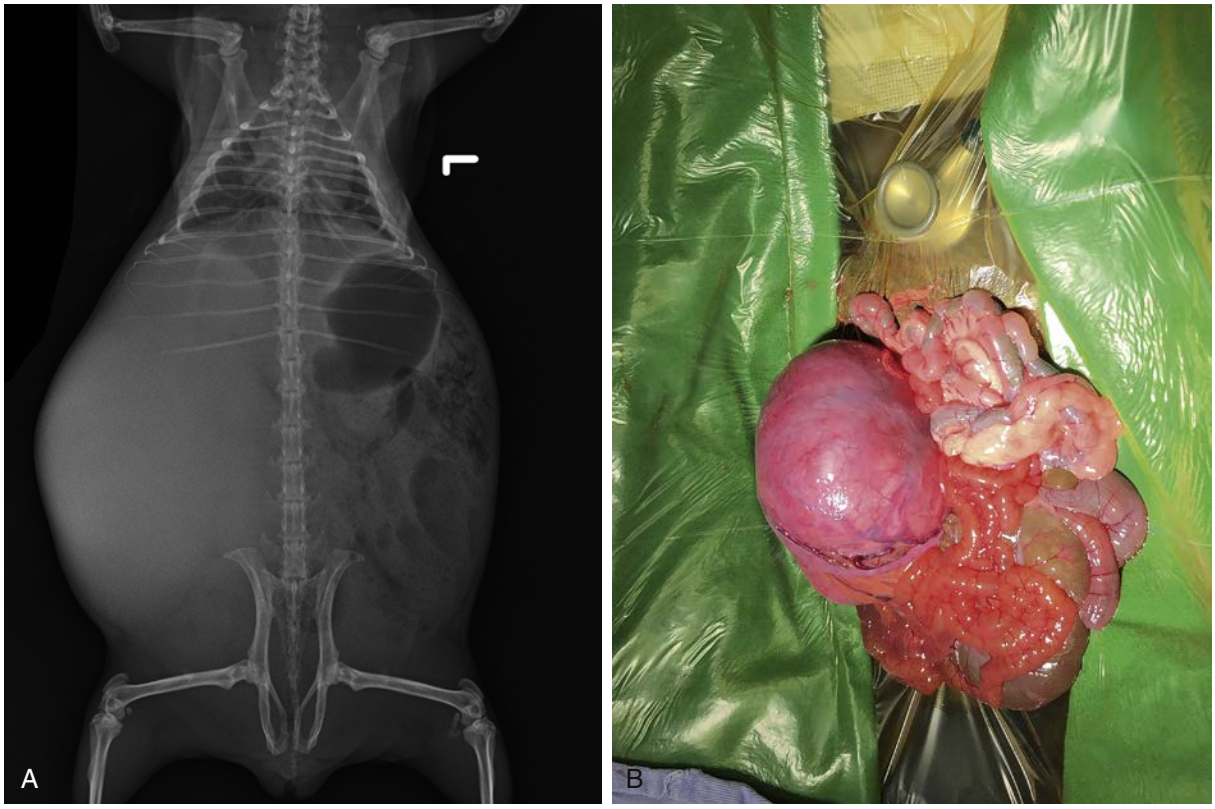


Fig. 21.17 Uterine neoplasia in a 2.5-year-old guinea pig. (A) Ventrodorsal radiograph shows a large soft tissue mass in the right abdomen, displacing internal organs. (B) Laparotomy in the same animal to remove the uterine neoplasm by means of an ovariohysterectomy. The histopathologic diagnosis was fibroleiomyosarcoma. (Courtesy Z. Szabo.)

be effective for the treatment of follicular cysts. Guinea pigs with a deslorelin implant can have an intermittent and prolonged vaginal opening, potentially a risk factor for vaginal infections.[48]

Endometritis and Pyometra

Bacterial infections of the uterus may manifest as endometritis or pyometra and are identified in breeding and nonbreeding animals.[6,7] The most commonly isolated bacteria are *B. bronchiseptica* and hemolytic *Streptococcus* species, but other possible pathogens include *E. coli*, *Corynebacterium pyogenes*, and *Staphylococcus* species.[7] Clinical signs are bloody or purulent vaginal discharge, depression, anorexia, and fever.[7] Endometrial hyperplasia and neoplasia are also common and should be considered as differential diagnoses.[6] Diagnosis is based on clinical signs, imaging, and cytologic results from the discharge. Ultrasound or computed tomography scanning are the best imaging modalities to diagnose uterine disease. Treatment involves stabilizing the animal with supportive care and broad-spectrum antibiotics. Ovariohysterectomy is the treatment of choice in nonbreeding animals. Long-term antibiotic therapy may be used in breeding sows if fertility needs to be maintained.

Uterine and Ovarian Neoplasia

Uterine leiomyomas are the most common uterine tumor in guinea pigs.[6] Other uterine tumors are leiomyosarcoma, endometrial adenoma, and adenocarcinoma.[6] Although ovarian tumors are not common in guinea pigs, rete adenomas, papillary adenomas, teratomas, and granulosa cell tumors have been reported.[6,29] Clinical signs of uterine and ovarian tumors may be mistaken for pregnancy and include hemorrhagic vaginal discharge, abdominal distention, palpable abdominal mass, and evidence of abdominal pain.[7] Uterine neoplasms can become very large and can lead to abdominal distension and displacement of internal organs (Fig 21.17A). In suspect cases, perform abdominal ultrasound scanning to discern the origin of the mass and possible involvement of other organs. Fine-needle aspiration and cytology may also help in diagnosis. Endometrial hyperplasia, usually associated with ovarian cysts, is also very common in guinea pigs and is a differential for uterine neoplasia.[6,63] Ovariohysterectomy is the treatment of choice for both uterine and ovarian tumors (Fig 21.17B). Consider early-age ovariectomy of the unbred sow as a preventive measure for reproductive system neoplasia.[10]

Dystocia

Guinea pigs are more predisposed to dystocia than other rodents or rabbits. This may be because of the large size of their pups, narrow pelvic canal, or inadequate separation of the pubic symphysis at parturition.[7] In a recent study, no evidence was found for ossification of pubic symphysis in either nonbreeding or breeding female guinea pigs.[39] Other possible causes for dystocia are uterine torsion, uterine inertia, obesity, and nutritional deficiencies.[7] Most dystocias occur in sows first bred after 8 to 12 months of age. Although some sows first bred after 1

year of age may deliver normally, most older primiparous sows have difficulty with parturition. Sows that are at risk must be monitored closely and may require cesarean section. Clients should be educated that continuous straining for 20 minutes or unproductive contractions for more than 2 hours is abnormal. Signs of dystocia in full-term sows are contractions and straining that produce a bloody or green discharge but no pups. Pressure from the gravid uterus or pups may also lead to temporary paresis or paralysis of the rear legs. Palpating the pelvic area for relaxation of the symphysis will help determine the need for a cesarean section. If the symphysis is separated approximately 2.5 to 3 cm, palpating the vaginal canal may reveal a pup that must be manually removed or assist-delivered. Sterile water-based lubricating gel placed in the vaginal canal helps ease pup removal. If the symphysis is relaxed and uterine inertia is suspected, treat with injectable calcium gluconate (100 mg/kg IM); if no response, treatment with oxytocin (0.2–3 IU/kg SC with fluids) may facilitate contractions. However, the use of oxytocin is controversial and may result in strong detrimental uterine contractions, particularly after IM administration. When conservative treatment is not effective or in cases in which the pubic symphysis is dilated less than 2.5 cm, cesarean section is indicated. Correcting electrolyte and fluid imbalances is crucial to the patient's stability during surgery. Because of the significant surgical and anesthetic risks, the prognosis is guarded to poor.

Uterine prolapse is most commonly associated with parturition. Acutely, the prolapse may be pink or red and smooth; however, depending on the duration of the prolapse, the tissues may be dry, darker, and covered with bedding or fecal material. In these cases, stabilize the sow with fluids, analgesics, and antibiotics and then perform ovariohysterectomy.

Toxemia of Pregnancy

Toxemia of pregnancy is most commonly seen in pregnant sows 2 weeks prepartum to 2 weeks postpartum. It can be caused by a negative energy balance of the sow resulting from the heavy demand of the growing fetuses. Predisposing factors include obesity, lack of exercise, large fetal loads, change in diet and/or environment, heat stress, and primiparity.[7,31] Pregnancy ketosis can also develop when the gravid uterus compresses either its own vascular supply or that of the kidneys or GI tract, leading to tissue ischemia, and hypertension, and in some cases, disseminated intravascular coagulation.

Signs of pregnancy ketosis are anorexia, lethargy, depression, uncoordinated movements, and dyspnea; this may progress to muscle spasms, paralysis, and death. Laboratory findings include ketonuria, proteinuria, aciduria, hypoglycemia, acidosis, hyperlipemia, and hyperkalemia.[7] Hepatic lipidosis frequently develops. Treat animals with pregnancy ketosis with intravenous (IV) or intraosseous isotonic fluids with dextrose and oral glucose. Critical care diets that contain readily available carbohydrates are recommended for assist feeding (e.g., Emeraid Herbivore, Lafeber Co., Cornell, IL). Treating pregnancy toxemia is often unsuccessful; therefore prevention is essential. Avoiding stress, obesity, and changes in the diet or environment during late pregnancy reduces the risk for pregnancy toxemia. Increase carbohydrate intake by supplementing with a critical care diet during the last 2 weeks of gestation and the early postpartum period, and make sure that food and water are readily available.

Male Reproductive Disorders

Bacterial infection of the scrotal area and prepuce are not uncommon and can develop from bite wounds, soiled bedding, or smegma accumulation in the prepuce.[63] Signs include unilateral or bilateral swelling of the scrotal area, preputial swelling or discharge, anorexia, and weight loss.[7] Smegma accumulation can result in enlargement and inflammation of the prepuce and glans penis, and the accumulated smegma can become very dry and hard (Fig 21.18). Treatment involves topical cleaning, appropriate antibiotics, supportive care, and analgesics and NSAIDs as indicated. Testicular neoplasia such as seminoma and embryonal carcinoma are rare but have been described in guinea pigs.[45] One enlarged testicle with or without testicular atrophy in the opposite gonad is the most common clinical sign of a testicular tumor and surgical castration is the treatment of choice.

Integumentary Disorders

To evaluate dermatologic disorders in guinea pigs, recognizing what is normal for a specific breed or for guinea pigs in general is important. All guinea pigs have minimal or no hair between the nose and lips, around the lips, on the outer pinnae, and behind the ears. The teddy, teddy satin, and texel breeds have a terrier-like coarse, kinky coat with curly whiskers. Occasionally hair or eyelashes may curl into the eyes of newborn pigs, causing irritation. The teddy and texel breeds also seem predisposed to dry, flaky skin.

Alopecia

Alopecia without inflammation is often related either to husbandry or hormonal conditions.[61,63,93] Nutritional deficiencies, as well as reaction to poor sanitation and bedding material, can cause alopecia. Hormonal causes of alopecia include follicular ovarian cysts (bilaterally symmetric, nonpruritic, Fig. 21.16) and hormonal changes common in late pregnancy or in lactating sows in poor condition or with large litters.[61] With barbering, the hairs are not completely epilated, and close examination of the skin reveals broken hair shafts. Self-inflicted barbering may occur out of boredom or poor nutrition; both are often caused by a lack of available hay or fiber. Adding hay and toys to the environment may resolve the problem. Dominant guinea pigs will barber their cage mates and may have to be separated. Examination of the barbering pattern will reveal whether it is self-inflicted (in which case the head and neck are spared).[61]

Dermatophytosis

Young to middle-aged and immunosuppressed animals are more susceptible to dermatophyte infections, which present as scaly, patchy lesions on the face, feet, and dorsum.[62,64,94] These skin lesions are usually circular areas of alopecia with inflamed and sometimes crusty edges (Fig. 21.19) and can also be pruritic.[61] Most infections are caused by *Trichophyton mentagrophytes* and *T. benhamiae,* but *Microsporum canis* can be isolated as well.[50] Diagnosis is based on clinical signs, results of cytologic examination, and dermatophyte culture. Because



Fig. 21.18 Severe accumulation of smegma in the prepuce in a guinea pig (A) leading to phimosis and inflammation. The smegma can dry out and become firm (B) and should be removed. (Courtesy C. Mans.)

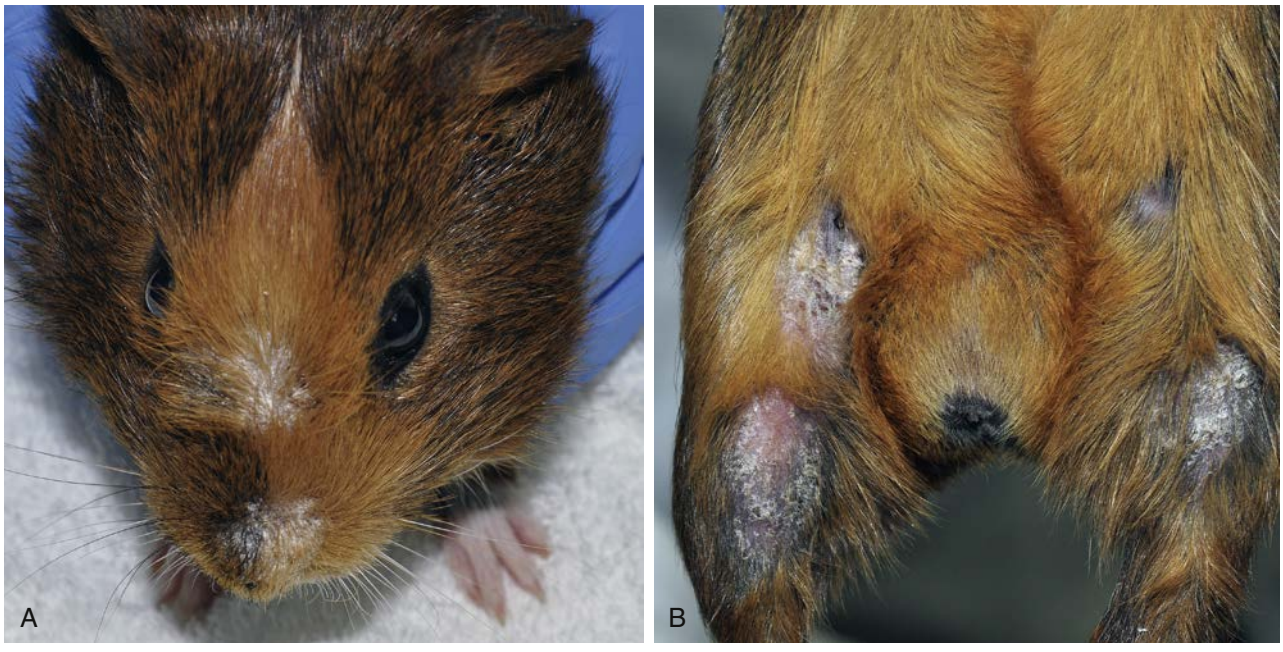


Fig. 21.19 Dermatophytosis in a guinea pig characterized by circular areas of alopecia with inflamed and crusty edges on the face (A) and on the medial aspects of the hindlimbs (B). (Courtesy C. Mans.)

T. mentagrophytes does not fluoresce with Wood's lamp, this test frequently produces false-negative results in guinea pigs.[61] Fungal culture is required for definitive diagnosis. Treatment includes oral antifungal medications such as itraconazole (5 mg/kg every 24 hours) or terbinafine (20 mg/kg PO every 24 hours), antifungal shampoos, and topical antifungal sprays.[61] Terbinafine has been shown to be more effective in guinea pigs against dermatophytosis than itraconazole.[62] Dermatophytosis is potentially zoonotic, and the organisms may survive in the environment, leading to reinfection.

Ectoparasites

The fur mite *Chirodiscoides caviae* (Fig 21.20A) is the most common ectoparasite of guinea pigs, whereas the most severe clinical signs are caused by the sarcoptic mite *Trixacarus caviae* (Fig 21.20B).[4,94] Infection with lice (*Gliricola porcelli*, *Gyropus ovalis* Fig. 21.20C–D) and, rarely, *Demodex caviae* also occurs.[4,93] Infection can be caused by direct or indirect contact. Fur mite infection can be subclinical or associated with severe clinical signs, depending on the severity of infection, including pruritis, alopecia, and restlessness.[4] Severe pruritus

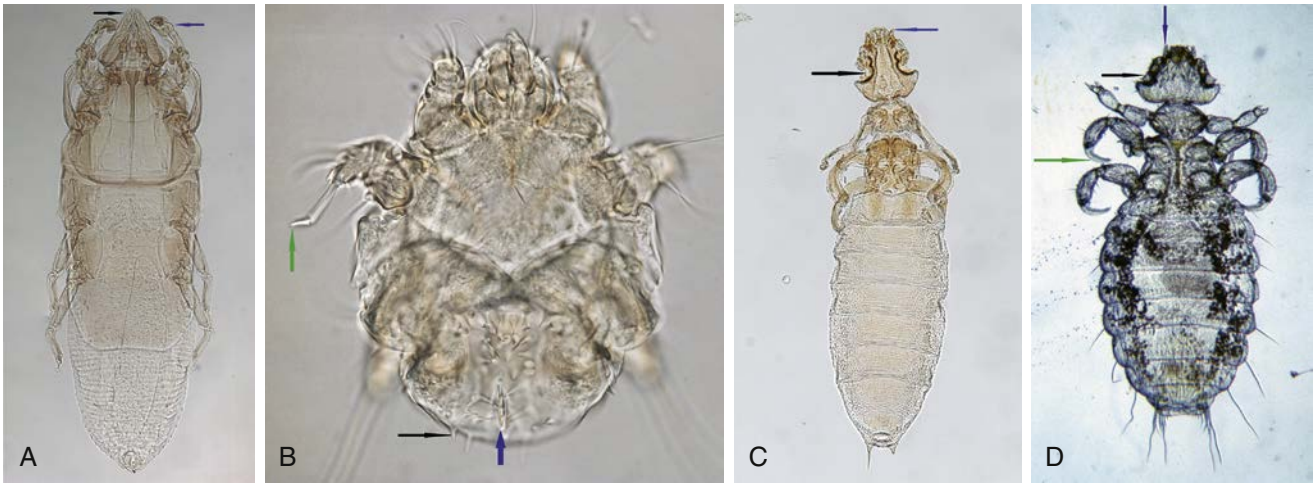


Fig. 21.20 Ectoparasites found in guinea pigs. (A) Fur mite (*Chirodiscoides caviae)* female mite with eggs visible. Elongated body, triangular rostrum *(black arrow)*. Anterior part of the body is very sclerotized (brown color). The first two pairs of limbs are hooked *(blue arrow)*. Magnification ×40. (B) Sarcoptic mite (*Trixacarus caviae)*. Oval body with triangle scale on the back *(black arrow)*, but without spikes. The anus is dorsal in the female *(blue arrow)*. The rostrum is pentagonal. The limbs are short and do not extend beyond the rostrum cranially. At their extremities, there is a sucker at the tip of a long and nonarticulated pedicle *(green arrow)*. Magnification ×100. (C) Lice of *Gliricola porcelli* with its elongated and thin abdomen, head with two antennas with four articles hidden in dimple *(black arrow)*, and two maxillary palps *(blue arrow)*. Each limb has a claw at its extremity. (D) Lice of *Gyropus ovalis* with its oval abdomen, head with two antennas with four articles hidden in dimple *(black arrow)*, and two maxillary palps *(blue arrow)*. Each limb has a claw at its extremity. (Courtesy the Parasitology Service, Alfort National Veterinary School.)



Fig. 21.21 White-yellow crusty areas with inflammation and abrasions from self-induced trauma in a guinea pig diagnosed with *Trixacarus caviae* mange. (Courtesy J. Mayer.)

is a hallmark sign of *T. caviae* infection; animals can scratch so intensely that they appear to be having a seizure. Severe pruritis can lead to severe self-induced trauma with secondary fungal or bacterial infections.[93] Lesions include white-yellow crusty areas with inflammation and abrasions from self-induced trauma (Fig. 21.21). Louse infestation usually causes a less severe dermatitis and, because lice spend their entire life cycle on the host, requires direct contact for transmission. Heavy lice infections can result in pruritic alopecia, crusty lesions, and an unthrifty-looking coat.[4,93] Guinea pigs housed with rabbits, other rodents, or birds may become transiently infected with other ectoparasites (e.g., *Sarcoptes muris*, *Notoedres muris*, *Myocoptes musculinus*).[4]

Ectoparasites are diagnosed by microscopic examination and direct visualization of the mites or their eggs. Treatment with ivermectin (0.4 mg/kg SC every 10–14 days for four treatments) or selamectin (15 mg/kg topical, single dose) has been shown to be effective for treatment of *T. caviae* infection in guinea pigs.[20] However, repeat treatment with selemectin may be needed. These macrocyclic lactones are effective against lice as well. Treat severe pruritus with antihistamines (diphenhydramine, hydroxyzine), NSAIDs, or both.[61] Asymptomatic animals should also be treated for ectoparasites and the environment disinfected.[61] Lice and fur mites are usually species specific; however, *T. caviae* can be zoonotic.

Pododermatitis

Pododermatitis is common in guinea pigs and can affect all four feet.[63,93] Lesions may originally develop from irritation due to improper husbandry (e.g., wire bottom cages, abrasive or soiled bedding, sharp pieces of wood chips). Clinical signs vary from mild to severe (Fig. 21.22) and include erythematous lesions with or without ulceration of the palmar or plantar surfaces of the feet, to granulomatous, callous-like swellings that, in severe cases, may result in bacterial invasion into the tendons, joints, and bone. Radiographs should be performed to rule out osteomyelitis or degenerative joint disease. Treatment in mild-moderate cases may include soaking the lesions with dilute chlorhexidine or iodine solutions, maintaining the animal on soft substrates, bandages, and administering systemic antibiotics based upon culture and sensitivity results, if indicated. More



Fig. 21.22 Pododermatitis on the left forelimb (A) and both hindlimbs (B) in guinea pigs. Swollen soft tissue and ulceration are present. (Courtesy J. Mayer and C. Mans.)

severe cases may require surgical debridement, placement of antibiotic-impregnated beads, and long-term wound management. If osteomyelitis or joint infection involves the digits of the front foot, amputation may be necessary. Analgesic and antiinflammatory medications are an important part of treatment.[61] Vitamin C deficiency may be an important predisposing factor in animals with pododermatitis, and supplementation may be beneficial as part of treatment protocols. The prognosis is poor in severe cases, and prevention is essential. Proper diet, husbandry, cleanliness, and preventing obesity are helpful in prevention.

Skin Neoplasia

Benign follicular tumors, in particular trichofolliculomas and less frequently trichoepitheliomas, are the most common skin neoplasm in guinea pigs.[40,93] Trichofolliculomas are benign and occur predominately in males; these often arise on the dorsal rump, incorporating the coccygeal gland (Fig. 21.23), and can be large, malodorous, ulcerated, and exudative. Complete excision is usually curative. Additional cutaneous tumors that have been reported in guinea pigs include sebaceous adenoma, fibrosarcoma, lymphoma, lipomas, liposarcoma, and fibropapillomas of the ear canal.[40,63]

Mammary Gland Disorders

Mastitis is uncommon in guinea pigs. Husbandry-related causes include poor cage hygiene, sharp objects, abrasive bedding, wire cage bottoms, and trauma from pups.[7,31] Bacteria cultured from infected mammary glands can include a wide variety of both gram-positive and gram-negative bacteria. The mammary glands are painful and swollen in cases of acute mastitis. Diagnosis is based on clinical signs and results of cytologic examination and bacterial culture of the discharge or milk. Treat guinea pigs with mastitis with antibiotics based on culture and sensitivity results, antiinflammatory medications, hot packing of the glands, and supportive care.[7]



Fig. 21.23 Trichofolliculoma in a guinea pig located over the caudal dorsum, close to the coccygeal gland. (Courtesy V. Jekl.)

Mammary gland neoplasms (fibroadenoma, adenomas and adenocarcinomas) are relatively common and reported in both sexes, with a higher prevalence in males,[63] and up to 75% are malignant (i.e., adenocarcinomas).[31,63] Clinical signs of mammary tumors are swelling of one or both glands with or without serous or bloody discharge (Fig. 21.24). Differentiate this condition from mastitis by cytologic examination, biopsy, or both. Because mammary tumors metastasize to the lungs, thoracic imaging by CT scanning or radiography is recommended.[43] Surgically excise mammary tumors with wide (5–10 mm) margins; also remove the local lymph node if possible. Because guinea pig skin is not as loose as in other rodents, a skin flap might be necessary to close the surgical site if the tumor is large.

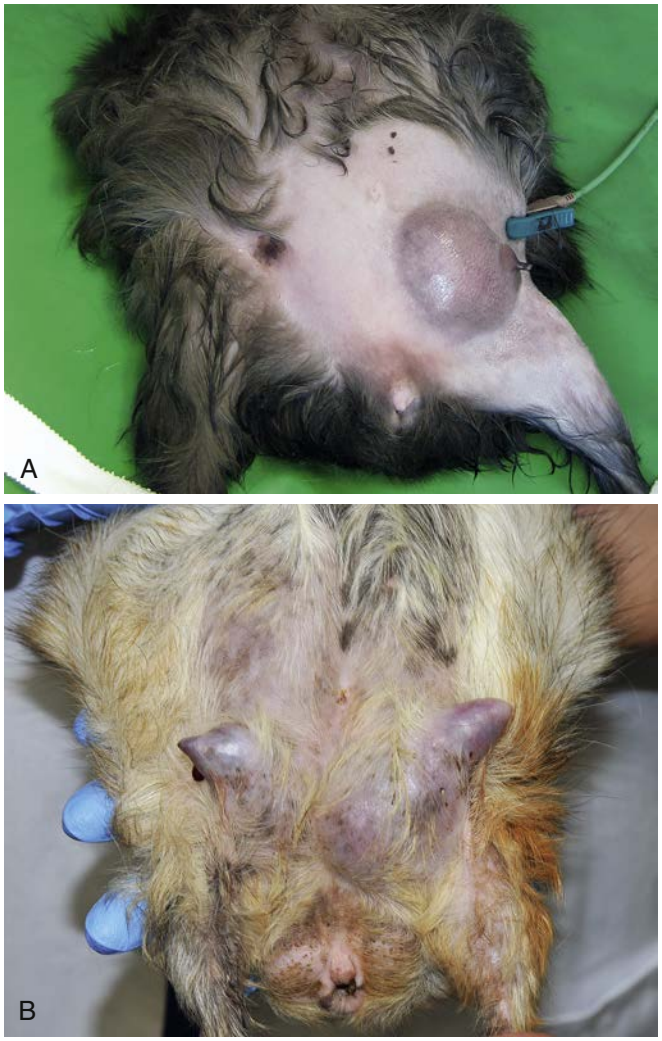


Fig. 21.24 Mammary neoplasms. (A) Mammary adenocarcinoma in a female guinea pig. (Courtesy Exotics Medicine Service, Alfort National Veterinary School.) (B) Mammary neoplasm affecting both mammary gland and leading to hemorrhagic discharge in a male guinea pig. (Courtesy C.Mans.)

Musculoskeletal Diseases

Vitamin C Deficiency (Scurvy)

Guinea pigs are incapable of endogenous synthesis of vitamin C because they possess a mutated gene for L-gulonolactone oxidase, which prevents the conversion of L-gulonolactone to L-ascorbic acid. Lack of dietary vitamin C results in defective type IV collagen, laminin, and elastin; this compromises blood vessel and joint integrity and results in joint and gingival hemorrhages.[57] Collagen is necessary to anchor teeth tightly; without it, teeth loosen and malocclusion develops. Young, growing animals are more susceptible to scurvy, and clinical disease can develop after as little as 2 weeks of ascorbic acid deprivation. Guinea pigs require 10 to 25 mg/kg per day of vitamin C in their diet; pregnant animals require 30 mg/kg per day.[31]

Guinea pigs fed an inappropriate diet, such as rabbit pellets, or fed outdated or inadequately stored pellets or pellets not supplemented with stabilized vitamin C are most at risk. Signs of vitamin C deficiency are a rough hair coat, anorexia or difficulty apprehending food, teeth grinding, vocalizing from pain, delayed wound healing, lameness, paresis, swollen joints (especially the stifle), and increased susceptibility to bacterial infections. Radiographically, long bone epiphyses and costochondral junctions of the ribs are enlarged. Pathologic fractures may also be evident. Postmortem findings may reveal hemorrhage into joints, skeletal muscle (Fig. 21.25), gingiva, intestine, and subcutaneous tissues from abnormal collagen production.

The diagnosis of vitamin C deficiency is based on history, clinical signs, and radiographic and pathologic lesions. Serum ascorbic acid levels can be used to confirm the diagnosis. Treat guinea pigs with vitamin C deficiency initially with parenteral ascorbic acid at a dosage of 50 to 100 mg SC or IM every 24 hours; subsequently, vitamin C can be given as an oral liquid at 10 to 30 mg every 24 hours. After recovery, ensure adequate levels of vitamin C in the diet. Fresh, commercial guinea pig pellets with stabilized vitamin C should be offered. Foods such as red and yellow peppers and strawberries provide good dietary

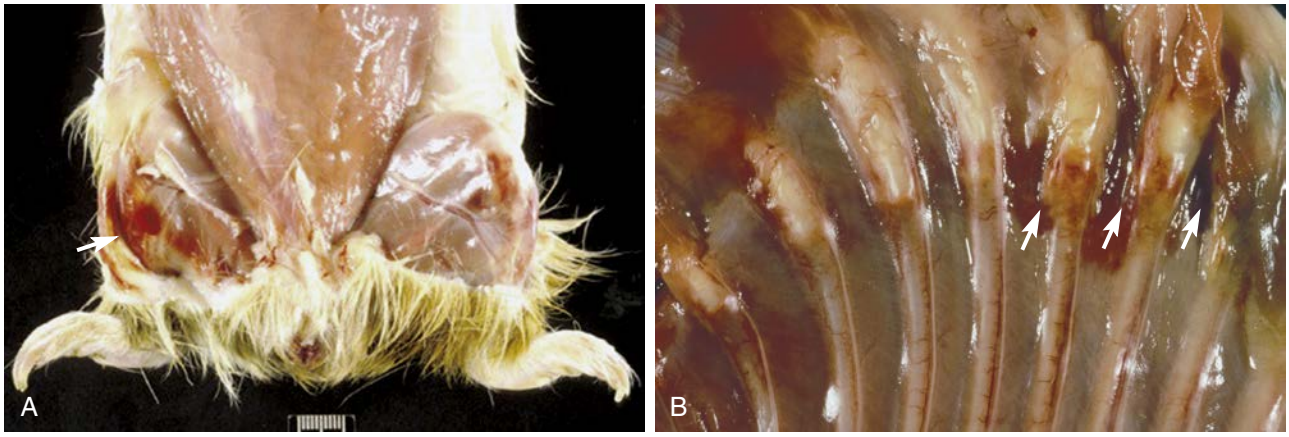


Fig. 21.25 Postmortem findings of vitamin C deficiency in guinea pig include (A) periarticular hemorrhage *(arrow)*, swollen joint (especially stifle), and (B) enlargement of the costochondral junction of the ribs *(arrows)*.

sources of vitamin C. Vitamin C added to the drinking water at a concentration of 200 to 400 mg/L daily has been advocated, but the vitamin is unstable in light and is most likely inactivated quickly. Also, adding any substance to the drinking water might alter the flavor and has the potential to prevent the guinea pig from drinking adequate amounts.

Osteoarthritis

Spontaneous osteoarthritis occurs in guinea pigs but can also be secondary to ulcerative pododermatitis (see above). Obesity, inadequate exercise, or improper substrate may be predisposing risk factors. Additionally, in one study, high-dose ascorbic acid supplementation (150 mg/day for 8 months) was associated with increased cartilage collagen content, suggesting that high-dose supplementation of ascorbic acid potentially worsened the severity of spontaneous osteoarthritis.[51] These results highlight the potential drawbacks of long-term, high-dose ascorbic acid intake on joint health, suggesting that dietary intake should not be supplemented above the currently recommended dietary allowance.[51] Treatment of osteoarthritis is palliative: soft clean bedding, pain management, physical therapy of the limbs to increase range of motion, and prevention of obesity or weight loss in obese animals.

Fibrous Osteodystrophy

Multiple cases of fibrous osteodystrophy in guinea pigs are reported.[26,42,85] Clinical reports suggest that fibrous osteodystrophy is more common in satin guinea pigs, suggesting a genetic factor in these animals.[26] Up to 30% of satin guinea pigs may be affected, with clinical signs usually occurring by 1 year of age. Fibrous osteodystrophy is caused by primary or secondary hyperparathyroidism and results in increased osteoclastic resorption of bone and replacement by fibrous tissue. Vitamin D deficiency, diets with a low calcium/phosphorous ratio, calcium malabsorption, or other calcium metabolism disturbances may play a role in the onset of disease.[69,81]

Clinical signs are secondary and include weight loss, anorexia or difficulty eating, hypersalivation, palpable enlargement of the mandibles, lethargy, difficulty walking, unwillingness to move, and pain on palpation of the bones and joints.[42] This disease must be differentiated from hypovitaminosis C, as the clinical signs can appear similar. Diagnosis is based on dietary history, physical examination findings, and radiographic findings (Fig. 21.26), which often include extensive changes to all bones in the body and skull, including osteopenia, osteosclerosis, and, less frequently, pathologic fractures.[42,81] In addition, alkaline phosphatase activity, plasma total and ionized calcium concentrations, serum 25-hydroxyvitamin D, and parathyroid hormone concentrations should be evaluated to confirm the diagnosis. Affected satin guinea pigs had lower calcium levels and higher alkaline phosphatase levels than healthy satin and nonsatin guinea pigs.[42] This disease must be differentiated from hypovitaminosis C, because the clinical signs can appear similar. At necropsy, findings include severely thinned trabecular bone, marked osteoclastic activity, resorption of cortical bone and extensive replacement with fibrous connective tissue, and hyperplastic parathyroid glands.[85] No renal lesions have been identified to date. The prognosis is guarded to poor. In affected animals, direct treatment at normalizing dietary Ca/P ratios and supplementing with oral calcium. Manage pain by including medications for skeletal pain, as well as antiinflammatory medications. Bisphosphonates are used in other species and humans to reduce osteoclastic activity and reduce bone pain, and have been used orally in guinea pigs suffering from fibrous osteodystrophy.[77] Provide supportive care, including assisted feeding and fluids as needed.



Fig. 21.26 Metabolic bone disease in a 3-year-old female satin guinea pig. Note the osteosclerosis and cortical hyperostosis and severe degenerative joint changes. (Courtesy C. Mans)

Neurologic Diseases

Otitis Media and Interna

Otitis media is common in pet guinea pigs and can progress to otitis interna. Many cases will remain subclinical. *Bordetella bronchiseptica*, *Streptococcus zooepidemicus*, *S. pneumoniae*, and *S. pseudointermedius* have been associated with otitis media.[43] Ascending infection via the eustachian tube is considered the most common route. Otitis media is often subclinical but might induce facial nerve paralysis with secondary exposure keratitis. Clinical signs of otitis interna include head tilt, ataxia, circling, and torticollis. Skull radiographs or preferably computed tomography is used to confirm the clinical diagnosis and to determine the presence and the extent of the disease. Treatment with appropriate antibiotics, analgesics, and antiinflammatory drugs may improve clinical signs, but it is usually not curative. Surgical treatment of otitis media in the form of total ear canal ablation and lateral bulla osteotomy has been reported in guinea pigs,[89] but this technique seems to induce more complications (facial nerve paralysis, anorexia, head tilt, death) in this species than in rabbits. Endoscopy-assisted myringotomy, combined with systemic antibiotics (based on culture and susceptibility

testing) and weekly endoscopic-assisted lavage of the tympanic bulla, has been reported in guinea pigs and appears to be associated with fewer complications.[75]

Insulinoma

Insulinoma can induce neurologic signs such as head tilt, ataxia, twitching, seizures, and weakness. These clinical signs, when present, are due to a severe hypoglycemia (see "Endocrine Disorders").

Response to Mite Infestation

Severe infestations with *T. caviae* can cause such severe pruritus that guinea pigs are often presented for seizuring (see "Dermatologic Diseases"). This is not a true seizure but a strong motor response to pruritis, with the animal sometimes in lateral recumbency.

Lymphocytic Choriomeningitis Virus

Lymphocytic choriomeningitis virus (LCMV) is an arenavirus that can cause meningitis and hind-limb paralysis in guinea pigs, although it is more commonly reported in mice, hamsters, and chinchillas. Lesions include lymphocytic infiltrates in the choroid plexus, ependyma, and meninges.[23] The virus is transmitted through inhalation, ingestion, or direct contact with contaminated urine, saliva, and feces. Biting insects can transmit LCMV, and transplacental transmission also occurs. The virus can be transmitted to humans.[2] Signs of LCMV infection in people include headache, vomiting, and fever; fatalities are rare (see Chapter 42).

Ophthalmologic Diseases

Several ophthalmologic conditions are common in guinea pigs (see also Chapter 40).

Corneal ulcer

Corneal ulceration is most commonly caused by trauma or foreign bodies such as hay and is diagnosed by fluorescein staining. Facial nerve paralysis caused by otitis media is another common cause for this condition in guinea pigs. Treatment is the same as in other species.

Conjunctivitis

Various bacteria can be isolated from the conjunctival sac of guinea pigs diagnosed with conjunctivitis. *Chlamydophila caviae* is a primary cause for conjunctivitis predominately in young guinea pigs.[56] Some infected animals remain asymptomatic, and clinical signs are usually mild with bilateral ocular serous discharge, and conjunctivitis.[56] Identifying intracytoplasmic inclusions in conjunctival scrapings and PCR on conjunctival swabs or scrapings can be performed to confirm the diagnosis. In a recent study, 48 of 75 symptomatic and 11 of 48 asymptomatic adult guinea pigs were PCR positive for *C. caviae*. Although the route of transmission is still unclear for this disease, nonetheless *C. caviae* could have zoonotic potential.[56] Disease is often self-limiting within 3 to 4 weeks, but the potential zoonosis warrants treatment consideration with a topical tetracycline ophthalmic ointment. Conjunctivitis is one of the many clinical signs seen with hypovitaminosis C. Lymphoma of the conjunctival lymphoid tissue has also been seen (J.M., personal communication, August 2017).

Exophthalmos

Exophthalmos is usually secondary to a retrobulbar process. In most cases, an odontogenic retrobulbar abscess associated with the maxillary cheek teeth is the underlying cause. Differentials for exophthalmos in guinea pigs include glaucoma, uveitis, and trauma.[64] Computed tomography is the recommended diagnostic test to assess the retrobulbar space, as well as the teeth and bones of the maxilla and orbit. Alternatively, ultrasonography can be used to assess the retrobulbar space. In mild cases with intact globe and vision, systemic antimicrobial therapy can be attempted, preferably based on culture and susceptibility results, obtained from an aspirate. In cases resulting from dental disease, treatment of the underlying dental abscess is indicated. In severe cases, enucleation may be indicated. Guinea pigs do not have a retrobulbar venous plexus, and therefore a transpalpebral enucleation technique can be performed. Prognosis is guarded to poor, depending on the severity of the underlying retrobulbar process and type of bacteria involved in the retrobulbar abscess.

Conjunctival Tissue Protrusion ("Pea Eye," "Fatty Eye")

Adult guinea pigs, especially purebred American shorthairs, develop a protrusion of the inferior conjunctival sac in one or both eyes, termed "pea eye" or "fatty eye" by owners (see Chapter 40). Histopathology of these tissues has demonstrated hypertrophy of the lacrimal or zygomatic glands or increased fat deposits within the conjunctiva.[44,64] Some lesions cause ventral ectropion, lagophthalmos, and secondary axial corneal degeneration.[44] This condition does not appear to be painful and usually resolves without treatment.

Heterotopic Calcification of the Ciliary Body

The clinical manifestation of this condition is a white lesion at the limbus, which corresponds to osseous metaplasia in the ciliary body (see Chapter 40). The cause is unknown but may be related to aging or genetic factors.[30] It is an incidental finding without clinical significance in most cases.[64]

Endocrine Disorders

Insulinoma

Multiple cases of guinea pigs with confirmed insulinomas have been reported.[21,35,88] All documented cases were older than 5 years of age and had an acute onset of neurologic signs secondary to hypoglycemia (head tilt, ataxia, twitching, seizures, and weakness). In addition, weight loss and lethargy may be seen.[54] Whipple's triad (symptoms of hypoglycemia, documented hypoglycemia, and response to treatment with glucose) can be used to diagnose the condition. Differentials for hypoglycemia are sepsis, hepatopathy, and prolonged anorexia. Repeated fasting blood glucose levels documenting hypoglycemia are suggestive of insulinoma. In addition, high blood insulin levels with concurrent hypoglycemia support the diagnosis, but reference intervals for insulin levels in guinea pigs have not been established. Confirmation of the diagnosis is usually by postmortem

examination of the pancreas. The prognosis is guarded to poor, depending on the general health status of the patient. In one report, a guinea pig was effectively treated with diazoxide (5–25 mg/kg PO every 12 hours).[35] Also consider treatment with prednisolone to increase gluconeogenesis in the liver and increase blood glucose levels.

Diabetes Mellitus

Spontaneous diabetes mellitus similar to adult-onset diabetes in people has been described in laboratory colonies of guinea pigs. Shortened life span (≤5 years), bladder hypertrophy, and voiding dysfunction have been reported.[5] A pet guinea pig was diagnosed with diabetes mellitus after the animal presented with cystitis and urination of small, frequent amounts; it responded to insulin therapy.[87] Diabetes mellitus may be transient in guinea pigs, and insulin therapy is generally not necessary. A low-fat, high-fiber diet is most important in treatment and prevention.[87]

Hyperthyroidism

Hyperthyroidism is the most common endocrine disorder in guinea pigs and usually is diagnosed in animals older than 3 years of age.[54] The underlying excessive thyroid hormone (thyroxine and triiodothyronine) production and secretion can be caused by thyroid hyperplasia, adenoma, and carcinoma. In a recent report, 8% (18 of 236) of guinea pig neoplasms were determined to be of thyroid origin.[28] Thyroid tumors in guinea pigs can be nonfunctional or functional (leading to hyperthyroidism).[54] Excessive circulating thyroid hormones lead to an increase in metabolic rate and exacerbate effects on the sympathetic nervous system. Presenting complaints are progressive weight loss, reduced body condition, normal or increased appetite, polydipsia and polyuria, hyperactivity, nervousness, and soft feces or diarrhea. Findings on physical examination can include poor body condition, palpable subcutaneous masses on the ventral neck, tachycardia, heart murmur, arrhythmia, hyperesthesia, and soft feces or diarrhea.[53,60]

If hyperthyroidism is suspected, submit a blood sample for a full thyroid panel (Table 21.3).[65] Imaging techniques such as ultrasonography, scintigraphy, CT, and magnetic resonance imaging may be helpful to assess the thyroid gland. An ultrasound examination of the thyroid can be done to detect any anatomic changes in the gland; perform fine-needle aspiration of palpable thyroid masses under ultrasound guidance.

The recommended treatment for hyperthyroidism in guinea pigs is radioactive iodine-131, which is considered to be the gold standard and preferred treatment for hyperthyroidism in cats. The radioiodine will primarily concentrate in the hyperplastic and neoplastic tissue and destroy it, whereas the normal tissue only receives a small dose of radiation because the tissue is suppressed. Treatment can achieve long-term control of the disease and is potentially curative. This treatment is less invasive than surgery and has a good success rate in guinea pigs. Radioactive iodine-131 treatment has been administered at 1 mCi/animal SC once with good results in multiple guinea pigs and with no adverse effects.[3,60] Other treatment options are drugs that inhibit thyroid hormone synthesis, such as methimazole (0.5–2 mg/kg PO every 12–24 hours: most cases respond to every-24-hour dosing) or carbimazole (1–2 mg/kg PO every 24 hours). These drugs are not curative, and therefore treatment is lifelong, and discontinuing medical therapy will result in relapse of clinical signs. Thyroidectomy is potentially curative if the neoplastic thyroid gland is not invading surrounding tissues and no ectopic neoplastic thyroid tissue is present.[49] Therefore advanced functional imaging (scintigraphy) is advised before performing a thyroidectomy to ensure that ectopic thyroid tissue is removed during the surgery. Surgery remains technically difficult and carries the risk of removing the parathyroid glands during the procedure, with subsequent adverse effects.

Hyperadrenocorticism

Pituitary and adrenal tumors leading to hyperadrenocorticism are uncommon in guinea pigs. Clinical signs observed in the cases reported were bilaterally symmetric, nonpruritic flank alopecia, thin skin, polyuria, polydipsia, bilateral exophthalmos, and muscle weakness.[27,54,63,96] Diagnosis of hyperadrenocorticism can be confirmed by an adrenocorticotropic hormone stimulation test, using saliva as a noninvasive approach to measuring cortisol levels.[96] Abdominal ultrasonography allows evaluation of the adrenal glands for enlargement or masses, which can support the diagnosis and rule out other anatomic abnormalities. Differential diagnoses include ovarian follicular cysts and hyperthyroidism. The medical treatment option for pituitary-dependent hyperadrenocorticism in guinea pigs is trilostane, which was used successfully in a single reported case.[96] This patient showed improvement in clinical signs within months of commencing therapy. Adrenalectomy has been described in a laboratory animal.[55]

Other Common Diseases

Cervical Lymphadenitis

Cervical lymphadenitis is usually caused by *Streptococcus equi,* subsp. *zooepidemicus*, which is considered part of the normal oropharyngeal/nasal flora of guinea pigs.[61] Oral abrasions caused by overgrown teeth, abrasive feed, or bite wounds lead to invasion of the bacteria into deeper tissues and cervical lymph nodes, which become abscessed.[61] Guinea pigs are presented with variably-sized swellings in the ventral neck region that are purulent and occasionally rupture. Rarely, *S. zooepidemicus* can spread systemically and cause pleuropneumonia, metritis, otitis media, and septicemia. Base the diagnosis on clinical signs and results of cytologic examination and bacterial culture from purulent material or lymph node aspirates.[61] Treatment requires surgical excision or lancing and drainage of the abscessed lymph nodes and systemic antibiotics based on culture and sensitivity results.

Lymphoma

Lymphoma is a common disease in guinea pigs and typically is a high-stage malignancy with poor prognosis. Epitheliotropic T-cell lymphoma has also been documented in several guinea pigs, presenting with pruritic alopecia and scaling.[47,58] Cavian leukemia caused by a type-C retrovirus was reported in laboratory guinea pigs; leukemic animals had a total white blood

cell count of 25,000 to 500,000 cells/mL, characterized by an increase in large lymphocytes.[31] Clinical signs include anorexia, lethargy, unkempt coat, and peripheral lymphadenopathy. Hepatomegaly, splenomegaly, and mediastinal masses are occasionally identified by diagnostic imaging. Diagnosis is based on the results of a complete blood count and cytologic examination of aspirates of enlarged lymph nodes or enlarged organs or body cavity effusion. The prognosis depends on stage of lymphoma at the time of diagnosis and the presence of signs of systemic disease (e.g., anorexia, lethargy). Overall prognosis is poor, although some animals have responded initially to chemotherapy. Treatment with prednisolone (1–2 mg/kg PO every 24 hours) can be used as palliative treatment. One report describes treatment of lymphoma in two guinea pigs with prednisolone (1 mg/kg PO) L-asparaginase (10,000UI/m^2 SC), and cytarabine arabinoside (300 mg/m^2 SC).[15] Both guinea pigs died after 3 weeks of treatment. Guinea pigs produce asparaginase[86] on their own, and this might render this drug less effective than in other species. Anecdotally, longer survival times (2–3 months) have been achieved with lomustine (12–15 mg/kg PO every 21 days) combined with prednisolone (1–2 mg/kg PO every 24 hours) (C. Mans, personal communication).

Only one case describing radiation therapy in a guinea pig with lymphoma has been reported.[66] A whole-body radiation with 1 Gy provided temporary remission in a 5-year-old guinea pig diagnosed with a lymphoma. A second total body irradiation with 1.2 Gy was performed 49 days later because of tumor progression. This resulted in a less noticeable response, which led to the euthanasia of the patient. Full-body radiation (1 Gy) for guinea pigs affected by leukemia could be considered because of the ease of use, the lack of significant adverse effects, and the better prognosis compared with chemotherapy trials. As with chemotherapy, radiation only provides a palliative and not a curative treatment of the patient. Radiation therapy can be supplemented by additional chemotherapy to try to achieve a longer remission time.

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22

Chinchillas

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BIOLOGY AND ANATOMY

Chinchillas *(Chinchilla lanigera)*, like guinea pigs, are hystricomorph rodents from South America. The common name *chinchilla* may derive from the Quechua words *chin,* "silent"; *sinchi*, "strong" or "courageous"; and *lla,* a diminutive. The Spaniards in the sixteenth century copied the word because Quechua Indians used chinchilla pelts to decorate their ceremonial dress.[76] Chinchillas are nearly extinct in the wild because of extensive hunting for their pelts. Wild chinchillas inhabit cool, semiarid, rocky slopes in relatively barren areas of the Andes at elevations from 3000 to 5000 m (10,000–16,600 ft) above sea level.[76] Consequently they have a high hemoglobin oxygen affinity.[76] Chinchillas live in burrows or rock crevices but are well adapted for running. They dust bathe, are herbivorous, and do not hibernate. They are gregarious, living in groups of several hundred.

The small-bodied, large-eared, and long-tailed form, *C. lanigera,* from central Chile, was domesticated in the United States from 13 individuals brought to California in 1927 by Matthew Chapman. It took nearly 12 months to capture them. These animals are the ancestors of all North American domestic chinchillas. The name *laniger* is from Latin, meaning "woolly."[76] The large-bodied, small-eared, and short-tailed form, *Chinchilla brevicaudata*, from the Altiplano (the highlands of Peru, Bolivia, northern Chile, and Argentina) was domesticated in Chile around 1931.[76] Comparison of the mitochondrial cytochrome-b gene sequence shows that both chinchilla species differ at 22 sites and the average genetic distance is approximately 6%.[76] A few reports suggest that some crosses between *C. lanigera* and *C. brevicaudata* have occurred because of captive breeding.[76] Hybrid males are infertile. Hybrid females are fertile, but when backcrossed, two-thirds of the second-generation hybrids are sterile.[76] In one study, although no traces of *C. brevicaudata* mitochondrial cytochrome-b gene variants were found in genetic sequences in any domestic *C. lanigera*, sequencing, results indicated a small genetic difference between domestic *C. lanigera* and wild *C. lanigera*.[76]

Behavior

In their natural habitat, chinchillas are active at dusk and at night; however, in captivity, they can be active during the day as well. They readily habituate to people if handled frequently. Flight is their defense mechanism, but animals, particularly females, not used to handling can sometimes bite and spray urine while standing upright. When frightened, chinchillas can shed patches of fur, a condition known as "fur-slip." The hairless patches take 6 to 8 weeks to fill in; it may take several months for the patches to become indistinguishable from surrounding fur.

The vocal repertoire of chinchillas comprises 10 different sounds.[51] These are attributed to the behavioral contexts of exploratory behavior, predator avoidance, sexual behavior, and social behavior, including social contact and antagonistic behavior (defensive and offensive). Chinchillas can raise and lower the tones of the calls they make. All chinchillas have a basic cry that is used commonly from birth.[76]

Color Mutations and Crosses

The hair coat is luxurious, soft, and very dense. As many as 60 hairs grow from a single hair follicle.[76] Captive chinchillas come in a variety of colors (Fig 22.1). The natural wild-type color is bluish-gray with yellow-white underparts. Through selective breeding, the most common color seen is dark blue gray (the dominant fur color gene). Other colors are mutations of the original standard color and include the dominant colors of beige, white, and black velvet; recessive colors include sapphire, violet, and ebony, which are varying shades of gray. Eye color may be black or pink to red due to coat color genes. White crossed with beige results in pink white, which is a cross, not a mutation. White crossed with standard results in white mosaic. Blue diamond is a double recessive cross between a violet and a sapphire. Homozygous white or homozygous black velvet combinations are lethal and a homozygous fetus from these combinations does not develop and is reabsorbed.

Anatomy and Physiology

The chinchilla has a slender body with short forelimbs and long muscular hind limbs with feet adapted for leaping. The long-plumed tail acts as a balance when the animal is jumping through the air. The head, eyes, and ears are relatively large, and the tympanic bullae are greatly expanded. Chinchillas have long whiskers and a bushy tail.

Chinchillas have four toes on both front and rear feet (digit 1 is rudimentary or absent). All toes have small primate-like nails, not claws. There is no fur on the palmar and plantar regions of the feet.

Chinchillas are virtually odorless; however, when frightened, they can release secretions that give off an odor, similar to that of scorched almonds, from glands inside the anus.[76] The average life span of chinchillas in captivity is 10–15 years. Animals as old as 22 years have been documented (Table 22.1).

The eyes are large and sit in a shallow bony orbit. A large and exposed corneal segment, a vertical slit pupil, and a heavily pigmented iris characterize the eyes of chinchillas. A third eyelid is only rudimentarily developed as a small conjunctival fold at the medial canthus and does not provide any protection to the cornea. The lacrimal drainage system consists of two lacrimal punctae at the medial canthus of the upper and lower eyelids; these drain into a single lacrimal duct and cannot be visualized macroscopically and therefore also not catheterized. The lacrimal duct runs in a similar course as in other rodents and lagomorphs.[16]

Chinchillas have very large, thin-walled tympanic bullae (Fig 22.2), which are readily visible on radiographs. The tympanic bulla is divided into a ventral and a dorsal bulla, which are separated by multiple bony septa. The ventral bulla is larger, extending caudally and reaching half the height of the skull.[76] The dorsal bulla forms the roof of the tympanic bulla and reaches to the inner side of the meatus (Fig 22.2). The eustachian tube connects the oropharynx with the tympanic bulla and enters the ventral bulla.[76] The ear canal diameter and tympanic membrane are both very large; because of these anatomic features, chinchillas are an animal model for human otologic research.

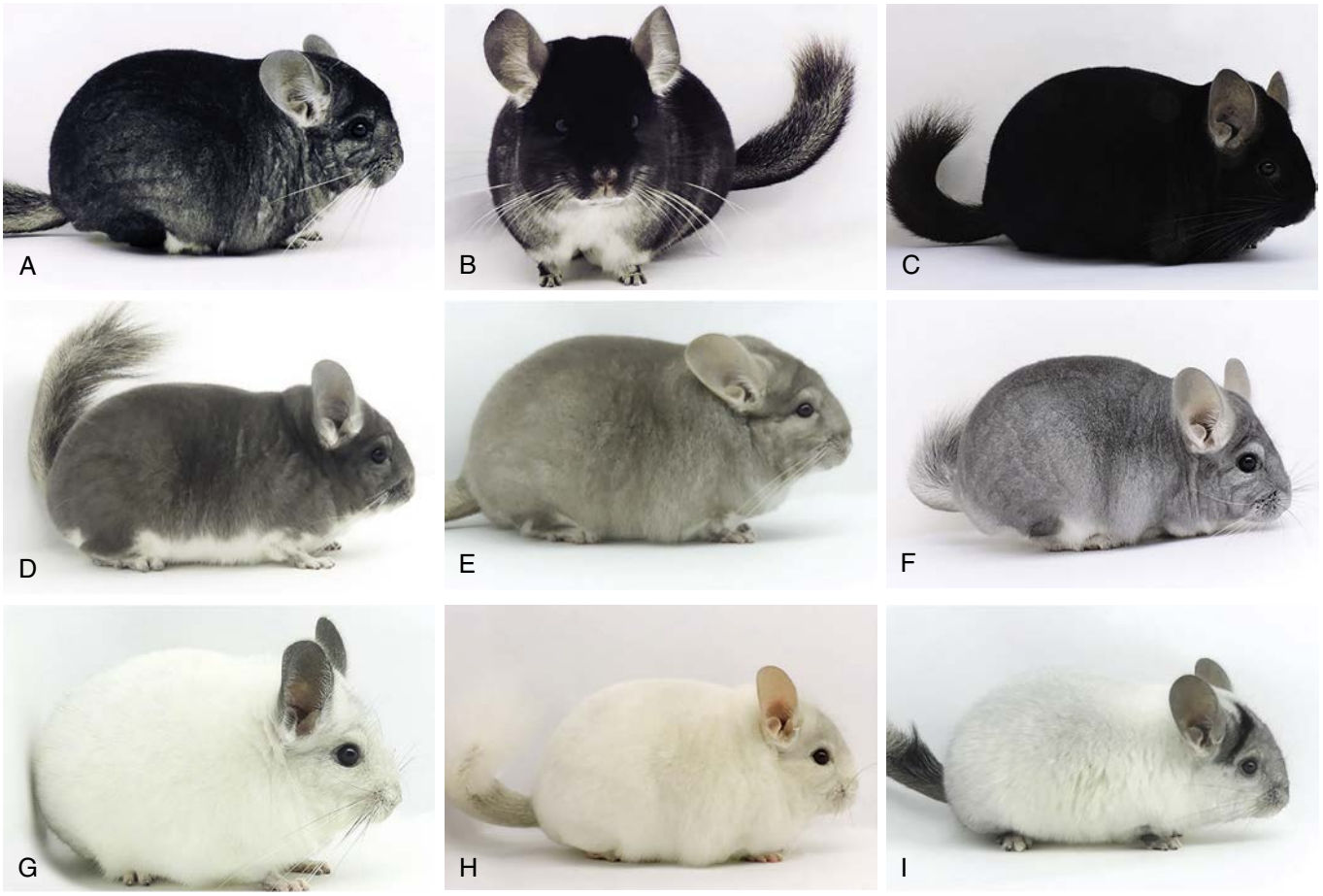


Fig. 22.1 Color mutations and crosses in chinchillas. (A) Standard, (B) black velvet, (C) ebony, (D) violet, (E) beige, (F) sapphire, (G) white, (H) pink white, (I) white mosaic. (Images courtesy of www.chinchillas.com.)

TABLE 22.1 Physiologic Values for Chinchillas

Life span	10–15 years (up to 22 years reported)
Adult weight	450–900 g
Rectal temperature	94.8°–100.2°F (34.9°–37.9°C) [66]
Heart rate	200–300 beats/min
Respiratory rate	40–80 breaths/min
Urine specific gravity	to > 1.060[23]
Urine pH	8.5–9.5[23]
Dental formula	2 (I1/1, C0/0, PM1/1, M3/3)
Intraocular pressure	4.7-14.7 mmHg (TonoVet)[82]
Schirmer tear test	1.07 ± 0.57 mm/min[50]
Phenol red thread tear test	14.6 ± 3.5 mm/15 seconds[64]

Gastrointestinal System

The dental formula of chinchillas is the same as that of guinea pigs: 2 (I1/1, C0/0, PM1/1, M3/3). Their teeth have adapted to a voluminous abrasive diet and have large chewing surfaces. All the teeth grow continuously throughout life (elodont) to compensate for the wear that occurs during prolonged chewing of their natural high-fiber diet. The labial aspect of the incisors is orange yellow in adult animals (Fig 22.3). The oral cavity is small and narrow.

Chinchillas have a long gastrointestinal tract. The small and large intestines in one adult animal measured 3.5 m (11.5 ft) long. In a wild chinchilla with a total body length of nearly 21 cm (0.7 ft), total length of the small intestine was 117 cm (3.8 ft) and of large intestine, without cecum, 145 cm (4.8 ft).[83] Compared with guinea pigs, the jejunum and descending colon are long.[14] The cecum is relatively large and coiled, and the colon is highly sacculated. The cecum holds less of the contents of the large intestine in a chinchilla than in a rabbit or guinea pig. According to one study, the cecum of a chinchilla holds 23% of the dry matter content from the large intestine, whereas that of a rabbit holds 57% and of a guinea pig, 44%.[76]

Chinchillas eat mainly at night, ingesting more than 70% of their total daily intake in the dark.[92] Fecal excretion is also predominantly at night.[76] Chinchillas produce two types of fecal pellets: one is nitrogen-rich, intended for coprophagy, and the other is nitrogen-poor, excreted as fecal pellets. Mean transit time of food in the gastrointestinal tract is 12 to 15 hours, similar to that of other rodents.

Urogenital System

Chinchillas produce concentrated urine. Reference values for urine specific gravity and urine pH are listed in Table 22.1.

The urethra in female chinchillas, as in other rodent species, terminates on the urinary papilla externally ventral to the

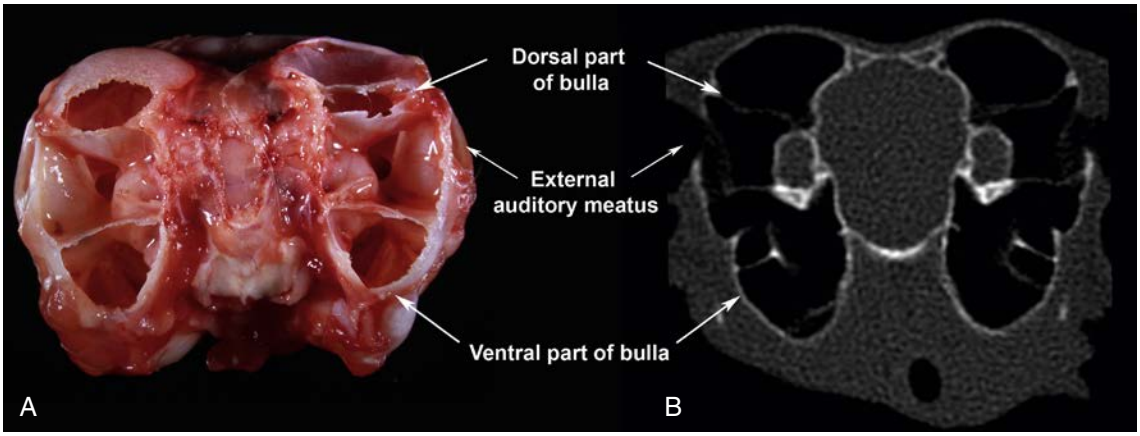


Fig. 22.2 (A) Caudal view of a chinchilla skull with the caudal walls of the tympanic bullae resected. (B) Computed tomography image at the level of the tympanic bullae. Note the large and multichambered tympanic bullae. (Photograph courtesy of A. Wuenschmann.)

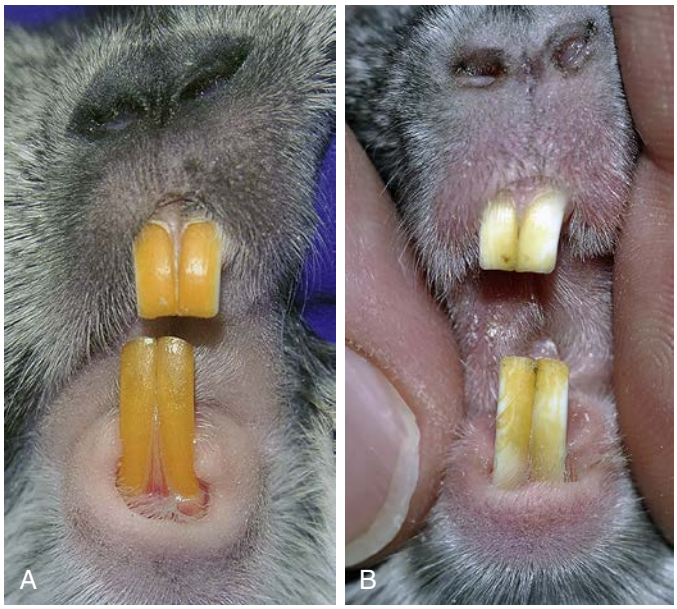


Fig. 22.3 (A) Normal incisor teeth in chinchillas. Note the yellow-orange pigmentation of the labial aspects of the teeth. (B) Abnormal incisors. Not the depigmentation of the labial surfaces. Depigmentation may be associated with calcium deficient diets.

vagina (Fig 22.4). The vulva (vaginal orifice) is U-shaped and situated between the anus and the mound-shaped urethral orifice; it is difficult to distinguish when closed and is "indicated" by a slightly, raised semicircular area (Fig 22.4).

Chinchillas have a uterus duplex bicollis vagina simplex, with two uteri, two cervices, and a single vagina.[42] Information regarding the uterine anatomy in chinchillas is conflicting, and some sources report a uterus bicornis with a single cervix.[42] Recent anatomic studies confirmed the presence of two separate distinct cervical canals and two cervices, consistent with a duplex uterus. However, the two external openings of the cervices are not discernable macroscopically and the two cervices appear as a single cervix.[42] Chinchillas have three pairs of mammary glands—one inguinal and two lateral thoracic pairs.

Male chinchillas do not have a true scrotum. Instead, the testes are contained within the inguinal canal or abdomen, and two small, movable sacs are next to the anus into which the caudal epididymis can drop (Fig 22.5). The penis in chinchillas is S-shaped, and the 1-cm long os penis (baculum) is present in the glans penis, which ends caudal to the anus.[20] As in other hystricomorph rodents, male chinchillas possess a structure termed variously as "intromittent sac," "sacculus urethralis," or "penile pouch." This structure is located ventral to the urethra, and its orifice should not be confused with the external urethral opening during catheterization (see Fig 21.5). The intromittent sac is lined with spurs and is everted during copulation, increasing the length and width of the glans penis.[20]

Male chinchillas possess unusually well-developed and elaborate accessory reproductive glands, which are paired and include the prostate, vesicular glands, and bulbourethral glands. The vesicular gland is very large, with finger-like projections. Secretions from the accessory glands form a hard plug that remains in the female tract after copulation. This 2- to 3-inch–long, irregularly shaped, firm waxy plug is often found in the cage after mating.[76]

Breeding

Reproductive data are summarized in the Table 22.2. Female chinchillas are seasonally polyestrous, and the breeding season in the northern hemisphere is approximately from November to May.[5] Estrus lasts 3 to 4 days, and the entire estrus cycle lasts 28 to 35 days.[76]

In females, a vaginal closure membrane seals the vagina at all times except during estrus and parturition and in cases of underlying disease. The closure membrane is open only during parturition and for 2 to 4 days during estrus (Fig. 22.4).[76] When the closure membrane covers the vaginal orifice, the urethral orifice can be mistaken for a genital opening. During estrus, a mucoid vaginal discharge develops; however, there is no obvious vulvar swelling. Cytologic characterization of vaginal smears can be helpful to differentiate between physiologic and pathologic conditions causing vaginal discharge.[5] The

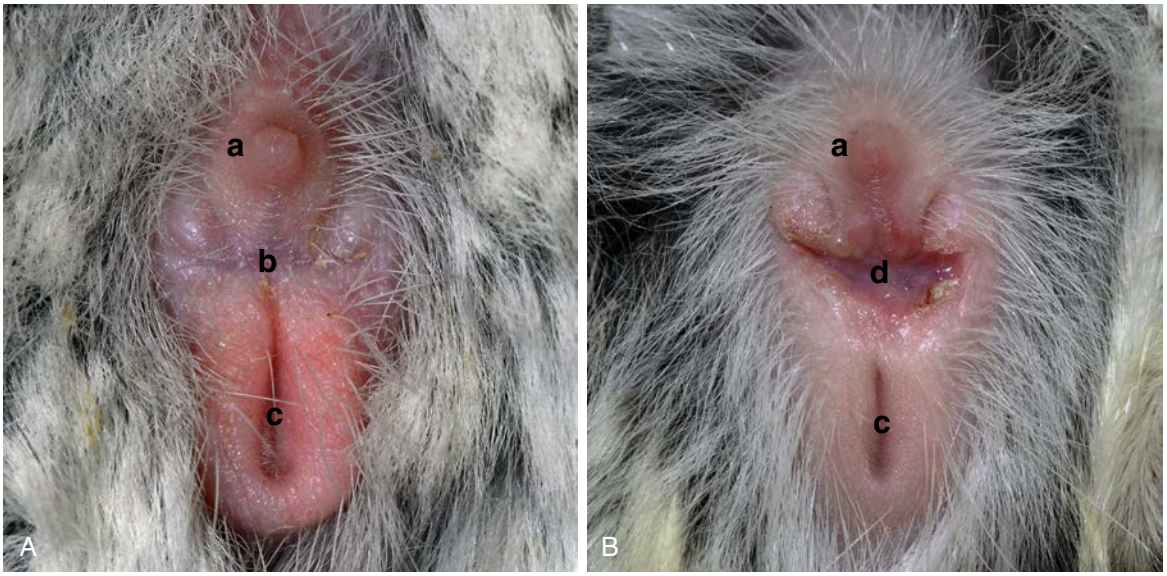


Fig. 22.4 (A) Normal female external genitalia in a chinchilla. The external urethral orifice is located on the urethral papilla (a). The vaginal orifice is sealed by a membrane (b) and located between the urethral papilla and the anus (c). (B) Normal female external genitalia in a chinchilla in estrus. Note the absence of the vaginal membrane and instead the open vaginal orifice (d). The vaginal closure membrane is also absent after birth and in most cases of underlying uterine disease.



Fig. 22.5 (A) Normal external genitalia of an adult male chinchilla. The anus is located caudally (a) and the prepuce (b) contains the glans penis. Note the large testicles left and right of the anus and prepuce. (B) Male chinchilla with penis protruding from prepuce.

TABLE 22.2 Reproductive Parameters for Chinchillas	
Sexual maturity	Female: 4–6 months, male: 8–9 months
Type of estrous cycle	Seasonally polyestrous (November–May)
Length of estrous cycle	28–35 days
Ovulation	Spontaneous
Length of estrus	4–5 days
Gestation period	105–118 days (average, 111 days)
Litter size	1–4 (up to 6 reported)
Normal birth weight	30–50 g
Weaning age	6–8 weeks

predominant cells during estrus are cornified superficial epithelial cells. Neutrophils are absent during estrus but common during proestrus and metestrus.[5]

For breeding, chinchillas can be housed in pairs or in polygamous units, with a single male and two to six females. The polygamous units used by breeders are set up with separate cages for the females, each with a rear door onto a common runway used by the male. The male can go through any open door at will, but the females wear collars that prevent exit from their cages. In a polygamous setting, the male is kept out of the female's cage during parturition and raising of young; however, in a pair setting, the male can often remain with the female if she tolerates his presence. Breeders facilitate mating by observing changes in the vaginal closure membrane and performing vaginal cytology.

Pregnancy is detectable by palpation at 90 days' gestation and may be determined by regular weighing. After 6 weeks, weight gain in pregnant chinchillas will increase rapidly. Gestation averages 111 days, and usually 1 to 4 young are in each litter (range 1-6). Parturition typically occurs in the early morning (before 8 A.M.) and only rarely late at night. All kits are usually born within 4 hours, and the time between kits can range from minutes to hours.[40] Dystocia is uncommon in well-managed breeding establishments. Although chinchillas do not build nests, the females can learn to use a nest box that, when heated, prevents the firstborn young from becoming hypothermic while the rest of the litter are being born. Chinchillas, like guinea pigs, are placentophagic. Blood on the nose and front paws of the female indicates that she has eaten the placenta and the birthing process is over.[76]

Chinchilla young are precocious, weighing 30 to 50 g at birth, and are fully furred with teeth and open eyes. They walk within 1 hour after birth. The dam stands rather than lays down while nursing, so infants often lie on their backs during suckling.[76] Weaning is normally at 6 to 8 weeks, and the minimal period of suckling necessary for survival is 25 days.[76] If the mother dies after birth, another lactating female will usually accept the newborn young, especially if they are close in age to her own. Hand feeding is necessary if a foster mother is not available or if supplemental nutrition is needed for litters of four or more. Chinchilla milk contains 11% to 16% fat, 6.4% to 8% protein, 1.7% lactose, and about 700 kJ/100 g.[26] A formula of equal parts evaporated milk and water can be administered with an eye dropper or pet nurser. For the first 3 or 4 days, the young should be hand-fed as often as possible during the day, with no more than 4 hours between feedings, and once or twice at night. After this time, the night feedings can be dropped and the intervals between daytime feedings gradually lengthened. Chinchillas begin to eat solid foods at 1 week of age.

In family groups, fathers are tolerant and friendly, sitting with the mother and young in a protective manner. Juveniles display frisky hop playing, including vertical leaps, body twisting, head tossing, racing and pivoting, and prancing with kicking back of the hind feet.

HUSBANDRY

Housing

Chinchillas are very active, acrobatic animals and require a lot of space. Large multilevel cages that provide room for climbing and jumping are excellent. Regular exercise opportunities outside the enclosure and provision of running wheels are strongly recommended. Chinchillas are easily housed in either mesh- or solid-bottom cages, although solid-bottom cages are recommended for pregnant females. Ensure that mesh spacing in cages is narrow, as tibial fractures commonly occur if a chinchilla catches its leg in a cage bar.

Chinchillas are nocturnal and shy animals, and in captivity they need a hide spot. Wild chinchillas conceal themselves in rock crevices. Plumbing pipes, clay pipes, or commercially available huts make ideal hiding places.

Chinchillas can be housed in pairs, colonies, or polygamous units, although colony housing is not advised for breeding chinchillas. Housing single chinchillas is discouraged because of their social nature.

Because of their thick fur and inability to sweat, chinchillas are very tolerant of cold but sensitive to heat. The recommended temperature range for housing chinchillas is 50° to 68°F (10°–20°C), with an ambient temperature preferably not higher than 70°F (21°C).[76] Temperatures lower than 65°F (18°C) and relative humidity lower than 50% promote good fur growth. Chinchillas do not tolerate dampness and are prone to heat stroke at environmental temperatures greater than 82° to 86°F (28°–30°C). Chinchillas will develop matted fur if kept in a warm (greater than 26.7°C [80°F]), humid environment.

Provide access to a dust bath daily, or at least several times per week (Fig 22.6). Dust bathing reduces fur lipids of chinchillas. Sanitized chinchilla dust is available commercially; beach or playground sand is not suitable for dust baths. The dust is placed in a pan, such as a plastic dishpan, that is big enough for the chinchilla to roll around in. The dust bath can be kept clean and free of feces by removing it from the cage after use. Excessive use of dust baths can lead to conjunctivitis.

Nutrition

In their natural habitat in the relatively barren areas of the Andes Mountains, chinchillas feed on any available vegetation, eating in the early morning and late evening by holding



Fig. 22.6 Chinchilla in a dust bath.



Fig. 22.7 Handling of a chinchilla. Note that minimal restraint is used to handle the animal. The front half of the body is maintained higher than the back end, which prevents the animal from trying to jump out of the hands.

the food with their forepaws while sitting on their haunches. Captive chinchillas eat mainly at night, with only small amounts of food ingested during the day.[92] Pet chinchillas should be fed a high-fiber diet consisting of grass hays and commercial chinchilla pellets containing 16% to 20% protein, 2% to 4% fat, and 15% to 20% bulk fiber. Although little has been published about the nutritional needs of pet chinchillas, growing animals and breeding females likely require more calories and higher levels of calcium, protein, and fat than do nonbreeding chinchillas. Offer treats such as such as grains, dried apples, raisins, and sunflower seeds only occasionally, in limited amounts. Fresh food items, such as vegetables, greens, or fruits, should not be fed to chinchillas, as these are not part of their natural diet and feeding these items will often lead to gastrointestinal dysbiosis and predispose to inadequate Ca/P ratio. Institute any dietary change gradually, because abrupt dietary changes may lead to temporary but often dramatic decreases in food intake. Hard foods for gnawing, such as nontoxic tree branches, can be offered and obtained commercially. A salt or mineral stone is not recommended.

Provide clean, fresh drinking water at all times. Chinchillas can be trained to use automated watering devices in a laboratory setting, or they can do equally well with cage-mounted water bottles. Chinchillas prefer water in a bowl over ball-tipped water bottles; therefore provide water bowls if increased water intake is desired.[33] Daily water intake of chinchillas fed hay or pellets is about 45 to 90 mL/kg body weight.[92]

CLINICAL TECHNIQUES

Handling and Restraint

Most pet chinchillas are easy to handle, but some may be shy or vocalize. Handle chinchillas calmly and gently. Do not grasp a chinchilla by the fur, as this may cause fur slip (see below). Chinchillas may be grasped gently around the thorax, taking care not to restrict breathing. If an animal is difficult to capture, remove it from the cage or carrier by grasping and lifting the base of the tail while using the opposite hand to support the body. Do not handle pregnant females unless necessary. Chinchillas tend to struggle if tightly restrained and are best examined with minimal restraint (Fig 22.7), instead letting the animal rest on the examiner's palms.

Physical Examination

On the initial examination, observe the chinchilla in its cage. Focus on the animal's movement, mentation, and rate and rhythm of breathing. A healthy animal has an alert demeanor with clear eyes. It should react to stimuli by moving or vocalizing; some animals will move very quickly. A healthy chinchilla has a spirited curiosity and a curled tail that is carried high. A sick animal often is indifferent, appears hunched, and has a dull coat.

Begin the physical examination by measuring the animal's weight. Measuring body temperature is not routinely performed unless a systemic disease process or hyperthermia (e.g., heat stroke) is suspected. For measuring rectal temperature, insert the thermometer 2 cm (0.75 inches) into the anus to obtain an accurate reading. Measure the temperature soon after restraint begins, since a stress-induced temperature increase occurs within 3 minutes of manual restraint.[66] The normal rectal temperature in chinchillas is 94.8° to 100.2°F [34.9°–37.9°C].[66]

Examine the eyes for any discharge or corneal or intraocular abnormalities. The tympanic membranes can always be visualized in chinchillas, and the ear canals should be clear of any debris (Fig. 22.8). The incisor teeth have an orange labial surface and should be even in length and occlusal surface (Fig 22.3). Manual restraint is not adequate for a thorough intraoral examination to rule out dental disease and is stressful to the chinchilla. Therefore anesthesia is necessary for a complete intraoral examination. Carefully palpate the skull for any asymmetry, in particular of the mandibles, which is usually associated with apical elongation of the mandibular cheek teeth.

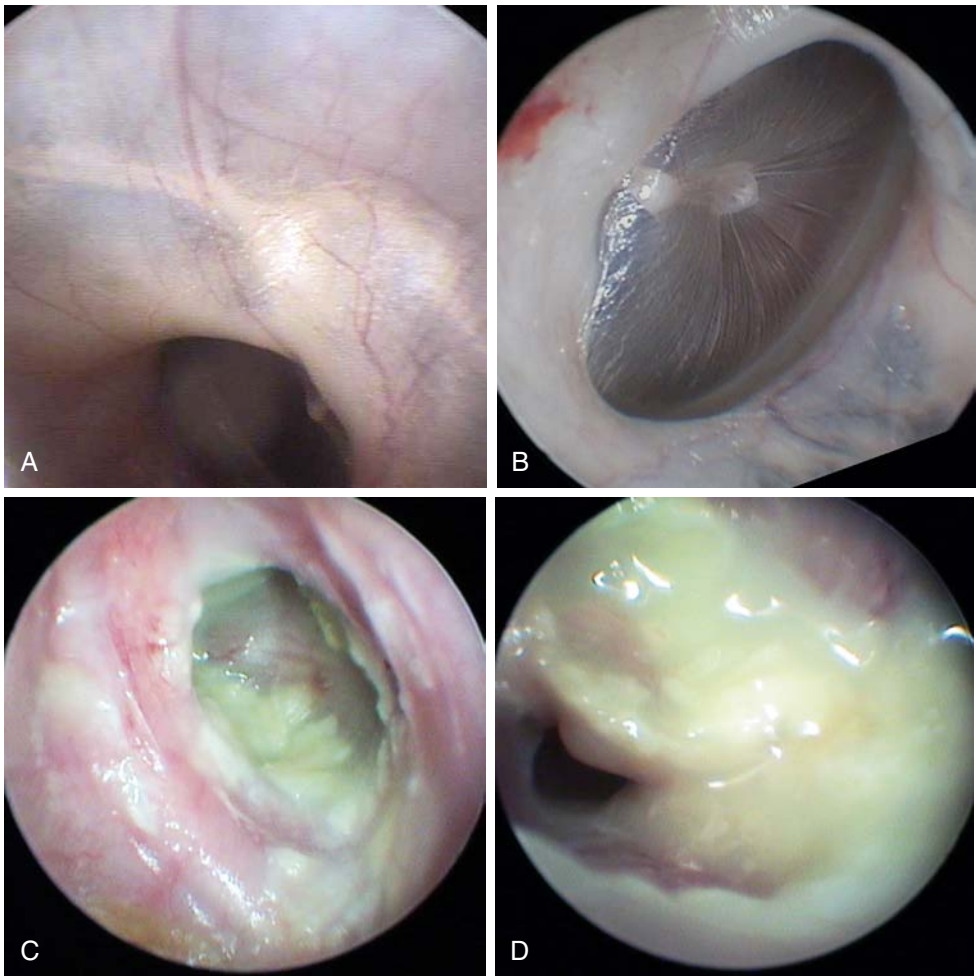


Fig. 22.8 Otoscopic examination in chinchillas. (A) Normal external ear canal. (B) Normal tympanic membrane. (C and D) Otitis externa secondary to otitis media. Note the purulent material in the external horizontal ear canal, partially covering the tympanic membrane which is abnormally opaque and vascularized (C) and perforated (D).

Next, examine the fur, skin, and mucous membranes. Wet fur around the mouth, ventral neck, or distal forelimbs is usually associated with hypersalivation indicative of intraoral (dental) disease (Fig. 22.9). Check the plantar surfaces of the hindlimbs for hyperkeratosis or pododermatitis. Auscultating the heart and lungs is best achieved with a pediatric stethoscope. Be aware that benign heart murmurs are common in healthy chinchillas. Abdominal palpation should not reveal any masses or abdominal distension.

As in other rodents, the anogenital distance is the best initial indicator of the animal's sex. Anogenital distance is greater in males than in females (Fig. 22.5). The urinary papilla of females can be mistaken for the penis; however, major differentiating features are that the penis is significantly larger than the urinary papilla, and the extruded glans penis can be separated and distinguished from the prepuce (Fig. 22.5). Morphologic differences between the sexes is evident at birth: the urinary papilla is adjacent to the anus in females (Fig. 22.4), whereas the penis is separated from the anus by a narrow band of tissue in males.

The glans penis should be completely extruded in all males during the examination (Fig. 22.5B) to rule out phimosis and remove fur or smegma accumulation.[58] Use dilute chlorhexidine



Fig. 22.9 Hypersalivation and staining of the fur around the mouth, neck, and forelimbs is very common in chinchillas with dental disease.



Fig. 22.10 Jugular venipuncture. (A) Dissection of the jugular veins in the neck of the cadaver specimen. Note the lateral location of the jugular veins along the neck. Use the sternum (a) and clavicles as landmarks. (B) The chinchilla can be restrained in sternal recumbence with the neck extended or (C) in lateral recumbence if anesthetized. The jugular veins cannot usually be visualized or palpated and jugular venipuncture is blind.

solution to aide in cleaning the glans penis, then carefully place it back into the prepuce. In females, examine for the presence or absence of the vaginal membrane (Fig. 22.4). Absence of the vaginal membrane can occur during estrus, after birth, or in cases of uterine disease, such as endometritis.

Blood Collection and Analysis

Venipuncture in chinchillas can be challenging because of the small size of the peripheral veins. The jugular veins are located laterally along the neck (Fig. 22.10) and are the preferred site for blood collection because venipuncture of this vein is most likely to result in a blood volume large enough for a diagnostic sample. For jugular venipuncture, use a 25- to 28-gauge needle and a 0.5- to 1-mL syringe. Manually restrain the animal with the forelegs pulled down over a table edge and the head and neck extended up like a cat; alternatively, sedate or anesthetize the chinchilla for venipuncture. Visualizing or palpating the jugular vein is usually not possible; needle insertion is done blindly, and the vein is located by aspirating blood.

The lateral saphenous and cephalic veins are accessible but very small and usually allow only minimal sample collection. Use a very small needle and insulin syringe to prevent collapse of the vein. Gingival vein venipuncture is less reliable compared with other rodent species. Femoral vein venipuncture can also be attempted in sedated or anesthetized animals. Venipuncture of multiple peripheral veins may be necessary to collect an adequate volume of blood for analysis.

Venipuncture of the cranial vena cava can be used for blood collection, but because of potentially fatal complications, this should only be performed in anesthetized animals in which blood cannot be collected by any other means.

Representative hematologic and biochemical references values are listed in Tables 22.3 and 22.4. Clinical laboratory values can vary according to the physiologic state of the animal, the sex, and the laboratory techniques used (See also Chapter 39).

Urine Collection and Urinalysis

Free catch urine can be collected by placing a chinchilla in a clean cage without a cage liner or bedding. Subcutaneous fluids can be administered to increase the chance of urination, but urine specific gravity cannot be interpreted in these cases. Cage floor urine samples are noninvasive, simple to obtain, and useful to measure urine pH and ketones using urine dipsticks. Anorexic chinchillas will readily become ketotic, and in more severe cases ketoacidotic, and therefore noninvasive urine testing is a simple, fast, and reliable method to determine metabolic status. Cystocentesis is sometimes necessary in animals with urethral obstruction. Anesthesia or sedation is necessary for cystocentesis, and the method is similar to that used in other small mammals.

TABLE 22.3 Hematologic Reference Intervals for Chinchillas

Analyte	Reference interval
Hematocrit, %	33–48
Hemoglobin, g/dL	10.5–15.2
Red blood cells, $\times 10^6/\mu L$	5.8–9.2
Reticulocytes, % RBC	0–1.8
Mean corpuscular volume, MCV, fL	49–59
Mean corpuscular hemoglobin, MCH, pg	14.5–20.5
Mean corpuscular hemoglobin concentration, MCHC, g/dL	29.3–36.0
White blood cells, $\times 10^3/\mu L$	2.1–17.6
Lymphocytes, %	31–95
Neutrophils, segmented, %	4–58
Monocytes, %	0–14
Eosinophils, %	0–3
Basophils, %	0–1
Platetlets, $\times 10^3/\mu L$	208–867

Data from Wuck A. Labordiagnostische Referenzbereiche bei Chinchillas [in German]. Thesis. Ludwig Maximillian Universiy of Muinch. 2010.

TABLE 22.4 Serum Biochemical Reference Intervals for Chinchillas[93]

Analyte	Reference interval
Alanine aminotransferase, U/L	2–24
Albumin, g/dL	2.3–4.5
Alkaline phosphatase, U/L	22–247
Amylase, U/L	1051–3391
Aspartate aminotransferase, U/L	19–247
Bile acids, μmol/L	1–92
Bilirubin, mg/dL	0–0.4
Blood urea nitrogen, mg/dL	30–81
Calcium, mg/dL	7.5–11.9
Chloride, mEq/L	105–126
Cholesterol, mg/dL	48–199
Creatine kinase, U/L	116–938
Creatinine, mg/dL	0.25–0.87
Fructosamine, μmol/L	119–223
γ-Glutamyl transferase, U/L	0–28
Glutamate dehydrogenase	0–3
Glucose, mg/dL	53–249
Lactate dehydrogenase, U/L	261–1108
Lipase, U/L	35–234
Magnesium, mg/dL	2/4–6.7
Potassium, mEq/L	3.3–6.1
Phosphorous, mg/dL	1.8–11.5
Protein, total, g/dL	4.1–6.7
Sodium, mEq/L	150–169
Triglycerides, mg/dL	22–205

Data from Wuck A. Labordiagnostische Referenzbereiche bei Chinchillas [in German]. Thesis. Ludwig Maximillian Universiy of Muinch. 2010.

Urinalysis is an important diagnostic tool in chinchillas (see Table 22.1 for reference values for urine pH and specific gravity). In healthy chinchillas, urine color can vary from yellow to red-brown. Amorphous crystals are present in most animals, and urine protein is present if measured by urine dipstick, which has been shown to not correlate with quantitative protein measurements.[23] In contrast to guinea pigs and rabbits, chinchillas do not excrete excess dietary calcium via the urine, but via the feces; therefore calcium carbonate crystals are not a normal finding in chinchillas.[23,34]

Urinary Catheterization

In male chinchillas, the most common indication for urethral catherization is urolithiasis. In sedated or anesthetized males, the urethra can be catheterized by using a 3.5- to 5-Fr nasogastric feeding tube or red-rubber catheter. Extrude the penis by placing gentle pressure on the scrotum at the base of the penis. The penis is S-shaped; therefore extend the penis caudally to facilitate passing of the catheter through the pelvic flexure of the urethra. Minimize handling of the penis itself to prevent irritation and trauma, which can lead to temporary partial prolapse. Identify the opening to the intromittent sac located ventral to the urethral opening to avoid accidental catheterization of this blind-ended structure.

Urinary catheterization in female chinchillas is rarely indicated but can be done easily because of the external location of the urethral opening (Fig 22.4).

Middle Ear Sampling Technique

Minimally invasive access to the middle ear through the dorsal roof of the tympanic bulla is a common surgical procedure in chinchillas used for human otologic disease research, and this transbullar sampling technique can be used in a clinical setting for sterile sampling of the middle ear in cases of otitis media.[13,54] The technique requires general anesthesia but is minimally invasive. For this technique, incise the skin over the dorsal aspect of the tympanic bulla, then perforate the bone forming the dorsal tympanic bulla with an 18- to 20-gauge needle (Fig 22.11). Once access to the middle ear has been established, insert a sterile 20- to 22-gauge intravenous (IV) catheter and aspirate samples for diagnostic testing, including bacterial culture and cytology.[13,54]

Diagnostic Imaging

Routine thoracic and abdominal radiographs are performed in chinchillas as in other species (Fig 22.12). Anesthesia or sedation is required for radiographic positioning. Vertebral heart size reference intervals based on thoracic radiographs (7.5–10.2), as well as computed tomography (CT) scans (7.1–9.4) have been established.[22] Echocardiographic measurements have been reported in chinchillas manually restrained and under isoflurane anesthesia (Table 22.5).[51] In chinchillas, CT is the preferred imaging modality in particular to evaluate the head.

Treatment Techniques

Fluid Therapy

The daily maintenance fluid rate for chinchillas is estimated to be 60 mL/kg body weight. Supplemental fluids are commonly



Fig. 22.11 Middle ear sampling technique in an anesthetized chinchilla using a transbullar approach. (A) Dorsal view of a chinchilla skull. The access to the tympanic bulla is obtained through the dorsal aspect of the bulla (arrow). (B) Following a small skin incision and perforation of the tympanic bone the middle ear content is aspirated using a sterile 22G catheter.

given subcutaneously into the loose skin of the dorsal neck and upper back areas. Volumes of 15 to 20 mL can be given in each subcutaneous bolus. To avoid unnecessary stress, animals that are drinking water can be given oral fluids unless they are azotemic or moderately to severely dehydrated.

Placement of peripheral IV catheters is challenging in chinchillas because of the small size and fragility of their veins. With the animal sedated or under anesthesia, small-gauge (24- to 26-gauge) indwelling catheters can be placed in the cephalic vein. Intraosseous catheters also can be placed, usually in the cranial tibia or femur. Monitor the catheter site closely in case the chinchilla attempts to chew the catheter or IV line. Placing e-collars on chinchillas to prevent chewing usually causes stress, and animals become inappetant. Avoid placing these, but if necessary, use a soft collar.

Nutritional Support

Anorexic chinchillas should receive assist feedings of commercial critical care formulas specifically designed for hindgut-fermenting rodents and rabbits. Feed 50 to 80 mL/kg/d of formula at an apple sauce consistency, divided into three to four feedings. Using a small 1-mL syringe facilitates feedings, because these can fit into the oral cavity to encourage swallowing and minimize spillage. Chinchillas frequently require prolonged syringe feedings because of the high risk of developing of ketoacidosis and hepatic lipidosis. Attempt to wean chinchillas off syringe feedings while monitoring urine ketones, which can be done by owners at home. Keep in mind that chinchillas do not ingest significant amounts of food or defecate during the day; therefore do not confuse this with anorexia or gastrointestinal hypomotility in this nocturnal species.

Antibiotic Therapy

Because they are hindgut fermenters that depend on the bacterial production of volatile fatty acids for energy, chinchillas are very susceptible to changes in enteric microbial flora. Although all orally administered antibiotics have the potential to affect normal gut microflora, drugs such as sulfonamides, fluoroquinolones, tetracyclines, chloramphenicol, and azithromycin are considered safe in chinchillas. Penicillins, cephalosporins, clindamycin, erythromycin, and other antibiotics with a predominant gram-positive and anaerobic spectrum should never be given orally to chinchillas. However, these antibiotics usually can be given parenterally without adverse effects, and long-acting penicillin G benzathine/procaine is routinely administered in chinchillas.

Oral metronidazole can cause significantly reduced food intake in chinchillas, which varies by individual and is dose dependent. The type of metronidazole, duration of treatment, compounding recipe, or concentration of the suspension do not play an important role. Reduced food intake is self-limiting and the appetite will return to normal after metronidazole has been discontinued.[27] A total daily dose of not more than 20 mg/kg is recommended.

DISEASES OF CHINCHILLAS

Hepatic Lipidosis and Ketosis

Hepatic lipidosis secondary to excessive fat mobilization in anorexic or hyporexic chinchillas is one of the most common findings in chinchillas at necropsy. The negative energy balance leads to increased mobilization of lipids and excessive beta oxidation of fatty acids in hepatocytes, promoting hepatic ketogenesis. Chinchillas with hepatic lipidosis often have a history of anorexia and decreased fecal output. In advanced cases, animals can be depressed and dehydrated. Biochemical parameters are frequently normal, but in severe cases hyperglycemia can develop, which should not be misinterpreted as consistent with diabetes mellitus. Urine dipstick testing is recommended to check for urinary ketones and decreased urine pH (Fig. 22.11). In severe cases, glucosuria can be present as well. Treatment should correct the underlying primary cause of anorexia (e.g., dental disease, gastroenteritis), along with correcting fluid deficits and providing nutritional support. Measure urinary ketones and pH repeatedly to monitor response to treatment.

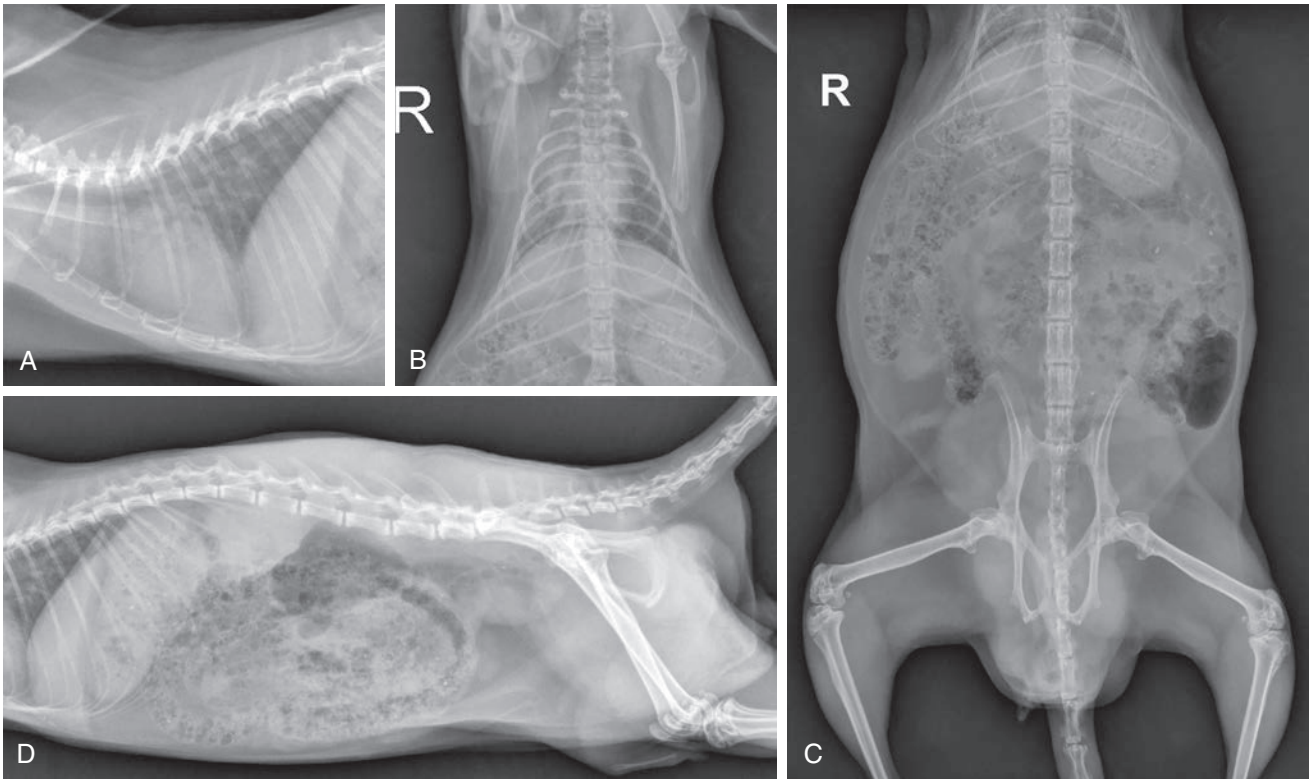


Fig. 22.12 Standard radiographic views in chinchillas. (A) Lateral thoracic and (B) ventrodorsal thoracic views. (C) Ventrodorsal abdominal and (D) lateral abdominal view.

TABLE 22.5 Echocardiographic Measurements (Mean ± SD) Obtained From 17 Clinically Healthy Chinchillas

Variable	Manual restraint	Isoflurane anesthesia
Heart rate, beats/min	169 ± 32	170 ± 22
IVSd, cm	0.2 ± 0.03	0.18 ± 0.03
LVPWd, cm	0.24 ± 0.04	0.26 ± 0.02
LVID, cm	0.59 ± 0.08	0.64 ± 0.05
LVIS*, cm	0.29 ± 0.06	0.38 ± 0.05
FS, %	50 ± 8	40 ± 5
LA*, cm	0.53 ± 0.06	0.49 ± 0.06
Ao*, cm	0.41 ± 0.04	0.36 ± 0.05
LA/Ao ratio[a]	1.28 ± 0.13	1.38 ± 0.2

Echocardiography was performed with animals positioned in right lateral recumbency under manual restraint as well as under isoflurane anesthesia.
Ao, aortic diameter; FS, fractional shortening; IVSd, interventricular septum in diastole; LA, left atrial diameter; LVID, left ventricular diastolic dimension; LVIS, left ventricular systolic dimension; LVPWd, left ventricular free wall in diastole.
[a]Anesthesia had a statistically significant effect on variable.
Data from Linde A, Summerfield NJ, Johnston M, et al. Echocardiography in the chinchilla. *J Vet Intern Med.* 2004;18:772-774.

Dental Disease

Dental disease is a common diagnosis in pet chinchillas of all ages (see Chapter 36). Historically dental disease in chinchillas mainly has been referred to as malocclusion and elongation of the cheek teeth. However, periodontal disease, caries, and tooth resorption are disease processes that frequently occur in chinchillas but are often missed during intraoral examination, even with general anesthesia.[55] Evaluation of 181 captive chinchilla skulls found signs of periodontal disease in 63% and dental caries lesions in 52%, characterized by brown discoloration and loss of tooth substance on occlusal and interproximal tooth surfaces due to a bacterial infection leading to demineralization (Fig. 22.13).[16] Nutritional (e.g., inappropriate dietary Ca/P ratio) and genetic causes have been proposed as predisposing factors.[55]

Common clinical findings associated with dental disease in chinchillas are reduced body condition and weight loss secondary to reduced food intake, changed food preferences toward more easily chewed feed items, weight loss, reduced fecal output with smaller, irregularly shaped fecal pellets, saliva-stained skin and fur with crusting and alopecia of the perioral area, wetting and crusting of the chin ("slobbers") (Fig 22.9) and forefeet, epiphora, poor fur condition, and fur chewing.[17,43,55] On clinical examination, palpable irregularities of the ventral borders of the mandible and overgrown depigmentation of the orange labial surface of the incisor teeth may be found (Fig 22.3B).[17,55] Facial abscesses of periodontal origin are seen infrequently but can occur.[43,55]

A limited examination using a pediatric laryngoscope, otoscope, or vaginal speculum can be performed in a conscious animal, but up to 50% of intraoral lesions can be missed, in particular periodontal disease, tooth resorption, and buccal spurs of the maxillary cheek teeth.[44] Instead, perform a thorough examination of the oral cavity under general anesthesia. Endoscopic-guided intraoral examination (stomatoscopy) provides superior

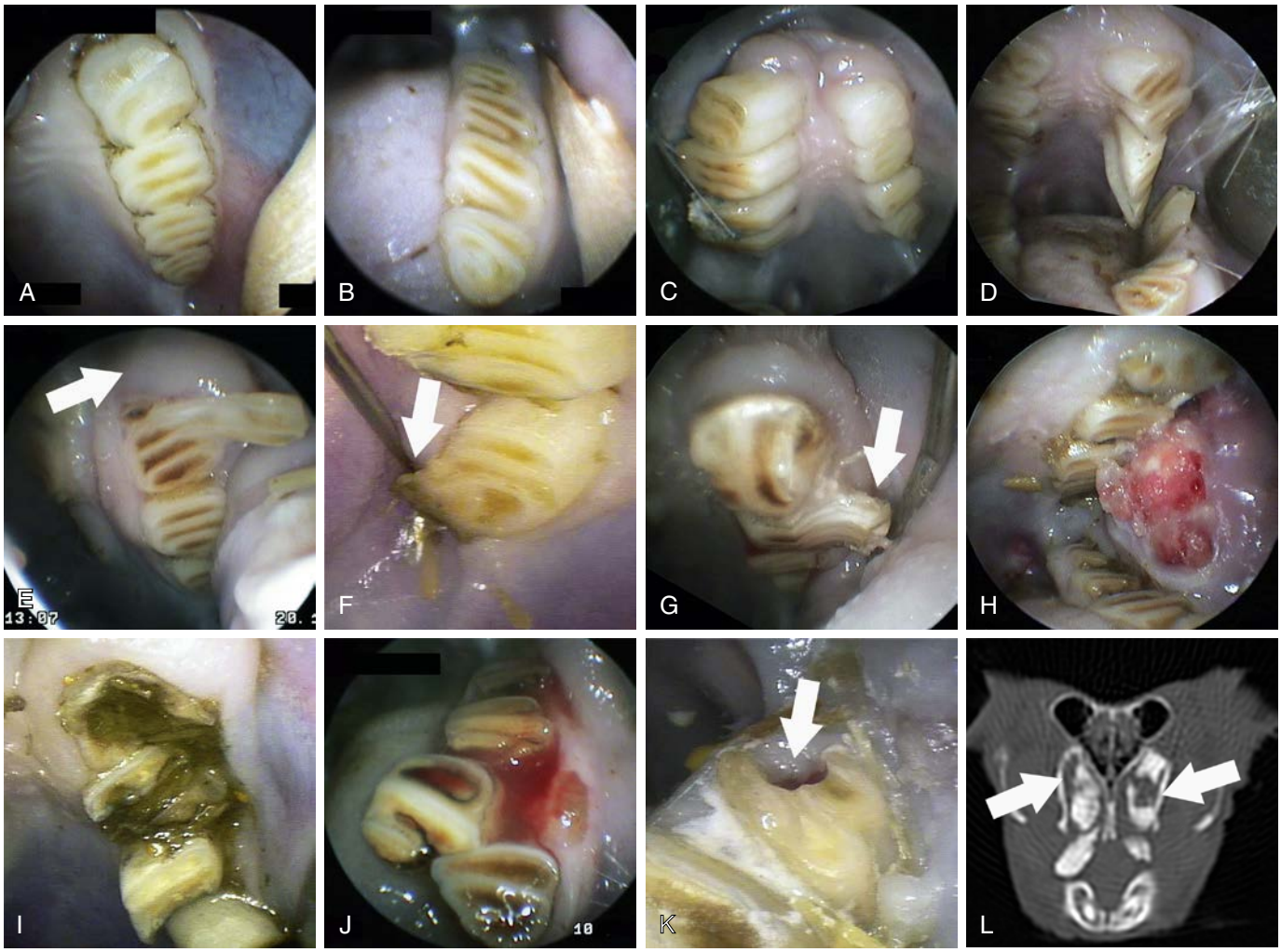


Fig. 22.13 Dental disease in chinchillas. (A and B) Normal appearance of the maxillary (A) and mandibular cheek teeth (B). (C) Clinical crown elongation of the left maxillary cheek teeth. (D) Clinical crown elongation and malocclusion of the left maxillary and mandibular cheek teeth. (E) Gingival hyperplasia (arrow) and buccal spur formation of the first maxillary left cheek tooth. (F) Buccal spur formation of the last right maxillary cheek tooth. (G) Buccal spur formation of the second left maxillary cheek tooth. (H) Buccal ulceration secondary to buccal spur formation. (I) Caries lesions affecting the clinical crowns of the first two left maxillary cheek teeth. (J) Periodontal disease and malpositioned second left mandibular cheek tooth. (K) Partial resorption of the clinical crown of the last left mandibular cheek tooth. (L) Computed tomography of a chinchilla skull, showing partial resorption of the reserve crowns of the upper cheek teeth and widening of the maxillary alveolar spaces.

visibility and increases the chance for detection of pathologic lesions and is considered a necessity by the authors for a complete intraoral exam in chinchillas.[55]

Inspect all cheek teeth for evidence of crown elongation, malocclusion, malposition, mobility, periodontal disease as well as caries and resorptive lesions (Fig 22.13). Sharp dental spur formation might be easily overlooked, particular if arising from the maxillary cheek teeth and directing buccally (Fig. 22.13E–G). These spikes frequently lead to ulceration of the buccal mucosa (Fig. 22.13H). Other common intraoral findings involving the cheek teeth are widened interproximal spaces, which facilitates food impaction and promotes development of periodontal disease. Loss of tooth substance and mobility of the clinical crowns are consequences of resorption of the reserve crowns (Fig 22.13L), whereas brown discoloration of occlusal and interproximal tooth surfaces is seen in cases of caries (Fig 22.13I).[17,43,55] Evaluate radiographs or, preferentially, CT scans of the skull in any chinchilla with a history or clinical signs suggestive of underlying dental disease. Radiography or CT are the only diagnostic methods to evaluate for subgingival disease, such as alveolar bone or tooth resorption (Fig 22.13L), apical elongation of the reserve crown and periodontal infections.[55]

The prognosis for chinchillas diagnosed with dental disease depends on the severity, the animal's general condition, and owner compliance. Repeated intraoral examinations and treatments under general anesthesia at varying intervals, often for the life of the animal, are usually necessary to control complications of dental and periodontal disease and maintain an acceptable quality of life for the animal. The goals of therapy include reducing periodontal infection and soft tissue trauma, which both lead to discomfort and pain, and recovering or maintaining the animal's ability to eat unaided.

After removing spurs and reducing elongated crowns (see Chapter 36), probe interproximal spaces and periodontal pockets and remove impacted debris. Rinse cleaned periodontal pockets carefully with topical hydrogen peroxide solution and use suction to remove debris.[55] Instilling doxycycline polymer filling (Doxirobe Gel; Pfizer Animal Health, New York, NY) in deep (> 3 mm) gingival and periodontal pockets may help delay reimpaction with debris and reduce periodontal inflammation.[55] If evidence of significant periodontal infection exists, begin systemic antimicrobial therapy with antimicrobials that are effective against anaerobic bacteria predominating in periodontal infections (e.g., penicillin G benzathine/procaine, 50,000 IU/kg subcutaneously every 5 days or azithromycin 30 mg/kg by mouth every 24 hours).[54,55] Managing pain and coexisting conditions such as ketosis and gastrointestinal hypomotility is critical. With animals in advanced stages of dental disease, offer easy-to-chew food items (soft leafy grass hay, moistened pellets, and critical care formulas offered in a dish). Many animals require short- and sometimes long-term nutritional support with syringe feeding after a dental procedure or with chronic severe disease.

Gastrointestinal Diseases

Dysbacteriosis and Diarrhea

Gastrointestinal disorders leading to soft feces or diarrhea are less prevalent in pet chinchillas compared with guinea pigs. Any systemic disease or a painful or stressful condition may result in secondary gastrointestinal problems with nonspecific clinical signs such as reduced food intake, reduced fecal output, and lethargy. Obtaining a thorough clinical history and physical examination are critical for formulating a sound diagnostic and therapeutic plan.

Various infectious and noninfectious causes of gastroenteritis and dysbacteriosis may affect chinchillas and result in a range of clinical syndromes including constipation, tympany, diarrhea, intussusception, and rectal prolapse. Gastrointestinal disorders were the major cause of morbidity and mortality in farmed chinchillas in the 1960s to 1990s. In pet chinchillas, noninfectious causes such as sudden dietary changes or inappropriate oral antibiotic therapy are more frequent and important. However, secondary infectious causes such as giardiasis, coccidiosis, and *Pseudomonas* species or enterobacterial overgrowth, such as *Escherichia coli* or *Proteus* species, can be seen.[60]

Feces smeared on the cage floor or matted, fecal-stained perianal fur are often the first signs the owner notices. The animal might be normal otherwise or, in chronic and severe cases, it can be anorexic, dehydrated, and depressed.

Identifying the underlying cause of gastroenteritis and dysbacteriosis is important to improve the outcome and reduce the chance of recurrence. Consider performing whole-body radiographs or CT and fecal parasite examination, cytology, and culture for enteric opportunistic pathogens (e.g., *E. coli, Pseudomonas aeruginosa, Proteus* species) in the initial diagnostic workup. Besides specific treatment for the primary underlying cause, provide nutritional support and fluid therapy, if indicated.

In chinchillas with severe dysbacteriosis when an infectious cause is suspected but unconfirmed, consider systemic parenteral antimicrobial therapy (e.g., enrofloxacin at 10 mg/kg SC diluted every 12 hours) for treatment of potential gram-negative opportunistic pathogens. Avoid oral drug administration because the absorption and effectiveness of oral drugs may be decreased when gastrointestinal function is abnormal. Parenteral administration is the preferred initial route for most drugs. Once an animal is eating and gastrointestinal function is improved, switch to the oral route.

Intestinal secondary yeast overgrowth, caused by *Cyniclomyces guttulatus* (previously *Saccharomycopsis guttulata*), which lines the stomach, is often seen in chinchillas with soft feces. However, increased numbers of this yeast in chinchillas with diarrhea or soft feces is considered secondary rather than a primary cause, usually promoted by an underlying disease process.[26] Offer well-dried, high-quality grass hay if the animal is still eating. Consider treatment with nystatin (100,000 IU/kg every 8 hours for 5 days) if *C. guttulatus* overgrowth is very high or no response to initial treatment is seen.

Tympany

Tympany of the stomach and intestines is less common in chinchillas compared with guinea pigs or rabbits and is often secondary to gastroenteritis, dysbacteriosis, ileus, luminal obstruction, or, very rarely, intestinal torsion.[53] The affected animal usually has a distended and tense abdomen. In severe cases, a depressed and dyspneic chinchilla may lie on its side. Signs of shock may be present. Prognosis depends on the severity and duration of tympany but is usually poor in severe or chronic cases. Institute treatment based on general guidelines for the management of gastroenteritis. Although gastric decompression is recommended for severe cases of tympany, this might result in collapse and death in a decompensated patient. Do not use motility-enhancing drugs if an infectious or obstructive cause cannot be ruled out.

Rectal Tissue Prolapse and Intussusception

Rectal tissue prolapse and intestinal intussusception frequently occur together, secondary to dysbacteriosis, enteritis, constipation, or diarrhea.[53] Intussusception of the descending colon and rectum is associated with most cases of rectal prolapse; however, the small intestine can also be affected.[53] Abdominal palpation might reveal a turgid cylindrical mass reflecting the intussuscepted portion of the intestine. The amount of intestine involved in the intussusception can be extensive and the affected portion is usually cyanotic, congested, and, in advanced cases, often nonviable. Besides treatment of the primary underlying cause, surgically correcting the intussusception is critical: intestinal resection and anastomosis may be necessary. Simple replacement or resection of prolapsed rectal tissue is insufficient. Assess the prolapsed tissue for viability and trauma. If an intussusception is ruled out, carefully clean and soak the edematous prolapsed rectal tissue in a 50% dextrose solution. Replace the prolapsed tissue and place a perianal purse-string suture.[53] Successful outcome after laparotomy and manual correction of more proximally located intussusceptions has been reported.[53]

However, the prognosis remains poor in most cases, and the outcome will depend on the location and duration of the intussusception, viability of the prolapsed and intussuscepted tissue, and the underlying primary cause. Recurrence and rapid deterioration of affected animals is unfortunately common, as rectal prolapse and intussusception usually reflect an acute complication of a more chronic underlying primary problem.

Esophageal Disorders

Because chinchillas cannot vomit, food items such as raisins, fruit, and nuts as well as bedding material and ingested placentas in post-parturient females can become stuck in the oropharynx and upper esophagus.[26] Clinical signs are a sudden onset of anorexia, drooling, retching, and possible dyspnea. Removing the foreign material is usually curative, and the prognosis is good if the problem is dealt with early. Megaesophagus was diagnosed in a 2-year-old chinchilla that presented for recurrent acute episodes of dyspnea and nasal discharge.[45] During hospitalization, the animal regurgitated food material episodically, followed by dyspnea, retching, gasping, and nasal discharge. Upper gastrointestinal contrast radiography aided the diagnosis of megaesophagus in this animal.[45]

Ophthalmic Diseases

Epiphora

Epiphora ("wet eye") is characterized by usually unilateral serous discharge and wetting of the periocular fur. Epiphora has been reported in 20% to 35% of chinchillas with dental disease.[17,43] Because of secondary bone remodeling, a common underlying cause for epiphora is elongated apical reserve crowns of the maxillary cheek teeth, causing complete or partial compression of the nasolacrimal duct (see Chapters 36 and 40).[16] In contrast to rabbits, obliteration of the nasolacrimal duct at the level of the apical portion of the maxillary incisor is uncommon in chinchillas.[43,53] If underlying dental disease is the cause of nasolacrimal duct obstruction, permanent patency of the nasolacrimal duct is unlikely to be regained, as there is no effective treatment for apical reserve crown elongation. Treat concurrent or underlying infection and inflammation with appropriate topical antibiotics and nonsteroidal antiinflammatory drugs. Because they cannot be visualized, flushing the nasolacrimal ducts is not feasible in chinchillas.

Conjunctivitis

Conjunctivitis is a common ocular disorder in chinchillas. Irritation from excessive sand bathing, inadequate cage ventilation, or underlying nasolacrimal duct obstruction can cause conjunctivitis. Normal conjunctival bacterial isolates in healthy chinchillas are predominantly (94%) gram-positive species (see Chapter 40).[50] In one study, most conjunctival bacterial isolates in chinchillas diagnosed with conjunctivitis were gram-negative (62%), with the most common isolate being *P. aeruginosa* in 50% of cases, followed by *Staphylococcus* species (27% of cases).[68] Chinchillas with an acute onset (1–3 days) of conjunctivitis were more likely to have gram-negative pathogens isolated, and *P. aeruginosa* was always associated with animals with concurrent upper respiratory signs. However, reduced appetite or activity, severity of conjunctivitis, unilateral versus bilateral conjunctivitis (Fig. 22.14), and presence of purulent discharge are not associated with a particular bacterial pathogen. In chinchillas diagnosed with conjunctivitis, always perform aerobic bacterial culture and susceptibility testing. Fluorescein staining is necessary to rule out damage to the corneal surface. Empirical therapy with topical gentamicin or polymyxin B combined with neomycin is recommended pending culture and susceptibility results.[68] Consider systemic antimicrobial therapy, especially if respiratory signs are present. Early recognition, systemic antibiotic therapy, and supportive care are critical for chinchillas suffering from systemic *Pseudomonas* infection.[28] Access to a dust bath should be restricted until the chinchilla has fully recovered.

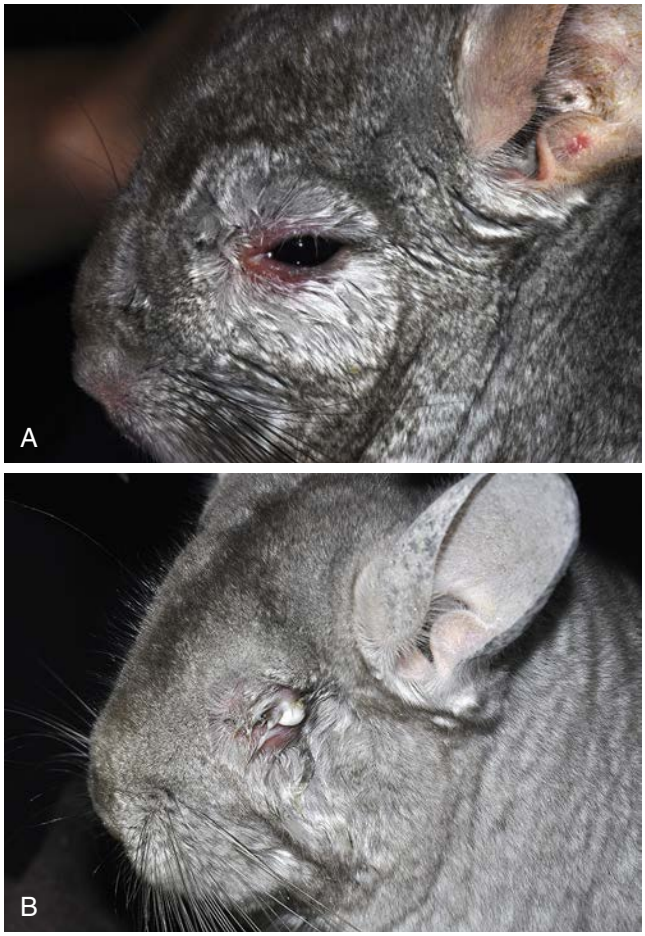


Fig. 22.14 Conjunctivitis in chinchillas. (A) Erythema and blepharospasm. (B) Large amounts of purulent discharge present in the left eye.

Corneal Diseases

Corneal damage and keratitis secondary to trauma are common clinical findings in chinchillas, usually associated with blepharospasm, discharge, and conjunctivitis.[63] The large, prominent corneal surface and the lack of a protective nictitating membrane likely predispose chinchillas to corneal trauma. Excessive sand bathing, inappropriate sand for bathing, and inappropriate housing conditions are possible underlying causes. Lack of a palpebral reflex secondary to facial nerve damage associated with otitis media has been reported as a cause for corneal disease.[63] Therefore, evaluate the palpebral reflex and the ears in all chinchillas with corneal

lesions. Diagnosis is by fluorescein staining of the corneal surface. Rule out possible nontraumatic underlying causes (e.g., exophthalmos) to avoid reoccurrence. Treatment of acute superficial lesions is topical ophthalmic antibiotics. In cases of chronic nonhealing ulcers, consider corneal debridement or grid keratomy after controlling any potential bacterial infection. Corneal lipid keratopathy has been reported in chinchillas.[63]

Miscellaneous Ophthalmic Diseases

Lenticular changes, in particular cataracts, are common in chinchillas.[63,71] Because diabetogenic cataracts have been reported, diabetes mellitus should be ruled out in chinchillas presenting with unilateral or bilateral cataracts.[63]

Asteroid hyalosis of the vitreous humor, in which lipid-calcium particles are formed as part of a degenerative process, can occur in older chinchillas.[71]

Exophthalmos can be caused by retrobulbar periapical abscesses of the maxillary cheek teeth.[63] A rare retrobulbar *Taenia* cyst has been described, leading to exophthalmos.[56] Although primary glaucoma has not been reported, secondary glaucoma can occur but is uncommon. Reference intervals for intraocular pressure in chinchillas have been published for rebound and applanation tonometer.[82]

A rare case of human herpesvirus I infection in a chinchilla, causing ulcerative keratitis, retinitis, neuritis, and meningoencephalitis, has been reported.[91]

Respiratory Diseases

Nasal discharge is relatively uncommon in chinchillas but can be associated with underlying dental disease, nasal foreign bodies, rhinitis, megaesophagus, cleft palate, or lower respiratory tract disease.[45,67] If conjunctivitis is diagnosed in addition to nasal discharge, *P. aeruginosa* infection should be ruled out.[68] Base treatment on the underlying cause.

Pneumonia is uncommon in pet chinchillas but common in farmed chinchillas if husbandry is inadequate.[53,60] Predominately gram-negative organisms have been isolated from chinchillas diagnosed with pneumonia. A case of pneumonia due to *Mycobacteria genavense* has been reported.[41] Clinical signs of pneumonia include tachypnea, dyspnea, and, in severe cases, open-mouth breathing. Presenting animals are often in poor body condition and have a poor hair coat. After ruling out other causes, such as congestive heart failure and diaphragmatic hernia,[1] initiate systemic antimicrobial therapy. Recommendations for treatment include oxygen therapy, systemic antibiotic therapy, and nebulization with antimicrobials (e.g., gentamicin). Once dyspnea is evident and an animal is in poor body condition, indicative of chronic disease, the prognosis is guarded to poor.

Cardiac Diseases

Only limited information on cardiac diseases in chinchillas is available. A chinchilla that presents with clinical signs consistent with cardiac disease, such as labored breathing, weakness, lethargy, and possible heart murmur, should be evaluated radiographically and echocardiographically. Echocardiographic abnormalities reported in chinchillas include mitral valve insufficiency, dynamic right ventricular outflow tract obstruction, tricuspid valve insufficiency, and left ventricular hypertrophy.[51,72] Reports of ventral septal defects and dilated cardiomyopathy also exist.[38,54]

While the prevalence of heart murmurs is high in chinchillas (23% in one study),[72] reports on cardiac disease in chinchillas are rare. Although echocardiographic abnormalities are detected in some animals, in many chinchillas these murmurs are considered benign.[54] In one report, 8 of 15 chinchillas with heart murmurs that underwent an echocardiogram had evidence of cardiac abnormalities, whereas 7 had none. Abnormalities included tricuspid or mitral regurgitation, left ventricular hypertrophy, and right ventricular outflow obstruction. Four of these 8 had grade 3 or higher murmurs.[72] Therefore, a cardiac workup may be indicated in chinchillas with pronounced murmurs.

Echocardiographic measurements for healthy chinchillas under both manual restraint and isoflurane anesthesia have been published (Table 22.5). Reference intervals for vertebral heart size have been reported in chinchillas and can be calculated based on radiographs (reference interval: 7.5–10.4) or CT scans (reference interval: 7.1–9.4).[22]

Clinical management of cardiac disease in chinchillas has not been reported. In animals diagnosed with cardiac disease, base therapy on treatment recommendations used in other similar species.

Urinary Tract Diseases

Urolithiasis is the most common urinary tract disorder in chinchillas and occurs predominantly in males. Most uroliths are composed of calcium carbonate.[54,59] Semen-matrix calculi have also been described in chinchillas.[36] Risk factors for development of urolithiasis in chinchillas are unknown, and it is unlikely that dietary calcium intake plays a role, because excess calcium is excreted in the feces and not the urine in chinchillas.[34]

The most common presenting complaints are hematuria, pollakiuria, and stranguria. Animals may be painful on abdominal palpation or have palpable stones.[59] Abdominal radiographs will show radiodense calculi in the bladder, urethra, or both.

Uroliths located in the urinary bladder offer a better prognosis compared with urethral stones, though both can occur alone or together.[59] Urethral calculi require urinary catheterization and retropulsion of stones into the bladder, which can be challenging because many of these calculi are embedded in the mucosa and cannot be dislodged. Therefore most (75%) chinchillas diagnosed with urethral calculi in one retrospective study were euthanized within 24 hours of diagnosis.[59] Cystotomy is recommended to treat cystic calculi; however, inform the owners that the recurrence rate is reported to be 50% after surgical removal of the calculi.[59] In one study, the median time to recurrence was 68 days (range 19–1440 days); median survival time was 391 days (74–1074 days) in chinchillas with calculi recurrence and 6 years (5–7 years) in animals without recurrence.[59] Closely monitor animals for recurrence and potential urinary obstruction after surgery.

Female Reproductive Diseases

Fetal resorption, mummification, retention, and abortion are common in chinchillas.[54] Fetal death may be caused by a variety of infectious and noninfectious causes. Incompletely



Fig. 22.15 Vaginal leiomyoma protruding from the vaginal orifice.

reabsorbed, retained, or mummified fetuses can remain in the uterus for extended periods and can predispose to sterility and endometritis. In chinchillas presenting with hemorrhagic vaginal discharge, consider abortion or fetal or placental retention if housed with a male conspecific.

Uterine neoplasms are increasingly reported and include leiomyosarcomas, leiomyomas, fibroma, and hemangioma.[7] Animals with uterine neoplasms usually have palpable abdominal masses and may have bloody vaginal discharge. Vaginal leiomyomas can present as soft tissue masses protruding from the vaginal opening (Fig 22.15).[9]

Endometritis and Pyometra

Endometritis and pyometra have been reported in farmed chinchillas and are increasingly reported in pet chinchillas.[32,47] Pyometra (purulent endometritis) is characterized by accumulation of purulent discharge within the uterine lumen, with cystic endometrial hyperplasia and secondary bacterial infection. The cause for endometritis or pyometra is often not determined during a diagnostic workup, but cases of stump pyometra secondary to incomplete ovariectomy have been reported in chinchillas.[47] Therefore complete and careful resection of all ovarian tissue should be performed during ovariectomy or ovariohysterectomy.

Affected animals can present with a history of acute onset of depression and anorexia or with mild lethargy or behavioral changes.[47,53] Clinical signs vary, but an open vulva and vaginal discharge are present in most cases. Vaginal discharge can range from mucoid or mucopurulent to hemorrhagic. Anogenital fur staining may occur. Some mucoid vaginal discharge is normal during estrus and should not be confused with pathologic vaginal discharge. Cytologic characterization of a vaginal smear can be helpful to differentiate between physiologic and pathologic conditions causing vaginal discharge.[5] The predominant cells during estrus are partially to completely cornified superficial epithelial cells. Neutrophils are absent during estrus but common during proestrus and metestrus. Uterine enlargement may be evident on abdominal palpation, and palpation may provoke vaginal discharge. Radiographs and abdominal ultrasonography are helpful to evaluate the uterus.[5] In some cases, lack of an open vulva and cervices and vaginal discharge does not rule out uterine disease, and cases without vaginal discharge may present with severe uterine enlargement leading to abdominal distension. Ovariohysterectomy has been recommended as the treatment of choice for endometritis and pyometra. In cases of mild endometritis with vaginal discharge, if the animal is in good condition, systemic antimicrobial therapy based on culture and susceptibility testing can be attempted. As in other species, prognosis will depend on the underlying and coexisting causes, such as hepatic lipidosis, ketosis, and possible complications in severe cases such as sepsis.

Dystocia

Signs of dystocia in chinchillas include restlessness, frequent crying, constant attention to the genital region, and a widened vaginal opening. Allantoic fluid or mucohemorrhagic discharge from the vagina is often present. Dystocia is usually associated with the presentation of a single oversized fetus or malpresentation of one or more kits. Uterine inertia is also a cause of dystocia. If more than 4 hours of labor have occurred without delivery of kits, intervention should be considered.[40] Use radiographs to assess the number, size, and position of the fetus(es). In an uncomplicated dystocia, lubrication and gentle traction of the fetus with feline obstetric forceps may allow delivery. Attempt treatment for uterine inertia with oxytocin (0.5–1 IU/kg SC) and calcium gluconate (25–50 mg/kg SC diluted). Surgical intervention is imperative if the chinchilla is in labor for longer than 4 hours and the kits cannot be delivered. Chinchillas respond well to cesarean section, and a survival rate of 67% has been reported in one study.[87]

Male Reproductive Diseases

Fur Rings

Accumulation of fur at the base of the glans penis within the prepuce, also known as "fur ring," is a common incidental finding during physical examination in chinchillas. In some cases, the accumulated fur can predispose to balanoposthitis and paraphimosis, secondary to acting as a nidus for bacterial infection or leading to constriction of the glans penis (Fig. 22.16). Therefore completely extrude the glans penis from the prepuce in any male chinchilla during physical examination. Remove any accumulated fur or smegma (Fig. 22.16A,B) and clean the penis with diluted chlorhexidine solution.

Balanoposthitis and Preputial Abscesses

Balanoposthitis is an inflammatory condition of the prepuce and glans penis usually secondary to infection. If no underlying



Fig. 22.16 Penile disorders in chinchillas. (A) Fur accumulation ("fur ring") around the base of the glans penis. (B) Smegma accumulation. (C) Paraphimosis secondary to **balenoposthitis** caused by *Pseudomonas aeruginosa*. (D) Phimosis causing secondary **balenoposthitis**. Note the purulent discharge. E) Preputial abscess.

fur ring or smegma accumulation is found, then consider the balanoposthitis a part of a systemic or localized *P. aeruginosa* infection (Fig. 22.16C)[21] or phimosis (Fig 22.16D).[58]

In cases of chronic balanoposthitis, preputial abscesses might develop, which can become considerably large and lead to swelling of the prepuce, preventing the penis from extrusion from the prepuce (Fig 22.16E). Preputial abscesses should be surgically explored and drained.

Paraphimosis

Acute severe balanoposthitis or fur rings can lead to paraphimosis (Fig. 22.16C), characterized by the prolapse of the glans from the prepuce and the inability to replace the glans back into the prepuce. In severe cases of paraphimosis, anuria might develop secondary to inflammation and trauma due to (self-)mutilation of the prolapsed glans penis. In any case of paraphimosis, try to identify the underlying cause. Flaccid paresis of the penis, due to excessive breeding or separation during copulation, has been reported.[26] The goal of treatment is to maintain or reestablish normal urination and to preserve the glans penis. Assess the glans and prepuce for viability; if viable, carefully clean the tissue with diluted chlorhexidine solution and apply a lubricant gel or petroleum-based ointment to facilitate replacement of the glans penis in the prepuce, if possible. Do not attempt to reposition the glans penis if significant preputial swelling is present and substantial force is necessary. Instead, continue to apply ointments or hydrogels to the everted prepuce and glans penis to prevent drying of the exposed tissue**.** Continue topical treatment three to four times daily until swelling has resolved. If self-mutilation or overgrooming occurs, consider placing a soft e-collar. However, ensure that the animal can eat unaided with the e-collar in place. Treat with systemic antibiotics if a bacterial balanoposthitis is present, and provide pain relief and anti-inflammatory drugs. If the prolapsed glans penis is not viable, then penile amputation and perianal urethrostomy could be considered, but the prognosis of this procedure in chinchillas is unknown.[26]

Phimosis

Phimosis is defined as the inability to completely protrude the glans penis from the prepuce or entrapment of the penis within the prepuce. Phimosis in chinchillas can develop secondary to preputial abscesses. Another common cause is adhesion formation between the visceral layer of the prepuce and the glans (Fig. 22.16D).[58] The cause of phimosis due to adhesions in chinchillas is unknown. In other species, phimosis can be congenital or acquired (i.e., secondary to chronic inflammation, trauma, or neoplasia).

Phimosis is often subclinical unless secondary balanoposthitis develops.[58] Treatment of phimosis is surgical by means of resecting any adhesions between the visceral layer of the prepuce and the glans penis or resolution of preputial abscesses. Remove adhesions under general anesthesia by using magnification.[58] After removing adhesions, completely evert the glans from the prepuce and examine for any abnormalities. After surgery, regularly extrude the glans penis manually and apply an ointment. The risk of reformation of adhesions exists, because the primary underlying cause is usually not revealed.[58] Regularly examine male chinchillas with a history of penile disorders and evert the glans penis completely for examination. Recurrence of penile disease is common, and prevention or early detection will lead to a better prognosis and less complications.

Ear Diseases

Chinchillas have very large tympanic bullae, large tympanic membranes, and a relatively short and simple external ear canal. These anatomic features have made chinchillas the gold-standard animal model for otologic research, in particular the

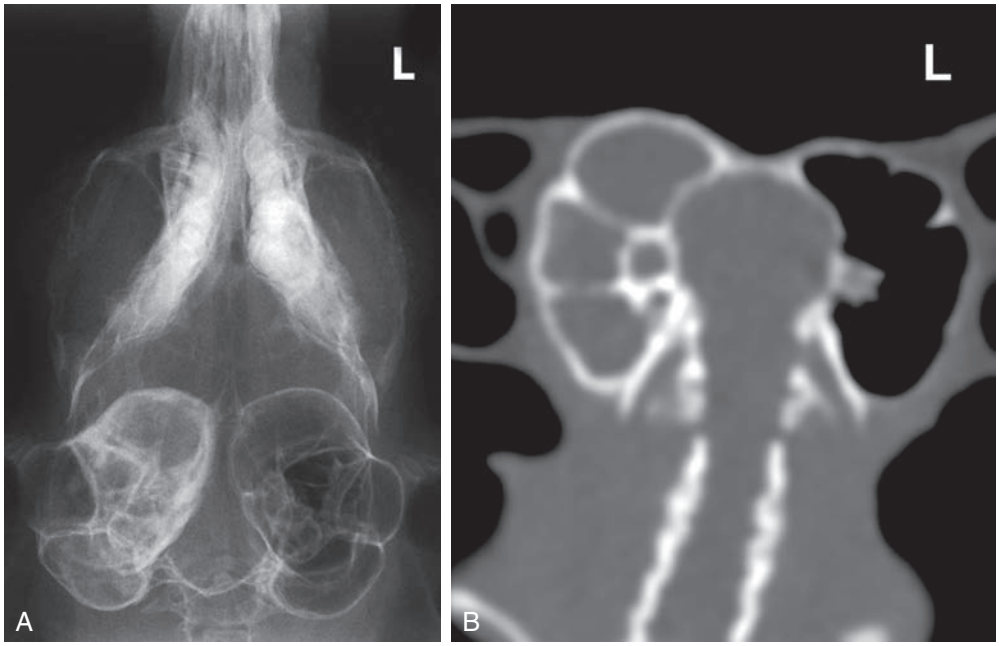


Fig. 22.17 Otitis media in chinchillas. Dorsoventral radiograph (A) and cross-sectional computed tomographic (B) view of the skull in a chinchilla with right-sided otitis media.

study of otitis media.[3] Hence, many studies on the pathophysiology and antimicrobial treatment of experimentally induced otitis media in chinchillas are available. Clinical signs caused by otitis externa, media, and interna can range from external ear canal discharge, head shaking, and mild head tilt to facial paresis and severe neurologic deficits.[8,11,78,90]

Perform an otoscopic examination in every chinchilla during physical examination. The normal ear canal is wide and free of debris or purulent material, and the large tympanic membranes should be visible in every chinchilla. The tympanic membrane appears avascular and semi-transparent (Fig. 22.8). Any changes in vascularity or opacity or bulging of the tympanic membrane are indicative of inflammation of the middle ear and should prompt further investigation. Primary otitis externa is rare in chinchillas, and most cases of otitis externa are a result of otitis media and a perforated tympanic membrane. Therefore purulent discharge present in the external ear canal should also prompt investigation of the tympanic membrane and middle ear by diagnostic imaging. A case of a leiomyosarcoma of the external ear canal has been reported in a chinchilla that was evaluated for purulent and hemorrhagic ear discharge. The neoplasm resulted in secondary otitis externa, media, and interna.[8] Skull radiographs in dorsoventral projection or, preferably, CT scans are used to diagnose otitis media (Fig. 22.17). A variety of bacteria may be cultured from the middle ear in chinchillas with otitis media, with *P. aeruginosa* being a common isolate.[78] Treatment of bacterial otitis media and interna remains challenging because of the formation of biofilms in the middle ear that can reduce the efficacy of antimicrobial drugs.[3] Bacterial isolation and antimicrobial susceptibility testing are critical. Minimally invasive access to the middle ear through the dorsal roof of the tympanic bulla has been reported (see clinical technique section of this chapter) (Fig 22.9). The prognosis for resolution of otitis media in chinchillas is poor, particularly if *P. aeruginosa* is isolated. Choose antibiotics based on susceptibility of the isolated organisms and the potential of the available drugs to eliminate bacteria effectively from the middle ear. Azithromycin (30 mg/kg PO every 24 hours) reaches tissue levels high enough to recreate sterile conditions within the middle ear of chinchillas, if the bacteria are susceptible.[2] Topical treatment of otitis media caused by *P. aeruginosa* by means of multiple fenestrations of the multichambered tympanic bulla has been reported but did not lead to resolution of the otitis media.[78] Ear canal ablation has been reported but is rarely indicated in chinchillas because diseases of the external ear canal are uncommon.[78]

Neurologic Disorders

Seizures

Several reports of seizures in chinchillas are described.[26,53] Encephalitis, septicemia, toxicosis, dietary deficiencies, hypocalcemia, hypoglycemia, hepatic or renal insufficiency, heat stroke, and idiopathic epilepsy are possible underlying causes.[26,90,91] Although uncommon in pet chinchillas, consider infectious causes of encephalitis, such as listeriosis, human herpes simplex virus, or cerebrospinal nematodiasis (see below).[79,91] Rule out extracranial causes, such as hypocalcemia, hyperthermia, hypoglycemia, organ failure, and lead poisoning.

Heat Stroke

The ambient temperature range to which chinchillas are adapted is 65°F to 80°F (18.3°C–26.7°C) in a low-humidity environment. Exposure to higher ambient temperatures, especially in the presence of high humidity and poor ventilation, can result in heat stroke.[60] Affected animals are recumbent or ataxic, exhibit rapid breathing, and have bright red mucous membranes, prominent ear vessels, and thick, stringy saliva. Treatment includes cooling the animal and, if the animal is in shock, administering

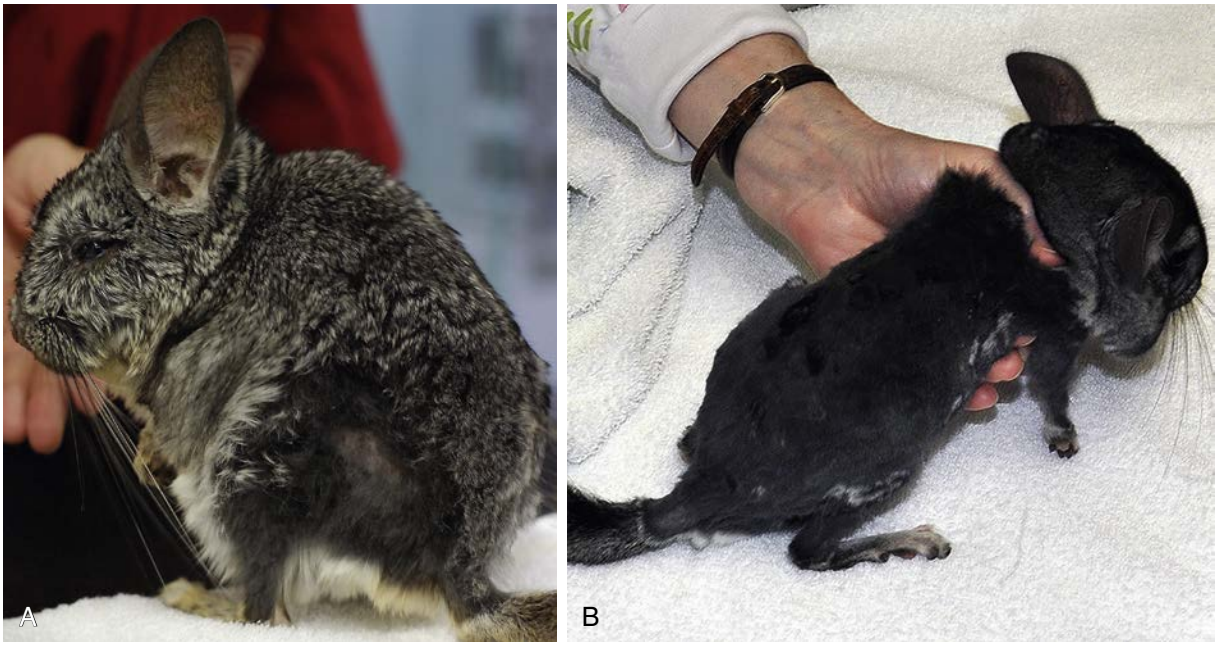


Fig. 22.18 Fur chewing in chinchillas. (A) Fur chewing is limited to the lateral aspects of the hindlimbs in this animal, which suffered from dental disease. (B) Generalized fur barbering affecting the entire body except the head and tail.

intravenous fluids. Long-term prognosis is guarded to poor, and animals often deteriorate after initial improvement.

Lead Toxicosis

Lead toxicosis is uncommon but has been reported in pet chinchillas. Seizures and blindness are possible clinical signs.[39] Blood lead concentrations of >25 µg/dL (0.25 ppm) are indicative of lead poisoning. Successful treatment with calcium disodium edetate (30 mg/kg SC q12h) has been reported.[39]

Dermatologic Disorders

Dermatophytosis

Dermatophytosis (ringworm) in chinchillas is most commonly caused by *Trichophyton mentagrophytes,* although *Microsporum canis* and *Microsporum gypseum* have been reported as well.[19,56] Infected chinchillas may have scaly patches of alopecia on the nose, behind the ears, or on the forefeet. Lesions may appear on any part of the body; in advanced cases, a large circumscribed area of inflammation with scab formation is typical. Because *T. mentagrophytes* does not fluoresce, ultraviolet light (Wood's lamp) is not useful for diagnosis. Diagnosis is made by dermatophyte culture. For topical therapy, use antifungal wipes (e.g., 2% chlorhexidine/2% miconazole wipes) or similar products. Adding miconazole powder to dust baths is routinely used by breeders to treat dermatophytes. Topical treatment removes spores from hair shafts, and systemic treatment acts at hair follicles. For systemic drug therapy, terbinafine (20–40 mg/kg PO q24h) is the preferred treatment, as it has been shown to be more effective than itraconazole (5–10 mg/kg PO q24h) in guinea pigs with dermatophytosis.[53] Continue treatment until two negative dermatophyte cultures have been obtained. Dermatophytes are zoonotic, and cases of chinchillas being the confirmed source of the infection have been reported.[35]

Fur Chewing

Fur chewing is a common problem in chinchillas; up to 20% of animals in breeding facilities can be affected (Fig. 22.18). Fur chewing is also commonly seen in pet chinchillas suffering from dental disease.[43] Many theories concerning the cause of fur chewing have been proposed, but scant scientific evidence exists for most proposed theories. Currently, the most widely accepted theory suggests that fur chewing is a maladapted displacement behavior triggered by stress and affecting predominately stress-sensitive animals. Adrenocortical hyperplasia and histologic changes of the skin, correlating with increased cortisol secretion, support this theory.[73] Typically, affected animals have normal fur on the head and distal extremities and shortened fur on the dorsum, from the lumbar area to the tail and laterally on the flanks (Fig 22.18). Diagnostic testing should be performed to rule out underlying disease, including painful conditions such as dental disease or otitis media. Obtaining a definitive diagnosis and identifying the primary underlying cause of fur chewing behavior may be difficult. Although fur chewing can be annoying for the pet chinchilla owner, it is not a significant threat to the animal's health if underlying medical conditions (e.g., dental disease) have been ruled out. Focus treatment on husbandry changes to reduce stress, such as reducing handling, light, and noise disturbances, avoiding offering multiple sleeping and feeding areas, avoiding keeping solitary pet animals, and offering enrichment items to redirect behavior.[53] Fluoxetine has been suggested as a potential treatment. However, in a recent study fluoxetine (10 mg/kg PO q24h) demonstrated limited success in reducing fur-chewing behavior.[28]

Fur Slip

Fur slip is a predator avoidance mechanism in chinchillas. When an animal is fighting or roughly handled, it can release a large patch of fur, thus enabling it to escape. A clean, smooth area of skin is left; hair may require several months to regrow.

Foot Disorders

In chinchillas, foot disorders predominately affect the hind feet. Lesions can include hyperkeratosis and erythema; less commonly, deep infections or open lesions of the plantar aspect of the hindfeet can develop. Possible predisposing factors are largely unknown, and foot lesions occur in pet as well as farmed chinchillas.[60] Treatment depends on the severity of disease. In mild cases, environmental improvements and application of petroleum-based ointment are often sufficient to resolve hyperkeratosis and erythema. Advise owners to reduce body weight gradually in overweight animals. In severe cases, perform surgical debridement followed by open-wound management and bandaging until healing is complete.

Miscellaneous Disease Problems

Diabetes Mellitus

Diabetes mellitus is rare in chinchillas. Treatment is difficult and the prognosis is poor. Only limited numbers of confirmed cases of diabetes mellitus have been reported.[25,57,63] Pancreatic atrophy and neoplasia have been identified at necropsy as the underlying cause for diabetes in some cases.[57]

When presented with an anorexic and hyperglycemic chinchilla, rule out common causes for anorexia (e.g., dental disease, pain). Many chinchillas will become ketoacidotic and hyperglycemic as a result of anorexia, not because of insulin deficiency, but rather a peripheral insulin resistance. Determine blood insulin levels to confirm a diagnosis of diabetes mellitus caused by endocrine pancreatic insufficiency. In cases with hyperglycemia secondary to peripheral insulin resistance, as seen with ketoacidosis, focus treatment on the underlying primary cause of anorexia and provide nutritional support.

Fractures

Traumatic fractures of the tibia are commonly seen. The tibia is a long straight bone with little soft tissue covering. It is longer than the femur, and the fibula is virtually nonexistent.[15] Tibial fractures are usually either transverse or short spiral fractures. Like the bones of rabbits, those of chinchillas are thin and fragile; surgical repair can be difficult, and complications are common (see Chapter 34). External fixation and intramedullary pins have been recommended for surgical stabilization of tibial fractures in chinchillas. Restricted exercise in a single-level enclosure, ideally without cage bars, is necessary. The prognosis for tibial fractures is guarded and complications after surgical fixation are common. These include bone-pin loosening and infection, nonunion, necrosis of the distal limb, and automutilation. Consider hindlimb amputation if surgical fracture stabilization fails or is not indicated. Chinchillas usually adapt very well after amputation.[53] Fractures of the fore limbs distal to the elbow can be managed by external cooptation and splinting; chinchillas usually tolerate such treatment well.

Diaphragmatic and Perineal Hernias

A diaphragmatic hernia was diagnosed in a chinchilla that presented with a history of anorexia, lethargy, and respiratory signs. Radiographs revealed pleural effusion and a soft tissue mass in the caudal thorax. Thoracic ultrasonography was not able to clearly identify the diaphragmatic hernia. Necropsy revealed a true diaphragmatic hernia, with parts of the stomach and omentum having passed through an approximately 0.8-cm diameter defect in the tendinous portion of the diaphragm.[1]

Perineal hernias have been reported in two adult intact male chinchillas that presented for swelling in the perineal area.[86] Ultrasonography confirmed the tentative diagnosis of a perineal hernia in both cases. The hernia sac contained the urinary bladder in one case and fat in the other case. Unilateral perineal herniorrhaphies, including an internal obturator muscle flap transposition technique, were performed, and both chinchillas recovered uneventfully.[86]

Neoplasia

Despite the long lifespan of chinchillas compared with other rodents, neoplasia is generally uncommon (1% to 2.3% prevalence) compared with guinea pigs and other rodents.[72] However, in the past 10 years, several cases of neoplasia in chinchillas have been reported. Female reproductive tract neoplasms are among the most frequently reported tumors in chinchillas and predominately affect the uterus, and less frequently the vagina, whereas ovarian neoplasms have not been reported. None of the uterine neoplasms were metastatic, and types included uterine leiomyomas, leiomyosarcoma, fibroma, and hemangioma.[7,9,53] Mammary adenocarcinoma with pulmonary, hepatic, and renal metastasis has been reported in a female chinchilla.[46] Cutaneous squamous cell carcinoma was diagnosed in three chinchillas that all had ulcerative skin masses ranging 2 to 5 cm in diameter, located on a limb.[85] In all cases, self-mutilation of the tumor was reported and all animals were euthanized within 2 months after initial diagnosis. Other integumentary and skeletal neoplasms reported include hemangioma of the subcutis, aural leiomyosarcoma,[8] fibrosarcoma at the tail base,[26] and nonmetastatic lumbar osteosarcoma.[80] Alimentary neoplasms reported include a cholangiohepatic carcinoma and a metastatic gastric adenocarcinoma.[52,53] A metastatic undifferentiated carcinoma of the salivary gland was diagnosed in a chinchilla that presented with a soft fluctuating ventral neck mass.[81] Other reported neoplasms include a metastatic iridociliary adenocarcinoma[89] and adenoma of the pituitary gland.[53] Lymphoma is very rare in chinchillas. Two cases of lymphoma have been reported in chinchillas; both animals had generalized lymphadenopathy and neoplastic cell infiltration in multiple organs.[53]

Infectious Diseases

Bacterial Infections

Opportunistic bacterial infections in chinchillas can cause disease either localized to one organ or septicemia. Affected animals are usually immunocompromised by age, underlying disease, nutritional status, or husbandry-related factors (poor hygiene, poor ventilation, contaminated feed). Enterobacteriaceae (e.g., *Proteus* species, *E. coli*) and *P. aeruginosa* have been associated

with significant morbidity and mortality rates, frequently causing enteritis and septicemia.[60]

Pseudomonas aeruginosa infections and enzootic outbreaks in chinchillas have been reported frequently, but this organism can also be found in apparently healthy chinchillas.[37,90] Initially, infections may be localized to one organ and are associated with conjunctivitis, enteritis, pneumonia, otitis media and interna, metritis, and abortion.[21,54,90] As the disease progresses, systemic spread is common. In addition, disease can manifest as an acute generalized form with septicemia and often sudden death.[54] Stress, concurrent disease, and contaminated water bottles can predispose to infection and clinical disease. Conjunctivitis is a common initial sign of *Pseudomonas* infection in chinchillas.[68] Anorexia, lethargy, and decreased fecal output often follow.[27,28,38] Multidrug-resistant and highly virulent strains of *P. aeruginosa* are widespread in chinchillas; therefore aerobic bacterial culture and susceptibility testing are strongly recommended.[37] Because affected animals are often in a critically compromised condition, empiric drug selection is frequently necessary while awaiting culture results. Susceptibility of *P. aeruginosa,* isolated from chinchillas with conjunctivitis, has been reported for potentiated sulfonamides (8%), enrofloxacin (36%), ciprofloxacin (63%), gentamicin (89%), and amikacin, ceftazidime, and piperacillin (100%).[68] In another study, susceptibility to gentamicin and ceftazidime was lower (41% and 73%, respectively), whereas susceptibility to ciprofloxacin was higher (77%).[37]

Streptococcus equi subsp. *zooepidemicus (S. zooepidemicus)* is a mucosal commensal, especially in the horse, but it is unrestrained in its selection of hosts, causing opportunistic respiratory, wound, and genital infections in most species. It has been reported in chinchillas with increasing frequency over the past decade, particularly in farmed chinchillas in the Midwest and California. Reports usually describe chinchillas with conjunctivitis and subcutaneous abscesses; however, pyometra and otitis media have also been described anecdotally. The first published report of *S. zooepidemicus* in a pet chinchilla was a 4-month-old male animal from Wisconsin with a rapidly growing midcervical subcutaneous mass.[6] The infection resolved after treatment with oral trimethoprim-sulfamethoxazole. In 2018, two 6-month-old female chinchillas from a laboratory animal facility in Colorado were diagnosed with subcutaneous abscesses caused by *S. zooepidemicus*.[62] Both animals were euthanized, and necropsy results showed evidence of sepsis. Although *S. zooepidemicus* is an emerging pathogen in chinchillas, the prevalence is unknown, and currently it is not a significant concern in pet animals.

Treatment of *S. zooepidemicus* abscesses involves curettage and drainage, with aerobic bacterial culture and susceptibility testing. Start antibiotic therapy with parenteral penicillin or ceftiofur or with oral trimethoprim-sulfa while awaiting susceptibility test results. In farmed chinchillas, sulfadimethoxine administered in the drinking water has been used to treat outbreaks. Chinchillas treated with antimicrobials could potentially be carriers and remain a source of infection for other chinchillas. *Streptococcus zooepidemicus* remains viable in water for 4 to 6 weeks but only for 1 to 3 days in feces or soil.[12]

Other bacteria, including *Yersinia pseudotuberculosis* and *Yersinia enterocolitica*, *Listeria monocytogenes*, and *Salmonella* species, have been reported as major pathogens in farmed chinchillas, but these are not significant pathogens in pet and research chinchillas.[31,60] *Mycobacterium genavense* was isolated at necropsy from the lungs and liver of a 1-year-old pet chinchilla that presented for emaciation, and radiographs were consistent with pneumonia.[41] Enterotoxemia and death caused by *Clostridium perfringens* enterotoxin have been reported.[53]

Parasitic Infections

Protozoal infections. Historically, group-housed chinchillas in fur ranches and research colonies have a high prevalence of giardiasis. However, the role of *Giardia duodenalis* (syn. *G. lamblia)* in causing disease in chinchillas is difficult to establish. *Giardia* are rarely found in fecal samples from wild chinchillas, but *Giardia* are found in both healthy and sick captive-bred animals. The prevalence of giardiasis and shedding in healthy pet chinchillas varies by study between 27% to 66%.[29,69,75] Predisposing factors, such as stress and poor husbandry, may cause an increase in parasite load, resulting in diarrhea and potentially death. Recently weaned juvenile animals are at higher risk of developing clinical signs.[49] Signs of giardiasis in pet chinchillas are a cyclic sequence of appetite loss and diarrhea associated with a declining body and fur condition.

Giardia cysts can be identified by zinc sulfate flotation, and trophozoites can be identified in fresh fecal smears in acute cases with heavy infection. Although enzyme-linked immunosorbent assays can detect *G. duodenalis* antigen in chinchilla feces, the clinical significance of a positive result of is questionable because clinically normal chinchillas can also shed the organism in the feces. Quantifying fecal cyst or trophozoite numbers in animals with diarrhea is more clinically relevant to determine if an infection is related to the clinical signs.

Treat chinchillas with giardiasis with metronidazole or fenbendazole. Treatment will reduce shedding and usually improve clinical signs but will not eradicate the infection; therefore treated animals may remain a source of chronic cyst shedding. *Giardia* cysts remain infectious for several weeks in a cool, humid environment. *Giardia*-infected chinchillas are a potential reservoir for zoonotic transmission. Direct transmission of *Giardia* from a pet chinchilla to a 1-year-old child from ingestion of the chinchilla's fecal pellets has been reported.[88] Molecular analysis of fecal samples from both hosts classified the *Giardia* cysts into assemblage B.

Eimeria chinchillae is strictly host-specific and can occasionally cause enteritis and diarrhea, predominately in young animals. Stress likely leads to clinical manifestation of a previously subclinical infection. The coccidia cause damage of the intestinal mucosa, with subsequent disturbance of the physiologic flora and possible secondary dysbacteriosis. Diagnosis is made by fecal flotation. Treat affected animals with sulfonamide compounds (e.g., sulfadimethoxine), which usually resolves clinical signs and cyst shedding but may not eradicate coccidia.

Although toxoplasmosis was common in fur-ranched chinchillas, it is now rarely seen. At necropsy, lesions include an enlarged spleen and mesenteric lymph nodes, as well as

hemorrhagic lungs.[53] In two chinchillas with focal necrotic meningoencephalitis caused by *Toxoplasma gondii,* several lobulated *Frenkelia* cysts were found in the brains, independent of and remote from the toxoplasmal inflammatory reaction.[61] Tissue cysts of *Frenkelia microti* were found in the brain of a chinchilla bred in Minnesota and used for biomedical research.[24] A case of acute hepatic sarcocystosis was reported in a pet female chinchilla.[77] Gastroenteritis associated with *Cryptosporidium* species was described in an 8-month-old pet chinchilla that originated from a pet shop, and the prevalence of *Cryptosporidium* species determined by polymerase chain reaction on feces of healthy pet chinchillas in China was 10%.[53,74]

Helminthic infections. The prevalence of nematode infections in pet chinchillas is low.[70] Disease outbreaks of cerebral nematodiasis caused by the raccoon ascarid *Baylisascaris procyonis* have been reported in chinchillas from western Canada.[79] Affected chinchillas showed ataxia, torticollis, paralysis, incoordination, and tumbling. Outbreaks of fatal central nervous system disease were linked to use of hay contaminated by raccoon feces.

Rodentolepis nana (previously *Hymenolepis nana*) infections are not uncommon in chinchillas.[18,53,65] This cestode does not require an intermediate host, and infection is by direct transmission via the fecal–oral route. Animals infected by high numbers of *R. nana* can show anorexia, diarrhea, weight loss, and death,[65] but subclinical infections are more common. *Rodentolepis nana* is zoonotic and can cause severe infections, particularly in immunocompromised people. Demonstrate *Rodentolepis* eggs by fecal flotation. Treat with praziquantel (5–10 mg/kg PO or SC every 10 days).

Chinchillas can serve as intermediate hosts for cestodes, including *Taenia serialis, Taenia pisiformis, Taenia multiceps, Echinococcus granulosus,* and *Echinococcus multilocularis.*[53] Carnivores are the definitive hosts, while rodents serve as intermediate hosts.[4,84] *Taenia crassiceps* infection in chinchillas can lead to hundreds of small cysts in the body cavities and subcutaneous space. Two cases in pet chinchillas from the Netherlands and Switzerland are documented.[4,48]

Fungal Infections

There are two case reports of *Histoplasma capsulatum* infection in chinchillas from the United States, one in a chinchilla imported from the United States to Switzerland and the second in a chinchilla from a commercial chinchilla ranch in Missouri.[53] At necropsy, pulmonary lesions included multiple hemorrhagic foci, alveolar consolidation, and bronchopneumonia, with the organism present in numerous giant cells. Multifocal pyogranulomatous splenitis and hepatitis, with *H. capsulatum* in giant cells, was also noted. The fungus was subsequently cultured from timothy hay used for food. Meningitis and optic nerve neuritis due to *Cryptococcus* species were reported in a chinchilla from California.[10]

Cyniclomyces guttulatus is normal intestinal flora in chinchillas. Animals with soft feces or diarrhea often show increased numbers of this yeast. This finding is indicative of dysbacteriosis, leading to opportunistic overgrowth of *C. guttulatus.*[26] Treatment should address the primary underlying cause of the dysbacteriosis. In severe cases of yeast overgrowth, consider treatment with nystatin (100,000 IU/kg by mouth every 8 hours for 5 days).

Aflatoxicosis is an acute, fatal disease resulting from improperly stored feed contaminated with *Aspergillus* fungi. This is predominately a concern in farmed chinchillas. In one report, the death of 200 chinchillas was attributed to high concentrations of aflatoxin B-1 in the feed.[30] The liver is the primary target organ of aflatoxin; in affected animals, it is enlarged, pale yellow, and friable. In the described cases, histopathologic analyses of hepatic parenchyma showed severe, diffuse cytoplasmic vacuolation of hepatocytes. Because the histopathologic changes caused by acute aflatoxicosis are nonspecific, the diagnosis is usually made in combination with mycotoxicologic feed analysis.[30]

Viral Infections

Viral infections in chinchillas are rare. Chinchillas are susceptible to human herpesvirus type 1 and may be a temporary reservoir for human infections. In a 1-year-old male chinchilla with a 2-week history of conjunctivitis and subsequent neurologic signs of seizures, disorientation, recumbency, and apathy, histologic examination showed a nonsuppurative meningitis and polioencephalitis with neuronal necrosis and intranuclear inclusion bodies; these findings were confirmed as indicative of herpesvirus type 1.[91] Both eyes displayed ulcerative keratitis, uveitis, retinitis and retinal degeneration, and optical neuritis. The clinical signs, the distribution of the lesions, and the viral antigen suggested a primary ocular infection with subsequent spread to the central nervous system.

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23

Degus

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Degus have become popular as pets in many European countries, are becoming more popular in North America, and are also exhibited in zoos. In laboratory animal medicine, degus are used as animal models for social behavior and brain function, diabetes mellitus, and cataract development, among other conditions. Compared with other commonly kept pet rodents, information on the medical management of degus is limited but has been increasing over the past decade.

TAXONOMY

Degus (*Octodon degus*) belong to the order Rodentia, parvorder Caviomorpha, and family Octodontidae. These porcupine-like small rodents are related to guinea pigs and chinchillas. Degus are native to a semiarid shrub land ecosystem, which is found on the western slopes of the Andes Mountains in north-central Chile, and live in areas of medium elevation, up to 1200 meters (4000 feet).[30] Degus live in social groups including two to five females and one to two males, which share a feeding range and an underground burrow system.[7,30] Although degus are commonly described as diurnal, they can display a variable chronotype. Within a colony, some animals may be preferentially diurnal, whereas others may be nocturnal or crepuscular.[17] Life expectancy of degus in captivity is 5 to 8 years.

ANATOMY AND PHYSIOLOGY

Degus typically weigh between 170 and 300 g and measure between 325 and 440 mm in length, including the tail.[2] Males tend to be larger than females. The pelage is yellow-brown above and creamy yellow below (Fig. 23.1). Five toes are present on each foot. The claw of the fifth toe on the front feet is flattened and nail-like. Long bristles extend over the claws on the hind feet. Degus have a moderately long, black-tipped tail with a tuft of fur at the tip.

The cartilaginous external auditory meatus is short and straight; the bony meatus is very short. The auditory bullae, which are relatively loosely connected to the rest of the skull, are elongated rostrocaudally, with a wider rostral end and tapering caudal end. The ventral surface of each bulla is composed of thin, translucent bone, through which are visible some of the internal septa that incompletely divide the middle ear into subcavities.[4]

The vertebral formula of degus is C7, T13–14, and S2–3, and 14 ribs are present. The proximal ends of the tibia and fibula are fused. The heart is localized between the third to fifth intercostal spaces and has the typical appearance of the mammalian heart. The left lung of degus has three lobes (cranial, middle, and caudal) and the right lung has four lobes (cranial, middle,



Fig. 23.1 Normal degu

accessory, and caudal).[28] Degus have a thymus with cervical and mediastinal components. The latter is multilobulated and amorphous, as in other rodents. The cervical part is bilobed and remains active and large for the entire life of the animal, unlike the mediastinal component.[29]

Degus are true herbivores and have a monophyodont (a single set of the teeth), full aradicular (lacking roots) hypsodont (long-crowned), elodont (continuously growing) dentition. Adult degus have 20 teeth in total, with a formula of 2(I1/I1, C0/C0. P1/P1, M3/M3). The labial surface of the incisors is orange pigmented, as in chinchillas. The apices of the maxillary incisors extend for two-thirds of the diastema to the apex of the premolars, and the apices of the mandibular incisors reach distal to the last molar. Premolars and molars, which are largely composed of dentin, have similar structure, and they form a uniform functional grinding unit in each quadrant of the oral cavity. The occlusal plane is almost horizontal in degus, as in chinchillas. Occlusal surfaces consist of alternating exposures of enamel, dentin, and cementum. As a consequence of the degu's strictly herbivorous diet, the occlusal surfaces are rough and uneven, with a succession of enamel folds and dentinal grooves. The occlusal surface of degu cheek teeth resembles the shape of the "eight" number, giving the name of their genus (Octodon: octo = eight; don(t) = tooth) (Fig. 23.2).

The glandular stomach is simple and has a regular, nearly oval shape (Fig. 23.3). The cecum has taenia (longitudinal muscular bands), separated by haustra, in which digesta are fermented by microbial organisms. The colon, in contrast to the cecum, lacks haustra. The degu spleen is unusual, with sinusoids lined by endothelial cells having cuboidal morphology that gives the spleen a glandular appearance.

The adrenal glands (Fig. 23.3) are rounded to ovoid and are large compared with other rodents of similar size. Kidneys (Fig. 23.3) of degus are relatively large and have a complex medulla with long nephrons. Degus have a well-developed adaptation for conserving water. Calcium is excreted mainly via urine.

The uterus is bicornuate and the vagina is located beneath the anus and forms a slit-like opening, which is covered by an epithelial membrane, except in proestrus and estrus. The external urethral orifice is located outside and cranial to the vagina on the urinary papilla (Fig. 23.4), similar to other rodents. There are three to four pairs of mammary glands, with the anterior three pairs located laterally in a line between the front and hind limbs.

The testicles are intraabdominal or in the parascrotal/cremasteric sacs, which are located parallel to the preputium (Fig. 23.4). The penis points caudally and is approximately 16 mm in length.[5] Like other hystricomorphic rodents, there are two external openings in the glans. The dorsal opening is the urethral opening and the ventral is the opening to the intromittent sac, in which four cornified spikes are located (Fig. 23.5). The small os penis is located dorsal to the urethra. Accessory sex glands are the prostate, seminal vesicles, and bulbourethral glands.[5]

REPRODUCTION

Degus are social rodents with colonies sharing one or more underground burrow systems.[7] Food and nesting material are accumulated in the burrows. In the wild, degus breed once per year, whereas in captive colonies, litters occur more frequently. Communal nesting groups include simultaneously lactating females, and allonursing of young has been observed among captive individuals.[2]

The average age of sexual maturity in degus is 4 to 6 months. Females are induced ovulators and require the presence of a male to induce ovulation. Degus have a chorioallantoic placenta that is hemochorial with slight lobulations. The gestation period is 87 to 92 days, and neonate degus are precocious, have a birth weight of about 14 grams, and are born with open eyes and well-developed fur.[19] Females usually have 4 to 6 pups in their first litter and 6 to 10 pups in subsequent litters.[19] During the first 3 weeks after birth, pups cannot regulate their body temperature and are unable to survive without their mother. They remain in the nesting site, where the dam closely attends them until they are about 2 weeks of age. By 2 weeks, pups begin gnawing on pieces of food and moving around the nesting site or cage. In the wild, they begin to emerge at the burrow opening at about 3 weeks of age.[19] Lactation is reported to last 2 to 4 weeks.

HUSBANDRY

Degus adapt readily to new environments and are easy to keep. A typical cage for a maximum of two degus should be a minimum size of 28 inches (length) × 28 inches (height) × 18 inches (depth) (70 × 70 × 45 cm). If kept in a minimum-size cage, degus should be let out to a larger roaming area for at least one hour, one or more times a day. Bar spacing needs to be a maximum of 2 cm. Any shelves/levels made of wire mesh should be avoided. Check that the cage is secured, because degus are highly intelligent and can soon learn to escape. The environmental temperature should be maintained at 18°C–20°C (64°F–68°F) to maintain diurnal activity patterns, and the light/dark cycle should be 12:12 hours. A variety of cage substrates, such as pine wood shavings, shredded (plain) paper, or other commercially available substrates, can be used. Cedar wood chips or cat litter should be avoided. Different kinds of running wheels, hay and grass cubes, ropes,

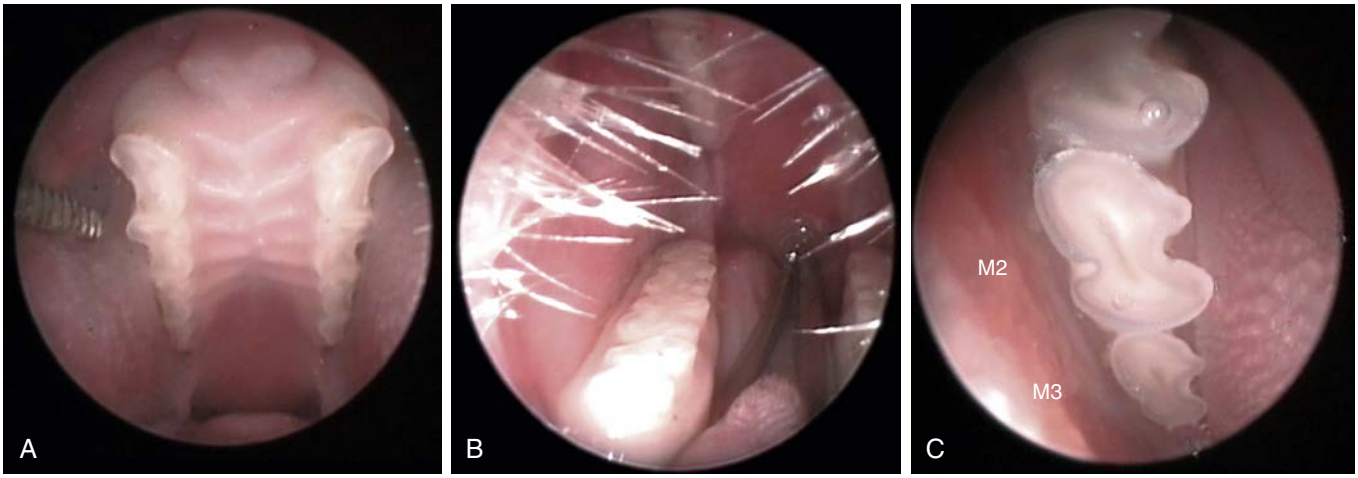


Fig. 23.2 Normal cheek teeth in degus. The occlusal surfaces of the maxillary (A) and mandibular (B) cheek teeth are flat. The clinical crowns of the cheek teeth are of the same height. (C) Detailed view of the right mandibular molars with whitish enamel ridges, displaying the typical shape, which resembles a figure of eight. (Courtesy Vladimir Jekl, with permission.)



Fig. 23.3 Topographic anatomy of the abdomen in a 2-year-old male degu. Degus are strictly herbivorous rodents with large gastrointestinal tract. (Scale in cm). *A,* Left adrenal gland; *white arrowhead,* right adrenal gland; *C,* cecum; *Co,* colon; *F,* mesenteric fat; *GB,* gall bladder; *J,* jejunum; *K,* kidneys; *L,* liver; *S,* stomach; *T,* testicle. (Courtesy Vladimir Jekl, with permission.)

edible fruit tree branches with leaves, digging boxes with sand, and other items will promote optimal social and foraging activity. Degus should be offered regular dust baths at least twice a week to keep their fur free from naturally secreted oil.

NUTRITION

Degus are generally herbivores and in the wild feed on the leaves, bark, stems, and seeds of shrubs and flowering plants. Degus are selective feeders and choose food items with reduced fiber and increased protein and moisture content and thus prefer young leaves and avoid woodier shrubs.[10] The gastrointestinal tract is structurally adapted to promote symbiotic microbial digestion of plant fiber (i.e., cellulose, hemicellulose) in the cecum. Degus are coprophagic, which allows for recovery of nutrients not initially absorbed from the feces. Approximately 38% of feces produced in 24 hours is reingested, mostly overnight.[18] Total gastrointestinal transit time measured in laboratory degus is about 5 hours.[25] The diet consumed by free-ranging degus is naturally lower in nonstructural carbohydrates such as sugars and starch.

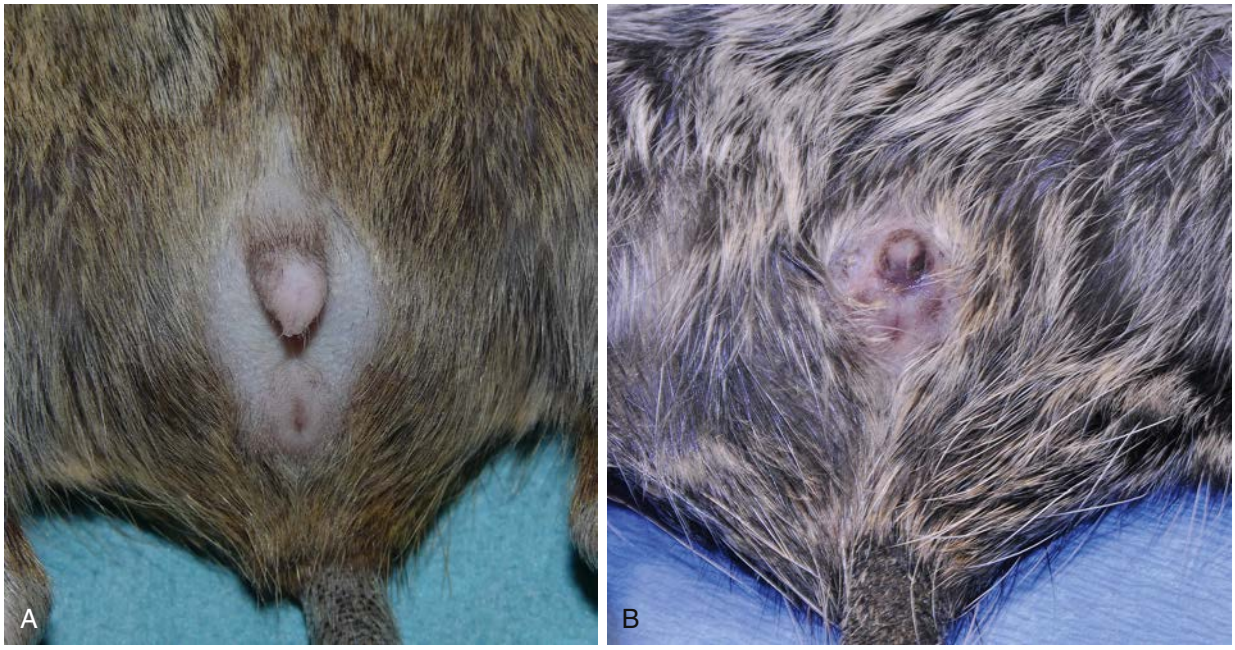


Fig. 23.4 The anogenital region of a male (A) and a female degu (B). The male degu has wider distance in between the anus and preputial orifice and testicles located in paranal sacs. (Courtesy Vladimir Jekl and Karel Hauptman, with permission.)



Fig. 23.5 Four cornified spikes are located in the intromittent sac of the glans penis of the degu. (Courtesy Vladimir Jekl and Karel Hauptman, with permission.)



Fig. 23.6 Tail slip in a degu caused by improper grasping of the tail for restraint. (Courtesy Vladimir Jekl and Karel Hauptman, with permission.)

Overconsumption of foods containing high levels of these carbohydrates can be detrimental to microbial organisms in the hindgut, as well as to the host animal, and has been implicated in the onset of clinical disease, including obesity, diabetes mellitus, and related illnesses. Degus require dietary essential amino acids, including lysine. For nonbreeding animals, a recommended diet should contain 0.6% lysine, 13.5% crude protein, 1.1% linoleic acid, and 3.0% crude fat on dry matter basis.[8,19]

Even though degus are adapted to survive during periods of limited water supply, water should be offered ad libitum in a ball-tipped drinking bottle. Degus are susceptible to *Pseudomonas* infections, especially until the age of 3 months; therefore water bottle sanitization is important.

CLINICAL TECHNIQUES

Restraint and Physical Examination

Restraint by the tail is not recommended because the skin over the tail can be easily damaged, and tail slip can occur (Fig. 23.6). Scruffing by the skin over the shoulders is also not recommended. Instead, grasping the animal around the neck and shoulders is the preferred method of restraint. A combination of midazolam (0.2–0.4 mg/kg intramuscularly [IM]), butorphanol (0.3 mg/kg IM), and ketamine (1–3 mg/kg IM), or midazolam (0.2–0.4 mg/kg IM) and ketamine (3–6 mg/kg IM), can be used for procedural sedation. Alternatively, isoflurane anesthesia delivered by face mask can be used to facilitate clinical procedures.

TABLE 23.1 Hematologic Reference Values in Adult Degus[14]

Parameter	Mean±SD	Range
Erythrocytes, $\times 10^6/\mu L$	8.7 ± 1.1	5.3–7.4
Hemoglobin, g/dL	11.7 ± 0.7	9.9–13.1
Hematocrit, %	50.0 ± 3.0	37–50
MCV, μm^3	51.4 ± 3.2	47.2–64.5
MCH, pg	13.4 ± 0.6	12.3–15.4
MCHC, g/dL	26.1 ± 1.1	226–289
White blood cells, $\times 10^3/\mu L$	7.4 ± 2.4	3.5–14.6
Neutrophils, $\times 10^3/\mu L$	3.1 ± 1.5	0.7–7.0
%	40.6 ± 13.1	19–72
Neutrophils, bands, $\times 10^3/\mu L$	0.0 ± 0.07	0.0–0.31
%	0.4 ± 0.73	0–3
Lymphocytes, $\times 10^3/\mu L$	4.0 ± 1.4	1.3–7.3
%	54.9 ± 12.7	27–77
Monocytes, $\times 10^3/\mu L$	0.1 ± 0.2	0–0.9
%	1.3 ± 1.5	0–6
Eosinophils, $\times 10^3/\mu L$	0.2 ± 0.3	0–01.45
%	2.6 ± 2.7	0–12
Basophils, $\times 10^3/\mu L$	0.0 ± 0.04	0.0–0.19
%	0.2 ± 0.45	0–2

MCH, Mean corpuscular hemoglobin; *MCHC,* mean corpuscular hemoglobin concentration; *MCV,* mean corpuscular volume.

TABLE 23.2 Plasma Biochemical Reference Values for Adult Degus[14]

Parameter	Mean ± SD	Range
Alanine aminotransferase, U/L	18 ± 8	10–48
Albumin	3.3 ± 0.5	1.9–4.5
Alkaline phosphatase, U/L	66 ± 15	41–106
Amylase, U/L	820 ± 234	481–1263
Aspartate aminotransferase, U/L	48 ± 25	19–138
Bile acids, µmol/L	13.5 ± 12.2	1.1–45.9
Bilirubin, mg/dL	0.16 ± 0.07	0.05–0.3
Calcium, mg/dL	10 ± 1.2	8–12
Chloride, mEq/L	103.4 ± 5.5	92–114
Cholesterol, mg/dL	77.2 ± 15	46–104
Creatinine, mg/dL	0.58 ± 0.11	0.34–0.87
Gamma-glutamyl transferase, U/L	6 ± 0.05	1.8–7.8
Globulin, g/dL	3.0 ± 0.6	1.7–4.8
Glucose, mg/dL	160 ± 31	97–236
Phosphorus, mg/dL	4.6 ± 1.1	2.0–6.5
Potassium, mEq/L	3.8 ± 0.4	3.1–4.7
Sodium, mEq/L	142.1 ± 6.3	123–151
Total protein, g/dL	6.3 ± 0.7	4.6–7.7
Urea (BUN), mg/dL	28.2 ± 5.0	18.5–41.7
Triglycerides, mg/dL	168 ± 105	39–429

All values reported are plasma samples unless otherwise indicated. *BUN,* Blood urea nitrogen.

Physical examination of degus involves a systematic approach as in other rodents. Be aware that in males, because of the large inguinal canals through which the testicles retract, testicles also can be palpated intraabdominally and should not be mistaken as abdominal masses. In degus that are presented in respiratory distress or in critical condition, placing the animal in an oxygen cage and stabilizing the patient before any diagnostic procedures are done is the priority.

Blood Collection

Obtaining a blood sample from a degu requires general anesthesia or deep sedation. The amount of blood that can be collected should not exceed 0.8% of the body weight. The cranial vena cava, lateral saphenous vein, and femoral vein can be used. Published reference intervals for hematologic and plasma biochemical parameters have been reported and are listed in Tables 23.1 and 23.2.[13]

Urine Collection and Urinalysis

Urine samples can be collected by cystocentesis under anesthesia or by free catch. The urine is turbid and ranges in color from white to brown based on the presence of pigments. Dipstick urine testing is recommended for quick evaluation of the metabolic status. The normal urinary pH is 8–9. Low pH, ketonuria, or both are poor prognostic factors. Glycosuria is commonly present in cases of diabetes mellitus. Because urine is a major route of calcium excretion in degus, the presence of calcium carbonate crystals in the urine sediment is normal.

Drug Therapy

To the author's knowledge, no pharmacokinetic data exist for any drugs in degus, and dosages are extrapolated or anecdotal. Similar to guinea pigs, antibiotics that can cause fatal dysbiosis of the intestinal flora include beta-lactams, lincomycin, clindamycin, and erythromycin. In the author's practice, the first-choice antibiotics are trimethoprim-sulfa drugs. Because of the risk of gastric ulcerations, corticosteroids are rarely used and should be avoided.

Intravenous and Intraosseous Catherization

Catheterizing peripheral veins in degus is very difficult because of small vein size, and jugular catheterization poses a high risk of fatal hemorrhage. Therefore, intraosseous catheterization of the proximal femur or humerus is preferred to obtain intravascular access in degus. Placing an intraosseous catheter is painful and therefore should only be performed with the patient under general anesthesia.

COMMON DISORDERS

The most common disorders in pet degus are dental disease, alopecia due to self-mutilation, and cataracts.[14] Other common disorders include diarrhea due to dietary causes, obesity, traumatic soft tissue injuries (bite wounds and tail slip), and fractures.

Dental disease

Dental disease is very common in degus, particularly in animals older than 2 years of age (see also Chapter 36).[14] Underlying causes for the development of dental disorders are dietary factors, traumatic injuries, lowered frequency of chewing movements, metabolic and infectious diseases, neoplasia, and developmental and genetic factors. Degus preferentially will eat seeds, grains, and other high-calorie food items over hay or hay-based pellets, likely contributing to the development of dental disease. Reduced chewing of a less abrasive diet in captivity

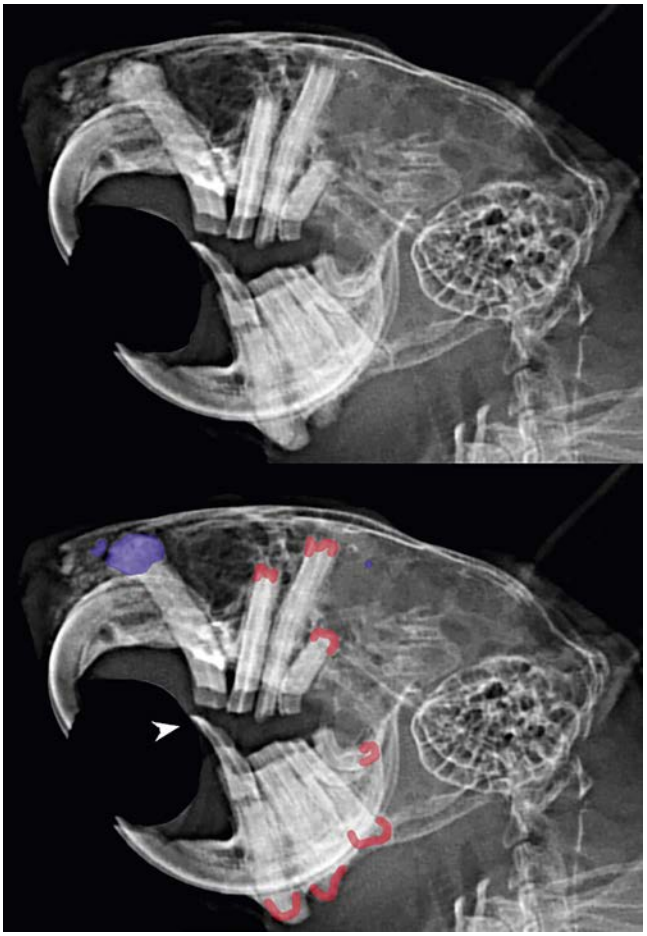


Fig. 23.7 Lateral skull radiograph of a degu that was presented with dyspnea. Radiographs show severe coronal elongation and apical deformities of cheek teeth with spike formation of the clinical crown of a mandibular premolar *(arrow)*. Diseased apices of all the cheek teeth are clearly visible *(red lines)*. The apical radiographic abnormality of a maxillary premolar was indicative of a dysplastic change (pseudoodontoma, *blue*). Histopathologic examination confirmed the presence of pseudoodontoma of the premolar and elodontoma within the nasal cavity. (Courtesy Vladimir Jekl, with permission.)

is hypothesized to diminish tooth wear (lack of teeth wear, lower amount of chewing movements), leading to elongation of continuously growing cheek teeth. Grains, seeds, and most high-calorie treats also have an undesirable high phosphorus content or inappropriate calcium/phosphorous ratio. Degus fed a pelleted diet with high phosphorus and normal calcium levels (1:1) developed disease of all teeth (incisor depigmentation, enamel hypoplasia, disruption in dentin and cementum formation, and apical and coronal cheek teeth elongation) within 6 months, in addition to significantly reduced mandibular bone density.[12]

Clinical symptoms are mostly nonspecific and include reduced food intake, change in feed preferences, and progressive weight loss.[21] Secondary hypersalivation often causes dermatitis and cheilitis. Barbering in many animals is associated with dental disease and correlates with excessive salivation. Secondary gastrointestinal disease, such as gastrointestinal (GI) hypomotility and diarrhea, is often associated with changes in feeding habits. Apical elongation of maxillary cheek teeth and elodontoma formation can result in dyspnea (Fig. 23.7).[15,16] The apices of affected mandibular teeth commonly perforate adjacent bone, resulting in the presence of palpable surface irregularities on the ventral mandibular surface (Fig. 23.7).[21] Formation of spurs and sharp spikes leads to buccal or lingual erosion and ulcerations and/or improper chewing patterns, which is associated with oral discomfort, pain, and dysphagia (Fig. 23.8).

Mandibular premolars (first cheek teeth) elongate below the tongue or above with typical formation of a "bridge" and subsequent entrapment of the tongue (Fig. 23.8B). In some cases, a "bridge" is formed below the tongue and can be missed during an intraoral examination.

For treatment, reduce the height of any elongated coronal crowns to a physiologic length and remove sharp spurs to promote healing of soft tissue. Extraction of cheek teeth may be indicated in cases of severe dental disease, but complete extraction is challenging because of apical elongation and ankyloses to the surrounding bone, which is frequently present.

Incisor malocclusion is usually secondary to coronal elongation of cheek teeth. Pathologies of enamel, dentin, and cementum (such as depigmentation, change in enamel color, horizontal enamel ridges, rough enamel surface, and cementum and dentin demineralization) develop secondary to germinal tissue disorders, especially in cases of metabolic imbalance (e.g., high-phosphorus diet, hypocalcemia, systemic diseases) or chronic trauma (biting the cage bars).[21] For incisor teeth, coronal reduction and correction of the occlusal plane can be done with a dental burr or cutting disc. Extraction of incisor teeth is rarely indicated in degus and should be reserved for severe periapical infections, severe malocclusion, and elodontomas. Extraction should only be performed after diagnostic imaging of the skull has been completed to assess the shape of the incisor teeth. Contoured hypodermic needles (24-gauge) are preferred as luxators.

Periodontal disease, resorptive tooth lesions, and caries are commonly associated with acquired dental disease because of disrupted dentogingival junction, abnormal tooth orthodontic movement within a jaw, and tooth eruption. Widened interdental spaces between the clinical crowns lead to food particle retention, gingivitis, and caries development. Also, abnormal dentin structure (because of dysplastic germinative tissue changes) and suboptimal diet (low-fiber, high-carbohydrate diet) predispose the animal to the caries and periodontitis. Odontogenic abscesses, as are commonly seen in rabbits, are rare in degus.

The most common tumor associated with the oral cavity and dentition in degus is elodontoma.[14,15] The exact pathophysiology of elodontomas in degus is not clear, but proposed causative factors include trauma, inflammation, age-related changes, acquired dental disease, and

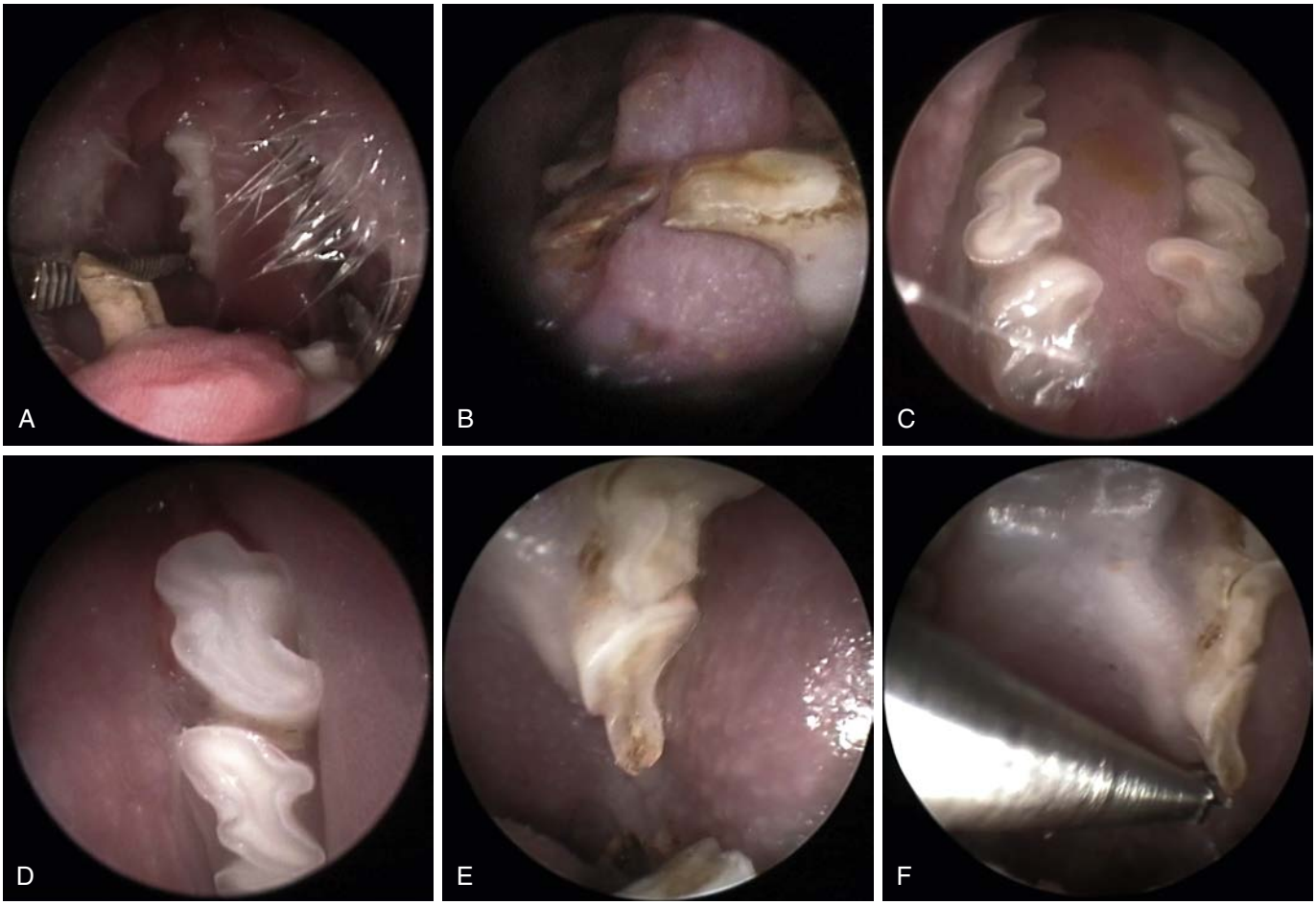


Fig. 23.8 Disorders of the cheek teeth in degus. (A) Coronal elongation with spur formation of the right mandibular premolar. (B) Bilateral coronal elongation of the mandibular premolars, with typical formation of a "bridge" and subsequent entrapment of the tongue. (C, D) Coronal elongation and lingual displacement of the mandibular premolar with widening of the interproximal spaces (D). (E) Spur formation at the distal aspect of the left maxillary last molar. (F) These spurs should be removed carefully, using a fine burr to prevent the risk of soft tissue injury and bleeding. (Courtesy Vladimir Jekl, with permission.)

subsequent impaired (arrested) eruption owing to apical elongation and germinal tooth tissue damage. Complete removal (if possible) of the tumor, supportive treatment, and analgesia are indicated. Elodontomas can be removed via dorsal or lateral rhinotomy. Other tumors seen in oral cavity of degus include melanoma, squamous cell carcinoma, and fibrosarcoma.

Gastrointestinal Hypomotility and Tympany

Gastrointestinal (GI) hypomotility or stasis usually occurs secondary to dietary change, low dietary fiber, pain, stress, obesity, or systemic disease. Gastrointestinal stasis can further lead to bacterial overgrowth (dysbiosis) or cecal or colonic impaction. Abnormalities of physiologic peristalsis lead to imbalance of the intestinal bacterial microflora, followed by increased fermentation process and gas production. The outcome is gastric or intestinal bloat, which worsens the abnormalities of gastrointestinal motility. Gas can accumulate in the stomach also in case of upper respiratory obstructive diseases, commonly associated with maxillary cheek teeth apical elongation and elodontoma formation.[14,15] Presence of gas in the stomach and gastric dilatation is also seen in premortal stages due to air gasping and aerophagia and immediately after isoflurane anesthesia. When GI stasis occurs, the animal rapidly develops hepatic lipidosis, which can be fatal.

The diagnostic plan should include a complete history, physical examination, fecal examination, and diagnostic imaging. Plasma biochemical analysis is helpful in identifying electrolyte imbalances or organ failure. Therapy consists of treating the primary cause and aggressive supportive care. The goal is to reestablish appetite and reverse negative energy balance. Fluid therapy, H2-receptor agonists, analgesia, and syringe feeding are recommended. Syringe feeding is critical, because the aim is to establish positive energy balance.

Gastrointestinal Dysbiosis

The cecum and colon of degus possess a predominantly gram-positive anaerobic and aerobic flora. As in all other herbivorous rodent species, the GI tract is well-balanced ecosystem. Any change in content, pH, and GI motility, including as a result of inappropriate oral antibiotic administration, can cause overgrowth of gram-negative microflora such as the *Enterobacteriacae* (e.g. *E. coli*) or some gram-positive anaerobes (e.g., *Clostridium difficile, C. spiriforme* or *C. perfringens*), which can result in enteritis/diarrhea or enterotoxemia. Clinical signs, diagnostic tests, and therapy are similar as for GI stasis. In the case of soft stool or diarrhea, fecal direct smear evaluation, fecal flotation, or fecal culture is indicated. If clostridial overgrowth is suspected, therapy also includes administration of metronidazole (30 mg/kg PO q12h) for 5 to 7 days and possibly oral adsorbents (kaolin).

Hepatic Lipidosis

Hepatic lipidosis occurs as a result of mobilization of stored fat, particularly in cases of prolonged anorexia (i.e., >24 hours). Obese animals are more sensitive because they already have fat accumulated in the liver. Negative energy balance leads to acidosis or ketoacidosis and metabolic failure. Clinical signs are mostly nonspecific and include lethargy and anorexia. Diagnosis of the cause of the anorexia is essential, and a positive energy balance should be provided. Nutritional support via syringe feedings, along with fluid therapy, are critical.

Diabetes Mellitus

The insulin of hystricomorph rodents is of different structure and has low physiologic activity (only 1%–10% active) compared with other mammals.[23] These species compensate for the reduced biologic activity of their insulin by increasing their insulin concentrations, slower insulin degradation rate, and increased numbers of insulin receptors. As a consequence, degus are unable to regulate glucose concentrations as tightly as other mammals. Degus that are fed easily digestible carbohydrates readily develop hyperinsulinemia initially with subsequent cataract formation and type 2 diabetes mellitus.[4,8] This ultimately results in a failure of beta cells of the pancreas and hypoinsulinemia. Degus also have physiologically increased aldosterone reductase activity in the lens.[6] This enzyme converts glucose to sorbitol, which increases the osmotic pressure and water influx in the lens and, in the case of high glucose concentrations, results in cataracts in as little as 4 weeks after experimentally induced diabetes.[6] When comparing the prevalence of diabetes and cataracts in degus, the lens appears very sensitive to a high-sugar diet, but cataracts can also develop independently of diabetes mellitus. Pathologic lesions associated with diabetes mellitus in degus include cortical cataracts, fatty liver, amyloid deposits in the pancreas, and hyperplasia and hypertrophy of islets of Langerhans. Clinical signs can include obesity, weight loss, anorexia, unilateral or bilateral cataracts (Fig. 23.9), dehydration, polyuria, polydipsia, and GI dysbiosis. Diagnosis is based on persistent hyperglycemia (> 200 mg/dL [11 mmol/L]), hypercholesterolemia, and glycosuria. Concurrent diabetic ketoacidosis is associated with a guarded to poor prognosis.



Fig. 23.9 Cataract formation in a degu with diabetes mellitus.

Medical management includes insulin at a dosage of 0.1–10 IU/kg every 8 to 24 hours subcutaneously. After insulin administration, monitor glucose concentration for 12 to 24 hours, depending on type of insulin, as fatal hypoglycemia may occur. The goal is to reduce blood glucose levels to < 200 mg/dL (11 mmol/L). Dietary adjustment toward a high-fiber diet and exclusion of simple carbohydrates, regular blood glucose monitoring, and weight management are essential to treatment. In some cases, after dietary change, the animal can become normoglycemic again without a need of insulin administration. Although cataracts are irreversible, animals usually can cope well with the visual impairment.

Dermatologic Disorders

Skin Wounds and Abscesses

Lacerations, subcutaneous abscesses, and ear pinna injuries commonly occur in degus secondary to aggression between cage mates. Depending on the lesions, debride and flush wounds, lance and drain or excise abscesses, and treat with local antimicrobials and administer systemic antibiotics as indicated for bacterial infection. Separate out aggressive individuals from the group or reduce the group size. With separated animals, visual and tactile contact (cages close to each other) is recommended, because some degus can be bonded to each other more than others, and individual separation can be stressful, even for an aggressive animal. If the group is not a breeding colony, neutering is recommended for all males.

Alopecia and Barbering

Barbering (automutilation, fur chewing) is the most common skin disorder and a common cause of alopecia in degus (Fig. 23.10).[14] The cause can be a primary behavioral disorder associated with anxiety or stereotypic behavior common in animals younger than 2 years. Common underlying triggers are insufficient cage size, lack of exercise, lack of cage substrate to burrow, caging as a solitary animal, inappropriate light–dark cycle, or high-calorie diets. In older degus, barbering can be associated with dental disease. Barbering can be also a sequela of social interactions within the group where the mostly dominant animal overgrooms other degus. Affected animals barber or lick distal parts of the feet, tail base, and medial aspects of the thighs. Alopecic regions do not show signs of inflammation

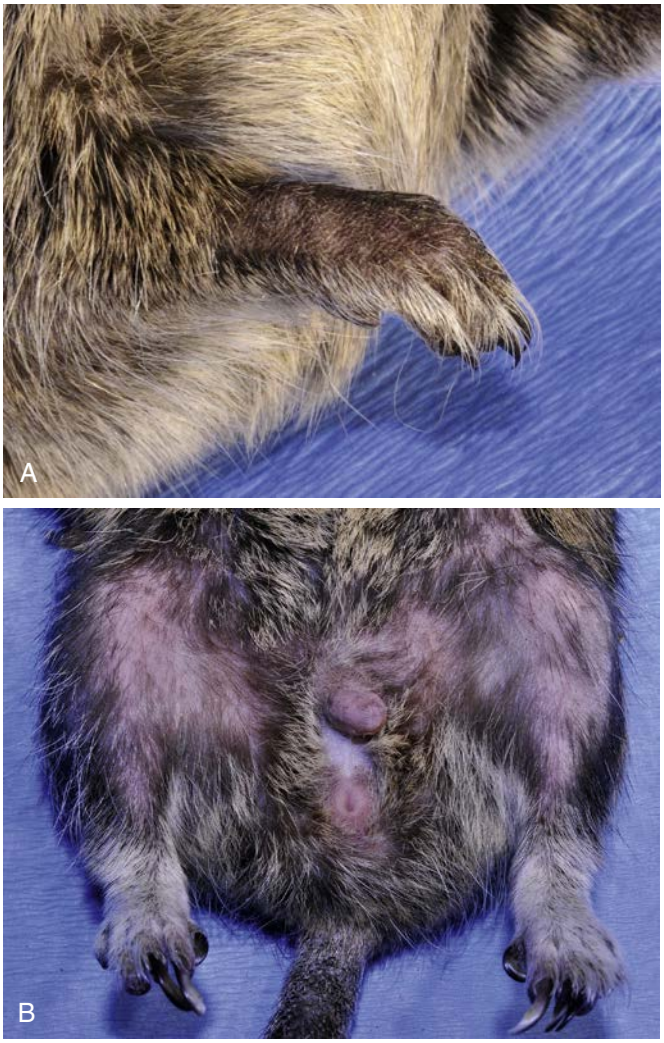


Fig. 23.10 Barbering leading to alopecia is common in degus and can affect various body parts, including the distal forelimbs (A) and inguinal area and medial thigh area (B).

or abrasion, unless they are secondarily infected. Treatment is challenging and includes changes in husbandry, such as a larger cage, group housing, providing substrate and sand baths, and feeding a high fiber diet.

Tail Slip

Degloving injuries of the tail (tail slip) are common as a result of improper restraint (Fig. 23.6). Treatment involves amputating the tail proximal to the affected part. All the tail vessels must be ligated to prevent blood loss.

Dermatophytosis

Dermatophytes reported in degus are *Trichophyton mentagrophytes* and *Arthroderma benhamiae*.[11,14] Hyperkeratosis and hair loss are common clinical signs. Diagnosis is made by cytologic examination and fungal culture. Therapy consists of local and systemic oral antifungal medications such as itraconazole (2.5–10 mg/kg PO q24h) or terbinafine (10–20 mg/kg PO q24h).

Ectoparasites

Ectoparasite infection in pet degus are rare. The zoonotic hematophagous tropical rat mite (*Ornithonyssus bacoti)* has been reported in degus.[14] Other ectoparasites (fleas, tick, *Demodex* species) have been reported anecdotally.

Respiratory Diseases

Because degus are obligate nasal breathers, any obstruction of the nasal cavity can lead to open-mouth breathing. Infectious diseases of the respiratory system are rare in degus. Rhinitis is a common diagnosis in degus and is frequently associated with elodontomas or overgrowth of the maxillary incisor or cheek teeth.[14–16] Noninfectious causes of dyspnea are elodontomas of the maxillary incisor teeth, maxillary cheek teeth apical elongation (Fig. 23.7), hyperthermia, traumatic head injury, metabolic acidosis, and kidney failure.[15,16] Diagnosis is based on physical examination and diagnostic imaging of the skull and thorax. Results of hematologic and plasma biochemical analysis are commonly nonspecific and are associated with anorexia and abnormal liver metabolism. Treatment depends on the underlying cause and severity of clinical signs.

Female Reproductive Tract Disorders

Dystocia, hematometra, pyometra, and vaginal tumors have been reported in degus.[14] Dystocia in degus can occur because of abnormal fetal size, stress during parturition, dietary change, overfeeding of carbohydrates, obesity, and uterine atony. Nonproductive straining and contractions for more than 20 to 50 minutes are abnormal. Dystocia most commonly occurs in primiparous females with a small number of unusually large pups.[14] Clinical signs of this life-threatening condition are apathy, anorexia, tachypnea, abdominal distension, continual straining, and vulvar discharge stained with blood. Diagnostic testing is based on history, abdominal palpation, and uterine and fetal ultrasonography. Survey radiographs are used to evaluate the size of the pup in relation to the size of the pelvic canal. Stabilizing the female involves providing a stress-free environment, thermal support, fluid therapy, and pain management. If the fetus is lodged in the vagina, it is sometimes possible to assist deliver the fetus under general anesthesia or sedation. If obstructive dystocia has been ruled out and uterine atony and general weakness is suspected, consider administering calcium gluconate (25–50 mg/kg SC IM) and oxytocin (0.1-0.8 IU/kg SC). Caesarian section is indicated in cases of prolonged parturition with the female showing general weakness, the presence of dead fetus/fetuses, or in animals with uterine pathology. Perform ovariohysterectomy at the same time as the C-section to prevent future pregnancies. The uterus is accessed via a ventral midline incision.

Male Reproductive Disorders

Penile prolapse and paraphimosis in degus can occur due to trauma, excessive breeding, fur ring, and debris accumulation.[14] In advanced cases, this condition can lead to penile or preputial ulceration or balanoposthitis. Necrosis of the penis can lead to urethral blockage. Diagnosis is based on results of clinical

examination of the prepuce and penis. Treatment for penile prolapse usually involves treating the underlying cause, nonsteroidal anti-inflammatory drugs, analgesics, and manual reduction. If debris or a fur ring is present, remove this manually and clean the area with chlorhexidine solution, preferably with the animal sedated or under anesthesia, and then gently retract the penis back into the preputial sac. Surgical intervention may be considered in cases when manual reduction is unsuccessful and the penis continues to prolapse. In cases where retraction of the glans penis is not possible, preputial amputation can be performed and is tolerated well in degus. Tacking the glans penis with suture to the preputial orifice so that the tip of the penis protruded slightly from the prepuce was used successfully for treatment of iatrogenic penile displacement after a neuter in a degu.[24]

Kidney Disease

Kidney disease, including nephrosis, pyelonephritis, glomerulonephritis, polycystic kidney disease, and renal neoplasms, has been reported in degus. Clinical signs are nonspecific and include anorexia, weight loss, and hunched posture. Diagnosis is based on the presence of azotemia, potentially hyperphosphatemia, and results of diagnostic imaging by abdominal ultrasound or contrast computed tomography.[9] Treatment consists of fluid therapy and supportive care.

Musculoskeletal Disorders

Among musculoskeletal disorders, limb fractures, arthrosis/spondylosis, bacterial arthritis and osteosarcoma, and fibrosarcoma are described.[14] Limb fractures are most common as a result of improper handling and falls. Traumatic fractures can be successfully repaired through extramedullary and medullary fixation.[3]

Ocular Disorders

Bilateral or unilateral cataracts are common in older animals and are associated with diets high in easily digestible carbohydrates or with diabetic animals (Fig. 23.9). Other described ocular disorders are eyelid injury, corneal erosions, keratoconjunctivitis, and uveitis.

Neoplasia

The prevalence of neoplasia in degu populations is low and mainly older animals are affected.[22] Tumor types reported in degus include renal transitional cell carcinoma with concurrent choristoma,[20] primary bronchioloalveolar carcinoma with renal and hepatic metastases,[1] parathyroid adenocarcinoma with metastasis and pulmonary adenocarcinoma,[27] reticular cell sarcoma of a cervical lymph node, hepatocellular carcinoma with pulmonary and renal metastases, hepatoma, splenic hemangioma, and mesenteric lipoma.[22] Other types of neoplasia described or seen by the author are fibrosarcoma, vaginal leiomyoma, vaginal leiomyosarcoma, melanoma, myxosarcoma, and malignant histiocytoma.[14,26]

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24

Prairie Dogs

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NATURAL HISTORY AND TAXONOMY

Prairie dogs (*Cynomys* species) are medium-sized burrowing rodents that live in colony groups in the plains of North America. Prairie dogs have been kept as household pets, are common in zoological collections, and have also been used as research models. Because of their small body size, relative longevity in captivity, and affectionate nature if properly handled, prairie dogs quickly grew in popularity as pets before 2003.[23,33] A zoonotic outbreak of monkey pox in 2003 resulted in 72 people residing in six U.S. states becoming ill after exposure (scratch, bite, or cage cleaning) to infected prairie dogs that acquired the viral infection while kept at the same holding facility with imported sick African rodents.[11,36a] As a result of this outbreak, both the United States and Japan issued a ban on the sale of prairie dogs.[36a] At present, legal ownership of prairie dogs in the United States varies from state to state, ranging from a complete ban on their ownership, requiring permits for possession, or no regulations at all.[36a] Potential owners of prairie dogs are advised to consult their local and national regulatory agencies before considering adoption of a prairie dog and, to minimize exposure to zoonotic diseases, to avoid adopting animals from the wild or from unverified sources.[36,56,72]

Black-tailed prairie dogs are nonhibernating, diurnal, and highly social.[31–33] Their name is derived from their habitat of grasslands and prairies and by their barking calls.[31] Prairie dogs belong to the order Rodentia, family Sciuridae, genus *Cynomys*. Five known species of prairie dogs have been identified—the black-tailed prairie dog (*Cynomys ludovicianus*), white-tailed prairie dog (*Cynomys leucurus*), Gunnison's prairie dog (*Cynomys gunnisoni*), Mexican prairie dog (*Cynomys mexicanus*), and Utah prairie dog (*Cynomys parvidens*).[31,32] Because black-tailed prairie dogs are the largest and the most abundant species in the wild and also the most common species in captivity, this chapter will focus on the husbandry and veterinary care of this species.

Approximately 150 years ago, black-tailed prairie dogs inhabited 14 states and provinces in the United States, Canada, and Mexico, with a population size in excess of 5 billion.[53] However, the population of black-tailed prairie dogs has faced numerous threats, including control activities by ranchers and farmers, government agencies, private individual hunting, sylvatic plague (*Yersinia pestis*), urban development, and habitat fragmentation.[22]

Anatomy and Physiology

The black-tailed prairie dog has a robust body with a stout head, small pinnae, and large eyes, with a neck nearly the same thickness as the head.[23] With the exception of rare albinos, the fur color is usually brown or reddish-brown above and whitish below, whereas individual hairs are black at their base (Fig. 24.1).[32] The tail is medium length, with a black terminal portion.[32] Prairie dogs molt their fur twice a year, with longer and



Fig. 24.1 Discoloration and abnormal "patchy" appearance of the fur can often be observed in sick prairie dogs.

thicker fur in the winter. The winter-to-summer molt begins at the head and moves caudally along the body; this process is reversed in the shift from summer to winter hair.[32] Basic physiologic data for black-tailed prairie dogs are listed in Table 24.1.

The prairie dog's skull anatomy has been described in detail.[32] Prairie dogs have prominent cheek pouches that are present under the skin, just lateral to the masseter muscle.[15] The dental formula is I 1/1, C 0/0, PM 2/1, M 3/3.[23] The cheek teeth (premolars and molars) are brachydont and consist of a series of ridges and cusps composed of soft dentin and an outer hard enamel.[23] As in all rodents, the incisors are aradicular hypsodont (or elodont) and grow continuously.[23] Prairie dogs are hindgut fermenters, with a large cecum occupying the ventral portion of the abdominal cavity.[15] The cecum comprises the body, tail, and ampulla coli, with both an ileocecal valve and an ileocolic valve.[15] The ascending colon consists of sacculations typical of rodents (haustra coli) that are created by muscular contraction of longitudinal bands, termed the *taeniae coli*.[15] The anal gland protrudes at the termination of the rectum as a triad of papillae, commonly referred to as the "flower."[23] The anatomy of the liver, biliary tree, and the pancreas has been described in detail.[28]

In males, the seminal vesicles are located between the dorsal surface of the urinary bladder and the rectum.[15] During the nonbreeding season, the seminal vesicles appear as translucent, thread-like structures; however, during breeding season, these vesicles become elongated and extend beyond the margins of the urinary bladder.[15] The accessory sex glands of male prairie dogs comprise the prostate gland and bulbourethral glands (Cowper's glands).[15] As the penis exits the body, it is directed ventrocaudally.[15] Males have open inguinal rings, and, during nonbreeding season, the testes are located intraabdominally.[15] Like rabbits and several other rodents, female prairie dogs have a duplex reproductive system structure with paired uteri that open into the two anterior cervices independently through lips that have a central swelling and channels that do not permit communication, followed by an opening into the vagina.[15,21]

The ocular anatomy and several clinical ophthalmic features of black-tailed prairie dogs have been reported.[41,42] Prairie dogs have a vestigial nictitating membrane in the medial canthus area.[42] The limbus is heavily pigmented, the iris is a dark homogenous brown, and the pupil is round.[42] There is no tapetum lucidum, and the retinal vascular pattern is holangiotic, with a horizontally elongated optic disk.[42] Measured tear production is 13.6 ± 7.8 mm/15 s (range 3–30 s) for the phenol red thread test and 1.2 ± 0.9 mm/min (range 0–4 mm/min) with the modified Schirmer tear test.[41] Intraocular pressure measured by rebound tonometry measurement (TonoVet, d setting [Icare Finland Oy, Vantaa, Finland]) is 7.7 ± 2.2 mmHg (range 3–11.4 mmHg).[41] *Staphylococcus* species are the most commonly isolated conjunctival bacteria.[41]

TABLE 24.1 Physiological Data for Black-Tailed Prairie Dogs[31,33]

Parameter	Range
Life span	8–10 years (wild), 12 years (females, captivity), 14 years (males, captivity)
Body weight	0.6–1.4 kg (males heavier than females)
Body length	300–450 mm
Heart rate	147–320 BPM
Respiratory rate	30–60 RPM
Rectal temperature	35.3°C–39.0°C (96°F–102°F)

BPM, Beats per minute; *RPM,* respirations per minute.

Reproduction

Black-tailed prairie dogs are unique compared with many other rodents because they are not highly prolific. Breeding starts after 2 years of age.[31] Within the basic social unit, a coterie, females commonly breed in synchrony (termed *synchronized breeders*), with gestation ranging from 32–35 days.[31,32] Litter size can range from 1 to 10 pups, with 4 being the average.[31,32] Pups are altricial, born naked and blind, yet exhibit rapid growth and are furred by day 27, open their eyes between days 33 to 37, and are characteristically weaned at day 49.[31] Pups exit the burrows in the sixth week of life to begin foraging[31] (Table 24.2).

Infanticide is common during this time, because the females will seek to kill the offspring of others, and can involve up to 39% of the litters.[32] However, once juveniles have emerged from the burrows, females will suckle not only their own pups but also the pups of other females.[32] During the breeding season, the males display large, scrotal testes and are often aggressive, whereas the vulva of the females becomes swollen and pigmented.[21,31]

Behavior

Prairie dogs are social animals, and wild colony sites can contain thousands of residents.[31] As mentioned above, the basic social unit is a coterie.[31,32] Typically coteries consist of 10 animals containing 1 adult male and 3 to 4 adult females, with the remainder consisting of yearlings and juveniles.[31] The females tend to remain for life, whereas the juvenile males disperse to new homes.[31] Many coteries make up the colonies that are sometimes referred to as *towns, villages*, or *complexes*.[31]

Despite a high level of social traits, prairie dogs have a tendency to cannibalism.[32] Additionally, intermale fighting is very common because young males are chased out of the group, and similar activities have also been recorded in females, often resulting in severe bite wounds.[32]

TABLE 24.2 Reproductive Data for Black-Tailed Prairie Dogs[31–33]

Parameter	Range
Breeding age, female	> 2 years
Breeding age, male	> 2 years
Ovulation type	Monestrous (5–6 hours on a single day/year)
Mating season	January–February
Estrus cycle length	2–3 weeks
Gestation period	≈35 days (33–38)
Birth	Always underground, usually in the morning
Mammary glands	8
Litter size	4 (1–10)
Birth weight	15 g
Eyes open	2 weeks
First fur	3 weeks
Weaning age	6 weeks (37–51 days)

Because of their diurnal nature, prairie dogs emerge from their burrows at dawn and undertake various activities such as foraging, fighting, chasing, kissing, vocalizing, and playing until dusk.[59] At dusk, they return to their burrows until the next morning.[59]

Prairie dogs communicate with unique vocalizations.[33,59] When on high alert, prairie dogs emit a series of repetitious barks.[59] Once a predator is detected, the prairie dog runs to a burrow mound and vocalizes an alarm call, which is heard as a sequence of "chatter barks."[59] Once the predator has left the area, a prairie dog will give a "jump-yip" while stretching to vertical with the front feet high in the air.[33,59] Many further vocalizations are heard, depending on the level of threat or communication desired.[59]

Prairie dogs are best acquired as pets at around 10 weeks of age and fully weaned.[31] At this age, they tend to imprint and accept their new owner more readily.[31] Adult prairie dogs can still make good pets with time and patience from the owner.[31] However, the source of these animals should be carefully and fully investigated to avoid adopting wild animals that might be carrying a variety of potentially zoonotic diseases.[1,36,50,72]

Husbandry

Caging

As pets, prairie dogs require an environment that tries to mirror what would be present in the wild. Pets require a large, safe cage to live in when they are not supervised.[31] Prairie dogs can be housed in same-sex pairs or groups or one male with multiple females.[52] If a female is present in a group of males, the males will have a tendency to fight over her.[52] In general, neutering can help prevent cage-mate aggression and prolong lifes pan.[31] Cage training for urination and defecation is possible because prairie dogs have a natural propensity to adopt certain areas for elimination.[33] The optimal number of prairie dogs per cage depends on the individuals and their personalities.[33] Housing prairie dogs requires several important considerations. The wire mesh of the cage should be very small (1.25 cm or 0.5 inch), because prairie dogs have a tendency to get their feet trapped in larger mesh.[52] Multilevel cages are an important consideration because prairie dogs enjoy having a high place to stand to overlook their surroundings and will generally climb to the highest point when there are signs of activity.[52] Prairie dogs are smart animals, and secure latches are essential to prevent inadvertent escape.[52] The cage bottom should be made out of solid material that is both safe if ingested and is also resistant to chewing.[52]

Bedding material is important in housing, and fibers such as woodchips, recycled paper, hay, and cotton cloths are examples of acceptable bedding material.[52] In the wild, prairie dogs create "burrow mounds," which they will try to replicate in captivity.[52] Providing prairie dogs with tubing and pipes they can climb and run through can simulate the tunnels of a burrow in the wild.[52]

Environmental enrichment is another key factor when considering husbandry for prairie dogs.[52] Toys that are used for dogs and parrots are good options, as are cardboard items.[52] A large solid-bottom running wheel can be placed in the cage to provide exercising opportunities and to minimize the risk of obesity.[52]

DIET

Precise dietary requirements for prairie dogs in captivity have not yet been determined. In the wild, prairie dogs are herbivorous, and the plant matter (a variety of grasses and forbs) they consume depends on the time of year and what is available.[62] Grasses consumed by wild prairie dogs may constitute as much as 85% of its wet weight as water, providing a large amount of the daily water intake.[2] The staple captive diet should include commercial rabbit pellets (2–4 g/100g body weight), free-choice grass hay, and some leafy green vegetables.[52] High-carbohydrate items or human food should not be offered because these can increase blood lipid concentrations.[12,52] In the wild, prairie dogs can diverge from their herbivorous tendency and consume items such as American bison scats and insects and practice cannibalism of other prairie dogs that have died of natural causes or infanticide of unweaned prairie dogs.[31,32]

Suboptimal diet and lack of exercise often lead to obesity in captive prairie dogs (ideal body weight <1.2 kg) and dental-related health issues.[52] Hypothyroidism is suspected in some of these cases; for example, one obese pet prairie dog that was fed a diet of human food composed mainly of hard cheese and potato chips had a low total T4 value of 0.4 µg/dL (5.15 nmol/L). In another case of an obese prairie dog, results of a full thyroid panel were as follows: total T4, 46 nmol/L; total T3, 1.0 nmol/L; free T4, 24 pmol/L; free T3, 7.6 pmol/L; and thyroid-stimulating hormone, 0.0 ng/mL However, results are difficult to interpret, as reference ranges for most of these parameters are not reported.[18,35] Although wild prairie dogs obtain most required hydration through their diet, captive animals need access to free-choice clean water provided in sipper bottles attached to their cages, as well in water bowls.[33]

CLINICAL TECHNIQUES

Preventive Medicine

An annual physical examination is recommended and, in addition, routine blood testing (complete blood count, plasma

biochemical analysis), nail trimming, and fecal examination should be performed. For population control purposes, animals over 6 months of age and those not intended for breeding should be neutered or spayed. Because of similarities in the abdominal viscera, size, and body conformation, ovariohysterectomy can be performed as in pet hystricomorphic rodents. In mature males, especially during their breeding season, the testicles can be palpated under the skin in the inguinal invagination, and a bilateral prescrotal technique can be performed in these cases. However, in young males and those outside their breeding season, the testicles are usually located in the abdomen, and a caudal abdominal ventral-midline approach is required for neutering. Avoid placing skin sutures because the animals have a propensity to remove them, and a protective E-collar is highly recommended to guard the incision site. Postoperative care includes appropriate analgesia, fluids, and assisted feeding. Chemical contraception has been reported in wild populations, but its use has yet to be evaluated in captive animals.[70,71] Currently there are no approved vaccines for captive prairie dogs.

Physical Examination

A complete physical examination including accurate body weight, thoracic auscultation, abdominal palpation, sex determination (Fig. 24.2), and oral examination should always be performed. Prairie dogs acquired at a young age and accustomed to people can sometimes be handled without the need for manual restraint or chemical immobilization. However, distressed animals and those unaccustomed to people can inflict severe bite injuries. The use of thick towels or leather gloves for protection can provide limited access for brief physical examination.

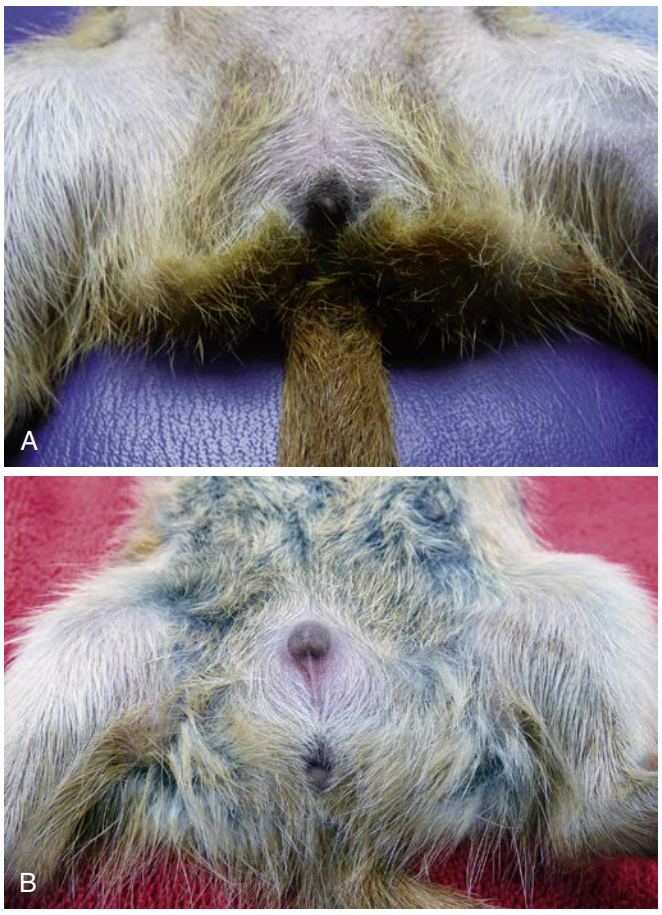


Fig. 24.2 As in most rodents, sex determination in prairie dogs is done by evaluation of the anogenital distance, which is shorter in the female. (A) Female prairie dog. (B) Male prairie dog.

Anesthesia

For a full clinical evaluation and subsequent diagnostic testing or surgical procedures, gas (isoflurane/sevoflurane) anesthesia is recommended. A small, low-resistance, nonrebreathing anesthesia system is appropriate, with a clear plexiglass chamber used for anesthetic induction and a tight-fitting face mask used for maintenance. Long anesthetic procedures can be maintained with either a tight-fitting face mask or by an endotracheal intubation (blind or endoscopic technique as in other rodents).[49] Keep prairie dogs normothermic (98°F–99°F [37°C]) during anesthesia. Most prairie dogs will develop respiratory acidosis and azotemia (relative/absolute) regardless of the time spent under isoflurane anesthesia; therefore provide corrective hydration to anesthetized animals (intravenous [IV]/subcutaneously [SC]) during surgery.[26] Body positioning under isoflurane anesthesia has no significant effects on selected biochemical and acid base parameters.[17]

At present, the fluid requirements are not yet determined for prairie dogs; however, 80 to 100 mL/kg per day of a balanced crystalloid solution can be used for maintenance. Intravenous catheters (24-gauge) can be placed in the cephalic veins and also in the femoral and medial saphenous veins as a secondary site. A fluid bolus of 30 to 40 mL can be given subcutaneously in the interscapular region. Dosages for chemical sedation and anesthesia are listed in the Appendix.

Phlebotomy

Despite their small body size, blood sampling is relatively easy to perform in this species. The jugular, cranial vena cava, cephalic, saphenous, and femoral veins are all good choices for phlebotomy. The exact total blood volume of prairie dogs is unknown. Total blood volumes in other rodent species are approximately 6% to 8% of body weight; therefore, in healthy, mature animals, remove no more than 10% of the total blood volume at one time.[29] Depending on phlebotomy site, use a 25- to 27-gauge needle and a 1- to 6-mL syringe for blood collection.

Complete immobilization of the prairie dog is indicated for accessing most phlebotomy sites. Collect blood samples immediately after anesthetic induction to avoid isoflurane-mediated hypotension and hypothermia, which can increase the difficulty of blood collection from peripheral venipuncture sites, and to prevent isoflurane-related artefactual changes in the results.[26,29]

Clip the fur around the blood collection site for visibility of the veins, and aseptically prepare the venipuncture site. For jugular venipuncture, position the prairie dog over the table in a cat-like fashion with the neck extended. Occlude peripheral veins by using a rubber band tourniquet clamped with a hemostat (Fig. 24.3). Syringes can be preheparinized to reduce the risk of clot formation.[29]

Clinical Pathology

Several studies have reported values for hematologic and biochemical (whole blood, plasma, and serum) analytes and coagulation parameters in prairie dogs (Tables 24.3–24.5).



Fig. 24.3 The femoral (or medial saphenous) vein in prairie dogs is useful for rapid collection of up to 1.0 mL of blood. The area is aseptically prepared, and a tourniquet using a rubber band and small hemostats can be applied above the stifle.

TABLE 24.3 Hematologic Reference Values for Black-Tailed Prairie Dog[5]

Parameter	Mean ± SD	Range
Erythrocytes, $\times 10^6$ /µL	6.59 ± 1.1	3.17–8.05
Hematocrit (calculated), %	37 ± 7	15–47
Hemoglobin, g/dL	12.0 ± 2.0	6.44–14.8
MCH, pg	18.5 ± 1.9	15.5–27.9
MCHC, g/dL	33.5 ± 2.2	31.4–44.0
MCV, μm^3	55.1 ± 5.2	44.2–68.2
MPV, μm^{-3}	6.1 ± 0.7	5.0–7.5
Reticulocytes, $\times 10^3$/µL	466 ± 157	138–783
RDW, %	17.9 ± 7.5	11.6–38.8
WBC, $\times 10^3$/µL	6.3 ± 1.9	3.3–10.5
Neutrophils, $\times 10^3$/µL	3.9 ± 1.6	0.8–7.9
Lymphocytes, $\times 10^3$/µL	2.2 ± 0.9	1.0–5.6
Monocytes, $\times 10^3$/µL	0.13 ± 0.11	0–0.42
Eosinophils, $\times 10^3$/µL	0.1 ± 0.13	0–0.5
Neutrophils segmented, %	69	43–87
Neutrophils band, %	0	0
Lymphocytes, %	25	8–54
Monocytes, %	4.1	0–12
Eosinophils, %	1.8	0–10
Basophils, %	0.2	0–2
Total solids, g/dL	7.5	6.9–8.0

MCH, Mean corpuscular hemoglobin; *MCHC,* mean corpuscular hemoglobin concentration; *MCV,* mean corpuscular volume; *MPV,* mean platelet volume; *RDW,* red blood cell distribution width; *WBC,* white blood cell count.

Interpret these values with caution because the animals and testing methods reported in each of these studies vary greatly; that is, between wild and captive animals and between different biochemistry analyzers.[35] Commercial reagent test strips can be used for prompt rule-out of azotemic prairie dogs.[46]

TABLE 24.4 Biochemical Reference Values* for Black-Tailed Prairie Dogs[5,18,35,69]

Analyte	Mean ± SD	Range
Albumin, g/dL	2.5 ± 1.1	1.7–9
ALP, IU/L	74 ± 22	45–128
ALT, IU/L	25 ± 16	2.9–8.4
Amylase, IU/L	323 ± 89	111– 499
AST, IU/L	35 ± 11	21–63
Bile acids, µmol/L	12.5 (median)	2–24
Total bilirubin, mg/dL	0.3 ± 0.1	0.2–0.6
Calcium, mg/dL	9.1 ± 0.4	7.5–10.2
Total CO2, mEq/L	34 ± 4.0	22–43
Chloride, mEq/L	98 ± 4	85–108
Cholesterol, mg/dL	104 ± 26	50–171
Creatinine, mg/dL	0.54 ± 0.17	0.3–0.9
GGT, IU/L	10.1 ± 1.2	8–13
Glucose, mg/dL	318 ± 90	138–510
Lipase, IU/L	50 ± 13	26–78
Phosphorus, mg/dL	6.3 ± 0.9	4.1–8.3
Potassium, mEq/L	5.1 ± 1.0	3.6–8.0
Sodium, mEq/L	144 ± 4	134–153
Total Protein, g/dL	5.7 ± 0.8	4.4–8.8
Thyroxine–total T4 (plasma), µg/dL	4.5 ± 2.4	0.6–8.0
Triglycerides, mg/dL	60 ± 38	16–142
HDL, mg/dL	70 ± 15	46–106
VLDL, mg/dL	12 ± 8	3–28
LDL, mg/dL	21 ± 12	3–45

*All values reported are serum samples unless otherwise indicated.
ALP, alkaline phosphatase; *ALT,* alanine aminotransferase; *AST,* aspartate aminotransferase; *BUN,* blood urea nitrogen; *CO_2,* carbon dioxide; *GGT,* gamma-glutamyl transferase; *HDL,* high-density lipoproteins; *LDL,* low-density lipoproteins; *VLDL,* very low–density lipoproteins.

TABLE 24.5 Coagulation Parameters in Black-Tailed Prairie Dogs (N = 16)[40]

Analyte	Median	Min–Max
Prothrombin time, sec	8.4	7.7–9.9
Activated partial thromboplastin time, sec	23.8	19.4–25.5
Fibrinogen, mg/dL	343	224–626
Fibrin degradation product, µg/mL	<5	<5

No studies have been published showing the specific serum protein fractions for prairie dogs. Data from an internal research study of agarose gel serum protein electrophoresis performed at the Kansas State University Clinical Pathology Laboratory in a small number (n = 17) of captive prairie dogs are presented in Table 24.6. The serum total protein (median: minimum–maximum) measured by the biuret reaction was 5.7 mg/dL: 5.1–6.6 mg/dL. The total albumin (median: minimum–maximum) measured by the immunoturbidimetric method with the Cobas

TABLE 24.6 Agarose Gel Serum Protein Electrophoresis Protein Fractions From Captive Prairie Dogs (N = 17)

Analyte	Median	Min–Max
Albumin, g/dL	2.6	0.8–3.2
Globulins		
Alpha-1, g/dL	0.5	0.3–2.0
Alpha-2, g/dL	0.6	0.3–0.9
Beta-1, g/dL	0.6	0.4–0.8
Beta-2, g/dL	0.8	0.5–1.4
Gamma, g/dL	0.5	0.1–1.3

Data courtesy Drs. Mark Morton and Lisa Pohlman, Clinical Pathology Laboratory, College of Veterinary Medicine, Kansas State University.

c 501 chemistry analyzer (Roche Diagnostics, Florham Park, NJ) was 3.4 mg/dL: 2.4–3.6 mg/dL.

Urinalysis

Unless required for a bacterial culture test, a urine sample is better obtained after it is naturally voided.[19] Daily urine volume production in the prairie dog is unknown and varies based on the water content of their diet. Prairie dogs exhibit the typical urine properties of rodents. The urine appears yellow and can be clear to cloudy from high protein content and inactive sediment.[19] The urine specific gravity has a wide range (1.005–1.059), and the pH is basic (8–8.5), as in all herbivorous rodents.[19] Contrary to what is often reported for rodents, crystals (calcium and others) were not found in urine samples from healthy prairie dogs.[19] Several urine biochemical properties (and their ratios) were reported for black-tailed prairie dogs and can offer an important clinical tool for renal function assessment.[19]

Radiology

Radiography can be used as either a screening test by taking at least two views (lateral and dorsoventral) of the whole body or collimated to the area of interest (dental, thoracic, etc.) with further views to be included. Ensure that the animal is completely immobilized and the limbs are extended and taped away from the main body to allow clear, symmetric, and diagnostic imaging (Fig. 24.4).

TABLE 24.7 Selective Electrocardiographic Measurements in Black-Tailed Prairie Dogs Under Isoflurane Anesthesia and in Right Lateral Recumbency

Parameter	Median	Range
Heart rate, beats/min	250	147–320
P-wave amplitude, mV	0.05	0.01–0.06
P-wave duration, sec	0.03	0.02–0.03
PR interval, sec	0.06	0.04–0.06
QRS duration, sec	0.02	0.02–0.03
QRS amplitude, mV	0.5	0.1–1.15
QT interval, sec	0.12	0.1–0.14
Mean electrical axis, degrees	—	–15 to + 120

Lead II was used for waveform analysis (N = 13).[64]

Cardiology

Prairie dogs have a unilobate left lung, and the heart lies in the midline of the body with the apex directed toward the left.[15] All prairie dogs show normal sinus rhythm, with a median heart rate of 250 beats/min (range 147–320 beats/min).[64] Most (62%) prairie dogs have a QRS complex demonstrating Rs morphology, and some also demonstrate qR and rS morphology.[64] All prairie dogs have positive P and T waves in lead II.[64] Although the ST segment is slightly raised (0.05 mV) in some prairie dogs, most show normal, relative to baseline, ST segments (Table 24.7).[64] Radiographic vertebral heart scoring (VHC) is used in prairie dogs, and reference values have been reported.[24] Reference values for echocardiograms have also been reported.[24]

Pharmacology

Although several references list select pharmacologic therapeutics in prairie dogs, most are based on anecdotal reports or individual experiences.[10,37] Pharmacokinetic studies on sustained-release buprenorphine and meloxicam have been

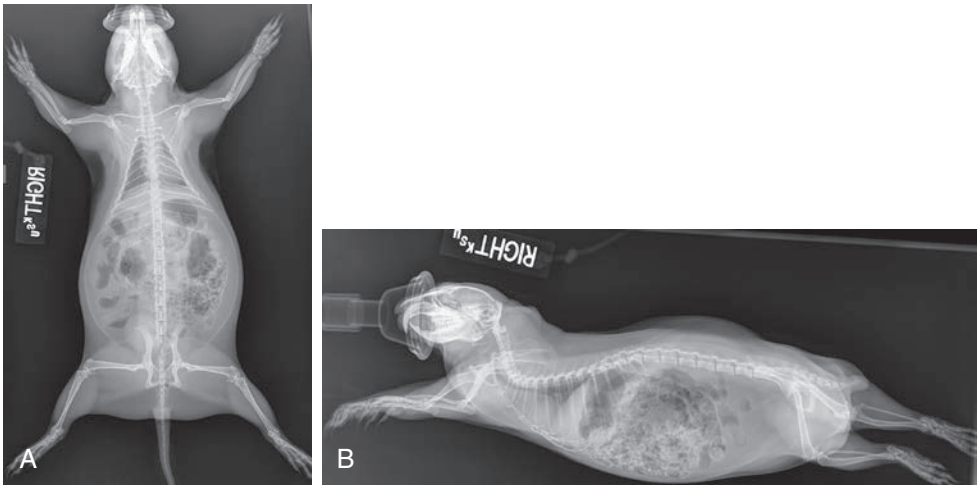


Fig. 24.4 Survey dorsoventral (A) and lateral (B) whole body radiography of a prairie dog. For diagnostic imaging, the animal should be completely immobilized and the limbs extended and taped in a 45-degree angle away from the body.

TABLE 24.8 Selected Drug Dosages for Black-Tailed Prairie Dogs[10,20,25,34,37,49,53,68,71]

Drug	Dosage and Administration	Comments
Analgesics		
Buprenorphine	0.03–0.05 mg/kg every 8–12 hours SC, IM, IV	
Butorphanol	0.1–0.5 mg/kg every 6–8 hours SC, IM	
Ketoprofen	2 mg/kg every 12 hours IM, SC	Not in azotemic animals
Meloxicam	0.3–0.5 mg/kg every 24 hours PO, SC, IM, IV	Not in azotemic animals
Antimicrobials		
Amikacin	2.5 mg/kg every 12 hours SC, IM, IV	—
Chloramphenicol	50 mg/kg every 12 hours PO, SC, IM, IV	—
Enrofloxacin	20 mg/kg every 24 hours PO, SC, IV	SC should be diluted 1:1 saline. IV should be given slowly.
Metronidazole	20 mg/kg every 12 hours PO, IV	
Procaine penicillin	25,000–50,000 every 3–5 days SC	Do not give orally
Trimethoprim-sulfa	30 mg/kg every 12 hours PO, SC, IM	
Antiparasitic		
Amitraz	Dip: Concentration of 250 ppm for 3–5 min at 4-day intervals for a period of 2 months	Demodex
Carbaryl	Weekly shampoo	Fleas, mites
Fenbendazole	10–25 mg/kg PO	Nematodes
Imidacloprid	Topical: ½ kitten dose, monthly	Fleas
Ivermectin	0.2–0.3 mg/kg SC every 7–10 days, 2–3 treatments	Mites
Ponazuril	30 mg/kg PO; two treatments, 48 hours apart	Coccidia
Selamectin	10–15 mg/kg topically, monthly as needed	Mites
Antifungals		
Chlorhexidine	2%–3% shampoo as needed	Dermatophytosis
Griseofulvin	250 mg/kg PO every 10 days for 3–4 treatments	Dermatophytosis
Ketoconazole	10 mg/kg every 24 hours PO	Dermatophytosis
Itraconazole	5–10 mg/kg every 24 hours PO	Dermatophytosis
Selenium disulfide	Shampoo once	Dermatophytosis
Sedation and Anesthesia (Use lower end of dose range when drugs are combined)		
Buprenorphine	0.03–0.05 mg/kg every 8–12 hours SC, IM, IV	
Butorphanol	0.1–0.5 mg/kg every 6–8 hours SC, IM	
Diazepam	0.2–5 mg/kg every 8 hours PO, IM, IV	
Ketamine	20–40 mg/kg SC, IM, IV	
Medetomidine	0.5 mg/kg SC, IM	
Propofol	3–5 mg/kg to effect IV	
K + X	20 mg (K) + 2 mg/kg (X) SC, IM	Premedication before gas anesthesia
M + K	50 µg/kg (M) + 10 mg/kg (K) SC, IM	Short anesthesia/deep sedation
M + K + P	80 µg/kg (M) + 10 mg/kg (K) + 4 mg/kg (P) SC, IM (M,K) + IV (P)	Short anesthesia or premedication followed by gas anesthesia
M + K + P	80 µg/kg (M) + 10 mg/kg (K) + 4 mg/kg (P) SC, IM (M, K) + IV (P)	Short anesthesia or premedication followed by gas anesthesia
D + K + M	0.25 mg/kg (D) + 40 mg/kg (K) + 1.5 mg/kg (M)	Short anesthesia

D, Dexmedetomidine; IM, intramuscular; IV, intravenous; K, ketamine; M, medetomidine; P, propofol; PO, by mouth; PPM, parts per million; SC, subcutaneous; X, xylazine.

described.[10,68] In the current absence of pharmacological studies describing efficacy and safety of drugs in prairie dogs, clinicians must be cautious before using any published dosages. Avoid using oral, narrow-spectrum antibiotics (such as β-lactam antibiotics and macrolides), because they may cause severe dysbiosis and clostridium-induced diarrhea.[45] Enrofloxacin (20 mg/kg every 24 hours) can be used if indicated.[20] Some pet prairie dogs can be given oral liquid formulations, whereas injectable drugs may need to be used with those that are more refractory to handling. Dosages for several commonly used drugs are listed in Table 24.8.

DISEASES

Very few medical conditions have been reported in detail in prairie dogs. Wild prairie dogs can harbor a wide range of viral, bacterial, and parasitic pathogens that are rarely reported in captive animals. A variety of external (fleas, lice, ticks, and mites) and internal (worms and coccidia) parasites have been reported in wild and, to a lesser degree, in captive animals, and dermal and fecal examinations should be performed routinely.[32,34,37] Noninfectious diseases are relatively common in captive prairie dogs and include obesity, dental disease (elodontoma/pseudo-odontoma and malocclusion),

neoplasia (hepatocellular carcinoma), trauma (bite wounds, falling), and pododermatitis (abrasive cage materials).[23,33,37,52]

Dental Diseases

The constant eruption of the incisors is leveled by an oppositional incisor abrasion from gnawing on objects or a high-fiber diet, at a suggested optimal rate of 1 mm/day. Captive prairie dogs offered a suboptimal diet (human food, low fiber) will commonly develop incisor malocclusion and sometimes secondary cheek tooth resorption. In these cases, perform dental examination with the animal anesthetized; the oral cavity and the teeth can be further evaluated by using an otoscope or endoscope. Diagnostic imaging (radiography and computed tomography) is indicated in cases of suspected dental disease. Dental-related abscessation is uncommon in prairie dogs and dental correction is performed as in rabbits and other rodent species with similar conditions (see Chapter 36). The offered diet should be optimized to minimize the recurrence of the condition.[7,38]

Captive prairie dogs are often presented for dental-related disease and sometimes secondary upper respiratory signs with respiratory distress. Differential diagnoses for dyspnea in prairie dogs include elodontoma, bacterial respiratory infection, obesity, cardiac disease (cardiomyopathy, congestive heart failure), pulmonary mites, and mediastinal mass.

Elodontoma

Elodontoma is defined as a hamartoma (benign mass-like overgrowth) of continuously developing odontogenic tissue and alveolar bone at the periapical region of the elodont incisors teeth.[4,16,60] Elodontoma has been referred to by various names that all relate to the same condition: "odontoma," "pseudo-odontoma," and "hamartoma."[4,8,9,14,16,38,48,49,51,60,66] The formation of elodontomas has been described in multiple rodent species other than black-tailed prairie dogs.[4,7,9,38,60] In prairie dogs, mainly the maxillary but also the mandibular incisors are involved.[60] The exact pathogenesis of elodontoma formation is unclear, but repeated biting of the cage wire in captive animals (from boredom or a stress-related stereotypic behavior) has been suggested as the main cause.[38] Dysplastic malformation and folding of the continuously growing tooth substance results in a severe, incisor-apical mass-like deformity.[38] This abnormal growth results in a space-occupying mass that, depending on its location, can invade proximal anatomic structures such as the nasal passages and the oropharynx.[38] Clinical signs are usually severe because the condition often is noticed in an advanced stage of the lesion. Depending on elodontoma location, prairie dogs will present for either respiratory distress (increased respiratory noises, open mouth breathing) or starvation.[38,66] Once an affected animal is stabilized in oxygen, sedate or anesthetize the prairie dog to allow a thorough physical and oral examination. Sedatives can also help improve the respiratory pattern before any further measures are taken: a combination of midazolam (0.5 mg/kg intramuscularly [IM], subcutaneously [SC]) and butorphanol (0.5 mg/kg, IM, SC) can be used to reduce respiratory distress. Results of diagnostic imaging (survey radiographs and computed tomography) will show mineralized opacities at the apical region of the affected incisors (Fig. 24.5).[38,48,49,66] Treatment of elodontomas is surgical. Multiple approaches have been suggested with the goal of removing either the affected incisor or the pathologic mass or both,

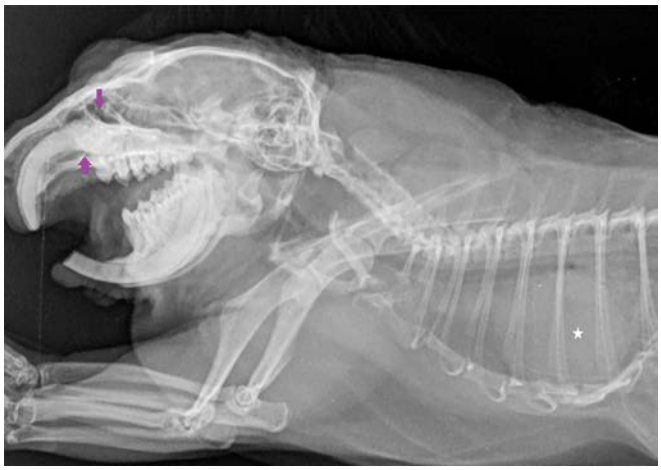


Fig. 24.5 Lateral radiograph of a sick prairie dog presented for respiratory distress. In this case, maxillary elodontoma *(purple arrows)* and cardiomegaly *(white star)* are possible contributing causes for this clinical presentation.

relieving the resultant respiratory obstruction.[38,49,66] Documented techniques include temporary and permanent rhinostomy and tracheostomy, transoral incisor extraction, transpalatal surgical extraction, and dorsal and lateral surgical extraction of the incisors.[4,6,8,14,49,60,66] These procedures can be technically difficult, and the outcome varies based on the specific condition (unilateral vs bilateral), the technique, and the experience of the surgeon. Some procedures, such as stenting, may only provide short-term resolution. Postoperatively, prairie dogs require intensive care, including analgesia, antiinflammatory drugs, assisted feeding, and nasal and stent flushing.[4,6,8,14,49,60,66]

Neoplasia

Hepatobiliary tumors are common in prairie dogs, with one study documenting 49% (26/53 cases) of tumors evaluated originating from the hepatobiliary system.[63] Hepatobiliary tumors that have been reported include hepatocellular adenoma, biliary cystadenoma, and hepatocholangiocarcinoma with most being hepatocellular carcinomas (HCC).[3,27,58,61,63,65] Hepatocholangiocarcinoma has been reported in other members of the Sciuridae family (woodchucks and ground squirrels) in association with a hepadnavirus (woodchuck hepatitis virus), similar to people infected with hepatitis B virus.[67] The similarity between HCC in prairie dogs and other Sciuridae suggests a viral cause.[67] In a single report of HCC in a prairie dog, deep sequencing of the tumor tissue identified the presence of a hepadnavirus, and electron microscopy showed the presence of viral particles similar in structure to other hepadnaviral particles.[67] Infection of the liver with *Helicobacter* species has also been suggested as an underlying cause.[3] Clinical signs in prairie dogs with HCC are lethargy, anorexia, weight loss, acute respiratory distress, or a palpable abdominal mass.[27,58,63,65] Results of clinical pathologic testing may show increased blood alkaline phosphatase concentration.[58,67] Abdominal radiographs may show hepatomegaly and a mass effect, and abdominal ultrasonography is useful in evaluating the hepatic echotexture.[30,58] Ultrasound-guided fine-needle aspiration and cytologic examination may show hepatoid cells with varying degrees of anaplasia, but liver biopsy is often required for a definitive

diagnosis. Metastasis to the lungs, kidneys, and lymph nodes were reported in up to 32% of prairie dogs diagnosed with HCC.[63,65] Attempted treatment of HCC in a prairie dog has not been reported. Liver lobectomy or resection of an isolated liver mass can be considered but may only be palliative given the suspected viral cause.

Other benign and malignant tumors have been reported in prairie dogs, including osteosarcoma, oral squamous cell carcinoma, lymphoma, intestinal leiomyoma, intrathoracic lipoma, anaplastic large T-cell lymphoma, and several others.[23,39,43,44,55,57,63]

Hepatobiliary Research and Disease

Because of the similarity to human bile and gallstone composition, and their tendency to form cholesterol stones, prairie dogs are used as a research model for gallstone etiopathogenesis and prevention, and gallbladder electrogenic bicarbonate secretion.[3,12] Studies have suggested a connection between infection with *Helicobacter* species and cholesterol cholelithiasis, cholecystitis, and gallbladder cancer.[3] In one study of wild-caught research prairie dogs, 12 of 34 were positive by polymerase chain reaction (PCR) testing for a novel *Helicobacter marmotae*-like species (*Helicobacter* sp. Prairie Dog 3) identified from the liver, and 10 of 34 were PCR-positive for a novel *Campylobacter* species identified in the intestine (*Campylobacter* sp. Prairie Dog).[3] Inflammatory lesions were present in the livers of five animals and a hepatocellular carcinoma in one *Helicobacter*-positive animal. Despite the suggested viral cause, pathology may be related to *Helicobacter* infection, similar to *H. marmotae* in woodchucks and mice, and *Campylobacter jejuni* experimentally can induce chronic hepatitis.[3]

Cardiac Diseases

Anecdotal and partial reports suggest that cardiomyopathy is a relatively common disease in captive prairie dogs.[23] Cardiomyopathy occurs in prairie dogs around 2 to 4 years of age,[23] and affected animals usually present in respiratory distress (Fig. 24.5).[64] Nutritional deficiency is speculated as a potential underlying cause.[23] There is a single case report of a membranous ventricular septal aneurysm in a black-tailed prairie dog.[13] As in all other species, the diagnosis of cardiac disease in prairie dogs requires both radiography and echocardiography.[24,64] Measurements of blood cardiac troponin I concentration should show near-zero values in healthy prairie dogs.[24]

Parasitic Diseases

Reports of parasitic infections (internal and external) are relatively uncommon in captive prairie dogs. *Baylisascaris nematodiasis* have been anecdotally reported.[33] A group of zoo-kept prairie dogs was diagnosed with passing oocytes of *Eimeria* species on routine fecal examination; all animals were successfully treated with ponazuril (30 mg/kg orally [PO]) administered in two treatments 48 hours apart.[25] Another group of captive prairie dogs showed bilaterally symmetrical alopecia extending from the mid-dorsum to the thighs and tail.[34] All life stages of *Demodex* mites were identified in skin scrapings, and treatment with amitraz (250 parts per million) resulted in resolution of lesions and hair regrowth.[34]

Zoonoses

Yersinia pseudotuberculosis, *Yersinia pestis,* and *Francisella tularensis* are reported in wild and captive prairie dogs.[1,35,36,50,54,72] Because of their tendency to cannibalize sick prairie dogs, any animal that is presented with sub-mandibular lymph node enlargement is considered suspect for any infectious disease. Leptospirosis is another important zoonotic disease, and captive prairie dogs may demonstrate exposure to leptospirosis, likely from wild rodent reservoirs.[47] Relocation of wild prairie dogs had led to clinical blastomycosis respiratory disease in their handlers.[56] Dermatophytosis (*Microsporum gypsum*) has been anecdotally reported in captive prairie dogs, and both can also affect people.[33] As in all mammals, rabies is a concern but to date, this disease has never been reported in a prairie dog.

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25

Rats and Mice

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TAXONOMY AND NATURAL HISTORY

The word *rodent* is derived from the Latin verb *rodere,* which means "to gnaw." This refers to the most distinguishing feature of this group, the elodont (continuously erupting) incisors possessed by all members of this order.[11] Although body size varies greatly, in general rodents possess a uniform body structure with various adaptations. Although the medical approach to the many small rodents species commonly kept as pets is similar, unusual species are sometimes encountered in practice, and more specific information about these species can be found elsewhere.[41] The chapter will focus on the biology and diseases of the two of most iconic species of rodents: rats and mice.

Mice

The mouse belongs to the family Muridae, subfamily Murinae. Most pet mice are domesticated from the wild house mouse (*Mus musculus*). Originally, house mice were bred by mouse fanciers for special coat colors and eventually were used for laboratory research.[27] Wild *Mus musculus* live in close proximity to humans, which has likely contributed to their success as a research model.[65] Wild mice are socially gregarious and associate in family groups called *demes*.[28] Each deme is composed of a dominant breeding male, a hierarchy of females, subordinate males, and juveniles. Because of this natural behavior, female mice usually do well when housed together, but intact adult males should not be kept together, because aggression, injury, and death can result. Mice are omnivorous and nocturnal, although they are easily roused during daylight hours. Adult mice weigh approximately 30 g. Mice make good pets for older children (10 years of age and up) because they move more quickly compared with rats, so younger children may not be able to handle them. Female mice or castrated male mice are recommended over intact males because of the strong odor of the latter.[44]

Other, less common species, including a variety of African spiny mice (*Heteromys* species), are kept as pets, but their

smaller size makes them more difficult for children to handle. Characterized by their dorsal, inflexible spine-like hairs, African spiny mice are likely more closely related to gerbils and are omnivorous.[15]

Rats

Rats also belong to the family Muridae, subfamily Murinae. Pet rats are derived from the brown rat or Norway rat (*Rattus norvegicus*). Domestication of this species was most likely begun in the 1800s, as a means to provide enough rats for the popular sport of rat baiting.[28] Wild rats are social, burrowing animals, and domestic rats will also burrow if given the opportunity. Rats are omnivorous and nocturnal, similar to mice. Unlike mice, rats are communal and do well housed in mixed groups of several males and females.[33]

Rats are common pets and are considered one of the better rodent pets because of their larger size and calm nature. Rats are most popular in the pet market in hooded color varieties, in which the coat color is present only over the head and shoulders. Rats are generally hardy as young animals but may suffer from obesity, chronic respiratory disease, and mammary tumors when older. Rats are large enough to be easily grasped by children, and they rarely bite. Some may be excitable and run when removed from their cages; however, rats have been known to return to their cages after "escaping."[33] Strange animals can be introduced successfully on neutral territory. Rats are relatively intelligent and can be trained to perform a variety of tasks for a treat.

ANATOMY AND PHYSIOLOGY

General Characteristics

Mice and rats possess a generic rodent body structure: a long body that tapers toward the head, short legs with four front toes and five hind toes, and a long tail. Rodents do not pant and have no sweat glands; therefore, their ability to withstand high temperatures is limited. Heat dissipation occurs through the ears and tails.

Sensory Organs

Both mice and rats have bulging eyes and may appear exophthalmic. Because of this feature, take care to keep the eyes moist while the rodent is under anesthesia. The Harderian gland, which lies behind the eyeball, produces lipid- and porphyrin-containing secretions that aid ocular lubrication and may play a role in pheromone-mediated behavior.[64] These secretions impart a red tinge to the tears and fluoresce under ultraviolet light. Normally, the lacrimal secretions are spread over the pelage during daily grooming. However, in stressful situations and in certain disease conditions, tears may overflow; this can be inaccurately diagnosed as bleeding from the eyes and nose.

The vibrissae, or sensory whiskers, are a very important sensory organ of touch for detecting objects and helping the animal navigate in dark environments.[34] This is especially true for albino rats, whose eyesight is poor relative to their pigmented counterparts.

Integument

Both mice and rats come in many different coat colors, bred specifically by fanciers. Generally, mice and rats are fastidious self-groomers and will keep their coats clean without baths. The white hair coat of rats often yellows with age, and the tail becomes drier and scaly. Aged male rats develop brown, granular sebaceous secretions at the base of their hair shafts, which some owners may mistake for ectoparasitism.

Gastrointestinal

Mice and rats have a common dental formula: 2 (I 1/1, C 0/0, M 3/3). The four prominent, incisors are elodont, or continuously growing throughout life, whereas cheek teeth are anelodont and do not grow after eruption. The enamel of most common rodents is white; however, some species may have enamel that is orange to yellow. The crowns of the mandibular incisors are longer than the maxillary incisors and may be mistakenly assumed to be overgrown. In general, the crown/length ratio for the upper to lower incisors is approximately 1:3.

Mice and rats are monogastric, with an aglandular forestomach that is separated from the glandular stomach by a limiting ridge (margot plicatus). It was thought that this limiting ridge was the reason that mice and rats do not vomit; however, other factors, such as the pressure and strength of the esophageal sphincter and crural sling and the innervation of the diaphragm, may also play a role.[60,66] It has also been suggested that rodents probably lack the critical brainstem circuitry required to generate an emetic response.[38] Because of their inability to vomit and high metabolic rate, mice and rats should not be fasted before anesthesia. The cecum is relatively large in these species, with an elongated colon. Most rodents practice some degree of coprophagy in which ingested fecal pellets presumably provide nutrients, such as B vitamins, produced by the colonic bacteria. Rats do not have a gallbladder.[27]

Urogenital

The urinary and reproductive tracts terminate in separate urethral and vaginal orifices in female rats and mice. Females are spontaneous ovulators and polyestrous, with stages of the estrous cycle that can be determined with vaginal cytology. Mammary tissue is extensive in rodents and ranges from over the shoulders to the perianal region. Mammary tumors can develop anywhere along this tract. Most female rats have six pairs of nipples, whereas mice have five; however, variations in numbers can be seen.

Like most other male rodents, mice and rats have open inguinal canals, an os penis, and a complex urogenital system that contains several prominent accessory glands. Male mice produce a characteristic musty odor. Pheromones play an important role in mouse behavior and are mediated through tissues such as the vomeronasal (Jacobson's) organ, which is located in the floor of the nasal cavity. Estrus is suppressed in female mice housed in large groups (the Whitten effect). Recently bred mice that are exposed to a strange male may have impaired implantation (the Bruce effect).[27,28] Normal physiologic, reproductive, and growth reference values are presented in Tables 25.1 and 25.2.

Sexing

Determining the sex of most rodents is easy in mature animals but can be more challenging in very young ones. In general, the distance between the anus and the genital papilla is a reliable method of determining the sex of young animals. The anogenital distance is greater in males than in females, and the genital papilla is usually more prominent and has a round opening in the

TABLE 25.1 Normal Physiologic Reference Values for Mice and Rats[a]

Value	Mouse	Rat
Average life span, months	12–36	26–40
Maximum reported life span, months	48	56
Average adult weight (male), g	20–40	267–500
Average adult weight (female), g	22–63	225–325
Heart rate, beats per minute	450–800	300–500
Respiratory rate, breaths per minute	106–7230	71–146
Tidal volume, mL	0.15–0.29	0.6–1.5
Minute volume, mL	24	220
Rectal temperature, °C	37.1	37.7
Approximate daily diet consumption of adult, g	3–5	15–20
Approximate daily water consumption of adult, mL	5–8	22–33
Approximate daily fecal production, g	1–1.5	9–15
Recommended environmental temperature, °C	24–25	21–24
Recommended environmental relative humidity, %	45–55	45–55
Total blood volume, mL/kg	70–80	50–65

[a]Average reference values from data given in references 7, 28, 32, 36, 40, and 50. Note that the ranges should be considered as guides; values are likely to vary between groups of animals according to such variables as strain, age, sex, fasted, and methodology.

TABLE 25.2 Normal Reproduction and Growth Reference Values for Mice and Rats[a]

Value	Mouse	Rat
Estrogen cycle length, days	4–5	4–5
Estrus (heat) duration, hours	9–20	9–20
Length of gestation, days	19–21	21–23
Pups per litter	7–11	6–13
Weight at birth, g	1–1.5	4–6
Eyes open, days	12–14	12–15
Ears open, days	10	2.5–3.5
Hair coat starts, days	10	7–10
Start to eat dry food, days	12	14
Optimal weaning age, days	18–21	21
Age of maturation of male, weeks	6	4–5
Age of maturation of female, weeks	6	4–5
Recommended minimum breeding age, weeks	8	9
Chromosome number, diploid	40	42

[a]Average reference values from data given in references 7, 8, 28, 50 and 80. Note that the reference values may not represent the mean or range for certain populations or strains of animals; the values should be interpreted as approximations.

male (Fig. 25.1). Examining multiple young animals to make a comparison is helpful. The testes of mature males are well developed, especially in rats. Holding the rodent vertically or applying gentle pressure directed caudally on the abdomen allows the testes to pass from the abdomen through the inguinal canal into the scrotum. Nipples are present only on the females of these species and can be seen at around 10 days of age.

HUSBANDRY

Housing

Suitable enclosures for rodents should be escape-proof and easy to clean. Although colorful and interesting, multilevel cages with tubes, wheels, and hide boxes may be so difficult to disassemble that basic cleaning is neglected. Manufacturers recommend that the entire cage be disassembled and washed thoroughly, which in reality is rarely done. Newer multilevel wire cages sit on a plastic base and can be separated to facilitate cleaning (Fig. 25.2). This type of cage provides the additional benefit of separating living space up and away from urine and feces. Features of optimal enclosures are slide-out or easy-to-remove bottoms for ease of cleaning, bottoms with high sides to contain bedding, adequate ventilation (aquariums are not ideal owing to poor ventilation), large doors for easy access to the pet, and a secure locking mechanism for each cage opening.

Frequent cleaning of the cage is critical in the care of pet rodents. Failure to clean the cage results in the buildup of ammonia and contributes to stress and illness. In mice and rats, *Mycoplasma pulmonis* organisms multiply more rapidly in the presence of ammonia levels of 50 to 100 parts per million.[71] Frequency of cage cleaning depends on the cage size and number of animals housed. Advise owners to notice the odor of the bedding; anything other than the scent of clean litter indicates that the cage should be cleaned. Provide food in heavy crocks or food dispensers so that the containers will not be tipped over.

Bedding choices include recycled paper, corncob, shredded paper, and wood shavings such as pine and various hardwoods. Much debate exists on the use hardwood and aromatic shavings such as cedar; anecdotally, their use is linked to skin and respiratory disease. Paper bedding is generally preferable, although these products are more expensive than wood shavings. Reclaimed wood pulp bedding is not recommended because of significantly increased intracage ammonia and nasal epithelium pathology seen in mice housed on this bedding material.[24] When compared with 20 other types of rodent bedding, paper bedding had the lowest levels of endotoxin and coliform levels.[86] In rats, the rate of sneezing and incidence of lung pathology was higher in animals housed on aspen shavings than in those housed on paper bedding.[10] However, results of one study in laboratory mice found no difference in growth, food intake, oxygen consumption, immunoglobulin E antibody concentrations, or general appearance and behavior in mice kept on paper bedding, cedar shavings, or pine shavings over a 4-month period.[6] Regardless of the bedding material chosen, emphasis should be placed on changing dirty bedding frequently to avoid development of disease.

Enrichment refers to providing mental stimulation and is appropriate for all captive animals. For rodents, enrichment usually includes such things as exercise wheels, hide boxes, materials to shred, treats wrapped in paper or hidden in toys, and time spent outside the enclosure interacting with the owner. Hide boxes can be commercially purchased or constructed from readily available materials such as polyvinyl chloride (PVC) pipe or cardboard boxes. Cardboard provides the additional advantage of a material that can be shredded, destroyed, and discarded when soiled. Smaller cat treat balls have been used successfully with

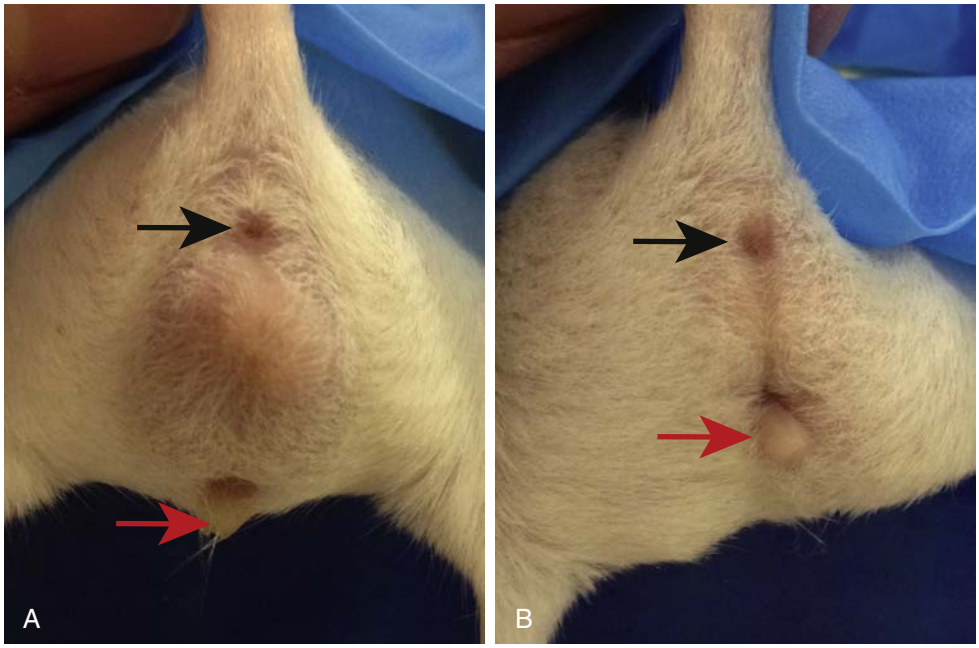


Fig. 25.1 Sexing mice based on anogenital distance, which is the length between the anus *(black arrow)* and the genital papilla *(red arrow)*. Males (A) have a greater anogenital distance compared with females (B).



Fig. 25.2 Ideal habitat for pet rats. The cage portion can be separated from the base for easy cleaning. Note the cloth and plastic "dens," exercise wheel, and cardboard box filled with paper for enrichment.

larger rodents. Many small rodents enjoy exercise wheels, and plastic exercise wheels that are almost noise-free are available.

Diet and Feeding

Rodents naturally hoard food items, and exactly how much food is actually being consumed is difficult to gauge by the rate of disappearance from the feeder. Water can be provided in bowls, but good-quality water bottles are preferred because they will prevent bedding from soiling the water. Water bottles can malfunction over time, resulting in blockage or leakage. Educate owners to change water and test water bottles daily.

Most rodents are omnivorous, often eating grasses, seeds, grain, and occasionally invertebrates in the wild.[44] Dietary requirements of species in laboratory settings are well established. In the pet environment, needs are best met with a formulated diet supplemented with small amounts of fresh foods and seeds for variety and interest. Although seed mixes are popular choices for rodents, these diets often lead to selective feeding and obesity. Animals usually consume high-calorie seeds (sunflower) and ignore formulated pellets, resulting in dietary imbalance. Although many rodents have such a short life span that dietary deficiency is rarely recognized, the most common adverse outcome in rats is obesity. Various studies have demonstrated increased longevity and reduction of certain diseases in rats maintained on a calorie-restricted diet.[56]

Protein requirements are 14% to 16% in mice and rats,[44] and formulated diets should reflect these requirements. Diets for actively breeding animals should contain higher levels of protein.

Breeding and Neonatal Care

Both mice and rats are successful breeders in captivity, and dystocia is uncommon.[79] The nesting instinct is strong in these species, with nest-building behavior occurring before parturition and even without a litter present (Fig. 25.3).[79] Therefore providing materials that can be used for nest building (such as shreddable paper products) is important. After the litter is born, the nest should be minimally disturbed for at least 2 days postpartum because increased stress, especially in mice, may increase cannibalism of pups by the dam.[33] Pups are born hairless with closed eyes and ear canals[79] and without the ability to thermoregulate; thus an adequate nest helps to improve breeding success.[29] Litter size can vary dramatically depending on the strain and age of the dam.[33] Weaning typically occurs at around 21 days in both mice and rats, once the young can eat solid food.[28,77]



Fig. 25.3 Nesting behavior in mice. Both mice and rats will naturally nest or burrow. Mice, in particular, have a strong drive to build a nest for thermoregulation and comfort, even in the absence of a litter of pups.

RESTRAINT AND EXAMINATION

The handling and restraint of mice and rats can be challenging. The key is to maximize diagnostic information while maintaining safety for both the examiner and the patient. If at any time the animal appears to be in distress, release it immediately and plan an alternative technique.

Many owners bring pet rodents to the clinic in their normal enclosures, which is helpful in terms of observing husbandry conditions and examining fecal output. However, attempting to retrieve a rodent from colorful caging tubes is time-consuming, can be stressful for the animal, and is best avoided. Therefore request that owners confine the pet to a separate carrier or a small travel cage within the home enclosure to facilitate capture and restraint.

The first step to rodent examination is close observation. Watch the rodent in its cage for quality of respirations, activity, condition of grooming, and the presence of a head tilt or discharges. If dyspnea or depression is observed, be extremely careful when handling the animal, as it is probably very sick and could die from the stress of a physical examination. At the same time, warn the owner of your guarded prognosis.

In general, restraint can be accomplished by three methods: (1) examining the animal as it is loose on the table; (2) restraining the animal with small towels or cloths; or (3) manual restraint. In some cases, combinations of the above methods are used. Scruffing is effective for mice, but rats do not tolerate this form of restraint. To scruff a mouse, gently grasp the base of the tail with one hand, and then grip the loose skin from the lateral aspects of the neck and over the shoulders with thumb and forefinger of the other hand (Fig. 25.4). Failure to incorporate enough skin allows the animal to rotate and bite the restrainer's fingers. For rats, the author's preferred method of manual restraint is by first gently grasping the base of the tail, and then restraining the shoulders and thorax using "the claw" or "baseball" method (Fig. 25.5). Place the index and third fingers on either side of the head, then gently wrap the thumb and remaining fingers around the thorax under the axillae, taking care not to squeeze too firmly on the thorax, which could restrict breathing.

Extremely fractious or distressed rodents benefit from mild sedation for examination or diagnostic testing, but use caution when sedating sick or debilitated patients. In general, if the animal is alert enough to defend itself vigorously, it will tolerate sedation. Induction with gas anesthesia in a small induction box or large facemask is the least stressful for both veterinarian and patient (Fig. 25.6). For further details on sedation and anesthesia for rats and mice, see Chapter 37.

Weight measurement is essential for calculating appropriate doses of medications and provides an opportunity for gauging the rodent's temperament before the actual physical examination begins. Rodents are easily weighed in metal or plastic containers placed on a small digital gram scale. The carrier in which the rodent is presented can sometimes also be used as the weigh basket.

The physical examination itself in rodents is similar to that in other species. However, special tools such as a transilluminator, binocular loupe, bivalve nasal speculum, and otoscope can improve visualization in small patients. An otoscope or bivalve nasal speculum can be used to examine the mouth and ears of rats. However, general anesthesia is usually required for a thorough dental examination. Lymph nodes and glands of the head can be observed for size and palpated for consistency. Assessment of the head is probably the most time-consuming part of the examination. Take care during abdominal palpation, because overzealous palpation can result in visceral rupture. In rodents, it is especially important to examine the anogenital region for discharges and staining of the fur or skin. When a rodent is picked up, it generally urinates and defecates. Have a dipstick ready to perform an immediate urinalysis or a syringe handy to aspirate urine off a clean surface for urinalysis; feces can be caught in a small tube and examined later if required. Palpate the limbs for tenderness or fractures and pay special attention to the paws, noting the length of the nails and the state of the footpads. Rodents are fastidious groomers and therefore can groom away evidence of underlying disease easily. Observe the medial aspect of the front legs for crusts, debris, alopecia, or porphyrin staining, which may occur from excessive grooming associated with nasal discharge. Also, keep in mind that some cage mates are aggressive groomers and can remove any evidence of illness by keeping their mates well groomed.

Respirations and heart rate are difficult to measure in rodents because they are rapid in healthy animals; instead, look for signs of dyspnea. A sensitive pediatric stethoscope is useful for auscultating larger patients. Some respiratory infections, such as mycoplasmosis, are clinically silent. These diseases can be better heard than seen; abnormal sounds called "chattering" in mice and "snuffling" in rats are noticeable without a stethoscope. It may be useful to put the rodent next to your ear and perform a few gentle chest compressions to evaluate audible respiratory excursions. Wheezing or snuffling may not be present at rest, but when chest compressions are performed to create deep respiration and exhalation, they may often become apparent.

The value of determining rectal temperature is questionable. Physical examination combined with attempts to measure rectal temperature causes stress, which can increase body temperature. Core body temperature in mice and rats varies daily from 96.5°F to 100.5°F (36°C–38°C) because of circadian variation, sex, and age.[73] Rectal temperatures can be measured safely with the use of small semiflexible temperature probes connected to a digital clinical thermometer.



Fig. 25.4 Restraint method for mice. First gently grasp the tail near the base (A), then scruff the skin around the dorsal neck (B). Be sure to include enough skin in the scruff so the mouse cannot turn its head to bite the handler.



Fig. 25.5 Restraint method for rats. Gently grasp the rat around the thorax with the index and middle fingers on either side of the head and the thumb under the axilla. (Courtesy Angela Lennox, DVM.)



Fig. 25.6 Induction of general anesthesia in a sedated rat by using a standard small animal mask as an induction chamber (A). Once the animal has lost its righting reflex, it can be taken out of the induction chamber and anesthesia can be continued by placing the nose into the gas inflow adapter (B) or in an extra small face mask (C). (Courtesy Angela Lennox, DVM.)

CLINICAL TECHNIQUES

Sample Collection

Diagnostic testing can provide the same benefits in rodents as it does in other species. Improved techniques and the ability to acquire meaningful results from small sample sizes make sample collection possible and practical in rodents. Reference intervals for hematologic and biochemical testing, serum protein electrophoresis, and urinalyses are presented in Tables 25.3 through 25.7. Reference values are often derived from laboratory populations and will vary with animal age, sex, strain, and husbandry, as well as with the method of sample collection and

TABLE 25.3 Hematologic Data for Mice

Value	Male[a] (n = 133)	Female[a] (n = 133)	Mixed sex[b]
Hematocrit, %	53 (39–74)	51 (38–64)	42–44
Hemoglobin, g/dL	14.4 (11.9–18.4)	14.0 (11.2–17.8)	13.4 (12.2–16.2)
Red blood cells, $\times 10^6/\mu L$	9.5 (7.3–12.3)	9.1 (7.2–11.4)	8.7–10.5
White blood cells, $\times 10^3/\mu L$	8.6 (4.4–14.0)	8.0 (4.6–16.2)	8.4 (5.1–11.6)
Neutrophils, %	23.5 (8.7–55.7)	19.1 (7.3–41.8)	17.9 (6.7–37.2)
Lymphocytes, %	67.2 (37.5–85.0)	71.4 (43.5–86.5)	69 (63–75)
Monocytes, %	6.8 (2.8–13.1)	6.8 (3.4–13.4)	1.2 (0.7–2.6)
Eosinophils, %	2.6 (0.3–5.2)	2.1 (0.2–6.6)	2.1 (0.9–3.8)
Basophils, %	0.4 (0.0–1.70)	0.4 (0.0–1.6)	0.5 (0–1.5)
Platelets, $10^3/\mu L$	1580 (736–2374)	1494 (469–2364)	600 (100–1000)
Mean corpuscular volume, fL	55.8 (46.5–69.0)	56.6 (47.5–66.7)	—
Mean corpuscular hemoglobin, pg	15.2 (13.1–18.0)	15.5 (12.9–18.1)	—
Mean corpuscular hemoglobin concentration, g/dL	27.5 (21.3–33.9)	27.5 (21.9–33.5)	—

[a]Values are given as mean with 95% interval low and high. Charles River outbred mice, Crl:CD-1 (ICR), 8–10 weeks, raised under optimal laboratory conditions. (Available at http://www.criver.com/files/pdfs/rms/cd1/rm_rm_r_cd1_mouse_clinical_pathology_data.aspx; information accessed on November 27, 2016.)
[b]Values expressed as means with range or range, from reference 28.

TABLE 25.4 Biochemical Data for Mice

Analyte	Male (n ≅130)[a]	Female (n ≅ 130)[a]	Mixed sex[b]
Albumin, g/dL	3.3 (3.2–3.9)	3.4 (2.6–4.1)	2.5–4.8
Alkaline phosphatase, IU/L	136 (101–207)	156 (37–249)	51–285
Alanine aminotransferase, IU/L	47 (28–64)	42 (18–71)	29–191
Aspartate aminotransferase, IU/L	78 (47–120)	84 (45–182)	—
Bilirubin total, mg/dL	0.3 (0.2–0.4)	0.3 (0.1–0.4)	0.1–0.9
Blood urea nitrogen, mg/dL	17 (16–22)	16 (9–24)	18–29
Calcium, mg/dL	11.0 (10.2–12.0)	10.9 (9.9–12.4)	8.7–10.1
Chloride, mEq/L	113 (106–114)	116 (107–131)	—
Cholesterol, mg/dL	185 (168–275)	148 (85–244)	—
Creatinine, mg/dL	0.3 (0.3–0.3)	0.3 (0.0–0.4)	0.1–0.4
Glucose, mg/dL	240 (147–361)	218 (137–319)	90–193
GGT, IU/L[c]	3 (0–13)	3 (0–19)	—
Phosphorus, mg/dL	11.2 (9.3–11.4)	10.6 (7.9–14.1)	5.4–9.3
Potassium, mEq/L	10.0 (9.3–14.2)	9.40 (7.84–11.34)	—
Sodium, mEq/L	154 (148–155)	154 (138–169)	—
Total protein, g/dL	5.8 (5.4–6.4)	5.7 (4.7–6.6)	4.6–6.9
Triglycerides, mg/dL	213 (128–288)	228 (75–449)	—

[a]Values are given as mean with 95% interval low and high. Charles River outbred mice, Crl:CD-1 (ICR), 8–10 weeks, raised under optimal laboratory conditions. (Available at http://www.criver.com/files/pdfs/rms/cd1/rm_rm_r_cd1_mouse_clinical_pathology_data.aspx; information accessed on November 27, 2016)
[b]Values expressed as range. Serum samples courtesy Carolyn Cray, PhD, University of Miami Miller School of Medicine. Ortho (Kodak:Ektachem) 700XR.
[c]The n value for GGT measurement was 30 for males and 29 for females.
GGT, Gamma-glutamyl transpeptidase.

TABLE 25.5 Hematologic and Serum Biochemical Data for Rats

Value/Analyte	Male[a] (n > 220)	Female[a] (n > 220)	Mixed sex[b] (n = 50)
Hematologic Testing			
Hematocrit, %	43.3 (28.3–49.2)	42.2 (39.6–45.9)	33.0–47.0
Hemoglobin, g/dL	15.4 (14.7–16.6)	14.6 (13.5–15.5)	11.2–15.9
Red blood cells, $\times 10^6/\mu L$	8.3 (7.9–8.9)	7.7 (7.2–8.1)	6.4–8.2
White blood cells, $\times 10^3/\mu L$	11.1 (9.8–12.9)	8.6 (7.0–10.7)	4.7–9.4
Neutrophils, %	11.1 (9.0–13.6)	9.7 (7.7–14.2)	7.0–32.0
Lymphocytes, %	83 (80.1–87.1)	85 (80.6–87.0)	57.0–91.0
Monocytes, %	2.6 (1.1–4.1)	2.3 (1.4–3.3)	2.0–5.0
Eosinophils, %	1.3 (0.7–2.0)	1.2 (0.6–1.6)	0–4.0
Basophils, %	0.4 (0.3–0.5)	0.4 (0.2–0.5)	0–3.0
Platelets, $\times 10^3/\mu L$	852 (765–1029)	841 (787–1021)	411–626
Biochemical Analysis			
Albumin, g/dL	3.7 (3.3–4.6)	4.2 (3.5–5.3)	2.8–5.3
Alkaline phosphatase, IU/L	125 (104–160)	83 (65–117)	87–381
Alanine aminotransferase, IU/L	35 (27–46)	32 (25–45)	36–80
Aspartate aminotransferase, IU/L	91 (77–110)	93 (72–116)	—
Gamma-glutamyl transpeptidase, IU/L	0.5 (0.0–1.0)	0.5 (0.0–1.0)	—
Bilirubin, total, mg/dL	0.6 (0.2–1.0)	1.1 (0.2–2.0)	0.2–0.7
Blood urea nitrogen, mg/dL	13.4 (10.0–16.0)	13.2 (11–17)	11–23
Calcium, mg/dL	10.2 (9.6–10.9)	10.3 (9.6–11.2)	5.7–12.4
Chloride, mEq/L	104 (101–107)	105 (101–108)	—
Cholesterol, mg/dL	65 (55–89)	78 (66–97)	—
Creatinine, mg/dL	0.6 (0.4–0.6)	0.6 (0.4–0.7)	0.3–0.6
Glucose, mg/dL	157 (121–197)	159 (120–186)	50–135
Phosphorus, mg/dL	7.7 (7.0–9.5)	6.6 (5.6–8.6)	6.5–12.2
Potassium, mEq/L	5.3 (4.6–6.1)	4.9 (4.3–5.9)	—
Protein, total, g/dL	6.4 (6.0–7.1)	6.7 (6.3–7.5)	5.6–7.4
Sodium, mEq/L	144 (141–149)	143 (141–148)	—
Triglycerides, mg/dL	76 (62–92)	61 (51–75)	—

[a]Values given as means with ranges. Charles River outbred Sprague-Dawley Crl:CD(SD) rats, 13–22 weeks of age, raised under optimal laboratory conditions. Bayer Technicon H1E and BMC Hitachi-Model 717 analyzers were used. (Available at http://www.criver.com/files/pdfs/rms/cd/rm_rm_r_clinical_parameters_cd_rat_06.aspx; accessed November 27, 2016.)
[b]Values given as ranges. Data courtesy Carolyn Cray, PhD, University of Miami Miller School of Medicine. Ortho (Kodak:Ektachem) 700XR; Automated analyzer for cell count, hemoglobin, and hematocrit. Differential based on 100-cell count by using blood smear made at the time of sample acquisition.

TABLE 25.6 Reference Intervals for Serum Protein Electrophoresis for Mice and Rats[a]

Analyte	Mouse	Rat
Albumin, g/dL	2.1–3.4	3.4–4.1
Alpha-1 globulin, g/dL	0.3–0.5	0.4–0.6
Alpha-2 globulin, g/dL	0.8–1.1	0.2–0.6
Beta globulin, g/dL	1.4–1.7	1.3–1.7
Gamma globulin, g/dL	0.2–0.3	0.1–0.5
A/G ratio	0.7–1.1	1.1–1.6

[a]Data courtesy Carolyn Cray, PhD, University of Miami Miller School of Medicine. Analytes measured by Beckman Paragon SPEP II gels in adult animals.

TABLE 25.7 Urinalysis Reference Values for Mice and Rats[a]

Value	Mouse	Rat
Urine volume, mL/24 h	0.5–2.5	13–23
Specific gravity	1.034	1.022-1.050
Average pH	5.0	5.0 -7.0
Protein, mg/dL	Males proteinuric	<30

[a]Average reference values from data given in references 7, 36, and 50. Note that the ranges should be considered as guides; values are likely to vary between groups of animals according to such variables as strain, age, sex, fasting, and methodology.

laboratory methodology used to derive the values. Therefore, these reference ranges should be used only as a guide, to be evaluated in conjunction with physical examination findings and other diagnostic tests to make a diagnosis.

Blood Collection

Because of their small size, blood collection in mice and rats can be risky. Venipuncture should be attempted only in normovolemic, normothermic patients; therefore, blood collection is often delayed until the animal's condition is stabilized. Before collecting a sample, know the sample volume required for the test in question and the maximum blood volume that can be safely acquired from the patient. Ascertain from the laboratory what type of sample (e.g., plasma or serum) and the minimum volume required for a given test. The blood volume of most rodents is approximately 6% to 7% of total body weight[85]; removing a maximum of 10% of the blood volume is generally safe (see Table 25.1). Make modifications to these guidelines according to overall patient condition and, in all cases, collect only the blood volume required for testing.

Recommended venipuncture sites in pet mice and rats are the lateral saphenous, femoral, jugular, and lateral tail veins, as well as the ventral tail artery.[53] In rats, the dorsal tail vein and cranial vena cava may also be used.[53] Collecting blood from the orbital plexus, facial vein, or by cardiac puncture is common in laboratory rodents; however, these are not recommended in pet rodents because of high complication rates and the availability of more suitable options.

Small-gauge needles (25- to 27-guage) with attached small syringes (1 mL or smaller) are recommended for blood collection. In very small patients or with vessels where negative pressure causes collapse of the vessel, consider puncturing the vessel with a clear-hubbed needle only and collecting blood with a heparinized hematocrit tube as it flows into the needle hub. Anesthesia or sedation may be necessary to obtain an adequate blood sample. Keep in mind that use of sedation or anesthesia, as well as different venipuncture sites, has been shown to alter the results of certain hematologic values.[37,53]

A technique for lateral saphenous venipuncture of laboratory rodents has been described that is minimally invasive, does not require anesthesia, can be performed by a single person when combined with the appropriate restraint, and can be repeated at the same location multiple times.[36,37] For use in a mouse, place the mouse head first in a large syringe case that has been punctured to provide several breathing holes near the end (Fig. 25.7). Extend an exposed hind limb by firmly grasping the skin just in front of or just behind the knee (Fig. 25.8). Shave the hair over the lateral tarsal area and apply sterile petroleum jelly or ophthalmic ointment to prevent blood from migrating into the hair. Puncture the vessel at a 90-degree angle to the skin with a needle of appropriate size (a 25-gauge needle is usually sufficient in the mouse). A drop of blood should immediately appear and can be collected into a microcapillary tube or a microtube container. After the required volume has been obtained, release the skin. This usually is sufficient to stop the bleeding; if it is not, apply gentle pressure to the puncture site. This technique may be too stressful for ill or debilitated animals.

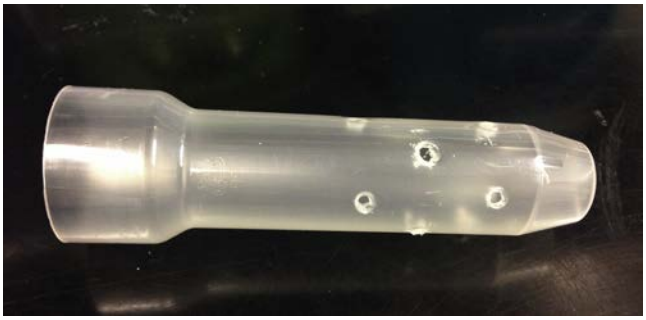


Fig. 25.7 Modified syringe case for mouse restraint. Air holes should be placed near the tip to allow for proper ventilation during restraint.



Fig. 25.8 Restraint of a mouse for lateral saphenous vein blood collection. With the mouse placed headfirst into the modified syringe case, expose one of the rear legs and extend it by pinching the skin behind the stifle. The leg can then be shaved and prepared with sterile ointment for blood collection.

Other site options for collecting blood samples are the lateral tail vein, the ventral tail artery of the rat, and the tarsal veins of larger rodents.[36,85] The lateral tail veins are located on both sides of the tail and are superficial; they can be seen easily in young animals and rats with nonpigmented tails. Warm the tail gently with a warm compress to increase blood flow and occlude the veins by placing a tourniquet around the base of the tail; a rubber band and mosquito hemostat are suitable for this purpose. With a needle of appropriate gauge for the species, enter the skin at a shallow angle at a point approximately one-third down the length of the tail (Fig. 25.9). If the initial attempt at collection is unsuccessful, try again at a site closer to the base of the tail. To avoid collapsing the vessel, use a small-volume syringe to withdraw the sample or collect the blood into a microhematocrit tube as it flows freely from the needle hub. A modified butterfly catheter (i.e., with all but the proximal 5 mm of tubing removed) may also be used.

The jugular vein can be used in both mice and rats, but this technique requires general anesthesia and usually needs two people to perform safely.[63] Shave the area of the ventral neck and gently restrain the patient with the neck hyperextended. The jugular veins should be visible about 2–4 mm lateral to the

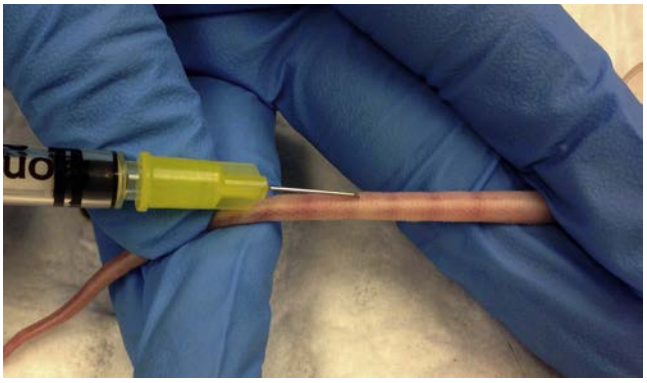


Fig. 25.9 Collecting blood from the tail vein of a mouse. Restrain the mouse using a large syringe case with air holes. The tail can then be exposed and warmed to vasodilate the lateral tail veins. Note the shallow angle of the needle and the starting point at about ⅓ of the way down the tail.



Fig. 25.10 Collecting a blood sample from the cranial vena cava in an anesthetized rat by using an insulin syringe with a 29-gauge needle.

sternoclavicular junction.[37,63] The needle should be inserted directed toward the tail, and the syringe should be withdrawn slowly so as not to collapse the vein. Light digital pressure may be applied at the venipuncture site to allow for hemostasis after the needle is withdrawn.

The cranial vena cava is the largest vessel that is easily accessible in rodents, but it should only be used in rats that are sedated or general anesthesia. Place the animal in dorsal recumbency and prepare the area over the manubrium for venipuncture. Using a 25- to 27-gauge needle with a 1-mL or smaller syringe, approach the vessel from the right or left of the manubrium, angling slightly medially and dorsally (Fig. 25.10). As you advance the needle, apply gentle negative pressure. Entry of the cranial vena cava will result in a flash of blood. If blood does not flow freely, the needle may have passed through or oblique to the vessel or the bevel may be contacting the vessel wall. Rotate or redirect slightly. The vessel is just under the manubrium; therefore deep needle penetration is not needed or recommended. Potential complications include vessel rupture and exsanguination, but this appears to occur rarely and is likely associated with excessive patient movement.

The ventral tail artery in the rat is another option for blood collection.[7] The artery courses along the ventromedial aspect of the tail, although it is not as superficial as the lateral tail veins. Place the sedated or anesthetized animal in dorsal recumbency. Use a 22-gauge needle and a 3-mL syringe from which the plunger has been removed. Alternatively, some practitioners prefer to use a 23-gauge butterfly needle with short tubing connected to a 3-mL syringe. Make the first puncture attempt at a point one-third down the tail's length. Enter the skin at a 20- to 30-degree angle to the tail, with the bevel of the needle facing upward. A perceptible "pop" usually indicates that the artery has been entered, and blood should quickly fill the syringe. The high blood pressure in this vessel negates the need for the negative pressure produced by withdrawal of the plunger. Indeed, the presence of the plunger within the syringe case impairs recognition of correct penetration of the vessel. After the required volume of blood has been collected, withdraw the needle and apply pressure to the puncture site. Note that more time is required to stop the bleeding from the tail artery than from the tail vein.

Urine and Fecal Collection

Many rodents will void during handling, sedation, and induction of anesthesia; thus, it can be difficult to collect an adequate sample volume for urinalysis.[85] Nonsterile samples may be collected by simply picking up the animal and holding it over a clean petri dish or other collection device.[49] Gently expressing the bladder and collecting the sample from the cleansed urinary orifice into a hematocrit tube can also yield enough urine for a dipstick or specific gravity. If neither of these methods is successful, another noninvasive method is lining an enclosed container (such as a plastic transport cage) with clean plastic wrap and allowing the animal time to urinate, then aspirating the sample from the bottom of the container.[49]

For sterile urine samples, cystocentesis may be attempted, although this may not be feasible in small patients. Deep sedation or full anesthesia is recommended. The bladder of all but the most obese rodents is readily palpable. With the animal in dorsal recumbency, use a very small–gauge needle and direct the needle caudally at an oblique angle through the abdominal wall into the bladder. Alternatively, use ultrasonography to locate the bladder for cystocentesis.

Collecting a fecal sample is simple in most rodents because of the large number of fecal pellets produced. Usually, most mice and rats will defecate when picked up or when the tail is lifted gently from the base. Avoid introducing fecal collection loops or devices into the rectum because of the fragile mucosa of the rodent colon.

Bone Marrow Collection

Collecting a bone marrow sample is possible, even in small rodents. Use the intraosseous catheterization technique described in the section below (Therapeutic Techniques) for the femur or tibia. Once the bone is catheterized, an empty syringe may be attached to the needle and aspirated to collect

bone marrow. Indications are the same as for any other species and include nonregenerative anemia of uncertain origin. For optimal quality, prepare samples immediately after collection.

Miscellaneous Sample Collection

Many types of samples can be collected safely in rodents, including skin scrapings, hair samples, fine-needle aspirates, biopsy samples, and thoracic fluid samples. For each patient, carefully consider the type of restraint (manual vs chemical), anatomic variations, and the size of collection equipment (needles and syringes). Use the equipment that is least invasive and as small as possible to collect diagnostic samples.

Diagnostic Imaging Procedures

Radiology and ultrasonography are commonly performed in small pet rodents (see Chapter 38). In brief, diagnostic-quality images require optimal films and settings and an immobilized, well-positioned patient,[12] which usually requires sedation or anesthesia. The increased availability of computed tomography and magnetic resonance imaging has allowed diagnostic imaging to become a useful ancillary examination.[74] Two excellent books designed to provide clinicians with normal anatomic and abnormal comparative diagnostic images are *Diagnostic Imaging of Exotic Pets: Birds, Small Mammals, Reptiles*[47] and *Radiology of Rodents, Rabbits and Ferrets: An Atlas of Normal Anatomy and Positioning*.[76]

Advanced Techniques

Technological advances have made possible electrocardiography and accurate and sensitive recordings of heart rate, respiratory rate, and blood pressure in research rodents.[46] The cost of the equipment for performing these measurements and the invasive procedures that are often necessary for achieving the recordings prohibit routine use of these testing modalities in most veterinary practices.

Therapeutic Techniques

As in most exotic species, therapeutic agents are not licensed for use in rodents, and such use is considered off label. Some medications may be too concentrated for small rodents and will require dilution or further compounding.[77]

Fluids can be administered by the subcutaneous, intravenous, intraosseous, and intraperitoneal routes; the method depends on the overall patient condition (see Chapter 41 Emergency and Critical Care).[18] Intravenous or intraosseous administration is most suitable for unstable, severely dehydrated patients. Placement of an intravenous catheter is difficult in most rodent patients; therefore, intraosseous catheterization is a better option.[52] Studies in multiple species have shown that drug and fluid administration by the intraosseous route results in similar onset of action and peak blood levels as use of the intravenous route.[83] Needles manufactured specifically for the purpose of intraosseous catheterization are available; however, in most small rodents, simple injection needles are appropriate (22- to 27-gauge, depending on patient size). The most commonly used site is the tibia; however, use of the femur has been described as well. Insertion of an intraosseous catheter is uncomfortable for the animal, hence, sedation with a local block or full anesthesia is required. To place a catheter into the tibia, infuse the skin, subcutaneous tissues, and periosteum with lidocaine at 1 to 2 mg/kg and wait for at least 10 minutes. Introduce the catheter at the tibial crest at the insertion site of the patellar ligament to avoid penetrating into the joint (Fig. 25.11). The size and shape of the proximal tibia determine the exact angle of placement, and correct placement is best confirmed by radiography in two views.[52]

Fluid needs for rodent patients that are stable but mildly dehydrated can be met with subcutaneous or oral fluid administration. Administer subcutaneous fluids in the loose skin between the shoulder blades (Fig. 25.12).[18]

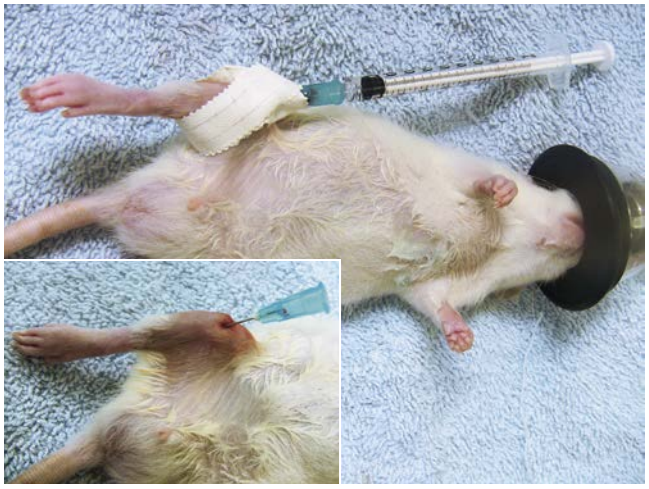


Fig. 25.11 Placement of a 25-gauge needle in the bone marrow cavity of the tibia of a young anesthetized rat. The site is prepared aseptically. The needle is taped in place and can be fitted with a standard injection cap or a small-gauge syringe for intermittent infusion. (Courtesy Angela Lennox, DVM.)



Fig. 25.12 Administering warmed subcutaneous fluids in a rat by using manual restraint.

Intramuscular injections should be given in the caudal aspect of the rear legs or epaxial musculature. Injecting into the lateral leg muscles carries a risk of damage to the sciatic nerve, which can result in lameness or self-mutilation.[18] Use a needle size as small as possible to allow passage of medication and penetration of the skin. Intraperitoneal administration of therapeutics is not advised because of the availability of other sites and potential risk of damage to abdominal structures or inadvertent injection into the gastrointestinal tract (especially the cecum).[18] Indications for intravenous administration of medications are rare; however, intravenous administration is possible in a larger sedated or anesthetized patient if done carefully. An alternative to intravenous injection is injection via an intraosseous catheter.

Oral administration of medications is generally uncomplicated in most rodents and accomplished by carefully restraining the animal and then introducing a syringe into its mouth. Because the volume of medication is often small, insulin syringes with the needle removed allow accurate measurement and ease of delivery. Compounding medication with sweet-tasting bases often increases compliance.

Administering medications in water or food is problematic because of the tendency of rodents to distrust unfamiliar tastes and to cache food, as well as the overall inability to control volume and frequency of administration.[18] Adding medications to water may reduce water intake. For these reasons, direct administration of medications is preferred.

Exercise caution in administering antibiotic therapy to rodents. Streptomycin and procaine are toxic in mice and nitrofurantoin causes neuropathologic lesions in rats. Commonly used antibiotics that are safe to use in rats and mice include amoxicillin/clavulanic acid, enrofloxacin, doxycycline, and trimethoprim-sulfa combinations. A comprehensive list of safe antibiotics and dosages can be found in the *Exotic Animal Formulary*.[13]

Because of the high metabolic rate of rodents, hand feeding is very important in anorectic animals. Hand feeding is generally easily accomplished with the use of a food supplement that can be fed through a small syringe. Hand-feeding products for herbivores, omnivores, or a mixture of both (Critical Care, Oxbow Animal Health, Murdock, NE; EmerAid Omnivore/Herbivore, EmerAid LLC, Cornell, IL) are nutritionally balanced and convenient for use. Strained vegetable baby foods such as mixed greens or sweet potato can be added to improve palatability if needed.

Hospitalization

Rodents are frequently hospitalized for advanced care or diagnostic testing. The hospital room should be quiet and free of visual or auditory signs of potential predators. Enclosures in the hospital must be escape-proof, even if the patient appears unable to attempt escape. Most rodents can be housed in clear square plastic pet carriers with snap-on tops. These carriers can be placed into most commercial pet incubators for temperature regulation (Fig. 25.13). Ideal bedding is light-colored towels or paper to allow easy identification of urine, feces, and abnormal discharges such as blood. Hospitalized rodents benefit from a hide box, which can be quickly constructed from a small cardboard box or paper. Stock a variety of rodent foods for feeding hospitalized animals or request a supply from the pet's owner before hospitalization.



Fig. 25.13 Hospitalized rodents are adept at escape. This rat is housed in an escape-proof plastic pet container inside a standard cage.

Preventive Medicine

Prevention of disease in rodents is far more successful than treatment. Disease prevention is based on ensuring the purchase of healthy animals and maintaining good husbandry practices. Measures that can be taken to ensure good husbandry are as follows: (1) providing balanced fresh food that is appropriate in protein and caloric content, (2) providing clean fresh water, and (3) cleaning cages on a regular basis to prevent accumulation of excess urine and fecal material. Adequate shelter, including providing shade from direct sunlight, avoiding drafts and extreme changes in temperature or humidity, and providing areas in which to nest and hide are also helpful in preventing disease development. If housing multiple animals, isolating sick animals from the rest of the group and protecting vulnerable animals from more aggressive members of their group (e.g., young animals from older animals) can be crucial to maintaining the health of the group. Stress reduction via separating natural predators living in the same household (e.g., mice from cats) is also ideal. Other sound husbandry practices include housing different species separately to prevent interspecies disease transmission (e.g., rats carry *Streptobacillus moniliformis,* a cause of septicemia in mice, in their nasopharyngeal cavities) and reducing obesity by limiting food intake and providing cage accessories (e.g., exercise wheels, tunnels, and ramps) that allow play and exploration.

Unlike larger companion animals, pet rodents are not vaccinated. Off-label treatment with avermectins (e.g., ivermectin, selamectin, moxidectin) has allowed routine systemic treatment of pet rodents for pinworms, mites, and lice. For ectoparasite and endoparasite treatment recommendations, refer to Table 25.8.

TABLE 25.8 Drugs for Treating Endoparasites and Ectoparasites in Pet Rodents

Active Substance	Dose	Application	Remarks
Ectoparasites			
Chlorpyrifos	6 g per 27 × 48-cm cage	Mix in bedding	For environmental control of ectoparasites.
Chlorpyrifos + Fenoxycarb	—	Spray	Used to treat environment against ectoparasites (insecticide + insect growth regulator)
Dichlorvos	5 g/kg mix/intersperse	Environment	Mix granules in bedding or hang strip 15 cm above cage for 24 hours, then 2×per week for 3 weeks
Doramectin	0.5 mg/kg	Subcutaneous	For fur mites, 3 times one week apart
Fipronil	≈7.5 mg/kg topically = 1 to 2 sprays in gloved hand	Spray	For fleas and ticks, apply to the whole body, repeat after 7 to 10 days.
Imidacloprid	10 mg/kg	Spot on	0.1 mL/kg of 10% solution
Imidacloprid + Moxidectin	10 + 1 to 2 mg/kg	Spot on	0.1 mL/kg of 10% solution. Flea species are used as an intermediate host and vector for tapeworms
Imidacloprid + Permethrin	10 + 50 mg/kg	Spot on	For fleas and ticks
Ivermectin	0.2 to 0.4 mg/kg 10% solution (propylene glycol)	Subcutaneous Topical	For fur mites and lice, every 7 to 10 days for 3 treatments For fur mites and lice, 1 drop behind the ear
Moxidectin	0.5% solution at 5 mg/kg 0.5% solution at 2 mg/kg	Topical Oral	For fur mite *Myocoptes musculinus*, repeat in 10 days. For fur mite *Radfordia affinis*, repeat in 15 days.
Permethrin	Dependent on size of animal	Topical	Powder: cover body with powder or cotton ball soaked in 5% solution
Permethrin + Methopren	As needed for environmental treatment	Spray	Used to treat environment against ectoparasites (insecticide + insect growth regulator)
Pyrethrins	As needed for environmental treatment	Spray Topical	Use "kitten-safe" product. Used to treat environment Use 0.05% shampoo every 7 days for four treatments
Selamectin	15 mg/kg	Spot on	For fleas and lice, repeat in 10 days. Strictly topical
Endoparasites			
Doramectin	0.2 mg/kg	Subcutaneous	For *Syphacia muris* (pinworm), every 7-14 days for 2-3 treatments
Fenbendazole	20 mg/kg	Oral	For pinworms, once daily for 5 days
Ivermectin	2 mg/kg	Oral or topical	For pinworms, once or twice 7-10 days apart
Metronidazole	10 to 40 mg/kg	Oral	For protozoa, twice 5 days apart
Praziquantel	25 mg/kg	Oral	For cestodes, trematodes, repeat twice every 10 to 14 days for three treatments. Stings if given SC
Toltrazuril	0.5% solution at 10 to 20 mg/kg	Oral	For coccidia, give daily for 2 to 3 days, pause 5 days and then repeat

DISEASES OF MICE

Oral and Dental

The most common problem in the oral cavity of mice is incisor malocclusion, especially the lower incisors. This is usually a genetic problem seen in younger mice, although it can occur in older mice because of trauma of the developing tooth buds. Prevalence of malocclusion was 3% (females) to 9% (males) in outbred mice in chronic toxicology studies.[54] Clinical signs are weight loss, anorexia, traumatic injury to the upper lip, ptyalism, moist dermatitis around the mouth and forequarters, and eventually death if not treated.[33] Trimming of the incisors with small nail clippers or scissors will temporarily correct the problem, but this needs to be performed routinely, as the incisors grow throughout the life of the animal. If the animal is fractious or if the handler is unable to attain proper immobilization of the head, brief sedation or anesthesia is recommended for the procedure. For more detailed information on dentistry procedures, see Chapter 36.

Respiratory System

Diseases of the upper and lower respiratory tracts are common in pet mice and rats. Animals may be presented with sniffling, sneezing, chattering, and labored breathing. If dyspnea is suspected, do not handle the animal more than is necessary during clinical examination, because it may die. Collection of tracheal and nasal secretions is not recommended because swabbing is highly traumatic, and the cause of disease is generally a mixed infection. Antibiotic treatment is helpful but does not eliminate the disease.

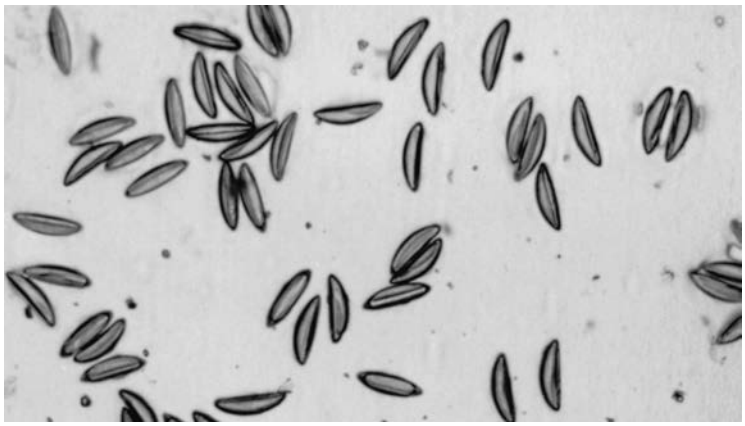


Fig. 25.14 Ova of mouse pinworm (*Syphacia obvelata*) as seen on a perianal tape test. Note the characteristic banana shape. (From Hendrix CM, Robinson E. *Diagnostic parasitology for veterinary technicians*. 3rd ed. St. Louis: Elsevier; 2006.)

The two most common causes of clinical respiratory disease in mice are Sendai virus and *M. pulmonis*. Sendai virus is associated with an acute respiratory infection in which mice display chattering and mild respiratory distress. Neonates and weanlings may die, whereas adults generally recover within 2 months. When the disease expression exceeds this pattern, the cause is most likely concurrent *Mycoplasma* infection. *Mycoplasma pulmonis* is the cause of chronic pneumonia, suppurative rhinitis, and occasionally otitis media. Chattering and dyspnea are caused by accumulations of purulent exudate in inflamed and thickened nasal passages. Survivors develop chronic bronchopneumonia and bronchiectasis and may develop pulmonary abscesses. Antibiotic therapy may alleviate clinical signs but does not eliminate the infection. Enrofloxacin (10 mg/kg) as an antimicrobial agent in combination with doxycycline hyclate (5 mg/kg) as an immunomodulator (not as an antimicrobial) given every 12 hours by mouth (PO) for 7 days is helpful. Additional treatments such as nebulization therapy, expectorants, and nonsteroidal anti-inflammatory drugs can be used to ameliorate the disease.

Gastrointestinal System

Endoparasites are relatively common in mice. However, only two parasites regularly encountered in the digestive tract, the protozoan parasites *Spironucleus muris* and *Giardia muris,* are considered pathogenic, even though they are not always associated with clinical signs in immune-competent animals. Diagnosis is based on demonstrating characteristic trophozoites in wet mounts of fresh intestinal contents or feces. Treatment for protozoa is metronidazole (see Table 25.8).

Pinworms are ubiquitous, considered nonpathogenic, and found frequently in mice purchased from a pet store.[16] Two species are commonly encountered in mice: *Syphacia obvelata* and *Aspicularis tetraptera*. Usually, pinworm infections are subclinical, although heavy infections may result in rectal prolapse, intussusception, enteritis, or fecal impaction.[28] Adult *S. obvelata* females deposit their ova on the fur around the anus. A quick way to diagnose *S. obvelata* infections is to make a clear cellophane tape impression of the perianal skin. Characteristic banana-shaped eggs will readily be seen under a light microscope (Fig. 25.14). *Aspicularis tetraptera* cannot be diagnosed this way because ova are deposited directly into the large intestine; therefore, fecal smear or flotation is required to confirm *A. tetraptera* infection. Fenbendazole, doramectin, or ivermectin treatments can all be used to eliminate pinworms (see Table 25.8). Importantly, in addition to treating the animal(s), environmental decontamination is recommended because pinworm eggs have been shown to persist in the environment.[55]

Another commonly isolated bacterial organism from pet mice is *Helicobacter* species.[16] Generally, mice infected with *Helicobacter* do not exhibit clinical signs; however, if an animal presents with rectal prolapse, *Helicobacter* should be a top differential diagnosis. Because this organism is difficult to grow in culture, the recommended test for detection is polymerase chain reaction (PCR) testing of fecal pellets. Recommended treatment is triple therapy with amoxicillin (1.5 mg/30 g mouse), metronidazole (0.69 mg/30 g), and bismuth (0.185 mg/30 g) PO every 8 hours for 2 weeks.[26]

Urinary System

Obstruction of the urethra in male mice has been described as resulting from infections of the preputial glands with *Staphylococcus aureus* and of the bulbourethral glands with *Pasteurella pneumotropica*. Accessory sex gland secretions and, rarely, urolithiasis have also been implicated. Mice are often presented to the veterinarian because they mutilate their penises as a result. In addition, occasional injury of the penis is seen in young males from aggressive breeding activity and abrasion on the cage. Treatment involves isolating the affected mouse, cleaning and debriding the affected areas, and treating the animal with antibiotics. A newly identified parvovirus, mouse kidney parvovirus, has recently been identified as the cause of a spontaneous nephropathy in mice.[72] This disease, previously known as "inclusion body nephritis," had puzzled pathologists for many years. Although incidence of viral

infection is believed to be widespread in laboratory mice, only severely immunocompromised mice develop clinically significant disease.[72]

Reproductive System

Mice experience relatively few complications associated with parturition. Occasionally, vaginal and uterine prolapse occurs after parturition. The prolapse can be reduced by placing a small, lubricated 20-gauge Teflon intravenous catheter (without needle) into the lumen of the uterus and vagina, and manually manipulating the tissue back into the proper anatomic position.[14] A purse-string suture using small-gauge (4-0 or smaller), absorbable suture material should be placed around the vaginal orifice before removing the catheter.

Integument

Many problems seen in pet mice are associated with the skin. In one survey from a large diagnostic laboratory that housed research animals, skin disease in mice represented 25% of all diagnostic cases (for all species) submitted.[48] Four groups of skin problems are categorized in mice: behavioral disorders, husbandry-related problems, microbiologic and parasitic infections, and idiopathic conditions.

Behavioral skin issues mainly stem from the hierarchical nature of the mouse's natural behavior. Mice naturally establish social dominance within a group, which can manifest as barbering and fighting. Barbering is commonly seen in group-housed mice, more often in females, where the dominant mouse nibbles off the whiskers and hair around the muzzles and eyes of cage mates. No other lesions are present, and only one mouse (the dominant one) retains all of its fur. Removal of the dominant mouse stops barbering; however, another mouse usually then assumes the dominant role. Barbering may also be seen associated with sexual overgrooming as a form of stress-evoked behavior, and lactating mice may display "maternal" barbering, produced in the process of suckling pups, in which alopecia is seen from tail to chin.[42] Barbering has a genetic-based behavioral background, because aggressive inbred strains of mice do not use barbering in their behavior.[42] Male mice, except littermates raised together from birth, are more likely to fight and can inflict severe bite wounds on one another, especially over the rump, tail, and shoulders. Recommended treatment involves isolating the aggressor and treating the wounds on injured mice. Bandages generally do not stay on mice, but small amounts of topical medications, such as triple antibiotic ointment or silver sulfadiazine, may be applied to provide antimicrobial activity and keep the wound moist.

Environmental causes of skin issues are hazardous cage equipment and poor husbandry conditions. Small patches of alopecia on the lateral surfaces of the muzzle are usually a result of chaffing on metal feeders, poorly constructed watering device openings, and metal cage tops. Unlike barbering, dermatitis may also be associated with the alopecic area. Individually housed mice can display aberrant stereotypic behaviors such as polydipsia and bar chewing, which results in mechanical abrasion and alopecia. Ringtail is a condition seen in young mice and rats under conditions of low humidity, in which annular constrictions can be seen around the tail and occasionally the feet or digits.[28] In severe cases, amputation may be required. In all of these cases, treatment consists of replacing poor equipment, ensuring proper humidity and husbandry, and providing environmental enrichment.

Many infectious causes of alopecia and dermatitis are associated with fur mites. Ectoparasites are common in mice purchased from pet stores.[70] In affected animals, the hair is generally thin, especially on difficult-to-groom areas such as the head and trunk. The coat often has a greasy appearance; in cases of heavy infestation, noticeable pruritus and self-inflicted dermal ulceration may occur. Three mites are commonly seen: *Myobia musculi, Myocoptes musculinus,* and *Radfordia affinis*.[28] Mites are spread by direct contact with infected mice or infested bedding. Diagnosis is based on the identifying adult mites, nymphs, or eggs on hair shafts with the use of a hand lens or a stereoscopic microscope (Fig. 25.15). Adults and nymphs appear pearly white and elongated (being about twice as long as they are wide); eggs are oval and are seen attached to the base of hairs or inside mature females. Treat mite infestations with avermectins (e.g., ivermectin, selamectin) or milbemycins (moxidectin).[13,68,69] Refer to Table 25.8 for dosages. Ringworm, caused by *Trichophyton mentagrophytes,* is uncommon in pet mice. Lesions, when present, are most often on the face, head, neck, and tail. The lesions have a scurfy appearance with patchy areas of alopecia and variable degrees of erythema and crusting. Pruritus is usually minimal to absent, and the lesions do not fluoresce under a Wood's lamp.[21]

Subcutaneous abscesses can also occur in mice, and fine-needle aspiration is recommended to aid in diagnosis and treatment. Three opportunistic bacterial pathogens—*S. aureus, P. pneumotropica,* and *Streptococcus pyogenes*—are often isolated from abscesses[3] and can cause abscesses in other organs (e.g., *P. pneumotropica* is sometimes associated with conjunctivitis, panophthalmitis, and swollen eye abscesses). Antibiotic therapy with penicillins or cephalosporins, concurrent with drainage and debridement of the abscess, is effective.

Idiopathic ulcerative dermatitis is a well-recognized disease in black laboratory mice on the C57BL/6 strain background with a characteristic distribution on the thorax and head (Fig. 25.16). The disease is often very pruritic, causing mice to inflict more damage to the skin from scratching. The cause of idiopathic ulcerative dermatitis is an underlying vasculitis attributed to immune complex deposition on dermal vessels.[43] Dietary factors and dysregulated fatty acid metabolism have been implicated in the development of the disease, and the severity appears to be modulated by dietary fat and vitamin E content. Gavaging affected mice with omega-3 fatty acids was associated with regressed lesions and resolved pruritus in a small sample of affected mice.[51] The ulcers may heal with fibrosis and resulting skin contracture or progress to a *Staphylococcus xylosus* secondary bacterial infection.[43,80] A recent study showed that nail trimming, added to topical treatment (Vetericyn [Innovacyn, Rialto, CA], Tresaderm [Merial, Duluth, GA], or triple antibiotic ointment), greatly improves healing compared with topical treatments alone.[2] Additionally, 0.005% sodium hypochlorite

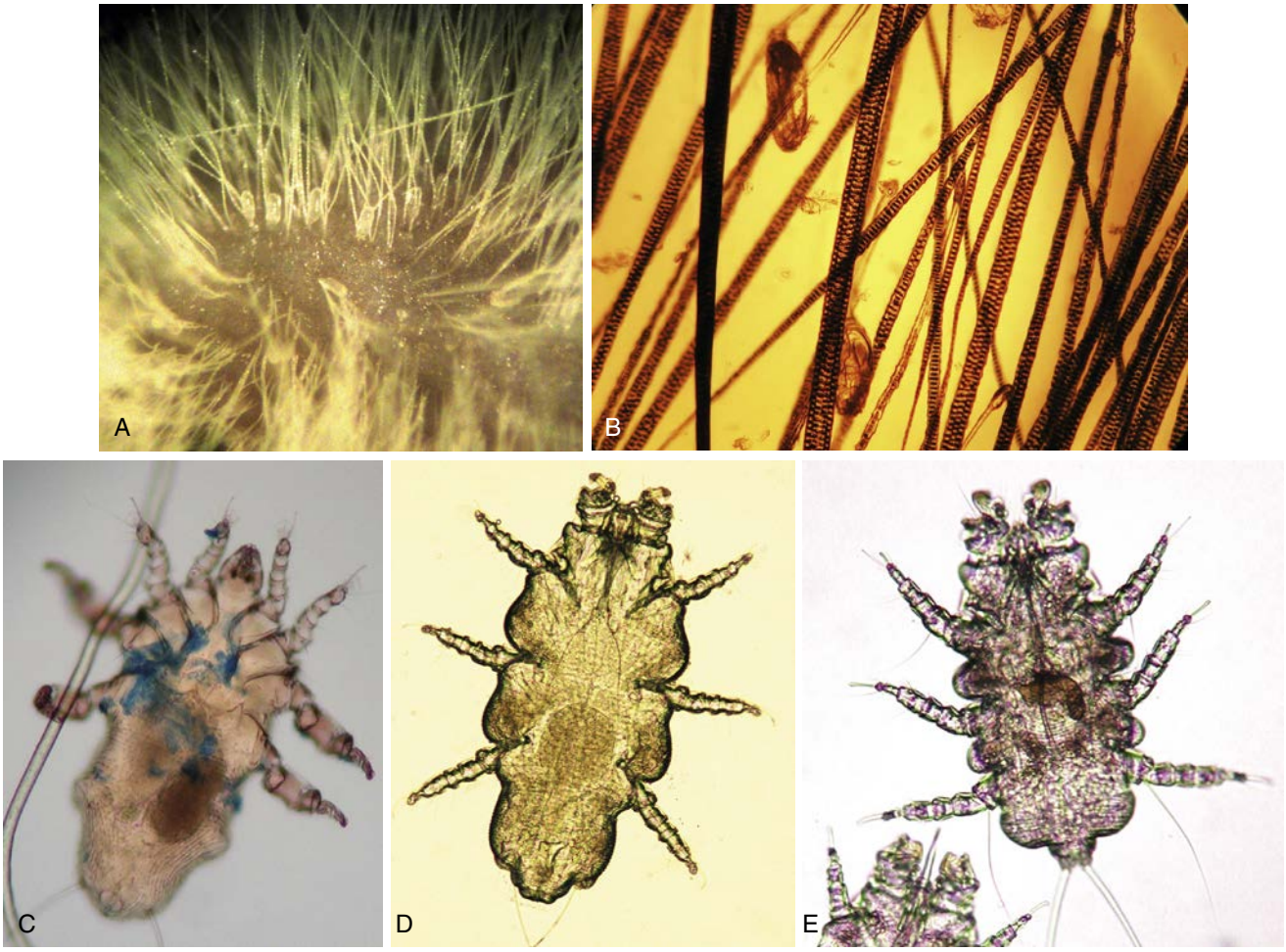


Fig. 25.15 Adult fur mites and ova. The ova are pearly white, oval, and attached to the hair base (A). Diagnosis of fur mite infestation can be made by visualization of ova attached to the hairs under a microscope (B). The adults of three species of fur mites that can infest mice: *Myocoptes musculinus* (C), *Radfordia affinis* (D), and *Myobia musculi* (E). (Photos courtesy Cheryl Yost)

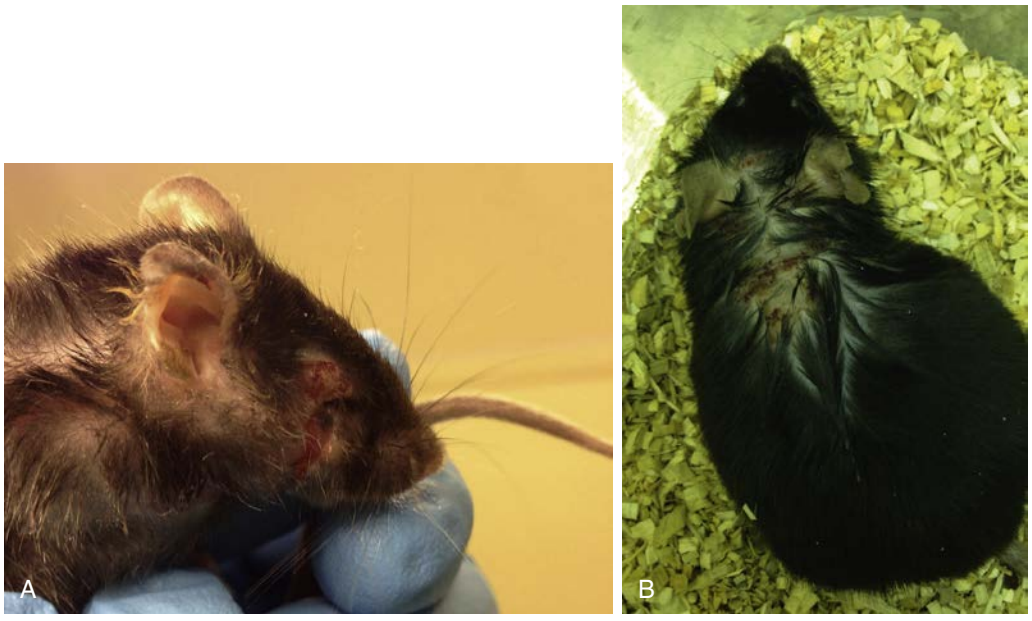


Fig. 25.16 Idiopathic ulcerative dermatitis in mice. This disease usually occurs in black mice with a C57BL/6 background strain. The lesions can occur anywhere, but are most often on the neck, back of head, and face. Note the excoriations on the face (A), likely worsened by scratching because of the pruritic nature of the disease. The appearance of a typical healing ulcer (B). Treatments include trimming toenails, topical medication, and fatty acid supplementation.

solution was more effective for wound healing than povidone-iodine/silver sulfadiazine or triple antibiotic ointment.[58] The author recommends using a multipronged approach for treatment of idiopathic ulcerative dermatitis, including toenail trimming, topical therapy, and omega-3 fatty acid supplementation (0.1–0.2 mL PO every 24 hours).

Neoplasia

Neoplasia, both spontaneous and induced, has been exhaustively studied in laboratory mice. Three types of cancer that occur frequently in pet mice are mammary tumors, lymphoma, and primary lung tumors. The most common mammary tumor is adenocarcinoma, followed by fibrosarcoma. The incidence of mammary tumors varies by mouse strain and the presence or absence of mouse mammary tumor viruses; the incidence is as high as 70% in some strains.[78] In wild and outbred mice, the incidence of fibrosarcoma ranges from 1% to 6%.[35] Subcutaneous tumors are nearly always malignant and have often ulcerated by the time a diagnosis is made. Tumors can be treated by surgical excision, but the chance of recurrence is high, and the prognosis is poor. Attempts to treat these tumors in pet mice by radiation or chemotherapy have not been reported.

Lymphoma of various types occurs spontaneously in multiple strains of mice, both inbred and outbred.[9] Because mice are used extensively in cancer research, many treatments for lymphoma are described in experimental studies; however, no treatments in pet mice have been reported.

Primary respiratory tumors are uncommon in other species but relatively common in mice.[9,28] About 95% of these are pulmonary adenomas, and these are prone to invade the pulmonary parenchyma and metastasize.[28] These cases are generally subclinical until the animal can no longer compensate for decreased lung capacity. Similar to lymphoma, no treatment of pulmonary adenomas in pet mice has been reported.

Zoonoses

Mice have the potential of carrying zoonotic diseases that can be transmitted to their owners. The diseases discussed are some of the more important zoonotic diseases of mice that the exotic pet veterinarian should be aware of.

Lymphocytic choriomeningitis virus is a virus that has been associated with many reports of human infection when in contact with laboratory or pet rodents, especially mice and hamsters.[61] The wild house mouse is the principal host for lymphocytic choriomeningitis virus, and it is widely distributed throughout the world. Transmission occurs when people are exposed to live mice or their excreta, or to mouse carcasses. Clinical signs in people range from asymptomatic to mild flu-like symptoms, to more severe signs of meningitis such as drowsiness, confusion, and motor abnormalities. Death has been reported in several cases where the central nervous system has become involved.[61] Owners of pet rodents that develop these symptoms are urged to contact their physicians immediately to seek proper diagnosis and treatment.

Salmonellosis is an important, worldwide zoonotic disease that is widespread in wild animals. Transmission is fecal-oral, and usually infection in pet rodents is associated with poor sanitation or contamination of food, bedding, or water by wild rodents.[61] The Centers for Disease Control and Prevention provides guidelines for small pet owners to help keep themselves and their families healthy: https://www.cdc.gov/healthypets/resources/safety-around-small-pets-H.pdf. Clinical symptoms of salmonellosis in people are gastroenteritis, abdominal pain, diarrhea, nausea, and fever.[61]

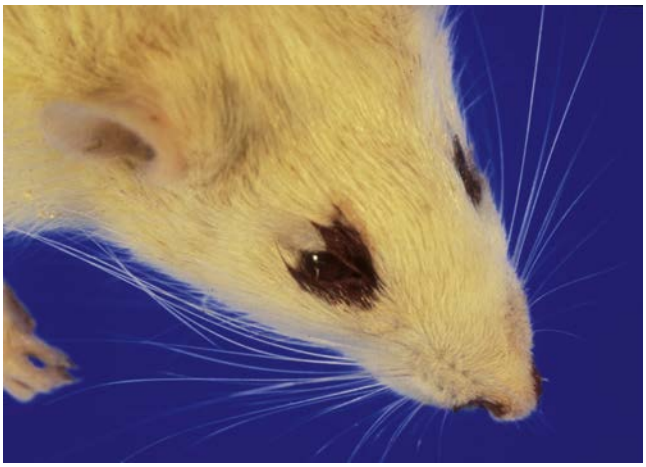


Fig. 25.17 Chromodacryorrhea, or red tears, in a rat. The color results from porphyrin pigments in the Harderian gland secretions, which are visible around the eyes and occasionally the nares.

Leptospirosis is another zoonotic disease with a reservoir in wild rodents. Rodents often do not show clinical signs but can shed leptospires throughout their life span.[61] Leptospires are shed in urine, so people can become infected by handling animals or contaminated bedding or through aerosol exposure during cage cleaning. Clinical signs in people range from asymptomatic to severe infection and even death, with potential renal, hepatic, pulmonary, and gastrointestinal involvement.[61] Refer to Chapter 42 for further information.

DISEASES OF RATS

Ocular

Chromodacryorrhea, or red tears, is a condition commonly seen in rats that present to the veterinarian. Owners will often claim that their pet rats are "bleeding" from the eyes or nose when they are actually seeing chromodacryorrhea. The red coloration of these tears is due to porphyrin pigments, which are produced by the Harderian glands located behind the eyes. Chromodacryorrhea is usually a response to stress and disease, and dried tears around the eyes and external nares can resemble dry crusts of blood (Fig. 25.17).[19] Because porphyrin will fluoresce under ultraviolet light, porphyrins can be differentiated from blood by using a Wood's lamp (Fig. 25.18). Red tears are often an indication of a chronic underlying disease, and their presence warrants thorough evaluation of the affected animal.

Oral and Dental

As with mice, the most common abnormality of the mouth in rats is incisor malocclusion. Treatment is the same as for mice; however, older rats have thicker incisors that may fracture when

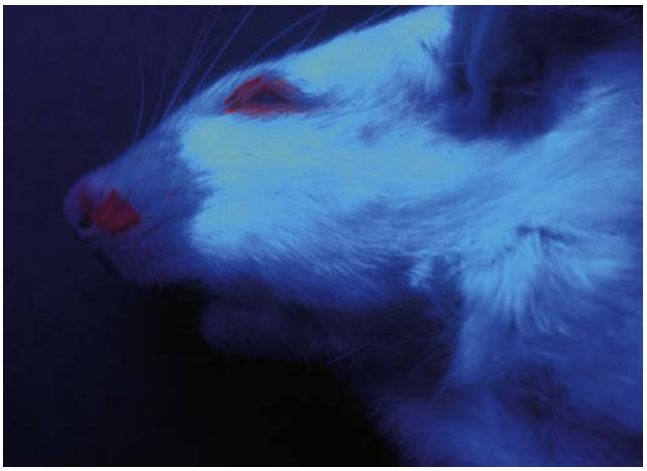


Fig. 25.18 Chromodacryorrhea in a rat viewed under an ultraviolet light. The porphyrins in the Harderian gland secretions around the eyes and nares readily fluoresce under ultraviolet light and can be distinguished from blood.

trimming with regular nail clippers. Instead, incisors should be trimmed using a hand-held drill (e.g., Dremel Rotary Tool; Dremel Co, Racine, WI) or a dental drill with diamond-disc attachment. Sedation or anesthesia is recommended to prevent injury to the patient. Place a wooden tongue depressor behind the incisors during trimming to protect the tongue and other soft tissues of the mouth. Refer to Chapter 36 for more details regarding small mammal dentistry.

Respiratory System

Respiratory disease caused by infectious agents is the most common health problem in rats. Three major respiratory pathogens cause overt clinical disease: *M. pulmonis, Streptococcus pneumoniae,* and *Corynebacterium kutscheri.* Other organisms such as Sendai virus (also called murine respirovirus; a paramyxovirus), pneumonia virus of mice (a paramyxovirus), *Pneumocystis carinii* (a fungus) cilia-associated respiratory bacillus, and *Haemophilus* species are minor respiratory pathogens that rarely cause overt clinical disease by themselves. However, the minor respiratory pathogens interact synergistically as copathogens with the major respiratory pathogens to produce two major clinical syndromes: chronic respiratory disease (CRD) and bacterial pneumonia.

The best-understood multifactorial respiratory infection in rats is CRD. The major component of CRD is *M. pulmonis,* and the disease is also known as murine respiratory mycoplasmosis (MRM). Rats may live 2 to 3 years with CRD. A survey of 28 pet ratteries in the United States found that all were positive for *M. pulmonis*.[17] Clinical signs are highly variable: in many cases no signs are present even though significant pulmonary lesions may exist. The prevalence and severity of signs typically increase with the age of the rat and the presence of environmental stressors. Initial infection commonly occurs without any clinical signs; early signs involve both the upper and the lower respiratory tracts and may include snuffling, nasal discharge, polypnea, weight loss, hunched posture, ruffled coat, head tilt, and red tears.[84] The most important aspect of CRD for clinicians is that respiratory mycoplasmosis varies greatly



Fig. 25.19 Fibrinopurulent pneumonia *(arrow)* caused by *Streptococcus pneumoniae* in a rat.

in disease expression because of the different factors that influence the host–pathogen relationship. Examples of such factors include intracage ammonia levels, concurrent infection with other respiratory pathogens, genetic susceptibility of the host, virulence of the *Mycoplasma* strain, and vitamin A or E deficiency.[84] Auscultation is insensitive in determining the severity of respiratory disease, and radiographs are often unremarkable. However, a computed tomography scan often reveals significant pulmonary disease. Serology is the preferred choice for diagnostic testing, as mycoplasma are difficult to grow in a laboratory. Younger rats naturally exposed to *M. pulmonis* may be seronegative for up to 4 months after exposure.[20]

The primary lesion of CRD is subacute and chronic bronchitis, a chronic inflammatory condition resulting in respiratory epithelial dysfunction.[45] The underlying airway inflammation and clinical signs result from damage and remodeling of airway epithelium, colonization of the airways with secondary infections, and infiltration and activation of neutrophils, macrophages, and lymphocytes. Bronchodilators are the primary treatment for subacute and chronic bronchitis. Inhaled nonselective muscarinic antagonists (e.g., ipratropium bromide) and beta-2 adrenergic agonists (e.g., albuterol, salmeterol), as well as oral theophylline provide significant although modest efficacy. Frequent treatment with broad-spectrum antibiotics is necessary, because microbial colonization is a common finding. Tetracycline antibiotics such as doxycycline are efficacious in CRD. Treating with doxycycline (5–10 mg/kg PO every 12 hours) or a long-acting depot such as doxycycline (70–100 mg/kg subcutaneously or intramuscularly every 7 days; Vibravenos; Pfizer Animal Health, Parsippany-Troy Hills, NJ), often helps affected rats.

Bacterial pneumonia is nearly always caused by *S. pneumoniae* (Fig. 25.19), but usually in combination with *M. pulmonis* (Fig. 25.20), Sendai virus, or cilia-associated respiratory

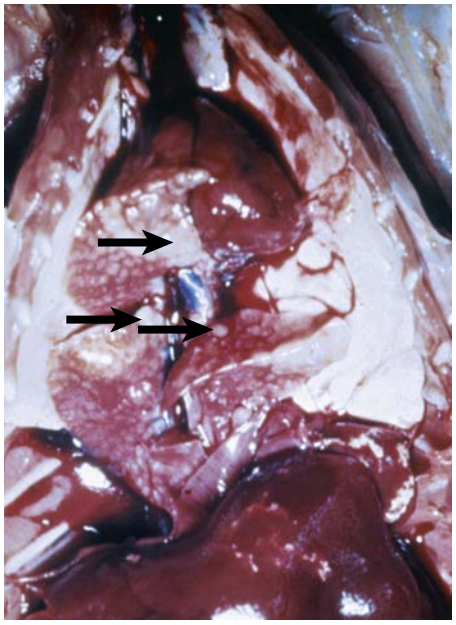


Fig. 25.20 Gross appearance of the lungs in a rat with pneumonia caused by *Mycoplasma pulmonis*. Compare the appearance of these lungs with that of the lungs in Fig. 25.19. Rats in the later stages of *M. pulmonis* chronic respiratory disease may show pulmonary abscesses *(arrows)*.

bacillus.[84] Pneumonia caused by *S. pneumoniae* can occur acutely. Young rats are more severely affected than are older ones, and often the only sign they exhibit is sudden death. Mature rats may demonstrate dyspnea, snuffling, and abdominal breathing. A purulent exudate may be seen around the nares and on the front paws (from wiping of the nostrils). A tentative diagnosis is based on identifying numerous gram-positive diplococci on a Gram's stain of the exudate or in a sample submitted for cytologic examination. Severe bacteremia is an important consequence of advanced disease and results in multiorgan abscesses and infarction. Treatment must be aggressive, and the use of beta-lactamase-resistant penicillins such as cloxacillin, oxacillin, and dicloxacillin (all of which can be administered orally) is recommended. The first-choice antibiotic treatment for *S. pneumoniae* pneumonia is amoxicillin/clavulanic acid (20 mg/kg PO every 12 hours).

Pneumonia caused by *C. kutscheri* occurs rarely, and only in conjunction with debilitation or immunosuppression.[84] In pet rats, immune suppression can result from diabetes, neoplasia, or dietary deficiencies.

Gastrointestinal System

Sialodacryoadenitis virus, a coronavirus, causes inflammation and edema of the cervical salivary glands. Owners of infected rats often describe their pets as having mumps. Sialodacryoadenitis virus is highly contagious and initially causes rhinitis, followed by epithelial necrosis and inflammatory swelling of the salivary and lacrimal glands. Cervical lymph nodes also become enlarged. There is no treatment for this disease. Glandular healing follows within 7 to 10 days, and clinical signs subside within 30 days, with few residual lesions remaining. During acute inflammation, affected rats are at high risk for anesthesia-related death because of the decreased diameter of the upper respiratory tract lumen; also, ocular lesions such as conjunctivitis, keratitis, corneal ulcers, synechiae, and hyphema can develop as a result of lacrimal dysfunction. The eye lesions usually resolve but occasionally progress to chronic keratitis and megaglobus.

Rats, like mice, are susceptible to pinworm infections. They may be infected with the rat pinworm (*Syphacia muris*), as well as the two common mouse pinworm species (*S. obvelata* and *A. tetrapetra*). Generally infections are asymptomatic in rats; however, heavy infections may cause failure to gain weight.[4] Various treatments have been shown to be successful, including ivermectin, fenbendazole, and levamisole (see Table 25.8 for dosages). However, topical selamectin and oral moxidectin have been shown to be ineffective.[28,30] Decontamination of the environment is also important to eliminate ova that can persist and remain infectious.

Urinary System

Chronic progressive nephrosis (CPN) is the best known of age-related diseases in rats. In CPN, the kidneys are enlarged and pale and have a pitted, mottled surface that often contains pinpoint cysts. Lesions consist of a progressive glomerulosclerosis and myriad tubulointerstitial disease primarily involving the convoluted proximal tubule.[31] The most striking change in renal function is proteinuria exceeding 10 mg/day that increases in severity progressively with age. The features of CPN are qualitatively similar among different strains of laboratory rats, but the onset, incidence, and severity of the disease vary considerably. The disease occurs earlier and is of greater severity in males than in females: urinary protein excretion averaging 137 mg/day has been documented in 18-month-old male Sprague-Dawley rats, whereas excretion averaging 76 mg/day was reported in female rats of the same age.[75] Dietary factors appear to have an important role in the progression of CPN. Caloric restriction, the feeding of low-protein diets (4%–7%), and limiting the source of dietary protein reduce the incidence and severity of CPN. Feeding soybean protein (as opposed to casein) and caloric restriction contribute substantially to reducing the incidence and severity of CPN; low-calorie diets that contain high protein levels do not decrease the incidence or severity. Drugs and exposure to chemicals can also exacerbate CPN. Diagnosis is based on clinical signs (polyuria/polydipsia), plasma biochemical results, and proteinuria. If only a small amount of blood is obtained, blood urea nitrogen concentration can be estimated with the use of a blood dipstick. Treatment is supportive and involves feeding a low-protein diet and administering anabolic steroids.

Uroliths and renal pelvic calculi are relatively infrequent in rats, especially compared with guinea pigs, rabbits, and chinchillas. Most uroliths that have been described were composed of struvite.[62]

Musculoskeletal and Peripheral Nervous System

Clinically, old rats show disturbances in motor function, posterior paresis and paralysis, loss of tail control, incontinence, and weight loss. Distinguishing between age-related peripheral or central nervous system changes, neurogenic muscular atrophy,

and primary age changes in muscles is very difficult. Posterior paresis is commonly caused by spinal nerve root degeneration (also known as *radiculoneuropathy*, *polyradiculoneuropathy*, and *degenerative myelopathy*).[87] Spontaneous tumors of the peripheral nervous system in rats are very rare; only isolated cases are reported in extensive tumor incidence surveys.[1] Allowing young rats to stand on their hind legs frequently is a predisposing factor in the development of avascular necrosis of the femoral head (Legg-Calve-Perthes disease).[59]

Integument

Ectoparasitic infestation is more common in rats than in mice. The most common fur mites that infest rats are *Radfordia ensifera*, although mouse fur mites (*R. affinis* and *M. musculi*) can sometimes be found.[28] Although *R. ensifera* infestation produces few ill effects, heavy infestation may lead to self-traumatization and ulcerative dermatitis. Other mites, including *Demodex* species, have been described in rats maintained in laboratories; however, they are seldom seen, and no contemporary reports of infestations in pet rats appear in the literature.[82] The tropical rat mite (*Ornithonyssus bacoti*) is an important opportunistic ectoparasite often found on pet mice and rats (Fig. 25.21). The mites spend a relatively short time on a host and penetrate the skin for feeding only; therefore cleaning the environment is essential for clearing up an infestation. Severe infestations can cause anemia, debilitation, and death in rodents. When an animal host is not available, humans can become the victims of mite infestation. Detect adult parasites by macroscopic examination of the host; the mites are orange red. Rats with ectoparasites can be treated with selamectin (15 mg/kg as topical spot on, repeat in 10 days). The environment can be decontaminated with either synthetic pyrethroids or fipronil (see Table 25.8).[5]



Fig. 25.21 The tropical rat mite (*Ornithonyssus bacoti*). Engorged with the host's blood, the mite appears red. It is an opportunistic ectoparasite often found on pet rodents including rats and mice. When an animal host is not available, humans can become victims of mite infestation. The mite spends only a short time on the host, penetrating the skin only for feeding. Severe infestations can resemble a rodent covered in fine sawdust; the sawdust is thousands of mites. Affected rodents can experience anemia, debilitation, and even death.

Ringtail is a pathologic condition of the tail of young rats that is typically characterized by dry skin and the formation of annular constrictions. In severe cases, blood vessels distal to the constrictions thrombose, resulting in pain, necrosis, and even autoamputation in some cases. This lesion is highly photogenic and probably for this reason is always described in textbooks and articles on diseases of rats. It occurs primarily during the preweaning period in rats aged 2 to 19 days and occasionally in young mice. Low environmental relative humidity (less than 40%) appears to be the cause, and it is more often seen in rats housed in hanging cages; it is rarely seen in pet rats. If ringtail is diagnosed, treatment options involve adding unsaturated fatty acids to the diet (e.g., 5% corn oil or an essential fatty acid supplement containing omega-3 fatty acids) or topical application of lanolin.[25,81] If avascular necrosis has occurred, amputate the tail proximal to the necrotic annular constriction.

Ulcerative dermatitis caused by *S. aureus* infection results from self-traumatization associated with fur mite infestation or, more commonly, from scratching of the skin over an inflamed salivary gland (see sialodacryoadenitis virus under "Gastrointestinal System," above). Rats have a remarkable ability to resist infection with *S. aureus*.[22] Treatment consists of clipping the toenails of the hind paws, cleaning the ulcerated skin, and applying a topical antibiotic. Systemic treatment is rarely necessary.

Neoplasia

The most common subcutaneous tumor in the rat is fibroadenoma of the mammary glands. The distribution of the mammary tissue is extensive, and the tumors can occur anywhere from the neck to inguinal region (Fig. 25.22). Tumors can reach 8 to 10 cm in diameter and occur in both males and females. Adenocarcinomas are less common and represent fewer than 15% of mammary tumors in pet rats. In a study of 105 subcutaneous masses in 100 pet rats, 53% were benign mammary fibroadenomas, and 12% were mammary carcinomas.[88] In the same



Fig. 25.22 Mammary fibroadenoma in the inguinal region of a female rat. The rat weighed 355 g before surgery, and the excised tumor weighed 40 g, representing 11% of the rat's body weight.

study, 14 of 35 rats with mammary fibroadenomas that were necropsied had concomitant reproductive tract abnormalities, such as endometrial polyps, hyperplasia, paraovarian cysts, and suppurative metritis.

Prevention and treatment of mammary neoplasia involves surgery and medical treatment. The surgical technique for mammary tumor removal ranges from straightforward to complicated (for high cervical or inguinal tumors) depending on the location and size of the tumor (see Chapter 33). However, recurrence of fibroadenomas is common in uninvolved mammary tissue, and repeat surgeries are often required. Although tumors do not metastasize, death is often caused by large tumors that ulcerate and become secondarily infected. The incidence of mammary tumors is significantly lower in early (<3 months) ovariectomized versus sexually intact rats due to influence of hormones.[39] Spaying sexually mature females (4–7 months old) has been shown to reduce mammary tumor formation[67]; efficacy of spaying rats older than 7 months to prevent mammary gland tumors is not known. It has been recommended that female rats be spayed when undergoing surgery for tumor removal. However, there are little data on efficacy of spaying at tumor removal in preventing tumor recurrence, and more tumors can develop in these cases.[88] In cases where an abdominal surgery cannot be performed or is not advised, subcutaneous deslorelin implants can be placed to suppress hormone production, although the effectiveness of this treatment at the time of tumor occurence is unknown and debated in practice. As with spaying, age may be a factor in efficacy of hormonal implants in prevention of mammary tumors. Placement of a deslorelin implant at the time of tumor removal has not been effective in preventing tumor recurrence in some cases.[88]

Another common neoplasm in rats is pituitary adenoma. Incidence increases with age, and many of these tumors secrete prolactin, which can cause spontaneous lactation.[8] Prevalence of pituitary adenomas does not differ significantly between rats with or without mammary fibroadenomas, and a causal role of adenomas in mammary fibroadenoma development is unknown.[88] Often older rats with pituitary adenomas will present with neurologic signs such as hind limb paresis or paralysis, changes in vision, etc. Advanced imaging, such as computed tomography or magnetic resonance imaging, is recommended instead of radiographs to make the diagnosis. Treatment with cabergoline (0.6 mg/kg PO every 72 hours) can decrease the size of the mass and even eliminate clinical signs.[57] However, this does not eliminate the tumor entirely, and regrowth can occur.[57] Surgery is not possible because of the location of the tumor.

Zymbal's gland tumor is a unique neoplasm that occurs in the specialized sebaceous glands of rats. The Zymbal's gland is an auditory sebaceous gland that lies ventral to the orifice of the external ear.[8] Most Zymbal's gland tumors are carcinomas and usually have abundant keratin production and papillary projections of epithelial cells. Many of these tumors can be mistaken for squamous cell carcinomas on histologic study.[8] The invasive, malignant nature of these tumors and location close to vital structures makes surgical removal difficult or impossible.

Zoonoses

One of the more important zoonotic diseases of rats is *S. moniliformis*, also known as "rat bite fever." *Streptobacillus moniliformis* is a gram-negative bacteria that can reside in the nasopharyngeal cavity of asymptomatic rats but can also cause otitis media.[23] Transmission to people occurs most commonly through a bite wound, so educating clients about gentle and appropriate handling of pet rats is very important. If a bite does occur, urge clients to seek medical attention. Symptoms of *S. moniliformis* infection in people are fever, malaise, headache, sore throat, lymphadenitis, myalgia, and petechial rash.[23] If one or more large joints are involved, septic arthritis can develop.[23] Screening PCR tests to detect the presence of *S. moniliformis* in pet rats are available.

As mentioned above, the tropical rat mite (*O. bacoti*) can bite humans opportunistically. This mite can also be a vector for transmission of hantavirus.[23] People generally develop pruritic dermatitis and a rash after exposure to this mite. Clients who develop these symptoms should treat their pet rodents for mite infestation (see Table 25.8). Emphasis should also be placed on proper cleaning and disinfection of the environment (nest, bedding materials, cage accessories, etc.), because these mites spend most of their time in the environment and not on the host.

Two other potential zoonotic diseases in rats, salmonellosis and leptospirosis, are also seen in mice. Refer to the previous section on zoonoses in mice for more information on these infectious agents. For further information on zoonotic diseases, see Chapter 42.

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26

Hamsters and Gerbils

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TAXONOMY, NATURAL HISTORY, AND GENERAL CHARACTERISTICS

Hamsters and gerbils belong to the suborder Myomorpha of the order Rodentia. Hamsters are in the family Cricetidae, which includes voles and lemmings, and gerbils are in the family Muridae, which includes rats and mice. The native habitat of the various species of wild hamsters ranges from the Middle East to areas of Europe, as well as Asia. They generally inhabit arid, warm environments such as steppes and the edges of deserts. Wild gerbils inhabit semi-desert or desert environments in Asia, Africa, and the Middle East.

Hamsters

Different hamster species are frequently encountered as pets in many countries (Fig. 26.1). The most common pet hamster species is the golden or Syrian hamster *(Mesocricetus auratus)*, which comes in a variety of coats, including the long-haired or teddy bear hamster.[30] The dwarf Djungarian or Russian winter white hamster (*Phodopus sungorus*) has become popular recently. Two other dwarf hamsters species that are common as pets are the closely related Campbell's hamster (*Phodopus campbelli*), also called the Campbell's Russian dwarf hamster, and the smaller Roborovskii or robo hamster (*Phodopus roborovskii*). Dwarf hamsters are all small (19–45 g body weight Russian; 18–28 g Roborovskii) and have furred short tails, white underparts, and a grayish to a tan dorsum with or without a dorsal stripe, depending on the species. Chinese hamsters *(Cricetulus griseus)* are similar in size to the Russian dwarf hamsters (19–46 g) but with longer tails.

Compared with the dwarf hamsters, Syrian hamsters are larger and often are more aggressive, with females more aggressive than the males. Dwarf hamsters are excitable and more difficult to restrain than Syrian hamsters, and they may bite when restrained. Dwarf hamsters are more social than golden hamsters and are more likely to live in family groups. Chinese hamsters are are not as social as dwarf hamsters and are best kept separately.

Hamsters are the least hardy of the small rodents when newly purchased, and stress-related diseases such as proliferative ileitis (often referred to as "wet tail" are common. Hamsters are nocturnal by nature, but if they are scooped up gently with two hands, they usually awaken without attempting to bite. Touching a hamster's back with a finger in an attempt to rouse it is likely to provoke a startle or threat response. Excited hamsters often jump from hands or tables when examined, and using appropriate caution when handling them is of utmost importance. Hamsters in general, but especially the Djungarian hamsters, are prone to a temporary exophthalmos when scruffed (Fig. 26.2). All hamsters are well known for their ability to escape from

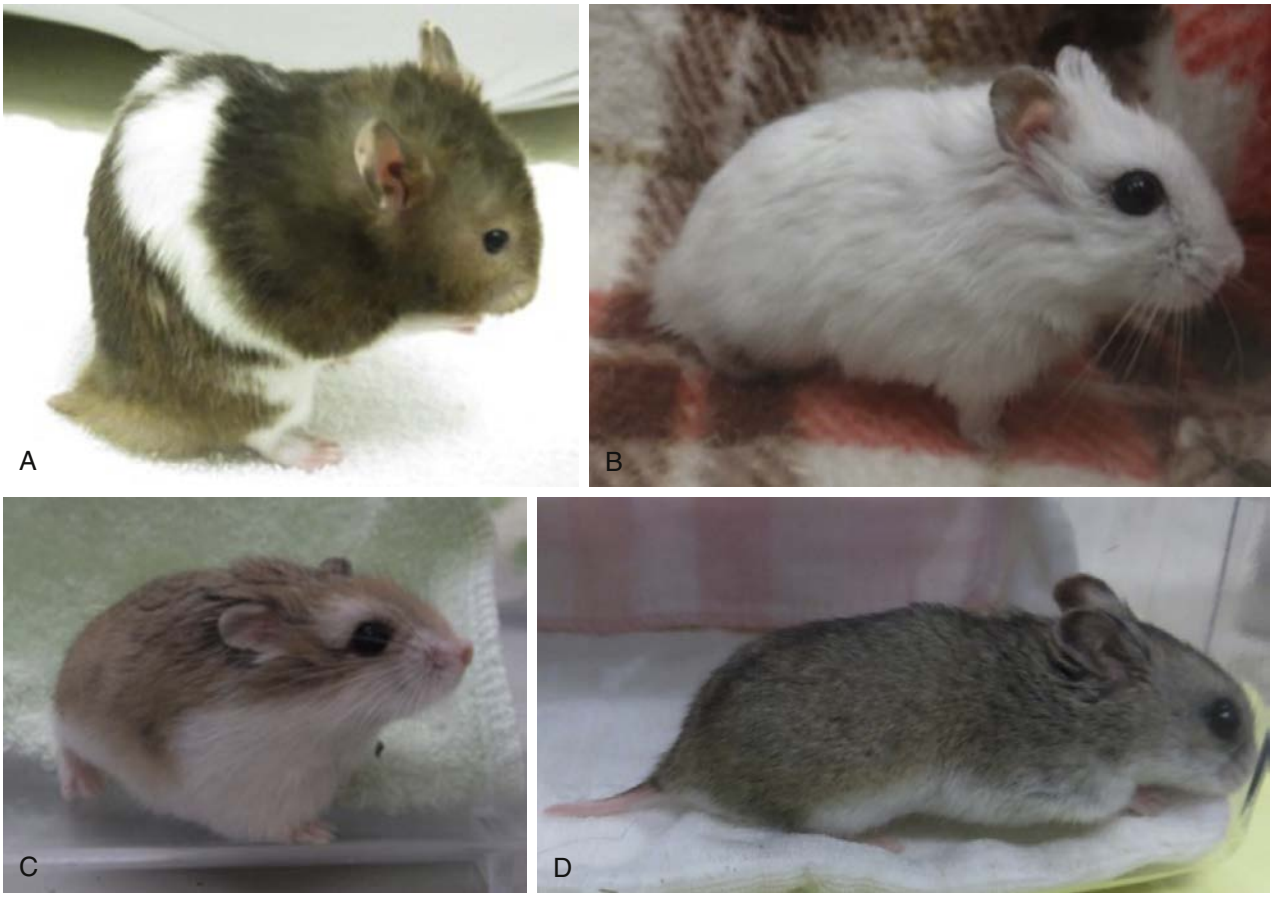


Fig. 26.1 Different hamster specie are frequently encountered as pets. (A) Syrian hamster *(Mesocricetus auratus)*. (B) Djungarian hamster *(Phodopus sungorus)*. (C) Roborovsky's hamster *(Phodopus roborovskii)*. (D) Chinese hamster *(Cricetulus griseus)*.



Fig. 26.2 Exophthaolmos during restraint in a Djungarian hamster.

enclosures. Chewed or broken cage parts should be replaced immediately; if a hamster is cared for by a child, an adult should regularly check the pet's cage for signs of wear. Hamsters may be stressed by hot, humid environments; therefore keep them in a cool area of the house during the summer months. The temperature inside a hamster burrow in the wild is around 62°F (16.5°C) and therefore significantly cooler than normal room temperature 75°F (25°C). Syrian hamsters, but not dwarf hamsters, will hibernate if environmental temperatures drops to 50°F (10°C) or lower. Short daylight periods and limited food availability can also induce hibernation. Most hamsters live in relatively dry areas (humidity around 30%–40%), so increased humidity (over 50%–60%) can be stressful.

Gerbils

Mongolian gerbils *(Meriones unguiculatus)* are desert dwellers with efficient kidneys for conserving water; the loop of Henle in their kidneys is longer than that of other rodents.[28,30] Pet gerbils are available in white, black, buff, gray, and spotted varieties. They are extremely active and may be difficult for small children to handle. Although gerbils are social and live in family groups, they are territorial and often will not tolerate the introduction of strangers. This is important to remember when reintroducing a gerbil into a group after a long separation or hospitalization. Cannibalism can result from attempting to keep incompatible pairs or males together.

Gerbils appear more disease resistant than hamsters, although older gerbils may develop a variety of neoplastic and degenerative conditions. Epilepsy has been reported in pet gerbil strains, and the gerbil has been used as a model in seizure and epilepsy research.[7] Seizures in gerbils in the United States may be genetic, because all gerbils in captivity in the United States originated from a population of 20 pairs that were caught from the wild in 1935.[7]

TABLE 26.1 Physiologic Reference Values for Syrian Hamsters and Gerbils[a]

Parameter	Hamster	Gerbil
Average life span, months	18–36	36–48
Maximum reported life span, months	36[b]	60
Average male adult weight, g,	87–130[c]	80–130
Average female adult weight, g	95–130[c]	70–100
Heart rate, beats/min	310–471	260–600
Respiratory rate, breaths/min	38–110	85–160
Rectal temperature, °F (°C)	97–102 F (36–39 C)	97–102 F (36–39 C)
Approximate daily diet consumption g/kg/d	150	80–120
Approximate daily water consumption mL/kg/d	50–150	40–80
Recommended environmental temperature, °F (°C)	70–75 (21–24)	64–72 (18–22)
Recommended environmental relative humidity (%)	40–60	30–50
Total blood volume, mL/kg	65–80	60–85
Urine specific gravity	1.060	—

[a]Average reference values from data given in references 16, 21, 27 and 34. Note that the ranges should be considered as guides; values are likely to vary between groups of animals according to such variables as strain, age, sex, fasted, and methodology.
[b]Life span of Roborovski hamster, 18–24 months.
[c]Syrian hamsters

TABLE 26.2 Reproduction and Growth Reference Values for Hamsters and Gerbils[a]

Parameter	Hamster	Gerbil
Estrogen cycle length, days	4–5	4–7
Estrus (heat) duration, hours	8–26	12–18
Length of gestation, days	15–22	24–28
Pups per litter	4–12	1–12
Weight at birth, g	1.5–3	2.5–3.5
Eyes open, days	12–14	16–21
Ears open, days	4–5	5
Hair coat starts, days	9	6
Start to eat dry food, days	7–10	16
Optimal weaning age, days	19–21	21–28
Age of maturation of male, weeks	8	9–18
Age of maturation of female, weeks	6	9–12
Recommended minimum breeding age, weeks	8	10–14

[a]Average reference values from data given in references 16, 17, 31, 34. Note that the reference values may not represent the mean or range for certain populations or strains of animals; as a result, the values should be interpreted as approximations.

ANATOMY AND PHYSIOLOGY

The anatomy and physiology of hamsters and gerbils are similar to that of other small rodents of the suborder Myomorpha, as described for mice and rats (see Chapter 25), with some differences. The dental formula of hamsters and gerbils is I1/1, C0/0, P 0/0, M3/3. The cheek teeth are brachydont and only the incisor teeth are hyposdont and elodont (continuously growing). Normal physiologic, reproductive, and growth reference values are presented in Tables 26.1 and 26.2.

Hamsters

Hamsters are short-tailed, stocky rodents known for their abundance of loose skin. They have large, potentially reversible cheek pouches; these are paired muscular sacs extending as far back as the scapula. The pouches are evaginations of the oral mucosa and are used for transporting food, bedding material, and occasionally young. Hamsters have a distinct forestomach that, like a rumen, has a high pH and contains microorganisms. Hamsters possess four front toes and five hind toes. The long fur of the plantar surface of the toes is a peculiarity of Djungarian hamster, which lives in relatively cold areas in the wild. All hamsters have tails; the tail is very short in golden hamsters, longer in dwarf hamsters, and especially long in Chinese hamsters.

Syrian hamsters have distinctive hip or flank glands that should not be mistaken for skin tumors. These dark brown patches are found bilaterally along the lumbar area (Fig. 26.3A). They are poorly developed in the female, but in the mature male they are prominent and become wet and matted during sexual excitement. Dwarf hamsters (*Phodopus* species) have a midventral sebaceous gland (Fig. 26.3B). Djungarian hamsters also have scent glands at both corners of the mouth (Fig. 26.3C). Secretions from this gland play a role in territorial marking and mating behavior.

Female Syrian hamsters are typically larger than males and produce a copious, off-white vaginal discharge, normally just after ovulation (day 2 of the estrous cycle). These secretions should not be misinterpreted as indicating a bacterial infection of the genital tract. The females also have paired vaginal pouches that collect exfoliated cells and leukocytes. Djungarian hamster males are larger than females, and the females do not normally produce a vaginal discharge after ovulation.

Syrian hamsters, but not other hamster species, are permissive hibernators. Low environmental temperatures stimulate them to gather food. At temperatures of about 41–50°F (5–10 °C), they may curl up and enter a deep sleep.

Gerbils

Mongolian gerbils are rodents adapted to a desert environment.[30] They require very little water and produce only a small volume of concentrated urine. In their natural habitat, they can obtain most or all of their water requirements from metabolic processes and any available fruit or vegetable matter. Despite this remarkable natural ability, pet gerbils should always have access to fresh water.

Gerbils of both sexes have a distinct orange-tan oval area of alopecia on the midventral region referred to as the *ventral marking gland* or *pad* (Fig. 26.4). This structure is comprised of large sebaceous glands that are under the control of gonadal hormones. In the pubescent male, the gland starts to enlarge and produces an oily musk-scented secretion. Gerbils can often be seen rubbing their abdomens on objects; this is thought to be a form of territorial marking. Females have four pairs of nipples.

Gerbils have a long furred tail. If the tail is caught or grasped too firmly, the tail skin can slough as a natural escape mechanism.

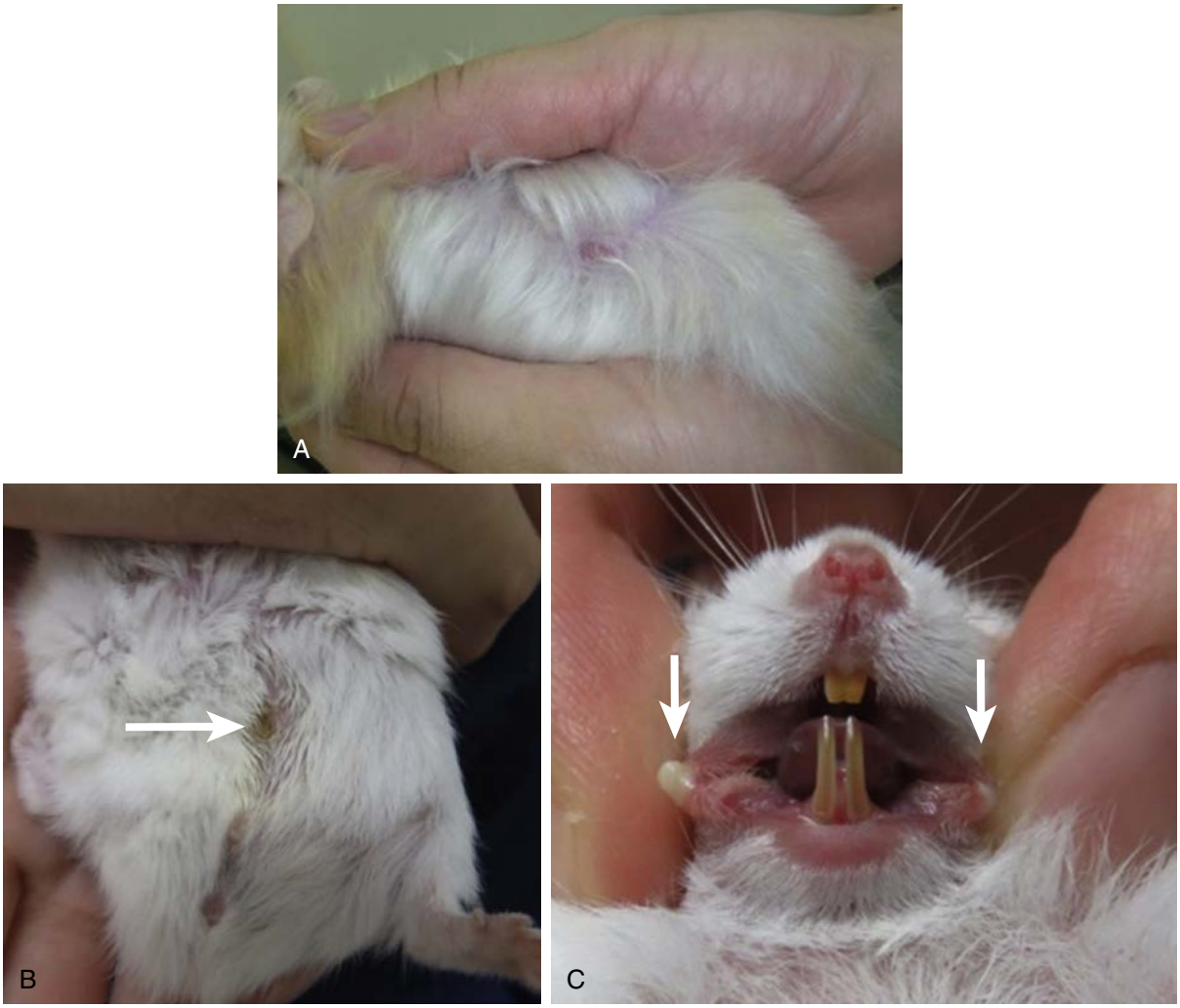


Fig. 26.3 Scent glands in hamsters. (A) Syrian hamsters have distinctive hip or flank glands. These dark brown patches are found bilaterally along the lumbar area. (B) Dwarf hamsters (*Phodopus* species) have a midventral sebaceous gland *(arrow)* and (C) scent glands at both corners of the mouth *(arrows)*.

HUSBANDRY AND DIET

The housing, bedding, diet, and enrichment of hamsters and gerbils is similar to that of other small rodents such as rats and mice (see Chapter 25), with a few differences. Syrian hamsters, especially females, are aggressive and are generally kept separately. Dwarf hamsters can be kept in groups, but they may fight occasionally. There are several cases reported of owners presenting anaphylactic symptoms such as respiratory distress after being bitten by their hamsters; warn owners of this rare but potential risk.[37]

Hamsters generally prefer bedding material more suitable as nest construction, and shavings are preferred over more granular material. In a study in Syrian hamsters that compared pine shavings, aspen shavings, corn cob, and wood pellets as bedding, all four bedding materials tested were deemed appropriate if short-term nesting material (e.g., paper towel) is added to the cage and if the litter is changed regularly.[36] Dust bathing is thought to be part of gerbils' normal grooming procedure. Sandboxes can be provided for gerbils in much the same way that they are for chinchillas.

Provide pet gerbils and hamsters with balanced commercial diets specific for the species. Pelleted diets are available (Oxbow Essentials Hamster and Gerbil Food, Oxbow Animal Heath, www.oxbowanimalhealth.com). Avoid generic seed mixes with small amounts of added pellets, because the animals will selectively consume the seeds and ignore the pellets. Gerbils have been used extensively in nutritional studies of dietary fat because of their sensitivity to high-fat, high-cholesterol diets with resultant changes in blood cholesterol levels.[10] Protein requirements vary from 14% to 17% in hamsters and up to 22% in gerbils.[30] Formulated diets for hamsters and gerbils should reflect these requirements.

RESTRAINT AND CLINICAL TECHNIQUES

In general, the handling and restraint, clinical techniques, and treatments used in hamsters and gerbils are the same as those for mice and rats (see Chapter 25), with some differences.

Restraint

Scruffing can be used for restraint of hamsters and gerbils (Fig. 26.5A). However, most hamsters and gerbils actively object to



Fig. 26.4 Gerbils of both sexes have a distinct orange-tan oval area of alopecia *(arrow)* on the midventral region referred to as the ventral marking gland or pad. The gland is androgen dependent, and therefore more prominent in males.

being scruffed, and scruffing also causes exopthalmos in hamsters. For relatively tame hamsters and gerbils, a better option is to use a small paper towel or tissue to grasp the animal around the back of the neck; then hold the rest of the body in the paper using the palm and other fingers. Using a paper towel or tissue when handling tame hamsters and gerbils can be helpful not only to avoid getting bitten but also to reduce stress of the patient and fear of human hands (Fig. 26.5B). The best holding technique for gerbils involves placing the palm of the hand over the gerbil's back and encircling the body with thumb and fingers (Fig. 26.5C). Gerbils will bite if they are not handled securely, despite the claim in many reviews that they rarely bite human handlers regardless of provocation. Do not grasp or hold gerbils by the tail, because this presents a risk of a degloving injury of the skin ("tail slip") (see below).

Before any sedation or anesthetic episode in a hamster, extract the food contents from the cheek pouches. Solid food such as seeds stored in the cheek pouches can be pushed from the posterior to the anterior side of the cheek pouch before gently squeezing the food out through the mouth. As in rats and mice, fractious or distressed hamsters and gerbils benefit from mild sedation for examination or diagnostic testing. Use techniques similar to rats and mice (see Chapters 25 and 37).

Clinical Techniques

Venipuncture of hamsters and gerbils follows the same guidelines as in mice and rats (see Chapter 25). As in other small rodents, venipuncture sites include the cranial vena cava, lateral saphenous and cephalic veins, and jugular vein. Venipuncture usually requires sedation or anesthesia, especially if accessing the cranial vena cava or jugular vein. In general, removal of a blood volume no more than 10% of the body weight is safe. Samples can be collected with small-gauge needles (25–28 gauge) with attached small syringes (1 mL or smaller) or with an insulin syringe. The cranial vena cava is the preferred venipuncture site of the authors (Fig. 26.6). The presence of a well-developed clavicle in the gerbil and hamster may complicate needle position. Collecting blood samples from the orbital plexus or by cardiac puncture is not recommended because of high complication rates and the availability of more suitable options.

In hamsters, administer subcutaneous injections, including fluids, over the middle body or more caudally (do not administer too cranially or laterally) to ensure that the injection is not accidentally given into the cheek pouches, which extends over both shoulders. As in other rodents, compounding oral medications with sweet bases often increases compliance. However, in hamsters especially, sugar should be avoided because this can cause gastrointestinal bacterial overgrowth. Reference values for hematologic testing and biochemical analysis are given in Tables 26.3 and 26.4.

COMMON DISEASES OF HAMSTERS

Gastrointestinal System

Oral cavity

Incisor malocclusion is often seen in hamsters, and the clinical signs include a change in preference of food, anorexia, loss of weight, rough hair-coat, and ptyalism. Often the owners may not notice any clinical signs, and malocclusion is found incidentally during physical examination. Inspect the incisor teeth and examine the oral cavity of a hamster by restraining the animal appropriately and pulling the skin of the cheek to both sides. Use cotton swabs or mosquito forceps to facilitate examination of the buccal aspects of the cheek pouches. Trim elongated incisors with a dental diamond disc cutter or reduce the length with a dental burr; regular trimming of every 2 to 3 weeks may be necessary. The distensible cheek pouches of hamsters sometimes are mistaken for lesions by owners.[5]

Cheek pouch impaction is not uncommon; a radiograph of the skull often shows the extent of the impaction. When this occurs, use fine forceps or cotton swabs to remove the impacted material if necessary. Determine whether predisposing causes of impaction are present, such as infection or malocclusion. If the contents cannot be removed easily or if a lesion is present (e.g., infection or inflammation) in the cheek pouch, anesthetize the hamster to extract the contents and collect samples for bacterial culture or cytologic examination. Clean the cheek pouch with saline solution or a chlorhexidine oral rinse, then administer systemic antibiotics and antiinflammatory agents as needed.

Everted cheek pouches are often seen. Incidence appears higher in Djungarian hamsters than in Syrian hamsters (Fig. 26.7A). Cheek pouches can evert when a hamster forces the contents (e.g., usually sticky or impacted material) out of the pouch. Other causes of everted cheek pouch are inflammation, neoplasia, or abscess; therefore perform a thorough examination in these cases. Consider biopsy if swelling is present. If the prolapse is acute or if the inflammation is mild, clean the tissue, reposition the cheek pouch with cotton swabs, and observe the hamster to see if the eversion reoccurs.

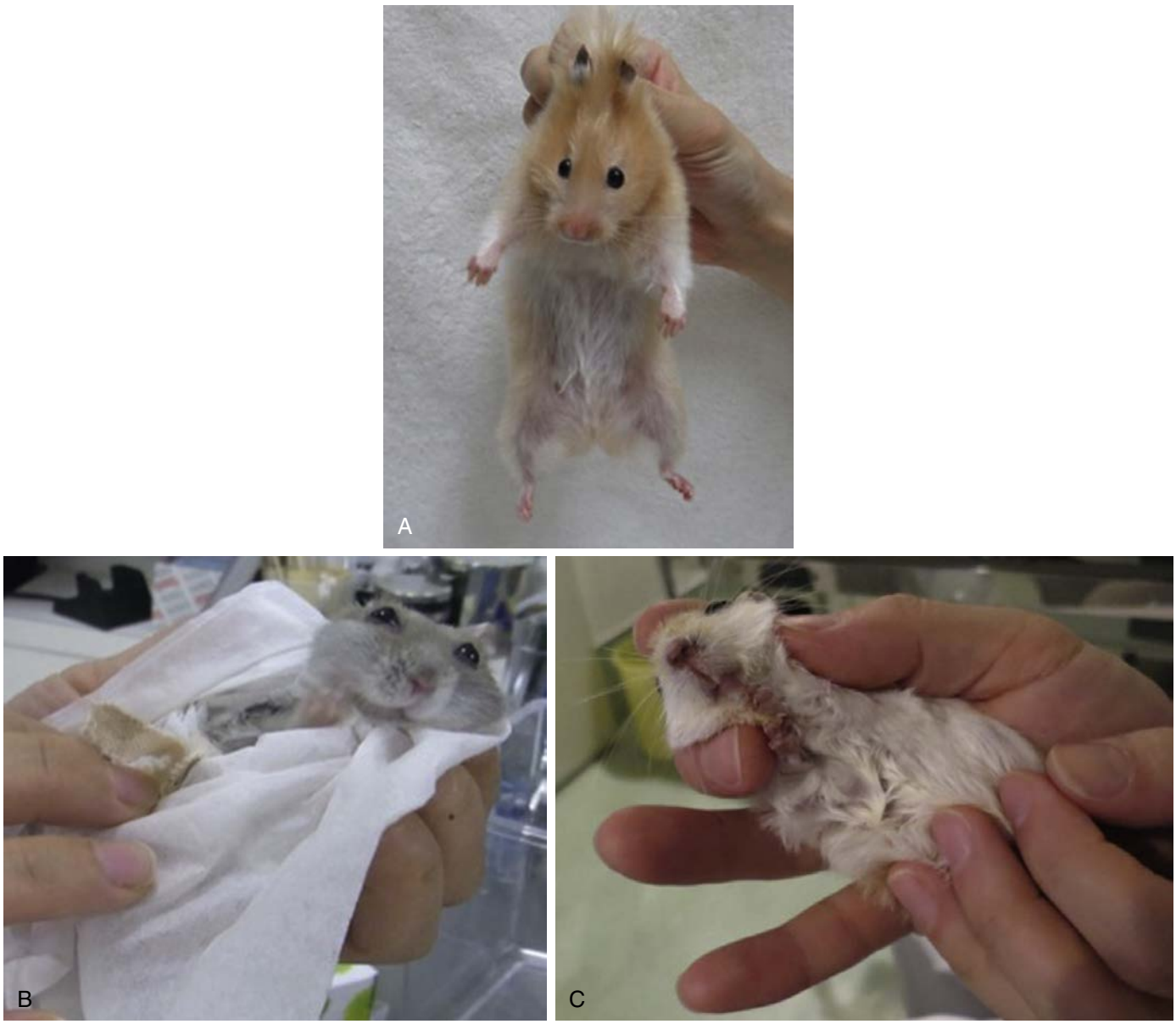


Fig. 26.5 (A) To scruff a hamster, grasp generous amounts of loose skin from the lateral aspects of the neck and over the shoulders with thumb and forefinger. (B) Restraining the animal with tissue papers or small towels can be helpful not only to avoid getting bitten but also to avoid them being afraid of human hands. (C) For gerbils, place the palm of the hand over the gerbil's back and encircle the body with thumb and fingers.

If the pouch everts repeatedly, use one or two sutures of monofilament nonabsorbable 5-0 suture material to suture the cheek pouch transcutaneously to the skin (Fig. 26.7B). If severe inflammation or edema is present, use hypertonic dextrose solution to try to reduce the edema before repositioning. Remove the sutures 5 to 10 days later. Inform the owner to avoid feeding sticky foods such as rice to prevent recurrence. If severe inflammation or necrosis is present in the cheek pouch, surgical excision of these lesions may be necessary. One author (Y.M.) has seen several cases of cheek pouch and salivary gland tumors present as mass lesions on the cheeks.

Enteric diseases

Enteropathies are among the most common problems in pet hamsters. Diarrhea can occur in hamsters of any age and is known as "wet-tail," although this euphemism is frequently used to describe the disease in young hamsters. Proliferative ileitis is the most significant intestinal disease of 3- to 10-week-old hamsters and results in a high mortality rate. This is caused by *Lawsonia intracellularis,* an intracellular bacterium that is also responsible for proliferative enteropathy in pigs.[46] Research studies have shown that strains of *Lawsonia* from pigs, ferrets, and hamsters are genetically similar.[11] Experimentally infected hamsters have significantly lower intestinal absorption of glucose, potassium, and chloride.[61] This malabsorption is the main mechanism involved in the physiopathology of diarrhea caused by *L. intracellular*. In suspect cases, treatment must be aggressive and involves correcting life-threatening electrolyte imbalances, administering antibiotics, and force-feeding. Several antibiotic treatments are recommended, such as tetracycline (400



Fig. 26.6 Collecting a blood sample from the vena cava in a golden hamster.

TABLE 26.3 Hematologic Data for Hamsters and Gerbils

Value	Hamster[a]	Gerbil[b]
Hematocrit, %	45–52	41–52
Hemoglobin, g/dL	15.2–17.4	12.1–16.9
Red blood cells, × 10^6/μL	6.5–7.5	7.0–10.0
White blood cells, × 10^3/μL	6.3–8.9	4.3–21.6
Neutrophils, %	16–26	5–34
Lymphocytes, %	65–80	60-95
Monocytes, %	0–4	0–3
Eosinophils, %	0–2	0–4
Basophils, %	0–2	0–1
Platelets, × 10^3/μL	300–570	400–600
Mean corpuscular volume, fL	68–74	—
Mean corpuscular hemoglobin, g/dL	19–24	—
Mean corpuscular hemoglobin concentration, g/dL	30–34	—

[a]Data courtesy of Carolyn Cray, PhD, University of Miami Miller School of Medicine. Automated analyzer for cell counts, hemoglobin, and hematocrit. Differential white blood cell count based on 100-cell count using blood smear made at the time of sample acquisition.
[b]Average values from data given in references 16 and 22. Note that reference values may not represent the range for certain populations or strains of animals; for this reason, the values should be interpreted as approximations.

mg/L of drinking water for 10 days or 10 mg/kg by mouth [PO] every 12 hours for 5–7 days), enrofloxacin (10 mg/kg PO or intramuscularly every 12 hours for 5–7 days), or trimethoprim-sulfa (30 mg/kg PO every 12 hours for 5–7 days). If diarrhea persists, treat symptomatically with bismuth subsalicylate and administer replacement electrolyte and glucose oral solutions and supplemental parenteral crystalloid fluids (10 mL/100 g subcutaneously [SC] every 24 hours). Definitive diagnosis often depends on necropsy and histologic examination, although fecal polymerase chain reaction (PCR) assays have been developed.[46] Sequelae to proliferative ileitis in surviving hamsters can include intestinal obstruction, intussusception, or rectal prolapse (Fig. 26.8).[13]

TABLE 26.4 Biochemical Data for Hamsters and Gerbils[a]

Analyte	Hamsters[b] (n = 50)	Gerbils[c] (n = 30)
Albumin, g/dL	3.5–4.9	2.5 (2.1–2.9)
Alanine aminotransferase, U/L	22–128	91 (56–165)
Alkaline phosphatase, U/L	99–186	118 (70–182)
Bilirubin total, mg/dL	0.1–0.7	—
Blood urea nitrogen, mg/dL	12–26	18 (11–32)
Calcium, mg/dL	5.3–12.0	—
Creatinine, mg/dL	0.4–1.0	0.3 (0.2–0.7)
Creatine kinase, U/L	—	363 (93–752)
Glucose, mg/dL	37–198	91 (24–117)
Phosphorous, mg/dL	3.0–9.9	—
Protein, total, g/dL	5.2–7.0	5.6 (4.6–6.3)

[a]Data courtesy of Carolyn Cray, PhD, University of Miami Miller School of Medicine. Values are given as means, reference intervals, or both. Samples are mixed plasma and serum.
[b]Ortho (Kodak Ektachem) 700 XR.
[c]Ortho Vitros 250 Analyzer.

Diarrhea in adult hamsters is associated with *Clostridium difficile* enterotoxemia. Suppression of normal enteric flora with resulting clostridial overgrowth and enterotoxemia can develop 3 to 5 days after the oral administration of antibiotics such as penicillin, lincomycin, cephalosporins, or bacitracin.[24] Detection of *C. difficile* by PCR assay is highly sensitive and can discriminate between toxigenic and nontoxigenic strains of the organism by detecting its toxin-producing genes. Oral administration of bovine antibodies against toxigenic *C. difficile* has been shown to protect hamsters against experimental antibiotic-associated enterotoxemia.[39] Antibiotic-associated enterotoxemia usually results from administration of antibiotics that have primarily a gram-positive spectrum; however, in any hamster that develops diarrhea after starting antibiotic therapy, immediately stop administration of all antibiotics and provide supportive treatment. The prognosis is guarded to poor in these cases.

Tyzzer's disease caused by *Clostridium piliforme* occurs in hamsters and gerbils. In an outbreak described in animals obtained from pet store suppliers,[43] there was a high mortality rate in hamsters and gerbils but not in rats and mice. Affected rodents appeared depressed and dehydrated, with scruffy coats and diarrhea; many animals had no clinical signs before death. Clinical outbreaks appear to be precipitated by severe stress, such as overcrowding, high environmental temperature and humidity, heavy internal and external parasite load, and nutritionally inadequate diets, illustrating the opportunistic nature of *C. piliforme* in immunosuppressed animals. The disease usually is not seen in healthy, immunocompetent animals. Tyzzer's disease is frequently listed as an intestinal disease of rodents and other animals in laboratory animal textbooks. However, the current true prevalence of infection in pet rodents is unknown.

Soft feces and diarrhea due to various causes are seen at all ages in hamsters and can develop from a sudden change of diet,

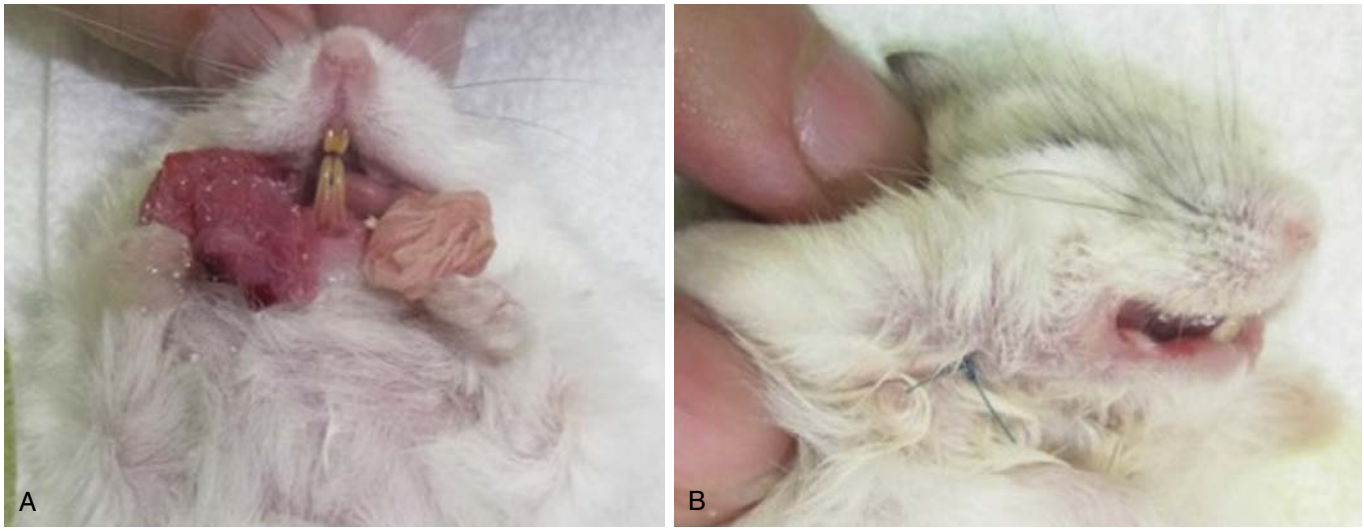


Fig. 26.7 (A) Everted cheek pouch in a hamster. (B) Monofilament nonabsorbable 5-0 suture material can be used to suture the cheek pouch transcutaneously to the skin with 1–2 sutures.

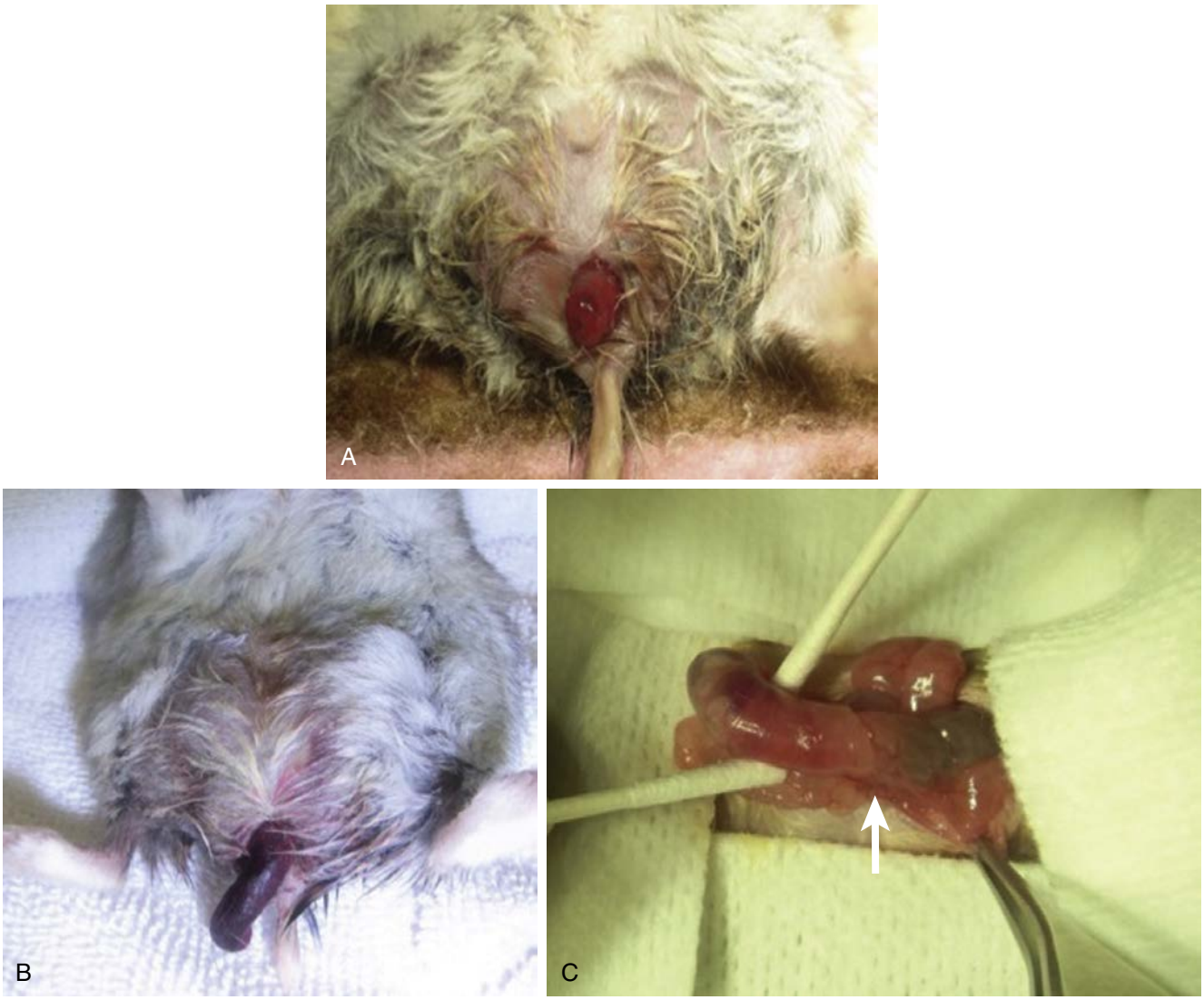


Fig. 26.8 (A) Rectal prolapse in a hamster. (B) Larger prolapse due to intussuception. (C) Note the intussusception of small intestine (↑).

feeding excess, high water–content foods such as vegetables and fruits, or spoiled food. In these cases, supportive care with probiotics, correcting the diet, and antibiotics will often be helpful. Hamsters kept in dirty environmental conditions such as soiled bedding or dirty cage components commonly present with periodic episodes of soft feces or diarrhea and inguinal and dermal lesions. Initially, no other symptoms may be present, but in more chronic cases, weight loss, hair-coat roughness, and general poor body condition may be seen. Aggressive supportive care such as parenteral fluid administration and thermal support in addition to the primary treatment may be needed in these cases.

Numerous protozoa can be identified on fecal examination of hamsters with soft feces or diarrhea. Whether these protozoa are the cause of the gastrointestinal symptoms or secondary is unknown; however, clinical signs often can be ameliorated by administering antiprotozoal agents. Therefore, if soft feces or diarrhea does not improve with supportive care, administer antiprotozoal agents such as metronidazole (see Formulary). Gastrointestinal parasites other than protozoa, such as cestodes, pinworms, and nematodes, are sometimes identified, and treatment is similar as in other small mammals. Some parasites in hamsters (e.g., *Hymenolepis nana*) are potentially zoonotic.

Rectal prolapse can be caused by severe diarrhea secondary to proliferative ileitis and prolonged tenesmus, among other causes. In hamsters where the prolapse is limited to the rectum (Fig. 26.8A), use a lubed small cotton swab to reposition the prolapsed tissue back into the rectum. After successful repositioning of the prolapse, place a purse-string suture to prevent recurrence. Make sure to check that the hamster can defecate normally after placing the purse-string suture. Remove the sutures after 3 to 7 days. In cases where a large section of the intestine is prolapsed (Fig. 26.8B), likely an intussusception has occurred in the abdominal cavity (Fig. 26.8C). Perform diagnostic imaging to accurately diagnose an intussusception or a foreign body. Alternatively, perform an exploratory laparotomy to investigate the cause of the rectal prolapse. If an intussusception is present, the treatment is often to resect the necrotic region, perform an end-to-end anastomosis, and perform a colpopexy to prevent a recurrence. Prognosis is poor in cases with intussusception; prognosis is better in cases with mild rectal prolapse that is quickly corrected.

Other diseases

Weight loss is seen in older hamsters and is often associated with hepatic and renal amyloidosis. In one report, amyloidosis was described in 88% of hamsters over 18 months of age.[19] Amyloidosis is the principal cause of death in hamsters in long-term research studies, and female hamsters have a higher incidence, increased severity, and earlier age of onset than do males.[53] In laboratory hamsters, social stress induced by crowding is correlated with amyloidosis.[18] Because overcrowding is uncommon with pet hamsters, clinical disease is not described, and the incidence may be low. However, edema and ascites caused by hypoproteinemia of hepatic and renal origin would be expected. Prognosis is poor, and treatment is supportive.

Hepatic cysts, which are thin-walled and of varying sizes, are occasionally found in the liver of hamsters (Fig. 26.9).



Fig. 26.9 Hepatic cyst in a Syrian hamster.

Initially, affected hamsters show no clinical signs, but as the cysts enlarge, animals may show abdominal enlargement, diffuse alopecia, dyspnea, decrease in activity, and wasting.[58] The cysts are often found on abdominal palpation, radiographic or ultrasonographic examination, or laparotomy. Grossly cysts protrude from the liver surface and contain a clear serous fluid. Hepatic parenchyma surrounding the cysts often shows pressure atrophy, necrosis, engorged sinusoids, hemorrhage, mild to extensive fatty or vacuolar degenerative changes, and occasionally proliferation of biliary ducts.[58] Hepatic cysts can slowly enlarge to occupy most of the abdominal cavity. Affected animals are generally over 2 years of age, and cystic proliferations may be found in other abdominal organs. The lesions are caused by developmental defects of the bile duct. Treatment for hepatic cysts is surgical excision; cysts confined to one lobe can be resected completely. In some animals that have cysts on multiple liver lobes or when surgical resection is not applicable, aspiration of cyst contents may alleviate the symptoms temporarily, but fluid will often reaccumulate. To aspirate cysts, use a 25-gauge needle or butterfly catheter and syringe to aspirate percutaneously with ultrasound guidance or while directly visualizing the cyst during surgery. Hepatic tumors are rare, but neoplasia such as biliary cystadenocarcinoma can be seen.

Urinary System

Normal hamster urine is yellow and cloudy and has a pH of around 8. Crystals such as struvite normally can be seen during urinalysis. Hematuria as a clinical sign can be seen in cases of cystitis, urinary calculi, or tumors of the urinary system. Because the urethra and the vagina have separate openings in all female rodents, bleeding can be distinguished as coming from either the urinary or the genital system by careful observation. Clinical signs such as pollakiuria, urinary scald, hematuria, and pyuria can be seen in cystitis. Often bacteria and white blood cells that show phagocytosis can be seen on urinalysis in these

cases. For treatment of cystitis, administer systemic antibiotics based on culture and sensitivity testing if possible.

Surgical removal of the urinary calculi may be indicated if there is urodynia (pain accompanying urination), urinary scald, or pollakiuria or dysuria, although it is rare. The cause of urolithiasis in hamsters is unclear. With hamsters that are presented with a history of urolithiasis, provide ample water (e.g., give vegetables or soak pellets in water) to try to prevent recurrence if subclinical dehydration is suspected as a risk factor.

Renal failure often can be seen in hamsters, especially in cases with renal amyloidosis.[8] However, determining and monitoring renal function by blood test results is difficult in these animals because blood sampling generally requires anesthesia. Therefore renal failure is often suspected based on clinical signs or findings on physical examination. Prognosis is poor with renal failure. Although it appears to be rare, one author (Y.M.) has seen renal tumors in four cases, all in Djungarian hamsters.

Reproductive System

Female Syrian hamsters have a 4-day estrous cycle characterized by a copious postovulatory discharge at the end of the cycle. The discharge is creamy white and has an acrid odor. Its stringy nature is distinctive; if touched, it can be drawn out as a long thread. Owners often describe the discharge as pus and mistakenly believe it to be abnormal.

Pyometra has been observed clinically, although rarely, in pet hamsters. The most common clinical signs are abdominal distension and vaginal discharge or hemorrhage. One author (Y.M.) has seen endometrial hyperplasia, endometritis, endometrial adenocarcinoma, endometrial adenoma, and uterine leiomyoma and rhabdomyosarcoma; these diseases were primarily seen in Syrian hamsters. Ovarian diseases that have been seen include follicular cysts, granulosa cell tumors, and theca cell tumors. Nonspecific clinical signs such as anorexia and lethargy may be the chief complaint. If ovarian or uterine disease is present, an abdominal mass is sometimes palpated. A tentative diagnosis is made by ultrasound examination of the abdomen; ovariohysterectomy is the treatment of choice. If a uterine or ovarian disease is suspected but cannot be confirmed, perform exploratory laparotomy to remove the reproductive tract. If the hamster otherwise is in relatively good condition (without severe anemia, sepsis, emaciation, or metastasis/dissemination of tumors), the prognosis is good. Mammary gland tumors are sometimes seen in hamsters (especially Djungarian hamsters), with a high incidence of mammary adenocarcinoma. In male hamsters, reproductive diseases are limited to tumors and inflammation of testis and accessory genital organs, which are rarely seen.

Cannibalism of the young accounts for about 95% of all preweaning mortality in group-housed laboratory female hamsters.[49] Other factors such as cold ambient temperatures (below 50°F [10°C]), lean diets, and low body weight (especially during pregnancy) appear to increase cannibalism.[54,55] To prevent this, instruct owners to give the mother ample food and water and to provide a quiet, warm nesting place for at least 1 week, or preferably 2 weeks. Disturbing the mother by handling the young or nest and not providing adequate nesting material, warmth, food, or water often results in the desertion of the litter and cannibalism. If a baby falls out of the nest or cannot go back to the nest and is not retrieved by the mother, use a utensil such as a plastic spoon to pick up the baby and replace it, so as not to impart a human odor on its body.

Respiratory System

Pneumonia has been reported as a common clinical condition in laboratory hamsters.[38,49] Histologic evidence of bronchopneumonia resembling bacterial pneumonia and interstitial pneumonia resembling viral pneumonia has been described, but there are no reports of observed clinical cases. Consequently, other authors have stated that respiratory disease is uncommon in hamsters.[23] The true prevalence remains to be established. Definitive diagnosis of pulmonary diseases in hamsters is difficult, and an important differential diagnosis is cardiomyopathy. Therefore diagnostic imaging and ultrasonography are important diagnostic tools.

In the authors' experience, respiratory diseases are occasionally seen in hamsters. Respiratory signs such as nasal sounds, dyspnea, and sneezing, as well as a decrease in activity and exercise intolerance, are sometimes seen. Incidence appears higher in Djungarian than in Syrian hamsters, whereas the incidence of cardiac disease and secondary respiratory distress appears higher in Syrian hamsters. Upper respiratory abnormalities (nasal cavity, etc.) are occasionally found in dyspneic Djungarian hamsters, but thoracic (lung and heart) abnormalities are rarely found on radiographic examination.

Purulent rhinitis associated with pneumonia and gluey eyelids has been described in hamsters and is associated with a poor prognosis. Children may inadvertently transmit bacterial pneumonia, especially that caused by *Streptococcus* species, to pet hamsters. Rapid diagnosis is based on identifying the characteristic gram-positive diplococci on a Gram stain of nasal and ocular discharges. Treatment with a broad-spectrum antibiotic such as trimethoprim sulfa or enrofloxacin is recommended until antibiotic sensitivity results are available. Hamsters exhibiting sneezing and nasal discharge often have stained fur around the nasal area and eyes due to nasal and ocular discharge. The nostrils may become irritated because of the nasal discharge or constant rubbing. In severe cases, lower respiratory tract signs due to pneumonia are seen, such as decreased activity, lethargy, and dyspnea. Affected animals show a rough hair coat and squinted eyes. Lower respiratory tract diseases can be diagnosed by radiography; however, detailed evaluation is often difficult with small hamsters except in severely affected animals with severe pulmonary edema, pleural effusion, or an enlarged cardiac silhouette (Fig. 26.10). Computed tomography is a potential diagnostic option to enable better evaluation of these conditions. In animals showing clinical signs, collect samples from nasal discharge for bacterial culture and sensitivity testing as needed.

For animals with suspected infectious disease, administer antibiotics either systemically orally or by nebulizer, or both. For chronic or severe cases with upper respiratory disease and pneumonia, nebulization therapy one to two times a day has shown good results for one author (Y.M.). Keep in mind to provide appropriate thermal support to avoid hypothermia during the nebulization because the animal will get wet. Regular



Fig. 26.10 Radiograph of a Syrian hamster shows cardiac enlargement and increased radiopacities of the lungs.



Fig. 26.11 Atrial thrombosis *(arrow)* in a Syrian hamster.

monitoring and oxygen administration during nebulization treatment are important in severely dyspneic patients.

Allergies, such as to bedding or strong aromas, are sometimes suspected to be the cause for sneezing. Allergy to beddings can be seen with conifer chip bedding; other clinical manifestations are erythema of the periorbital area, limbs, and lower abdomen. For suspect cases of allergic rhinitis, change the bedding to a less irritant, more absorbent material to reduce ammonia odor and improve sanitation.

Cardiovascular System

Atrial thrombosis has been described in aging research hamsters by many authors. In certain strains, it occurs with a high incidence (up to 73%).[52] Most thromboses develop in the left atrium secondary to heart failure and lead to a consumptive coagulopathy (Fig. 26.11). Although the incidence does not differ by sex in geriatric animals, atrial thrombosis occurs at a younger age in females (13.5 months) than in males (21.5 months).[66] Aged pet hamsters present with clinical signs of cardiomyopathy such as hyperpnea, tachycardia, and cyanosis. In untreated hamsters, death usually follows within a week after these signs become evident. The incidence of atrial thrombosis is influenced by the endocrine status of the animal and especially by the amount of circulating androgen. Castrating male hamsters is linked to an increase in the prevalence of atrial thrombosis.[56]

Cardiomyopathy should be suspected in aged pet hamsters (older than 1.5 years) that present clinically with signs of tachypnea, lethargy, anorexia, peripheral edema, and cold extremities.[52] In one author's experience (Y.M.), most cases are Syrian hamsters presenting with dilated cardiomyopathy. Diagnosis of cardiomyopathy in hamsters is based on clinical signs and results of radiography and ultrasound examination of the heart (see Fig. 26.10). Treatment of heart disease is symptomatic and involves the empiric use of pimobendan (0.2–0.6 mg/kg PO every 12 hours), furosemide (1–4 mg/kg PO every 8–24 hours), angiotensin-converting enzyme inhibitors, and prophylactic anticoagulants. Verapamil, a calcium antagonist, administered at a dose increasing from 0.25 mg to 0.50 mg given SC every 8 hours over 4 weeks, prevented severe myocardial lesions in untreated 2-month-old inbred female myopathic hamsters.[33]

Endocrine System

Surveys of spontaneous lesions in laboratory hamsters describe a high incidence of adrenocortical hyperplasia and adenoma.[53] However, despite extensive histopathologic study, hyperadrenocorticism or Cushing's disease has been reported in only four hamsters, with high serum cortisol concentrations documented in only one of the four.[2,40] Hamsters with clinical signs resembling those of Cushing's disease are occasionally seen in practice. Diagnosis is based on identifying classic signs similar to those seen in dogs, such as a history of polydipsia, polyuria, and polyphagia; clinical signs of alopecia and hyperpigmentation; and high concentrations of plasma cortisol and serum alkaline phosphatase. Normal hamster cortisol concentrations are low compared with those of other species and range from 0.5 to 1.0 µg/dL in normal males and females.[65] Hamsters may secrete both cortisol and corticosterone[45]; therefore meaningful measurement of plasma cortisol concentrations is empiric at present. If hyperadrenocorticism is suspected, the cause—such as hypersecretion by a functional tumor, primary adrenal hyperplasia, or excess adrenocorticotropic hormone production—is often more difficult to determine. Hamsters respond to exogenous adrenocorticotropic hormone stimulation.[65] In reported cases, treatment with both ketoconazole (5 mg/kg every 12 hours for 1 month) and mitotane (5 mg PO every 24 hours for 1 month) were ineffective, and metyrapone (8 mg PO every 24 hours for 1 month) was effective in one of two hamsters.

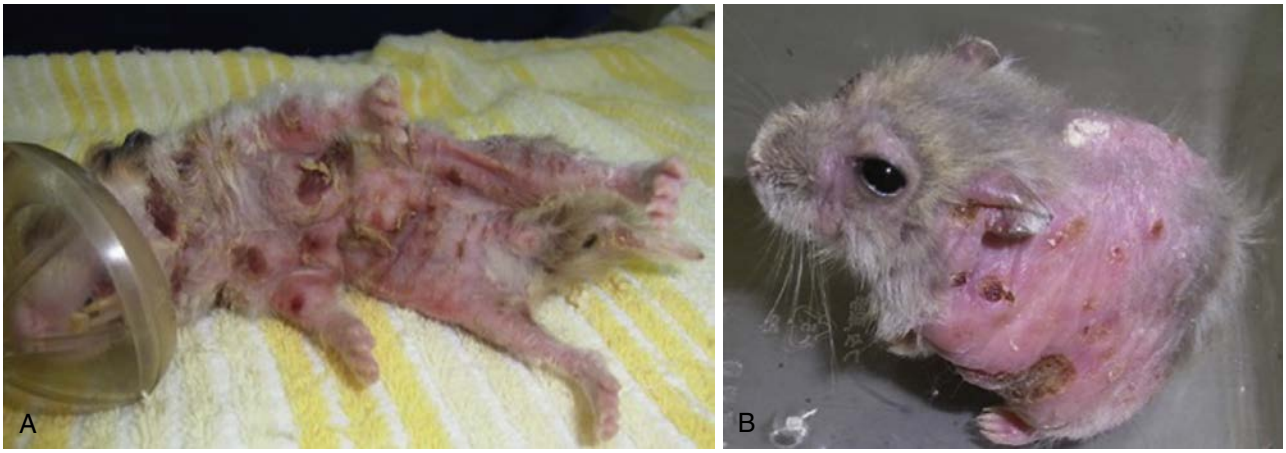


Fig. 26.12 Cutaneous lymphoma confirmed by histopathologic examination in a (A) Syrian hamster and (B) a Djungarian hamster. Cutaneous lymphoma is seen more commonly in Syrian hamsters.

Integumentary System

The most common skin problem seen in Syrian hamsters is a rough hair coat. This is a nonspecific sign of fighting, aging, or a variety of diseases. The length of hair in the long-haired teddy bear Syrian hamster is influenced by testosterone. Males from the age of sexual maturity have significantly longer hair than females or castrated males, which display fluffy, shorter hair.[51]

Melanomas are frequently reported in Syrian hamsters, not only of the flank glands but also of the skin. There is a striking 10:1 male/female melanoma ratio.[60]

Djungarian hamsters show a high prevalence of neoplastic disease (five times greater than Syrian hamsters), and most tumors are integumentary (e.g., mammary tumors, atypical fibromas, and papillomas).[32] Masses on the body surface of hamsters can be neoplasia, abscesses, or ventral hernias. The causes of a ventral hernia can be congenital or due to bites from cagemates.

Cutaneous abnormalities such as alopecia, eschar, and pruritus are often caused by bacterial or fungal infection or parasites, similar to other pet animals. Bacterial pseudomycetoma has been described in several dwarf hamsters; treatment is excision.[15] Fur mites are described as ectoparasites of hamsters.[42] *Acarus farris* is found in Syrian hamsters and identified by skin scrapes. *Demodex criceti* and *Demodex aurati* also occur in hamsters. Infestation manifests with immunosuppression or secondary to other cutaneous diseases. Clinical signs are similar to those in other species. For treatment, consider use of ivermectin, selemectin, or lime sulfer dip (see Formulary for dosages). Use of 0.017% coumaphos and medicated bath in 0.013% amitraz was reported as sucessful in one case.[26]

Cases of nonpruritic symmetric alopecia associated with adrenal disease are reported,[2,65] and there are some cases in which those diseases are suspected, but antemortem diagnosis is difficult. Alopecia of the snout is seen due to sticking the nose out of the cage and continuously biting the cage.

Lymphoma

Lymphoma is the most common neoplasm in hamsters, particularly in Syrian hamsters. Clinicians see three variations of lymphoma. Cutaneous lymphoma is frequently seen in adult hamsters and resembles mycosis fungoides, an epitheliotropic T-cell lymphoma in people (Fig. 26.12).[25] Lethargy, anorexia, weight loss, patchy alopecia, and exfoliative erythroderma are seen in affected animals. On histopathologic examination, dense infiltrates of neoplastic lymphocytes are present in the dermis with extension into the epidermis. To date, no cases of cutaneous lymphoma have been reported in Djungarian hamsters, although cases have been seen by one author (Y.M.). A second variation is seen in aged hamsters and is the most frequently observed neoplasm of the hematopoietic system.[32] These tumors are often multicentric and involve the thymus, thoracic lymph nodes, mesenteric lymph nodes, superficial lymph nodes, spleen, liver, and other sites. The third variation is epizootic lymphoma in young hamsters, caused by hamster polyomavirus (HaPV).[1] When HaPV is first introduced into a naive population of breeding hamsters, it can result in epizootics of lymphoma, with an incidence as high as 80% among animals. Once the viruse is enzootic in a hamster population, the occurrence of lymphoma declines to a much lower level, and infected hamsters develop HaPV skin tumors rather than lymphoma. Hamsters with HaPV lymphoma appear thin, often with palpable masses in their abdomens. Tumors associated with HaPV often arise in the mesentery but can also arise in the axillary and cervical lymph nodes. The tumors are often lymphoid, but erythroblastic, reticulosarcomatous, and myeloid types occur.

Base a diagnosis of lymphoma on the history, clinical findings, and results of diagnostic testing. If enlarged lymph nodes are noted, perform a fine-needle aspiration for cytologic examination. Cutaneous lymphoma is best diagnosed by a full-thickness skin biopsy. For treatment, prednisolone (1–2 mg/kg PO every 12–24 hours) may result in a short period of remission. There are no detailed reports regarding other chemotherapy. One author (Y.M.) has administered L-asparaginase (10,000 U/m^2 or 400U/kg SC) to affected hamsters with no adverse effects but only limited beneficial effects.

Although no clinical data are available regarding whole-body radiation for hamsters, it has been shown that hamsters are

considered the most radioresistant of all the small laboratory animals.[12] The LD50 regarding whole body radiation was determined to be significantly longer than for other species in experimental trials. The Syrian hamster showed an LD 50(40) at 611 rads whereas the Chinese hamster had an LD 50(40) at 856 rads (for males) and 816 rads (for females).[12] This is an important finding when considering whole-body radiation for lymphoma or leukemia.

Musculoskeletal System

Bone fractures are common in hamsters. Many of the fractures occur on the hind limbs, with most involving the lower leg (i.e., tibia). The most common cause of fractures is entrapment of a limb in the wires of the cage or wheels or getting stepped on by the owner. Some hamsters with a fracture show lameness and bite their injured limb, but many explore their environment actively with no evidence of abnormality other than a dangling limb on presentation. In cases of hamsters being dropped or stepped on, hind-limb paralysis can be evident due to fracture or dislocation of a vertebrae in addition to a fracture of the limbs. Open fractures are most common; therefore examine the skin thoroughly if there is evidence of a penetrating trauma. In trauma cases, obtain whole-body radiographs to scan for any other fractures or lesions in the body cavity and the exact position of the fracture.

In cases of femur fractures or other fractures with surrounding soft tissue swelling that limits mobility, the bone may heal with cage rest alone. However, with lower limb fractures, nonunion, necrosis of the skin, or infection can develop because of excess mobility and further trauma. External coaptation sometimes can be applied with tape or adhesive bandage (Fig. 26.13). For surgical repair, 25- or 27-gauge needles can be used as intramedullary pins or external fixation. Remove the pins after confirming bone healing with radiographs; intramedullary pins can be left in place if there is no problem after healing. In many cases, an Elizabethan collar is needed after surgical repair to prevent self-mutilation. However, hamsters often bite the external coaptation or external fixation devices and feel severe stress from Elizabethan collars. Oral sedation with benzodiazepines may be helpful to reduce the stress behavior of the patient. Intramedullary pins cause minimal stress compared with external coaptation or fixation. Cases with severe self-mutilation of the lesion, open fractures, or a poor outcome after external coaptation or surgery or cases that are presented a long time after injury may require amputation of the injured limb. Some owners choose amputation initially because of the difficulty of management at home, need for repeat veterinary visits, or economic constraints. Therefore good client education is needed to choose the treatment plan for fractures in hamsters and inform the client of the high risk of complications. Include information not only on the risks of anesthesia and surgery but also postoperative management and problems and the possibility that amputation ultimately may be necessary.

One author (Y.M.) has seen several cases of osteosarcoma on the limbs of hamsters. A recent paper documented an osteosarcoma on the scapula of a Chinese hamster.[14] At this time, amputation is the first choice of treatment in most cases. Hamsters adapt well to amputation of one limb. Change the cage after amputation to accommodate the hamster, for example, from two levels to one level or from a complex cage to a simple and barrier-free structure, and remove any wheels to avoid secondary injuries during exercise.



Fig. 26.13 Use of a tape splint in a hamster to provide external coaptation of a tibial fracture.

Ocular System

Hamsters have a shallow eye socket and well-developed orbital sinus.[68] Exophthalmos is commonly seen in hamsters and usually occurs because of ocular infection, trauma to the periorbital area, or if scruffed tightly at the back of the head during restraint (Fig. 26.2). Obese hamsters are more prone to exophthalmos. Hamsters with sialodacryoadenitis may develop keratoconjunctivitis sicca and exophthalmos and subsequent proptosis. Exophthalmos associated with restraint is usually reversed once restraint is stopped. For exophthalmos from other causes, the prognosis for saving the eye is good if the hamster is treated soon after exophthalmos occurs. Cleanse the ocular area gently with an ophthalmic wash and lubricate the eye with sterile ophthalmic lubricant. Gently retract the lid margins around the globe until the eye returns to its normal position. If exophthalmos has been present for a prolonged period, treat the eye with an antibiotic ophthalmic ointment for a minimum of 7 to 10 days. Occasionally, tarsorrhaphy will be needed to prevent recurrence. Rinse the exposed tissues carefully with eye flush, replace the globe into the socket as soon as possible, and do a tarsorrhaphy with one to two sutures to prevent repetitive proptosis. Damage to the optic nerve due to excessive pull can result in permanent blindness. Administer antibiotics systemically as needed, and apply topical antibiotics as well as lubricants to the eye for 7 to 14 days. Remove the sutures after 4 to 7 days. Enucleation is indicated in cases with severe trauma of the eyeball, severe infection, or other causes of proptosis such as orbital abscess or tumor.

Meibomian gland inflammation is common in hamsters and presents as a small, round, white mass on the eyelid. Lacrimation or ocular discharge may be seen if the mass causes corneal irritation or difficulty in closing the eye. Treat this lesion by incising the swelling with a bent 25-gauge needle, and then compressing

the gland with forceps or small needle holders to remove exudate. Apply antibiotic eye drops for several days after treatment. Treatment is often curative.

Other ocular conditions of hamsters include corneal damage and bleeding into the anterior chamber caused by trauma. Ocular discharge is often seen in hamsters with eye disease such as corneal ulcers or conjunctivitis or those with a severely weakened general condition secondary to other diseases. Ocular discharge is especially severe after sleeping, and the hamster might not be able to open the eyes due to the discharge. In these cases, treat the underlying disease at the same time as washing the eyes, removing the ocular discharge, and applying topical antibiotic eye drops. Cataracts can be seen in geriatric hamsters, and Campbell's hamsters are reported to be prone to glaucoma.[50]

COMMON DISEASES OF GERBILS

Integumentary System

Facial eczema, sore nose, and nasal dermatitis all describe a common skin condition seen in gerbils. Clinical lesions adjacent to the external nares appear erythematous initially; these lesions progress to localized alopecia and then to an extensive moist dermatitis (Fig. 26.14). The cause is believed to be an increase in the secretion of porphyrins by the Harderian gland (as in chromodacryorrhea in rats), which acts as a primary skin irritant.[6] Various staphylococcal species (*S. aureus* and *S. xylosus*) may act synergistically to produce dermatitis.[57] Stress may cause excessive Harderian gland secretion. Two examples of stress are overcrowding and exposure to an environmental humidity of greater than 50%, which causes the fur coat to stand out and appear matted. Gerbils require sand baths to keep their coats from becoming oily. Keeping the gerbil in a dry environment, cleaning its face, and providing soft clay or sand bedding instead of abrasive wood chip bedding will usually alleviate the problem. Use topical or parenteral antibiotics (except streptomycin) or disinfectants such as diluted chlorhexidine gluconate for local disinfection in gerbils with severe dermatitis. Sand for dust (sand) bathing and in the litter box should be removed from the cage during treatment, especially with moist dermatitis or dermatitis involving exudate or lacrimation. If dust bathing is necessary to keep or improve the condition of the fur, skin, or both, make sure it is done under the owner's supervision, the dust is hygienically managed, and there is no dust left on the fur or skin after bathing.

As in other rodents, self-mutilation of the fur or skin from barbering or being chewed by other cagemates can be seen. In severe cases, the lesion can be complicated by secondary infection or bone fractures. Abscess and moist dermatitis due to urine leakage can also be seen in some gerbils.

The tail of the gerbil is covered by thin skin. Unlike rats or mice, if a gerbil is picked up by the tip of its tail, the skin often slips off, leaving a raw, exposed tail that eventually becomes necrotic and sheds (Fig. 26.15). If the tail skin is lost, surgically amputate the degloved tail where the skin ends. The tail usually sloughs if it is left untreated.

Gerbils have large ventral abdominal marking glands that are androgen-dependent (see Fig. 26.4). Therefore the marking glands are larger in males than in females. Owners may mistake these normal glands for tumors. In aged animals, the gland may become infected or neoplastic (Fig. 26.16). Local debridement and topical antibiotics are indicated for the treatment of infected glands. Do a wide excisional biopsy if you suspect a tumor such as an adenocarcinoma.[29]

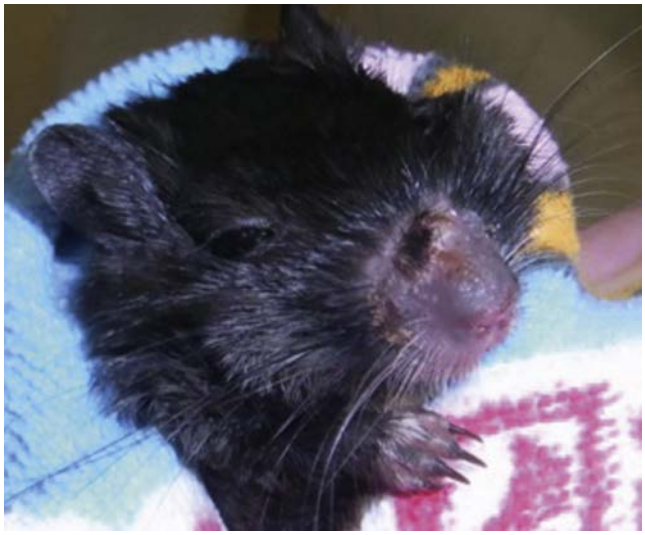


Fig. 26.14 *Facial eczema, sore nose,* and *nasal dermatitis* all describe a common skin condition seen in gerbils.

Ectoparasites are rare in gerbils but can be seen in situations where other animals such as dogs, cats, or rabbits share the same environment. Debilitated gerbils can present with demodicosis, and *Demodex merioni* is reported.[50] Selemectin or ivermectin is used for the treatment of demodicosis as in hamsters.

Other dermatoses such as dermatomycoses due to *Trichophyton mentagrophytes* and *Microsporum gypseum*, hormonal alopecia from ovarian cysts, cutaneous neoplasms such as squamous cell carcinoma,[29] lymphoma,[59] and melanoma[48] are also reported in gerbils.[50]

Gastrointestinal System

Tyzzer's disease, due to *Bacillus piliformis,* is the most frequently described fatal infectious disease of gerbils.[67] Common findings are acute death or death after a short period of illness and the presence of multiple foci of hepatic necrosis. Diarrhea and gross and microscopic lesions in the intestinal tract are variably present. Experimentally induced Tyzzer's disease in gerbils has confirmed that these animals are extremely susceptible to infection.[64] The probable route of infection is oral, explaining why gerbils exposed to infected bedding contract the disease.

Diarrhea and loose feces (soft stool) sometimes can be seen in gerbils. Dietary factors, stress, and other illnesses can be causative. Treat by reducing stress, improving the sanitary conditions, and treating underlying diseases. Administer fluids and probiotics as needed. Protozoa as a cause of diarrhea and loose feces is rare. And the treatment is the same as in hamsters. Endoparasites such as *Hymenolepsis nana* and *Taenia crassicollis*[50] and pinworms such as *Denstomella translucida* are reported in gerbils.[47]



Fig. 26.15 Degloving of the tail skin of a gerbil. The skin of the tail is occasionally slips off (A), leaving a raw, exposed tail that eventually becomes necrotic and sheds (B).



Fig. 26.16 Neoplasia of the ventral marking gland in a gerbil.

As in other rodents, malocclusion caused by incisor teeth fracture or other causes can occasionally be seen in gerbils as well, and regular trimming may be needed. Use dental drills or small clippers (see Chapters 25 and 36) to trim incisors. Gerbils fed on standard rat and mouse diets for more than 6 months can develop spontaneous, insidious periodontal disease due to the accumulation of plaque and calculus-like accretions.[43a,63] On the same diets, about 10% of the animals become obese, and some may develop diabetes.[63] When feeding pelleted diet to gerbils, always use diets labeled specifically for gerbils.

Central Nervous System

Approximately 20% to 40% of gerbils develop reflex stereotypic epileptiform (clonic-tonic) seizures beginning around 2 months of age. The susceptibility is inherited, seen in selectively bred lines, and caused by a deficiency in cerebral glutamine synthetase.[35] There is no treatment. Most animals outgrow the behavior with time. The seizures pass in a few minutes; they may be mild or severe and have no lasting effects. Other neurologic disorders seen by the authors include torticollis and stagger walking. Encephalitis due to naturally occurring infection with *Bacillus piliformis* has been reported, and this should be considered when a gerbil is presented with neurologic signs.[62]

Reproductive System

Cystic ovaries are reported to occur frequently in laboratory Mongolian gerbils.[44] Removal of the affected ovary is recommended. Ovarian granulosa cell tumors are the most common tumors in gerbils. In young gerbils (less than 2 years of age) tumors are often incipient and not macroscopically visible.[20] However, in older gerbils, local invasion is seen in the ovarian hilum, periovarian fimbriae, and large ligaments. Metastases occur in the abdomen, with the omentum being the most affected organ. Metastases are not found in the thorax. The incidence of granulosa cell tumor is higher in virgin females than in breeding females; therefore ovariectomy is recommended in pet gerbils that are not destined for breeding.

Tumors and Aging

After 2 to 3 years of age, approximately 25% to 40% of gerbils develop neoplasia.[41] After granulosa cell tumors, tumors of the skin are the next most frequent. Squamous cell carcinoma of the sebaceous ventral marking gland in males and melanoma, usually of the ear, foot, or base of the tail, are seen.[48] Besides neoplasia, older gerbils have a high incidence of chronic interstitial nephritis.[4] Aged gerbils are at risk for the development of aural cholesteatoma, a nonneoplastic keratinizing epithelial mass that occurs in the middle ear and mastoid region; it erodes bone and invades the labyrinth and cranial cavity.[9]

ZOONOSIS

Significant public attention has focused on the zoonotic risk of rodents, in particular lymphocytic choriomeningitis virus and hantavirus (see Chapter 42). Although the natural reservoirs of these diseases are various species of wild rodents, there are documented cases of human infection with lymphocytic choriomeningitis from exposure to pet rodents.[3] Pet hamsters, in particular, carry a wide variety of potentially infectious agents. In general, use standard precautions in handling pet rodents, including thorough handwashing. Because hamsters and gerbils are popular pets for children, discuss potential anthropozoonosis with clients, especially if pets are kept in a school setting.

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Sugar Gliders

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BIOLOGY

Natural History

Sugar gliders (*Petaurus breviceps*) are small, nocturnal arboreal marsupials that are native to New Guinea and the eastern coast of Australia. There are at least seven recognized subspecies.[2,17] Wild sugar gliders inhabit open areas in tropical or coastal forests and dry, inland, sclerophyll tropical forests. They are social animals, with colonies of 6 to 10 animals occupying a territory of up to 1 hectare. Dominant males mark territory and other



Fig. 27.1 The patagium, or gliding membrane, of sugar gliders stretches between the front and hind legs. (Courtesy Dr. Y. Miwa.)

group members with scent gland secretions. Animals in a group will nest communally in leaf-lined tree holes. During periods of extreme cold or food scarcity, sugar gliders conserve energy by going into torpor for as many as 16 hours per day.[17]

Recently in the pet trade in the United States, sugar gliders are being called "sugar bears," which leads to confusion. They are being marketed in shopping malls, fairs, and on the internet. With this rise in distribution, practitioners may see joeys that are in poor condition because their owners have been poorly educated on their behavior, diet, husbandry, and social and health requirements.

The life span of sugar gliders is longer than that of other comparably sized pets; they can live from 10 to 12 years in captivity.[34]

Anatomy and Physiology

Sugar gliders have soft, velvety fur that is gray with a central black stripe dorsally and cream-colored ventrally. Sugar gliders have a patagium (gliding membrane) that stretches between their front and hind legs (Fig. 27.1) and gliding distances are reported to be as long as 50 m.[40] The female has a pouch, containing four teats, in which she raises one or two young. Epipubic bones are unique to certain marsupials and are absent or diminished in gliders. The cloaca is a common terminal opening of the rectum, urinary ducts, and genital ducts. Being a nocturnal prey species, sugar gliders have large, protruding, widely spaced eyes. They have five toes on their hind feet, with an opposable first digit and syndactyly of the second and third digits. Dominant males mark both territory and group members with secretions from androgen-sensitive frontal (forehead) (Fig. 27.2A), gular (throat/chest) (Fig. 27.2B), and paracloacal scent glands[39] (Fig. 27.2C). Sugar gliders also have an enlarged cecum, which functions principally in microbial fermentation of complex polysaccharides in gum. The rest of the gastrointestinal tract is similar to most carnivores. The dental formula is 2(I 3/2, C1/0, P 3/3, M 4/4) for a total of 40 teeth in the adult (Fig. 27.3A–B). Body weight of adults in captivity is between 100 and 160 g for males and between 80 and 130 g for females. Body length ranges from 16 to 21 cm and tail length from 16.5 to 21 cm.

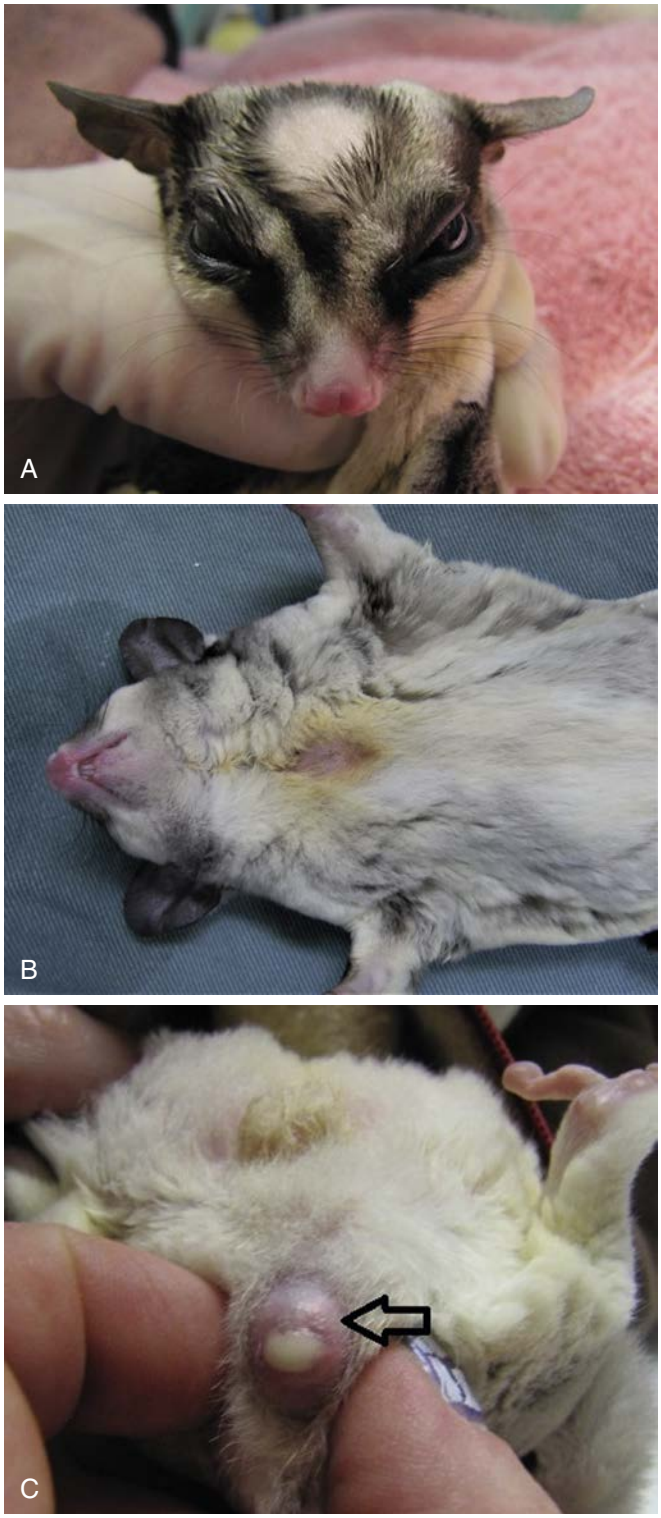


Fig. 27.2 The scent glands in sugar gliders. (A) Male sugar gliders have a frontal scent gland on their head. Secretions from this gland are used to mark territory and group members. (B) Male gliders also have gular scent glands, located on the ventral aspect of the throat/chest. (Courtesy Dr. Y. Miwa.) (C) Although more developed in males, paracloacal glands of either sex may become impacted and infected, requiring manual evacuation and in some cases surgery. The arrow marks location of a paracloacal gland in female sugar glider, with gentle pressure applied. The material is thick and white to yellow in color.

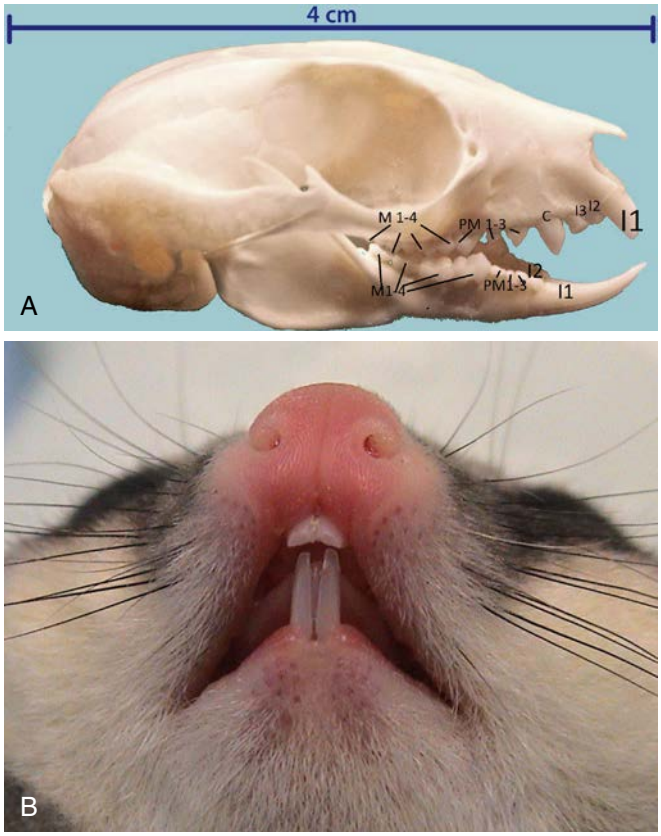


Fig. 27.3 (A) Skull of the sugar glider. I = incisor, C = canine, PM = premolar, M = molar. (Courtesy Dr. V. Capello and K. Lennox.) (B) The lower incisors are adapted for gouging into tree bark. These teeth normally angle forward, thus they are not maloccluded and should never be trimmed. (Courtesy of Dr. V. Capello.)

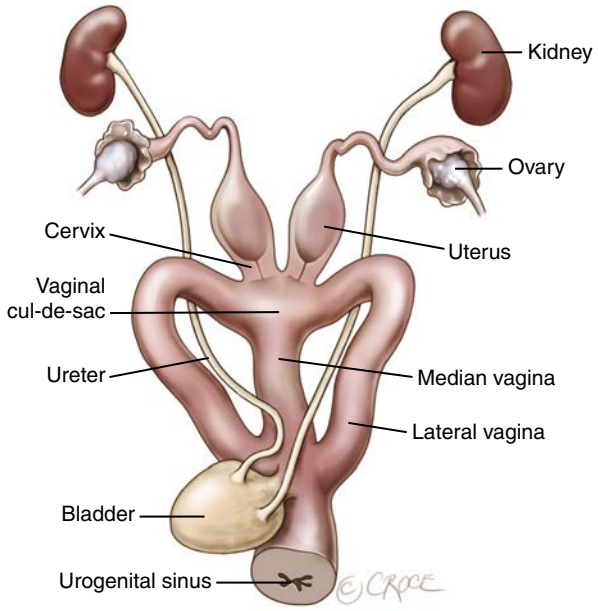


Fig. 27.4 Schematic drawing of the female urogenital tract in marsupials. (From Miller RE, Fowler ME (eds). *Fowler's zoo and wild animal medicine*. Vol 8. (St. Louis: Elsevier, 2015:257. Adapted from Vogelnest L, Woods R. *Medicine of Australian mammals*. CSIRO 2008. Reprinted with corrections 2010, Illustrator: Beth Croce, Published by CSIRO Publishing, Collingwood, Victoria, Australia. Reproduced with permission.)

The metabolism of marsupials is approximately two-thirds that of placental (eutherian) mammals. Cloacal temperature is lower than the actual body temperature; the average cloacal temperature is 89.6°F (32°C).[2,14,20] True rectal temperature in marsupials can be measured by directing the thermometer dorsally into the rectum from within the cloaca. The rectal temperature is usually 97.3°F (36.3°C).[14] The normal heart rate of a sugar glider is 200 to 300 beats/min, and the respiratory rate is 16 to 40 breaths/min.[2]

Color Variations and Genetics

In recent years, sugar gliders have become available in a variety of colors through selective genetic breeding. Several color variations have been described and accepted as "standard" mutations. These variations of the natural gray line include white face, white tip, leucistic, and mosaic. A white face mutation lacks the black bar below the ears and will have lighter or broken eye rings. Gliders with white fur on the tail tip are considered a white tip coloration mutation. The leucistic sugar glider, also referred to as black-eyed white, is all white with black eyes. The albino sugar glider differs from the leucistic in that it is all white with red eyes, as seen in other albino animals. Mosaic sugar gliders have characteristic white patches on the body, feet, or tail. If the mosaic coloration involves the tail, the sugar glider is referred to as a ring-tail mosaic. Certain lines of mosaics may produce sterile males, although the females are fertile. Red series classification includes red cinnamon, lion, butter cream, and chocolate. Other color varieties are continually being produced by fanciers, although there has not been a coordinated genetic breeding program. As more unusual mutations and colorations are produced, inadvertent selection for genetic disorders likely will develop.

Reproduction

The reproductive anatomy of sugar gliders is typical of marsupials.[27] Female sugar gliders have two uteri and two long, thin, lateral vaginas that open into a single cul-de-sac divided by a septum (Fig. 27.4). Both sexes have three paired paracloacal glands, which are more developed in males.[27] Males have a large prostate with a constriction at the anterior third. Males also have two pairs of Cowper's (bulbourethral) glands. The testes are located in a prepenile pendulous scrotum, and the penis is bifid with the external urethral opening located at the base (Fig. 27.5). Therefore the distal penis can be amputated in cases of penile trauma or paraphimosis.[27]

Sugar gliders are seasonally polyestrous, with the natural breeding season in the southern hemisphere occurring between June and November. They are polygamous, with a dominant male that breeds with the mature females in the colony.[17,27] The estrous cycle is 29 days long.[2,22,27] Young (joeys) are typically born in the spring, when insects are plentiful. Litter size is usually two and less commonly one.[17] Two litters in a single breeding season are common if food is abundant.

Young weigh only 0.2 g at birth when they migrate to the pouch after a 15 to 17 day gestation period. They remain in

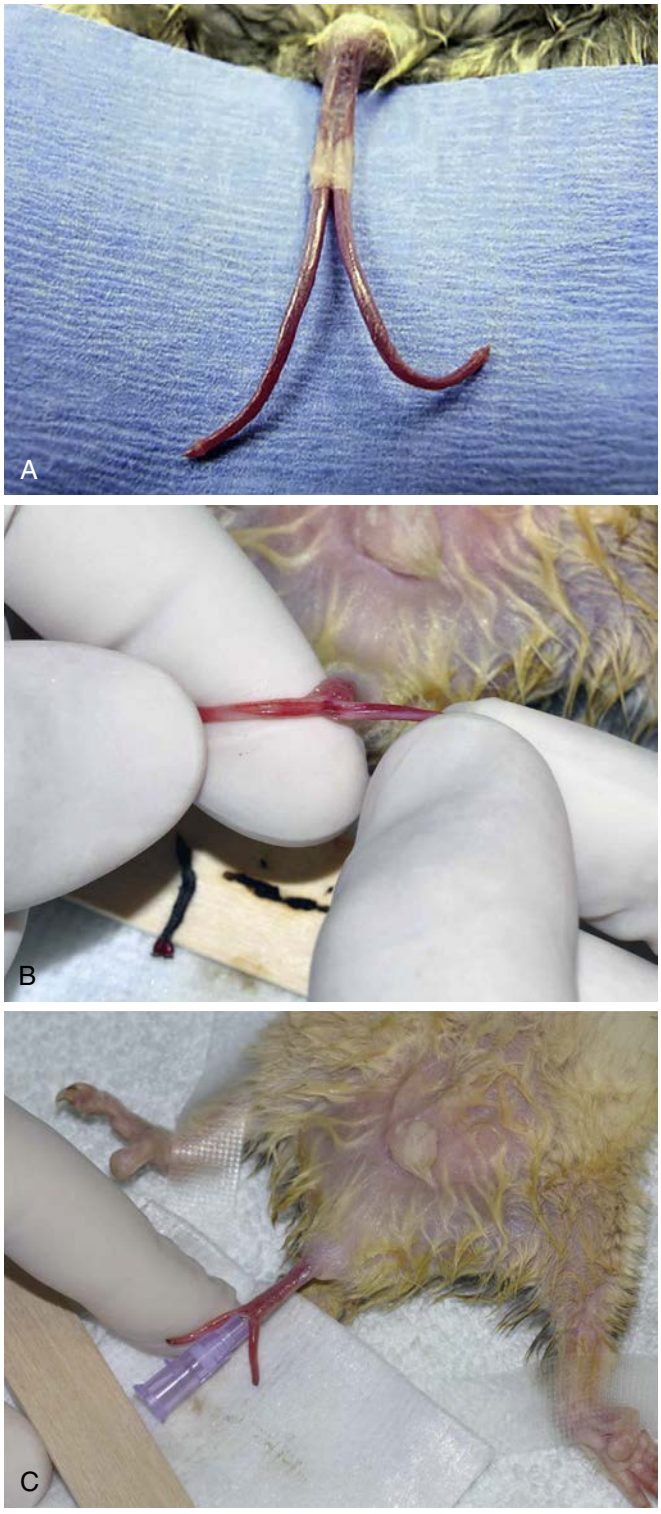


Fig. 27.5 (A) In male sugar gliders, the penis is bifid. (B) Male gliders do not urinate from the tip of the forked penis, but from its base. (C) The urethral opening can be catheterized. (Courtesy Dr. C. Mans.)

the pouch for 70 to 74 days. After they outgrow the pouch, the young are left in the nest until they are weaned at 110 to 120 days of age. From day 75 to day 100, the young are left in an insulated nest while the mother is foraging. The joey will begin exploring outside of the pouch during this time. Table 27.1 lists the expected growth rate and specific developmental milestones as the joey ages.[2,34] The young remain with the colony until they are forcibly dispersed, at 7 to 10 months of age.[2,17] Sexual maturity is reached at 8 to 12 months of age in females and 12 to 15 months in males.[2,22,23]

TABLE 27.1 Growth and Development of Young Sugar Gliders[2,3,20]

Age (days)	Weight (g)	Milestones	Total Daily Intake (mL)
1	0.2	Birth	—
20	0.8	Ears free from head; papillae of whiskers visible	0.2
40	3.2	Ears pigmented; whiskers erupted; eye slits present	0.6
60	12	Intermittently detached from teat; dorsal stripe, fur, and gliding membrane developing	2.5
70	20	Left in nest; eyes open; fully furred	4
80–90	35–44	Fur lengthens	6–8
100	54	Emerging from nest; starting to eat solids	8–10
120–130	78	Weaning	Feed up to 20% of body weight in pureed solids
200	100	Subadult	Feed up to 20% of body weight in solids

Behavior

Both sexes mark territory with secretions from scent glands and urine. The female's scent glands are within the pouch, and she will secrete and increase marking to indicate breeding readiness to the male. Adult males will rub the frontal scent glands on the female's chest.

Sugar gliders are quite vocal, with a whole series of alarm yaps and screams. They are highly social animals and should not be kept as a solitary pet; they become clinically depressed when housed singly. Self-mutilation is not uncommon in solitary gliders. Those without proper socialization or exercise and territory space may become aggressive. Males will fight if there is not enough distance between nest boxes. Both sexes may fight and become irritable at the beginning of breeding. Gliders without adequate stimulation may become aggressive toward humans. Sterilization may help, but they will continue to scent-mark and will not be "human-socialized" like a domesticated animal. New introductions to a single glider or social group needs to be done gradually and under supervision because established gliders may defend their territory and attack a new animal.

Sugar Gliders as Pets

Sugar gliders are acceptable pets if they are given sufficient socialization, ample space, an enriched environment, and an

appropriate diet. When hand-reared or handled daily while just emerging from the pouch, they adapt well to captivity and develop a strong bond with their human companions. They are time-consuming pets, with recommended human interaction of at least 2 hours per day. Basic handling for socialization and companionship is best achieved at night, when the animals are more interactive and playful. If awakened and handled during the day, sugar gliders become agitated and irritable and are more likely to bite.

Sugar gliders are most responsive to and trusting of individuals they know, but they respond well if approached with patience and gentle handling. They enjoy cuddling and curling up in shirt pockets or pouches, where they feel safe. They should not be allowed to crawl into tight-fitting clothes, such as pants pockets, because of the risk of injury.

Advantages of sugar gliders as pets include their small size, playfulness, and intelligence. Disadvantages include their nocturnal nature, housing requirements including social needs, specific dietary needs, and musky odor.

Husbandry

Caging

Because of their active nature, sugar gliders need large cages to climb, run, and jump. Minimum cage size for a pair is 36 × 24 × 36 inches (91 × 61 × 91 cm), but larger is better. Cages should be made of wire for good ventilation, with wire spacing no more than 1.0 × 0.5 inch (2.5 × 1.3 cm) wide. Keep sugar gliders at temperatures between 65° and 90°F (18° and 32°C).[14,34] Most pet gliders are kept indoors year-round, although in warmer climates, outdoor enclosures constructed like psittacine aviaries may be used. Place several food and water dishes in various locations throughout the cage to decrease competition. Place branches, perches, and shelves at various levels of the cage to satisfy the natural behavior of climbing and jumping. Sugar gliders enjoy playing with bird toys, such as swings and chew toys made of wood; avoid any toys containing wires, soft plastic, or rubber that could be ingested, or reflective surfaces. Plastic wheels without open rungs, such as a hamster wheel, can be provided for exercise.

Sugar gliders need permanent access to a nest box for sleeping and hiding, with minimal daytime disturbances. Position the nest box high in the cage. A sleeping pouch constructed of washable, tightly woven fabric can be used if only a non-breeding pair is housed in the cage. This should be laundered frequently, but gliders will re-scent it on replacement in the cage. Worn or frayed fabric can be a hazard by catching toenails, so inspect the pouch frequently and replace as needed. Nest box size depends on colony size, but boxes should be at least 6 × 6 inches (15 × 15 cm).[2,17,34] Nesting material can consist of hardwood shavings, recycled paper products, or equivalent materials. Artificial wool, cloth strips, and similar materials are not suitable because fibers have been known to entrap an animal's limbs. Clean the nest boxes and change bedding material regularly, at least every 1 to 2 weeks.

To prevent injury, ensure that there are no hazards for exercise outside of the cage. Sugar gliders can become injured by household accidents, such as falling into toilet bowls; chewing on electrical cords; landing on hot lightbulbs; getting caught in upholstery, rugs, curtains, or window blinds; being shut in a door or window; or being stepped on by family members.

Nutrition and Feeding

Sugar gliders are omnivorous, and in the wild the diet includes sap and gums (carbohydrate-rich) from eucalyptus and acacia trees, nectar and pollen, manna and honeydew, and a wide variety of insects and arachnids.[17,26] Trees produce "manna," a deposit of white encrusting sugars from wounds made by sap-sucking insects, birds, other gliders, or possums. Honeydew is secreted by sap-sucking insects. Sugar gliders possess specialized lower incisors for chewing and gouging into the bark of trees. The lengthened fourth digit on the forelimb aids in extracting insects from crevices. The diet varies with the season. During the spring and summer months, sugar gliders are primarily insectivorous. Field energetics studies have demonstrated that wild sugar gliders consume 182 to 229 kilojoules (kJ)/day.[26] This is equivalent to approximately 17% of body weight in wet weight of food.[26] Captive gliders expend less energy in exercise and consume more easily assimilated foods than do those in the wild; therefore the total "energy" (i.e., kilojoules) offered to gliders in captivity should be less.

Captive diets must satisfy the numerous specializations of these insectivorous omnivores. The captive diet should include nectar, adult insects such as gut-loaded crickets and Dubia roaches, and other protein sources, as well as very limited amounts of fruits and vegetables.[12,22,26] Commercial diets are available that claim "complete" nutrition, yet there are few published studies using these diets in scientific feeding trials.[12,13] Several commonly fed diets that include commercial products, as well as produce and supplements, were found to be inadequate, with evidence of iron storage overload.[10,12,13] Guidelines for feeding commercial glider pelleted food suggest that commercial pellets should comprise 75% of the diet, with the remaining 25% a variety of fruits and vegetables. When fed, fruits and vegetables should be finely chopped together into the diet so that the glider cannot pick out a favored item and leave the rest. A calcium-based multivitamin supplement can be added to fresh produce such as mango, banana, apple, and broccoli. Treats should not be more than 5% of the daily diet and can include insects such as calcium gut-loaded large crickets and yogurt.[5] If gliders are being bred, additional protein, such as insects (e.g., gut-loaded crickets), cooked eggs, and lean cooked meat, as well as calories may be required.

If a commercial diet is not used, then approximately 50% of the diet should be sources of fruit sugars, preferably in the form of a sap or nectar. Nectar sources include fresh nectar, maple syrup, honey, and artificial nectar products.[12,26] Examples of nectar products include prepared lory diets and Gliderade (Avico, Fallbrook, CA). Gum arabic (acacia) can be purchased as a powder, mixed into a thick paste, and used to simulate native gums; it can be placed in holes in branches and on surfaces, with insects or bits of fruit stuck to it for enrichment and foraging. The remaining percentage of the diet should include lean protein sources, such as an insectivore diet, and supplemental live insects. An example of portions for an adult

glider: 1 tablespoon Leadbeater's (see below), 1 tablespoon zoo-based insectivore diet (Insectivore Fare; Reliable Protein Products, Phoenix, AZ), ½ teaspoon chopped mixed fruits such as mango and banana, and 1–3 adult gut-loaded insects such as crickets or Dubia roaches. Because sugar gliders are nocturnal, offer fresh food items in the evening.

The Leadbeater's recipe as an artificial nectar has been recommended as a base mixture for sugar glider diets. This was originally formulated for Leadbeater's possums (*Gymnobelideus leadbeateri*).[12,26] The Leadbeater's recipe consists of 150 mL water, 150 mL honey, 1 shelled hard-boiled egg, 25 g high-protein baby cereal, and 1 teaspoon vitamin and mineral powder. This mixture is kept refrigerated or frozen until served. The original Leadbeater's recipe is often modified, with adjustments usually being made for palatability rather than nutritional content. Several modified versions are found on the Internet, such as the Bourbon's modified Leadbeater's diet (bmldiet.com) and the Wombaroo High Protein Supplement (Wombaroo, Food Products; Glen Osmond, South Australia, Australia; wombaroo.com.au/resources, adult sugar glider feeding guidelines). Diets posted on owner/breeder websites should be scrutinized closely, because none of them have undergone thorough nutritional dietary trials and analysis.

Contrary to the nutritional needs observed in the wild, much of the information found in lay publications and on the Internet lists fruits and vegetables as a major portion of the captive diet. Fruit-based diets are harmful to captive sugar gliders because these provide inadequate protein and calcium and predispose animals to osteoporosis and periodontal disease.[12,26] Although sugar gliders readily accept fruits, nuts, and grains, these are not a substantial part of their natural diet.

Hand-Rearing

Orphaned marsupial-pouch young must be maintained at a stable temperature close to the body temperature of the mother, which may range from 86° to 93°F (30° to 34°C). An artificial pouch can be made from a child's cotton sock and placed in a temperature-controlled box. By the time the pelage is thick and complete, the orphan has reached a homeothermic state and no longer requires an artificial heat source. If the age of the orphaned young is not known, estimate age from the body weight and stage of development (Table 27.1). The artificial nest can be a fleecy cotton bag that is big enough to accommodate the joey and a soft toy the size of an adult sugar glider; it should be placed in a box maintained at 77°F (25°C).

Feed unfurred young every 1 to 2 hours (including throughout the night), and feed just-furred young every 4 hours. Gradually reduce the frequency to twice daily, then once daily, until the young are weaned. Feed a low-lactose milk formula (e.g., Esbilac Puppy [PetAg, Inc., Hampshire, IL]).[26] Marsupial milk increases in energy at the time of pouch exit to provide for the young's increased energy demands of locomotion and thermoregulation. This change can be simulated by adding canola oil to the milk at the rate of 1 mL of oil per 20 mL of milk. Marsupial milk formulations are also commercially available for different ages of joeys (Possum Milk Replacer, Wombaroo; Impact Colostrum Supplement, Wombaroo).



Fig. 27.6 Manual restraint of a sugar glider in a towel.

Juvenile sugar gliders usually lap readily from the tip of a syringe, or they can be taught to lap from a small plastic lid. Start offering solids at about 100 days, at which time the young glider should weigh approximately 54 g, and wean at 130 days, when body weight is approximately 78 g. Pureed baby food with meat and vegetables or blended adult diet is suitable starter food.[26]

CLINICAL TECHNIQUES

Handling and Restraint

Sugar gliders are rather easy to handle but can be difficult to restrain, especially in the evenings. Therefore clinical examinations scheduled early in the day when the animals are normally less active may be advantageous. Sugar gliders will readily bite the handler if they are frightened or irritated. Methods of restraint include grasping the glider at the base of its tail or cupping the animal in the palm of your hand. The ventrum and hindquarters can be examined by lifting the animal by the base of its tail while allowing the glider to grasp a surface with its front feet. This method also permits palpation of the abdomen and examination of the pouch. If the glider is not well-tamed, there is a risk of the handler being bitten. To examine the head and chest, hold the sugar glider in a small towel with its head exposed (Fig. 27.6). Sugar gliders typically do not tolerate being scruffed.[34]

Full clinical examination or diagnostic sampling is best performed with the animal under isoflurane- or sevoflurane-induced general anesthesia. Measure cloacal temperature, heart and respiratory rate, and weight before the animal recovers from anesthesia. Maintain animals on a heated surface while under anesthesia and during recovery.

Blood Collection

Collecting a blood sample from a sugar glider can be difficult, particularly if the glider is ill or dehydrated. Anesthesia is required for diagnostic sampling. Use a 0.5-mL insulin syringe or a 1-mL tuberculin syringe with a 25- to 27-gauge needle to



Fig. 27.7 The cranial vena cava is a common venipuncture site in sugar gliders. The vein is accessed by using a 1-mL tuberculin syringe with 25-gauge needle inserted at the thoracic inlet and directed caudally. This glider is under gas anesthesia with the face mask on the right.

collect blood samples. In a healthy glider, blood volumes of 1% of body weight can be safely collected (e.g., 100 grams body weight equals 1 mL of blood). Less volume should be drawn if the glider is ill.

Reliable venipuncture sites in sugar gliders are the jugular vein and the cranial vena cava (Fig. 27.7).[21,34] These sites yield the greatest blood volume. For jugular venipuncture, insert the needle midway between the point of the shoulder and the ramus of the mandible on the ventral aspect of the neck, lateral to the trachea and esophagus. The cranial vena cava can be sampled at the thoracic inlet. Direct the needle caudally at a 30-degree angle off midline toward the opposite hind leg.[21,29,30] As in other species, complications may include laceration of the cranial vena cava or potentially puncturing the heart.

Small blood samples can be obtained from various peripheral veins. The medial tibial artery can be accessed to collect up to 0.5 mL of blood.[2,33] Although this vessel is readily visible, it is quite mobile. For venipuncture of the cephalic, lateral saphenous, femoral, or ventral coccygeal veins, use a 0.5-mL insulin syringe with a 27- or 28-gauge needle. These veins are superficial and easily collapse if too much negative pressure is applied. Up to 0.25 mL of blood can be drawn from these veins.[34]

Hematologic and plasma biochemical values obtained from captive sugar gliders are listed in Table 27.2.

Treatment Techniques

Subcutaneous fluids should be administered along the dorsal midline of the thorax. Take care not to administer the fluids laterally into the patagium because fluids are more slowly absorbed from this area and can cause discomfort and distress. Owners need to be aware that subcutaneously administered fluids may still move to the patagium despite site of administration. Intraosseous fluids are delivered in the proximal femur by using the same technique to place an intraosseous catheter as is used in other small mammals. The author suggests using 50–100 mL/kg every 24 hours as daily maintenance requirement.

TABLE 27.2 Hematologic and Plasma Biochemical Reference Values for Captive Sugar Gliders[a]

Measurement	Reference Range[a-c]
Hematologic Values	
Hematocrit, %	53 ± 6 (51–54)
Red blood cell count $\times 10^6/\mu L$	8.6 ± 1.0 (8.3–8.8)
Hemoglobin, g/dL	16.3 ± 1.9 (15.8–16.9)
Mean corpuscular volume, fL	64.1 ± 14.8 (60.2–68.1)
Mean corpuscular hemoglobin, pg	19.1 ± 1.1 (18.8–19.4)
Mean corpuscular hemoglobin concentration, g/dL	30.8 ± 0.7 (30.6–31.0)
Platelet $\times 10^3/\mu L$	346 ± 201 (292–400)
White blood cell count $\times 10^3/\mu L$	7.4 ± 7.7 (5.5–9.3)
Neutrophils $\times 10^3/\mu L$	1.8 ± 1.5 (1.5–2.2)
Lymphocytes $\times 10^3/\mu L$	5.4 ± 7.0 (3.7–7.2)
Monocytes $\times 10^3/\mu L$	0.1 ± 0.1 (0.1–0.2)
Eosinophils $\times 10^3/\mu L$	0.2 ± 0.2 (0.1–0.3)
Basophils $\times 10^3/\mu L$	0.0 ± 0.0 (0.0–0.1)
Biochemical Values	
Alanine aminotransferase (ALT), U/L	117 ± 28 (97–137)
Alkaline phosphatase (AP), U/L	102 ± 57 (89–137)
Amylase, U/L	2734 ± 890 (2117–3351)
Aspartate aminotransferase (AST), U/L	77 ± 71 (54–100)
Bilirubin, total, mg/dL	0.4 ± 1.3 (0.1–0.7)
Blood urea nitrogen (BUN), mg/dL	17 ± 8 (15–18)
Calcium, mg/dL	8.7 ± 0.8 (8.5–8.9)
Chloride, mEq/L	107 ± 7 (106–109)
Cholesterol, mg/dL	118 ± 28 (112–124)
Creatine kinase (CK), U/L	1359 ± 972 (1081–1637)
Creatinine, mg/dL	0.5 ± 0.3 (0.5–0.6)
Glucose, mg/dL[c]	162 ± 45 (153–172)
Magnesium, mEq/L	1.9 ± 0.5 (1.6–2.1)
Phosphorus, mg/dL	5.2 ± 3.6 (4.4–6.1)
Potassium, mEq/L	5.1 ± 2.3 (4.6–5.5)
Protein, total, g/dL	6.9 ± 0.7 (6.7–7.0)
Albumin, g/dL	3.9 ± 0.4 (3.1–4.6)
Globulin, g/dL	3.0 ± 0.5 (2.9–3.1)
Sodium, mEq/L	141 ± 11 (139–143)

[a]All data in this table were obtained from healthy males; blood values later obtained from healthy females reportedly fell within those ranges (D. Brust, personal communication, 2019).
[b]Mean ± SD (ranges shown are the 95% confidence intervals after outliers were removed. Statistically, 90% of the population should have values within these limits).
[c]Glucose levels measured immediately after collection.

Subcutaneous injections are safely administered along the dorsal midline of the thorax. Volume may be up to several mL. Administer intramuscular injections in the epaxial muscles of the neck and upper thorax or in the muscle mass in the anterior thigh. Volume is usually limited to less than

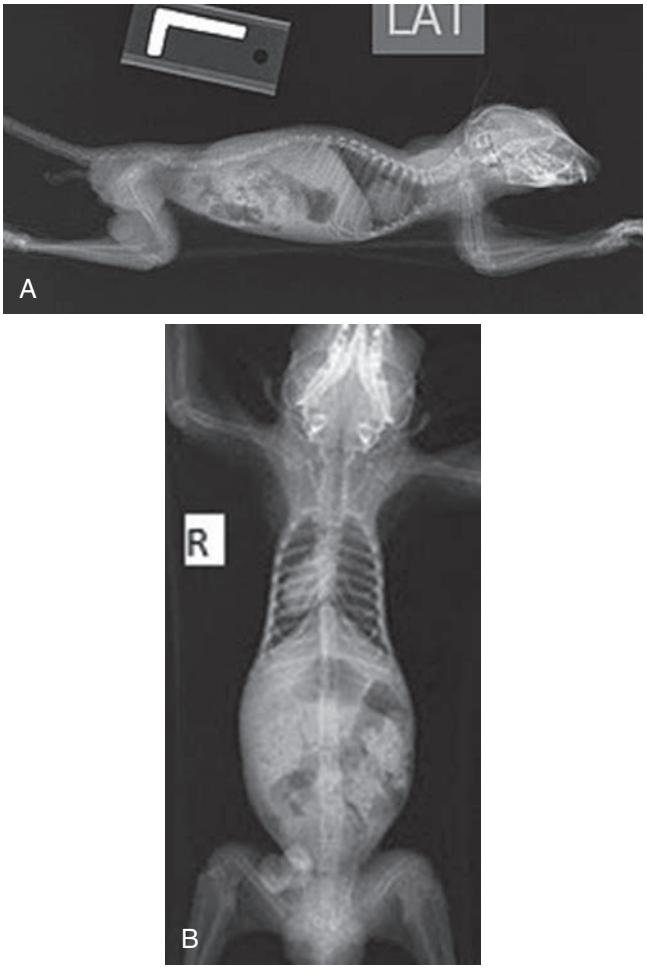


Fig. 27.8 Radiographs of a normal sugar glider. (A) Lateral view. (B) Ventrodorsal view.

0.1 mL per muscle site. Intravenous injections are difficult and can be administered in the cephalic or lateral saphenous veins with the animal under anesthesia; the intraosseous route can be used instead.

Diagnostic Imaging

General anesthesia is required to position a sugar glider for diagnostic radiographs. If young are present in the pouch but detached from the teat, remove them before anesthesia. Reflect the patagium away from the body wall to minimize artifact and improve visualization on lateral views. Standard equipment used for very small animals is adequate for imaging sugar gliders. Digital radiography or mammography film yields excellent definition of both soft tissues and skeletal elements (Fig. 27.8).

Ultrasonography is a valuable tool for use in sugar gliders. Probes should be at least 7.5–12 mHz. Quick images can be obtained by using manual restraint (e.g., for checking free fluid in the chest or abdomen), but detailed images usually require anesthesia. Limit clipping of fur to avoid hypothermia after the exam, and warm the ultrasound gel before application. Echocardiographic reference measurements have not yet been published in sugar gliders.

DISEASES AND SYNDROMES

Gastrointestinal Disease

Malnutrition

Because of the misinformation regarding dietary requirements, sugar gliders in captivity commonly suffer from malnutrition. Common diet-related conditions are hypoproteinemia, hypocalcemia, hypoglycemia, and anemia. Hypocalcemia is primarily caused by an imbalance of dietary calcium, phosphorus, and vitamin D. Lack of dietary protein is a cause of anemia and hypoproteinemia. With chronic malnutrition, hepatic and renal biochemical values can be abnormal. Malnourished sugar gliders are weak, lethargic, thin, and dehydrated on presentation. If they are severely hypocalcemic, seizures and pathologic fractures can occur. Pale mucous membranes, edema, and bruising may be present in anemic and hypoproteinemic patients, and secondary infections are common in debilitated animals. Treatment involves general supportive care and correction of the underlying dietary problems.

Oral and Dental Disease

Sugar gliders possess specialized lower incisors for chewing and gouging into the bark of trees (Fig. 27.3B). These incisors do not grow continuously and therefore should never be trimmed. Trauma to the teeth may result in pulp exposure and infection, potentially requiring extraction.

Periodontal disease, caries, and tartar buildup are common in sugar gliders fed soft, carbohydrate-rich diets.[2,28] Tartar and calculus can be scaled while the patient is anesthetized. Associated gingivitis and periodontitis can be treated with systemic antibiotics. Including insects with hard exoskeletons in the diet may help deter tartar buildup. In extracting diseased teeth, be careful not to damage adjacent tooth roots.

Oral Abscesses

Young sugar gliders may present with abscesses in the gingiva and mucosa of the oral cavity. Enteric bacteria, including *Proteus* and *Enterobacter* species, have been cultured.[3] It is postulated that fecal bacteria on the toe nails is introduced into the oral cavity when the glider scratches its head and mouth or potentially from grooming the vent. Whenever possible, base antimicrobial therapy on culture and sensitivity results. The author uses a fruit-flavored children's antiseptic mouthwash on cotton buds to daily swab out the mouth.

Diarrhea

Diarrhea is a common symptom of digestive disease in sugar gliders and can be secondary to bacterial enteritis (caused by *Escherichia coli*, *Clostridium* species, or other bacteria), intestinal parasites (such as various nematodes, cestodes, and protozoa including *Giardia* species and *Simplicomonas* species), viruses (rotavirus), metabolic disorders, malnutrition, or stress.[32,36] Diet changes can also precipitate diarrhea, particularly in joeys.[3] Giardiasis may be asymptomatic in some adults but can be associated with intermittent diarrhea, particularly in young, breeding, or stressed gliders. Metronidazole administered at 25 mg/kg by mouth every 12 hours for 14 days[25] is usually effective

along with stringent sanitation of the environment. The author prefers the benzoate form, compounded with a flavored syrup for palatability. Treat all gliders in the habitat.

Standard diagnostic tests including fecal analysis, bacterial culture, fecal cytology, complete blood cell count, plasma biochemical profile, and radiographs are useful in discerning the cause of the digestive disorder. Specific therapy is directed at the underlying cause, along with nutritional support and fluid therapy.

Rectal and Cloacal Prolapse

Rectal or cloacal prolapse can occur secondarily to tenesmus and is more common in malnourished gliders in poor health. Prolapse has been linked to diarrhea and gastroenteritis from any cause, hypocalcemia, and pain, although in some cases the primary cause may be hard to diagnose. Because of the structure and function of the cloaca, reducing the prolapsed tissue is similar to the procedure done in birds. First, irrigate the prolapsed cloaca with a hypertonic solution (50% dextrose) and inspect it closely to identify anatomic structures as well as any necrotic tissue. Irrigate the prolapsed tissue with diluted 2% lidocaine (0.05 mL diluted with sterile water to 0.1 mL). Remove and resect any necrotic tissue if the necrosis extends beyond the superficial mucosa. Replace the tissue gently by using moistened cotton-tipped applicators. After replacement, gently massage the caudal abdominal area to assure that the tissue has been replaced into normal anatomic position. One or two vertical sutures using monofilament suture can be placed to reduce the size of the cloacal opening; take care not to obstruct the urogenital opening. Place an antibiotic cream into the cloaca after placing the sutures. Postoperative care includes addressing the cause for the prolapse, as well as continued antibiotics and a nonsteroidal antiinflammatory drug (NSAID).

Cloacal Disorders

Paracloacal gland impaction. The paracloacal glands are similar to anal glands in placental mammals. As such, these glands similarly can become infected or impacted. The condition is more frequently seen in older gliders, particularly if they have been neutered or spayed, as there is some decreased expression of the glands with decreased sexual activity and scent marking. Expression of the impacted glands produces a thick mucoid to caseous discharge, depending on the degree and type of infection, usually with a foul odor (Fig. 27.2C). Bacterial culture and sensitivity testing may reveal a variety of bacterial species and help determine the best course of antimicrobial therapy. Meloxicam for 3–5 days after expression will help with inflammation and discomfort. The glands can be surgically removed if they become repeatedly or chronically impacted (see surgery section below). One differential diagnosis for paracloacal gland impaction and infection is neoplasia.[7,30]

Paracloacal masses. Swellings closely associated with the cloaca but not originating from the paracloacal glands have been reported in several sugar gliders and can be caused by various underlying causes (Fig. 27.9). A fluctuant 1-cm swelling in a 5-year-old castrated male sugar glider suffering from stranguria was diagnosed as a paracloacal cyst not associated with the paracloacal glands. Surgical resection of the cyst was curative.[42]



Fig. 27.9 Paracloacal cyst in a castrated male sugar glider. The cyst originated from the cloacal wall and was not associated with the paracloacal glands. (Courtesy Dr. C. Mans.)

In a 3-year-old female sugar glider, a pericloacal mass was diagnosed as urinary bladder herniation with cystolithiasis. Cystotomy and cystopexy were curative.[8] Neoplasia of the paracloacal glands has also been reported as the cause for paracloacal swelling.[7]

Respiratory Disease

The differential diagnoses in sugar gliders that are presented with signs of tachypnea or dyspnea include trauma (hemothorax, fractured ribs causing pneumothorax), bacterial pneumonia, congestive heart failure, heat stress, and secondary to abdominal distention from various causes. Anesthesia is needed for diagnostic radiographs. Fluid obtained by thoracentesis can be cultured as well as examined cytologically. Ultrasonography is useful to evaluate the heart, determine whether fluid is present, and view abdominal organs. Perform a standard complete blood count and biochemical analysis to aid in diagnosis. General symptomatic therapy includes oxygen, nebulization, and bronchodilators. Treat underlying conditions as in other species with antibiotics, cardiac medications, diuretics, antihistamines, and NSAIDs as needed.

Urinary Tract Disorders

Cystitis, Crystalluria, and Urolithiasis

Hematuria, stranguria, and dysuria are common signs of urinary disorders. Underlying causes for development are poor nutrition, dehydration, lack of exercise, and improper environmental and social conditions that decrease normal, frequent urination as part of the urine marking behavior. Diagnosis and therapy of cystitis, crystalluria, and urolithiasis therapies are

performed as in other species. Stones may be struvite and usually are radiodense. Ultrasonography is useful to assess stones as well as the condition of the bladder wall. Urolithiasis may require surgery.[7] Correcting the underlying factors affects the prognosis for resolution of the condition. Recurrence is possible but is uncommon if underlying causes are corrected.

Urolithiasis can lead to urethral obstruction, particularly in male sugar gliders. Radiography for radiodense stones or ultrasound scanning can assist in locating the obstruction. Because of the bend needed to get into the bladder, catheterizing the sugar glider's bladder through the urethra is not possible anatomically, even with cloacal endoscopy. Treatment is indicated with NSAIDs, analgesics, antimicrobials, and fluid therapy as needed.

Renal Disorders

Like other mammals, renal disease can be evaluated in sugar gliders by biochemical analysis, specifically blood urea nitrogen, creatinine, phosphorous, and electrolyte levels, as well as results of urinalysis. Polyuria and polydipsia may be present with moderate to severe renal compromise. More commonly, geriatric (>8 years of age) gliders are presented for nonspecific signs of illness such as anorexia, poor grooming, and decreased activity. Imaging including radiography and ultrasonography are indicated. Renal klossiellosis has been diagnosed in two pet sugar gliders with the parasite (*Klossiella dulcis* n. sp.) associated with tubular dilation and mild interstitial nephritis.[1] Bilateral hydronephrosis has been reported in an intact male. Clinically, this glider had caudal abdominal swelling, and ultrasonography showed bilateral hydronephrosis and hydroureter.[11]

Prognosis is guarded to poor in many cases of renal disease, as age-related decrease of function may be irreversible. Therapy is based on that used in other species, which may include fluid therapy.

Reproductive Disorders

Female Reproductive Tract Infections

Because the cloaca is the common opening for the reproductive tract, as well as digestive and urinary systems, infection of the reproductive organs can be an extension of disease in these other systems. Ascending infections into the lateral vagina and uterus from the cloaca can occur (Fig. 27.4). Clinical signs may include anorexia, depression, and weight loss. Exudate from the cloaca may or may not be present. Diagnostic testing should include bloodwork, radiographs, and ultrasonography. Although pyometra/vaginal infection medical treatment with antibiotics can be attempted, surgical removal of the uterus and ovaries may be necessary. Removing the central and lateral vaginal canals is challenging in marsupials and requires identifying and maintaining the ureters, which pass between the lateral canals and central canal and insert into the urinary bladder (Fig. 27.4). Therefore medical treatment with antibiotics is usually more feasible than surgical treatment of infected lateral vaginas.[27]

Pouch Infection and Mastitis

Various bacteria and yeast have been isolated from infected pouches. These can be infections of the pouch itself or mastitis.



Fig. 27.10 Self-mutilation of the penis in a sugar glider, resulting in necrosis of the bifid glans penis. (Courtesy Dr. C. Mans.)

In these cases, perform culture and sensitivity of the exudate from the pouch or mammary glands. Therapy may be complicated by joeys remaining in the pouch, and systemic antibiotics may be the most feasible treatment option. If the joeys are old enough to spend time out of the pouch, gently swab the empty pouch daily with a dilute chlorhexidine solution on cotton buds to remove exudate.[27] Improving environmental hygiene and optimizing the health of the dam may prevent these infections.[27]

Infertility

Failure to breed in female sugar gliders can be related to obesity or inappropriate social situations, as well as underlying medical conditions. Infection within the uterus, vaginal canals, or both is possible.[27] In suspect cases, perform a full workup, including blood tests and diagnostic imaging. Review the diet, social situation, and environment as well. Infertility, predominantly in males, is also common in certain lines of the mosaic color mutations.

Failure-to-Thrive Joey

Joeys are born in a fetal stage and migrate to the dam's pouch, where they further develop. This is a very delicate stage for the joey, where detachment from the nipple or dislodgement from the pouch is often fatal. Trauma to or infection in the pouch may contribute to developmental and growth problems. Diet for the dam needs to be optimal. Environmental stress and disruption must be minimized while joeys are in the pouch.

Self-Mutilation of the Penis and Scrotum

Self-mutilation of the penis and scrotum is commonly seen in single-housed or stressed males (Fig. 27.10). Amputation of the bifid penis may be necessary if it is severely damaged. Males urinate from the base of the penis, so amputation does not interfere with urination (Fig. 27.5). The urethra only can be

catheterized. Closely monitor the urethral opening for patency after amputation of the penis, because postoperative swelling may occlude the orifice. Because sexual frustration may be a factor, castration is recommended for a pubescent male that mutilates its penis or scrotum.[20,22] A necrotic penis may be associated with systemic sepsis and bacteremia. Institute parenteral antibiotics and supportive care and pain management as needed.

Dermatologic Disorders

Stress-Related Disorders and Self-Mutilation

Stress in sugar gliders can manifest in numerous ways. Self-mutilation is a common manifestation. Stressed gliders can also present with coprophagy, hyperphagia, polydipsia, and pacing.[34] Alopecia has been seen, theorized to be caused by increased adrenal activity, although increased cortisol levels have not been reported.

Self-mutilation of the tail, limbs, scrotum, and penis is common (Fig. 27.10), particularly in singly housed pet gliders. Underlying causes include stress due to lack of proper socialization with other gliders, disruption to their normal nocturnal activity and daytime rest time, poor nutrition, and poor husbandry including caging that is too small and lacks enrichment and an environment that is noisy or too cool in temperature. Correcting these underlying problems must be undertaken in conjunction with treating the wounds. Degloved tail or limb tissue may require amputation. Treat with analgesics and antimicrobials, although gliders may need psychotropic medications, such as antidepressants, gabapentin, and even mild sedatives, to prevent further trauma. Elizabethan collars, bandaging, and custom-made jackets to protect the traumatized tissue can assist in preventing further trauma while treating the glider for underlying causes and allowing the lesion to heal. Reduce stress by providing proper nutrition, normal social grouping, appropriate housing with room for exercise, nests, branches, and cage accessories, appropriate ambient temperatures, and protection from potential predatory species. Dogs and cats can be considered predators; prevent access of these animals to sugar glider environments.

Endocrine Alopecia

Alopecia in a bilateral symmetrical pattern has been reported primarily in older female gliders (Fig. 27.11). A similar condition is frequently reported in older female short-tailed opossums (*Monodelphis domestica*) and has been linked to prolactin-secreting pituitary adenomas.[19,22] Cause of the condition in gliders has not been documented.

Ectoparasites

Mites, lice, and fleas are all potential parasites of sugar gliders, particularly if there are other pets in the household.[2,20] Mites recovered from sugar gliders include trombiculid (*Guntheria kowanyam*), astigmatid (*Petauralges rackae*), and atopomelid mites.[2,20] Imidoclopid, selamectin, and ivermectin can all be used to control ectoparasites. Dosages have been based by weight using feline products.[2,5]



Fig. 27.11 Endocrine alopecia is a recognized but poorly understood syndrome in the sugar glider.

Ophthalmic Disorders

Ocular Injury

Ophthalmic traumas occur frequently in sugar gliders because of their slightly protruding eyes. Corneal scratches with ulceration and conjunctivitis are most common. These may be inflicted by cage mates or from rubbing against cage accessories. Treatment is similar to that in other species. Correcting the caging or social situation may also be needed.

Cataracts

Nutritional imbalances and congenital predisposition are both potential causes for cataracts in sugar gliders. Hypovitaminosis A and hyperglycemia can both contribute to acquired cataract formation. Correction of the causative imbalance can halt progression but may not restore vision, depending on the severity of the opacity. A hereditary predisposition is also suspected in captive sugar gliders.[22]

Retrobulbar Abscesses

Bite wounds to the eye from competing males can lead to retrobulbar abscesses. The glider will be presented with a large, semi-fluctuant mass extending from the eye to the ear. Radiographs or preferably computed tomography help to determine the extent of the abscess and if there is underlying osteomyelitis from penetration of the orbit or skull. Treatment involves surgical removal of the abscess material and debridement. If the globe has been penetrated and is infected, enucleation may be necessary. Systemic treatment involves antibiotics, as well as pain management. Separating males or incompatible gliders and reorganizing the social structure can be attempted but may not eliminate future aggression with resulting trauma.

Musculoskeletal Disease

Nutritional Osteodystrophy

Also known as nutritional secondary hyperparathyroidism or metabolic bone disease, nutritional osteodystrophy is a common cause of hind limb paresis and paralysis in sugar gliders. The condition resembles the syndrome seen in calcium-deficient

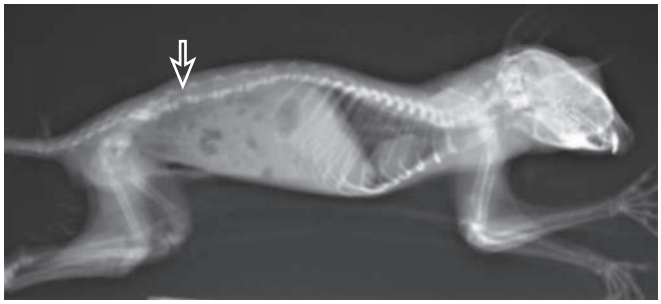


Fig. 27.12 Lateral radiograph showing spinal trauma (arrow) in a glider presented for hindlimb paresis.

captive reptiles. The importance of ultraviolet B lighting is well established in reptiles; however, sugar gliders are nocturnal and rely on gut absorption of vitamin D_3 rather than the conversion of vitamin D_2 in the skin from exposure to UVB.[20] The clinical presentation of nutritional osteodystrophy is sudden onset of hind limb paresis. Differential diagnoses include spinal trauma and general malnutrition. Radiographs may reveal long bone, pelvic, and possible pathologic fractures and vertebral osteoporosis (Fig. 27.12). Plasma biochemical changes include hypocalcemia and hypoproteinemia. The clinical history often indicates a calcium-deficient diet comprised of mostly fruit and minimal protein.[2] Treatment includes cage rest, parenteral calcium, and vitamin D_3 with dietary correction. Because this is considered painful, provide analgesics. Stabilize fractures if possible, although healing times may be prolonged until bone metabolism is corrected.

Diets should contain about 1% calcium, 0.5% phosphorous, and 1500 IU/kg vitamin D_3 on a dry weight basis.[2,34] Insects should be gut-loaded with an appropriate diet containing calcium before being fed to sugar gliders.

Obesity

Captive sugar gliders easily become overweight when fed a diet that is too high in fat or protein (Fig. 27.13). Excessive sugary treats and lack of exercise also contribute to weight gain. Obesity may contribute to cardiovascular or hepatic disease as is seen in other species.[2] Lipid deposits can form in the eyes of juvenile sugar gliders if the mother is fed a diet too high in fat. These deposits appear as small white spots within the eyes and can affect the glider's sight. Treatment of obesity includes modifying the diet and increasing exercise. Encourage owners to weigh their gliders on a weekly basis using a kitchen or postage gram scale. Recommend a weight loss schedule to the owner and provide counseling with written instructions on how to accomplish this.

Fractures and Limb Amputation

Because of their small size and propensity to chew injured extremities, severe fractures of the limbs may be most successfully treated with amputation, although internal fixation and external splinting can be performed similarly to that in rodents of equivalent size. The patagium often interferes with placing splints and bandages. Three-limbed gliders can often locomote well, particularly if cage furnishing adjustments are made. Limb amputation usually requires some alteration of the patagium itself, as the normal attachment to the limb has been removed. Use of analgesics and antiinflammatory drugs are an important compliment to any orthopedic procedure.



Fig. 27.13 Severe obesity in a sugar glider.

Neurologic Disease

The most common neurologic condition of pet sugar gliders is paresis or paralysis secondary to nutritional spinal osteodystrophy. If a sugar glider presents with neurologic signs, differential diagnoses should include trauma and, less commonly, otitis media/interna, bacterial meningitis, toxoplasmosis, *Baylisascaris procyonis*, vitamin E nutritional encephalomalacia, and toxicosis. Reflex testing is often difficult even in tame gliders because they tend to resist limb and joint manipulation in preference to "clinging" to the handler. Lack of proprioception or clutching along with prick sensitivity and toe/tail pinches, balance, and righting response may help the clinician determine if the deficit is central or peripheral. Observing the awake glider exhibiting locomotion and postural or neurologic signs can be done using a clear-sided anesthetic chamber. A full diagnostic workup will include blood tests and diagnostic imaging.

Tremors and Seizures

Seizure activity to any degree constitutes an emergency condition regardless of the cause. Common causes of seizure are hypocalcemia, hypoglycemia, polyvinyl chloride toxicosis, exposure to chemicals in the environment, and possibly heavy metal toxicosis. Administer a benzodiazepine anticonvulsant (i.e., midazolam or diazepam) to the glider to stop the seizures. Full anesthesia may be needed to control the seizure while a

diagnosis is pursued. Intubation is recommended, as many gliders may vomit during the seizure or while attempting anesthesia.

Polyvinyl Chloride Toxicosis

There have been numerous anecdotal reports of gliders that were housed in polyvinyl chloride–coated wire cages developing tremors that progressed to full seizures. Many of these gliders also showed partial paralysis. The onset was usually within 2 months of being placed in the cage. Onset of neurologic signs tended to be quicker in younger gliders than in adults. Several brands of caging were linked to this problem. Clinically gliders were found to have appropriate diets, and other health conditions were ruled out. Treatment involved anticonvulsants and supportive care, and removing the animal from the caging.[41]

Other Neurologic Disorders

Toxoplasmosis causes a fatal encephalitis similar to that seen in other species. Antemortem diagnosis may be aided by serology, although specific serologic tests are not validated commercially for sugar gliders. Treatment may be tried in suspect cases by using trimethoprim sulfa (15 mg/kg by mouth every 12 hours) and supportive care.[25,34] Bacterial and fungal organisms have been implicated in neurologic disease, often confirmed at postmortem examination. Cerebrospinal fluid for culture, biochemical analysis, and cytologic examination can be obtained from the cisterna magna, although the volume is usually less than 0.05 mL. The procedure is similar to that done in rodents of comparable size and should be practiced first on a cadaver.

Infectious and Parasitic Diseases

Bacterial Diseases

Infectious diseases continue to be reported in captive sugar gliders. Gliders are presumed to be susceptible to the same pathogens as are other marsupials in their family. Sugar gliders have died from infection with *Pasteurella multocida* contracted from rabbits kept in the same area.[20,22] The disease is characterized by generalized abscessation in various organs and subcutaneous areas, as well as sudden death. *Clostridium piliforme* infection (Tyzzer's disease) has been diagnosed in captive sugar gliders.[20,22]

Listeria monocytogenes infection was found in a sugar glider with sepsis. The diet included cantaloupe, which at the time was implicated in a United States foodborne *L. monocytogenes* outbreak from cantaloupe. The bacterial strains from the humans and the glider were genetically distinct, however, in this case.[35]

Parasitic Diseases

Parasites are most often found in wild sugar gliders or in captive gliders kept outdoors. Various nematodes, trematodes, tapeworms, mites, lice, and fleas are all potential parasites of sugar gliders.[2,20] Specific parasites identified in sugar gliders include trematodes (*Athesmia* species) in the liver and nematodes (*Parastrongyloides*, *Paraustrostrongylus,* and *Paraustroxyuris* species) in the gastrointestinal tract.[2] Giardiasis and cryptosporidiosis have also been diagnosed in captive sugar gliders.[20,22] The nematode *Ophidascaris robertsi* was found on necropsy with third-stage larvae recovered from two heart chambers and one free in the peritoneal cavity. Pathologic findings included intraluminal and perivascular pulmonary hemorrhage. The glider had been bred in captivity but had contact with wild-caught Australian pythons, which were believed to be the source of the infection.[15] Marsupials are susceptible to *Toxoplasma gondii*, which causes neurologic signs and sudden death.[20]

A recently recognized disease syndrome has been reported that includes diarrhea, wet and "sticky" joeys, pouch exudate, and frequently death in joeys. The furred but still largely pouch joeys have the appearance of not being groomed or of having tacky mucus covering them. Clinical signs include lethargy, dehydration, diarrhea, anorexia, and death. Adults may be asymptomatic, although mild, intermittent diarrhea has been reported. The glider community describes this as "ick," although joeys in this condition can result from other diseases. A wet mount of the affected joey's stool or often of the dam's reveals a trichomonad organism. Polymerase chain reaction testing of the organism has identified it as a newly recognized genus, although published reports identify it both as *Simplicomonas* and *Simplicimonas* (Tritrichomonadae).[24] Affected joeys can be treated with metronidazole benzoate at 25 mg/kg by mouth every 24 hours, usually for at least 14 days, along with supportive care.[25] Also treat all adults in the environment with the same dosage of metronidazole. The benzoate form is used because of its palatability. It is unknown if the adults are lifelong carriers or can be cleared of the organism.

Neoplasia

Neoplasia, in particular lymphoid neoplasia, is relatively common in captive gliders.[2] Benign tumors reported include subcutaneous fibroma, histiocytoma, and sebaceous epithelioma.[30] A pericloacal mass that caused colonic obstruction was diagnosed as a transitional cell carcinoma arising from the urothelium.[30] A dermal hemangiosarcoma was reported in a mass growing on the lateral margin of a patagium.[38] Many tumors, including mammary neoplasia, are treated with surgical excision. Table 27.3 summarizes reported neoplasms.

SURGERY AND ANESTHESIA

Anesthesia

Isoflurane and sevoflurane are the anesthetics of choice for sugar gliders. The use of either of these agents facilitates physical examination, venipuncture, and radiographic examination, as well as anesthesia for general surgery. Anesthesia can be induced with the use of a large face mask as an induction chamber to deliver 5% isoflurane. As soon as the glider is recumbent, remove it from the chamber and place a small face mask until the glider is sufficiently anesthetized for endotracheal tube placement. A 1-mm Cook endotracheal tube (Global Veterinary Products, New Buffalo, MI; www.globalvetproducts.com) can be used to deliver isoflurane at 2% to 3% for maintenance. Transient apnea may occur during induction; therefore monitor the heart rate closely. If the heart rate is stable, gentle pressure to the thorax usually stimulates breathing. Intubation of gliders can be aided by using a stylet and fine-bladed laryngoscope. While extending the glider's head to maximally lift the soft palate, extend its tongue and use the laryngoscope to see the larynx.

For longer anesthetic procedures, in particular surgical procedures, a balanced anesthetic approach, including

TABLE 27.3 Reported Neoplasms in Sugar Gliders [2,7,9,16,19,29,30,38]

Neoplasm	Tissue
Adenocarcinoma	Abdominal, chest gland, duodenal, lung, mammary, metastatic
Carcinoma	Adrenal cortical, bronchoalveolar, intestinal, mammary, paracloacal gland
Carcinoma, squamous cell	Vagina
Dysgerminoma	Not specified
Epithelioma, sebaceous	Skin
Erythroid leukemia	Spleen
Fibroma	Subcutis
Fibrosarcoma	Not specified—listed as incidental finding
Hemangiosarcoma	Dermal
Hepatocellular tumor	Liver
Histiocytoma	Subcutis
Lymphoid or myeloid leukemia	Not specified
Lymphosarcoma	Cutaneous, various tissues
Melanoma	Cutaneous
Myxosarcoma	Not specified
Pheochromocytoma	Adrenal gland
Spindle cell tumor	Not specified

the use of preemptive analgesics, anxiolytic tranquilizers, and local anesthetics, followed by gas anesthesia results in fewer fluctuations in heart rate and blood pressure, as well as a decreased concentration of inhalant gas anesthetic, and a smooth, rapid recovery. Commonly used drugs for premedication, analgesia, and anesthesia are summarized in the Appendix Formulary. Maintenance of preoperative body temperature prevents prolonged recovery and the trigger of torpor and decreased overall metabolism associated with the drop in body temperature.

Inserting an intravenous catheter for intraoperative fluid and venous access may be difficult; instead, an intraosseous catheter placed in the femur or tibia can be used. For surgeries predicted to last less than 1 hour or surgeries that do not enter the abdominal cavity, subcutaneous fluids administered as part of the preanesthetic medication regimen may be sufficient.

A local anesthetic can be used to infiltrate the incision site, operative area, or achieve a dental nerve block and has the further advantage of providing postoperative site analgesia, which decreases the possibility of the glider chewing at the incision site. For castrations, bupivacaine at 2 mg/kg or lidocaine at 4 mg/kg (diluted 1:10 in saline solution) can be administered, with 50% of the total volume injected directly into each testicle. The use of these local anesthetic agents should reduce the contraction of the cord during ligation and help prevent chewing of the surgical site.[31]

The use of tiletamine hydrochloride and zolazepam hydrochloride (Telazol, Fort Dodge Animal Health, Fort Dodge, IA) in sugar gliders is controversial and reportedly caused neurologic signs and death in apparently healthy sugar gliders when administered at 10 mg/kg.[18] Other reports suggest that it can be used in sugar gliders at 8.4 to 12.8 mg/kg without problems.[6]

Soft Tissue Surgery

General Surgical Considerations

Sugar gliders should be fasted for about 4 hours before surgery.[37] For gastrointestinal surgery, a longer fasting period may be indicated. Magnification with a binocular head loupe during surgery aids in identifying small structures and vessels. Minimize blood loss during surgery by using a radiosurgery unit or carbon dioxide laser and ligate small vessels with fine nonreactive monofilament suture. To discourage self-trauma, skin sutures must not be tight. Sugar gliders can reach almost all parts of their body, even with a fitted Elizabethan collar.

Sugar gliders typically recover smoothly from anesthesia. Additional analgesics are continued after surgery to minimize self-trauma to the incision and to provide postoperative pain relief (see Appendix Formulary). To maintain body temperature, allow the patient to recover from anesthesia in an incubator. Restricted activity and usual postoperative procedures are recommended as in other species.

Castration and Scrotal Ablation

For castration, several methods have been described for exposure of the spermatic cords, including a longitudinal incision by scalpel, radiosurgery electrode, or carbon dioxide laser made close to the body wall in the stalk skin (Fig. 27.14). With the laser, place a tongue depressor between the glider's body and the scrotal stalk. Then apply the laser to the stalk, rapidly cutting in transverse section close to the body wall, leaving no excess tissue. The laser cuts and cauterizes instantly, although the skin will appear to puff up. No sutures are needed if using the laser, which minimizes postoperative mutilation compared with scalpel-based surgery.[31] Traditional scalpel surgery necessitates clamping the cords with hemostats and ligating using 5-0 PDS suture. The scrotal sac containing the testicles and the distal portion of the stalk is then removed. The ligated stalks can be incorporated with a suture in the abdominal fascia to prevent herniation.[23,32] Close the skin incision by using tissue glue. Regardless of the technique used, be sure to provide appropriate postsurgical analgesia.

Ovariohysterectomy

For ovariohysterectomy, make a 1- to 2-cm skin incision paramedial to the pouch, leaving enough skin along the edge of the pouch for closure.[23,34] Identify the linea alba by blunt dissection, then incise into the abdominal cavity. The bladder is visible as the abdominal cavity is entered. Carefully exteriorize the bladder to bring the reproductive tract into view. The ovaries appear as small, red, granular structures. Identify and ligate the ovarian branch of the ovarian artery. Ligate and remove the uterus at the level of the cervix above the lateral vaginal canals. Close the linea alba; then close the skin routinely with subcuticular sutures.

Patagium Repair

Small wounds (less than 5 mm) to the patagium may be left to heal by second intention, but they should be thoroughly clipped, debrided, and cleaned. Carefully remove hair from the

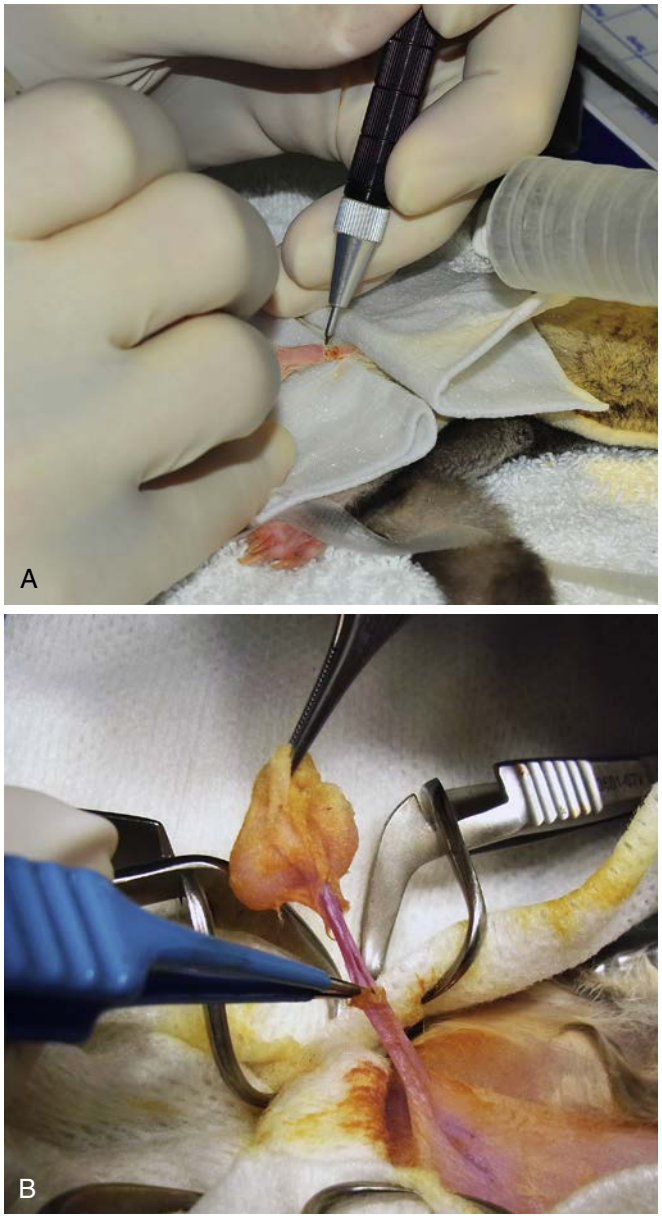


Fig. 27.14 Castration of male sugar gliders. (A) Use of a CO2 laser. (B) Castration can be performed using radiosurgery to incise the skin, stalk, and cords. (Courtesy Drs. C. Mans and Y. Miwa.)

wound edges. Larger wounds may require suturing; take care to correctly align the two skin layers and use fine absorbable suture material. Magnification will assist this process. If the gliding membrane is extensively damaged, it may need to be reshaped to remove any skin tags or flaps that could become snagged on wire enclosures. Some patagial repairs will result in contraction of the gliding membrane, and mobility may be reduced.

Paracloacal Gland Removal

The surgical removal of paracloacal glands is similar to that of anal gland removal in other species. A single skin incision over the center of each firm swollen gland will reveal the gland and allow the skin to be peeled away from the thin connective tissue and glandular wall (Fig. 27.15A). Take care to prevent rupturing of the glands, especially if the glands are infected or impacted.



Fig. 27.15 (A) Dissection of the impacted paracloacal gland from the surrounding connective tissue reveals a small stalk-like attachment for ligation and excision. (B) Closure of paracloacal gland removal surgery is similar to anal gland removal in the ferret. (Courtesy R. D. Ness, DVM.)

The bulk of the procedure is performed with blunt dissection of the gland from the surrounding connective tissue around the cloaca. A single ligation or use of radiosurgery or carbon dioxide laser may be necessary to ligate the small blood vessel at the base of the gland. Close the incision with a single subcuticular suture and a small drop of tissue glue on the surface (Fig. 27.15B). Inject a small amount of diluted local anesthetic at the surgery site to reduce the chance of postoperative self-trauma.

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28

African Pygmy Hedgehogs

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Hedgehogs are members of the family Erinaceidae and were previously classified in the now obsolete Order Insectivora. Hedgehogs are now grouped in the Order Eulipotyphla, which includes other small mammals like shrews and moles.

BIOLOGY AND ANATOMY

Taxonomy and Natural History

The two most familiar hedgehog species are the central African hedgehog *(Atelerix albiventris)* and the European hedgehog *(Erinaceus europaeus)*. The central African hedgehog, also known as the white-bellied, four-toed, or "African pygmy" hedgehog, is native to the savannah and steppe regions of central and eastern Africa.[55] Some pet African pygmy hedgehogs are descended from hybrids of the central African and similar Algerian hedgehog *(Atelerix algirus)*. In the pet trade, *Atelerix* species are generally referred to as African pygmy hedgehogs. Unless otherwise noted, the information in this chapter refers to pet African pygmy hedgehogs. Because of the ban on importation, pet hedgehogs in the United States are captive bred; numerous color varieties exist, and at least one show standard has emerged.

Wild African hedgehogs are found in diverse dry open habitats including grassland, scrub, and suburban yards.[45] They are nocturnal and spend their daylight hours hidden in burrows or other cavities. At night, they are active invertebrate predators, traveling several miles in search of insects, earthworms, slugs, and snails.[55] Males and females are territorial and solitary except during courtship and when females raise young.

Because of their small size, spiny coat, and relatively recent appearance in the pet trade, African hedgehogs can be challenging patients. Hedgehogs are illegal in some states and municipalities; in other states, a permit is required. Additionally, a permit from the United States Department of Agriculture (USDA) is required for persons who breed, transport, sell, exhibit, or use hedgehogs for research or teaching purposes. Even breeders who give away their progeny must be registered with the USDA, although breeders with three or fewer intact females are now excluded from this requirement. Hedgehog owners are advised to check with appropriate regulatory agencies, including state fish and game or wildlife departments and their regional USDA office for specific regulations.

Anatomy and Physiology

Hedgehogs are adept at climbing, digging, swimming, and constant jogging. The tibia and fibula are fused distally. The stance is plantigrade. The manus has five digits, the pes has four. The normal hedgehog gait is a slow and steady waddle, but they are capable of bursts of speed.

Hedgehogs have brachydont (closed-rooted) teeth (Fig. 28.1). The first incisor in each quadrant is large and projects forward. The mandibular first incisors occlude into a space between the maxillary first incisors, an arrangement that is suited to spearing insects. This noticeable gap between the first maxillary incisor teeth is significantly larger in female than in male African pygmy hedgehogs, which may be because of the female's overall larger size and prehension of relatively larger prey items.[17] The molar teeth are relatively flattened with multiple cusps and are suited for crushing food items. The stomach is simple, and a vomiting reflex is present. There is no cecum, and the colon is smooth. Feces are normally soft but formed.

The crown and dorsum (collectively called the *mantle*) are covered in a dense coat of several thousand smooth spines. The epidermis in this area is thin, and there is a thick fibrous dermal layer that contains much fat and few blood vessels. Hedgehog spines are composed of keratin and have a complex internal structure that confers lightness, strength, and elasticity. Each spine has a round basal bulb that firmly attaches it within the follicle, whereas a more narrowed portion at the skin surface allows each spine to bend when force is applied. Healthy spines are difficult to pull from the follicle without breaking at this narrowed portion. Spines may last up to 18 months and are replaced individually. Spines are absent from the midline of the crown, and hair on the feet and muzzle is sparse to absent. The haired skin and the soles of the feet are rich in sweat and sebaceous glands. The toenails are round in cross section and are highly curved.



Fig. 28.1 Oral examination in a hedgehog; note the large gap between the maxillary incisors, which is a normal finding.

A wary hedgehog will raise the spines and crouch. If an alert hedgehog is frightened by touch or noise, contraction of the panniculus muscle pulls the loose spiny skin over the entire body. Several muscles assist in pulling the panniculus over the body and tucking in the legs and rump. The panniculus is thickened at the rim to form the orbicularis muscle, a purse-string-like muscle that closes the loose skin over the animal. A hedgehog may remain rolled up for hours with relatively little muscular effort.

An unrolled hedgehog's sex is easily determined; the male has a conspicuous prepuce that opens on the midabdomen (Fig. 28.2A), whereas the female's urogenital opening is a few millimeters cranial to the anus (Fig. 28.2B). The penis has a prominent glans that protrudes laterally into horn-like structures.[5] There is no scrotal sac; the testes are located in a para-anal recess (Fig. 28.2A),[5] are surrounded by fat, and can be palpated in reproductively active males. The accessory sex glands in the African pygmy hedgehog are not well described. Male accessory glands in European hedgehogs include paired prostate

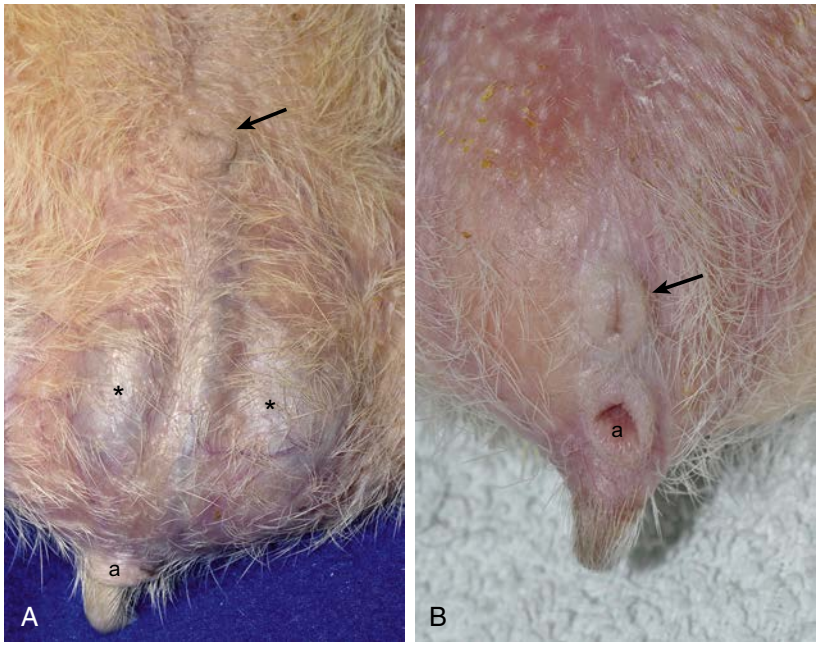


Fig. 28.2 (A) Adult male hedgehog; note the midabdominal prepucial opening *(black arrow)* located a significant distance from the anus *(a)* and the testicles *(asterisks)* located in a para-anal recess. (B) Adult female hedgehog; note the close proximity of the anus *(a)* and the more cranial vulvar opening *(black arrow)*, a much shorter anogenital distance when compared with the adult male.

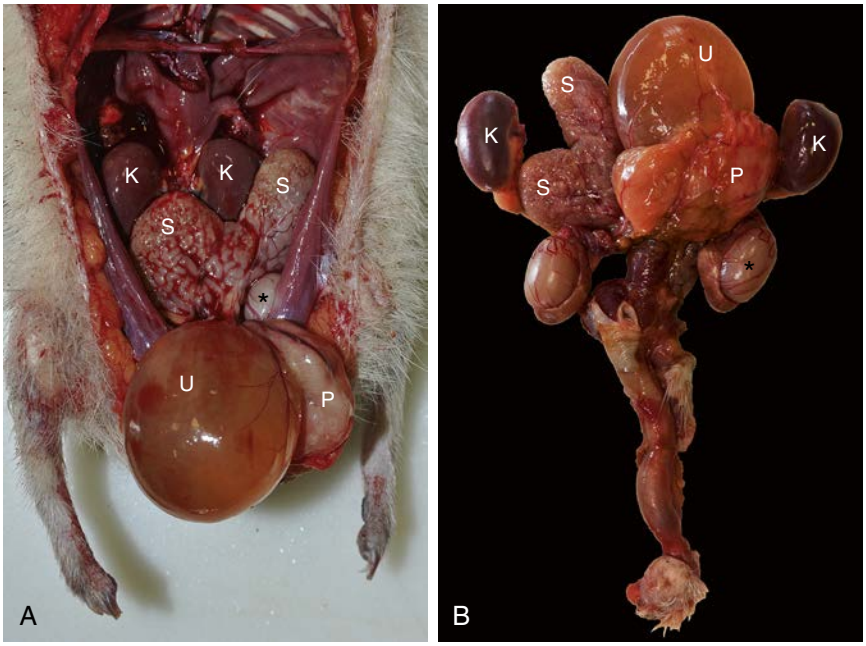


Fig. 28.3 (A) Postmortem photographs illustrate the accessory sex glands in a male hedgehog; note how the glands fill a large portion of the caudal abdominal cavity. Shown are the seminal vesicles *(S)*, kidney (K), and prostate *(P)* adjacent to the urinary bladder *(U)*; the left testicle *(black asterisk)* is also partially visible. (B) The urogenital tract ex situ shows the accessory sex glands. (Photos courtesy Dr. G Doss, DVM.)

glands, seminal vesicles, bulbourethral glands, and Cowper's-like glands (Fig. 28.3).[55]

In female hedgehogs, the uterus is bicornate with no uterine body but rather a continuous lumen over the cervix. There is a single cervix and a long vagina that is always patent. A fan-shaped gland, homologous to the Cowper's-like gland of the male, lies on each side of the vagina in female hedgehogs.[55] The urethral opening is located in the distal vagina, several millimeters from the vulva.[55] The mesosalpinx and ovarian bursa are fat-laden, and the fallopian tubes are relatively short and emerge from the side of each uterine horn.[5] Females have three pairs of mammary glands.[45]

Neurology and Behavior

Hedgehogs have a very sensitive olfactory system and well-developed olfactory lobes. The vomeronasal organ is also prominent, and hedgehogs may occasionally exhibit a flehmen response.[28] It is believed that olfaction plays a key role in a wild hedgehog's ability to navigate within its home range, detect food, avoid predators, and communicate with conspecifics.[28] Hedgehogs also have sensitive hearing, especially in the ultrasonic range. Their sense of vision is not as well developed and is essentially monochromatic.[55]

Foraging hedgehogs normally emit a variety of snuffling sounds. Frightened or agitated hedgehogs make a distinctive hissing sound that may be punctuated with various puffing and cough-like sounds. With intense distress, and occasionally impatience for food, a scream may be emitted.[28] Other vocalizations include grunts, squeals, clucking, snuffling, and high-pitched sounds, but these are uncommon except during courtship and between mothers and offspring. The cerebrum of the hedgehog is relatively small, and their learning abilities seem to be less



Fig. 28.4 Self-anointing or anting behavior in a hedgehog. This behavior is elicited by a variety of substances; the hedgehog takes the material or object into the mouth, mixes it with frothy saliva, and applies the mixture to its spines with its tongue. (Courtesy Lyndsey Smith, Manhattan, KS.)

than those of rodents or carnivores.[55] They do demonstrate the ability to recognize their owners and with patient training may learn simple commands. With patient, gentle handling, most hedgehogs will learn to accept and even enjoy human contact.

Both sexes of wild and captive hedgehogs demonstrate a unique behavior called *self-anointing* or *anting* (Fig. 28.4). This behavior may be elicited by a variety of substances, particularly those with a strong or unusual odor, such as fish, wool, and various plants and vegetables. The hedgehog takes the material or object into its mouth, mixes it with frothy saliva, and applies the mixture to its spines with its tongue. Many speculations have

been offered about the purpose of this behavior, the most plausible of which seems to be one of imparting an individual odor to the animal and its home range.[55]

HUSBANDRY

Housing

Hedgehogs are solitary in the wild; in captivity they are usually maintained in individual cages. Some fanciers successfully keep groups of females with or without a single male or even groups of males, but this can lead to disproportionate feeding and injuries from fighting. Although young animals raised together may tolerate each other as adults, hedgehogs typically become aggressive toward cage mates when they reach sexual maturity. Should multiple animals be housed together, provide at least one hide box for each animal.

Healthy hedgehogs are very active, and as large a cage as possible should be provided; 2 × 3 feet (0.6 × 0.9 m) are minimal floor dimensions. Hedgehogs are able to climb and escape through small holes, so the cage must be secure and lidded; smooth walls are ideal. Hedgehog droppings can be soft and messy, making wood cages difficult to keep clean. Plastic-bottomed cages with wire walls are suitable provided that the wire spacing is appropriate (1 in. [2.54 cm] square is acceptable). Widely-spaced wires can lead to limb entrapment or death if the hedgehog puts its head between the wires and becomes ensnared by its spines. A hiding place is an essential furnishing. The cage substrate should be soft and absorbent and will require frequent changing. The substrate should be 3 to 4 inches deep to allow for digging; hiding mealworms or other treat items in the bedding is a good way to stimulate foraging behavior. Cloth or string in the cage poses a risk, as hedgehog digits and limbs are easily entrapped by loose fibers (Fig. 28.5).



Fig. 28.5 Discolored distal digit in a hedgehog secondary to fiber constriction.

Hedgehogs should be maintained at ambient temperatures between 72°F and 90°F (22°C and 32°C); 75°F to 85°F (24°C to 29°C) is optimal. African hedgehogs may go into torpor if they are too cool or too warm. A heating pad placed under part of the enclosure or a ceramic heat emitter may be used to provide a constant source of heat without affecting the photoperiod. Low humidity (less than 40%) is preferred, and a day cycle of 10 to 14 hours of low-intensity light should be provided.

Placing all the droppings in a litter tray on a daily basis may facilitate litter training. Natural plant litters used for cats make the best litter substrate. Clay, clumping-type litter, or sand may stick to the animal and should not be used.

Exercise wheels are highly recommended. The wheel must have a solid or fine plastic mesh for hedgehogs to run on because their legs tend to become entrapped by traditional wire rodent wheels. Hedgehogs should also be let out into a large area on a daily basis for supervised exercise. Cardboard tubes, straw, safe climbing structures, swimming tubs, and other toys provide enrichment. Dirty hedgehogs may be bathed with a mild pet shampoo and a soft-bristle brush.

Diet

Wild African hedgehogs feed on a diversity of invertebrate prey as well as plant materials and occasional eggs, vertebrate prey, and carrion.[55] Insectivorous mammals are traditionally fed diets that are 30% to 50% protein and 10% to 20% fat (dry-matter basis).[11] Hedgehogs seem to require a higher level of dietary fiber than carnivores, which may be related to the large quantity of insect exoskeletons in their natural diet.

The base of the captive diet consists of a commercially prepared, dry kibble formulated for insectivores or hedgehogs specifically. If commercially prepared hedgehog food is not used, premium food for less active cats or dogs should form the basis of the diet. Ferret food is too high in fat and therefore not recommended. With many individuals, food must be rationed to prevent obesity. Depending on the animal's weight and activity, three to four teaspoons of the main diet is typically fed daily. Growing animals and reproductively active females may be fed the usual diet ad libitum, and calcium-rich foods are recommended.

In addition to the main diet, provide a small amount of varied moist foods (e.g., canned cat or dog food, cooked meat or egg, or low-fat cottage cheese) and vegetable/fruit mix (e.g., beans, cooked carrots, squash, peas, tomatoes, leafy greens; bananas, grapes, apples, pears, berries). Invertebrate prey (e.g., mealworms, crickets, earthworms) should also be provided occasionally for enrichment. Gut-load the invertebrate prey with a calcium-rich diet before feeding, and feed sparingly due to their poor nutritional value and often high fat content. Invertebrate prey and other dry food items can be hidden in the bedding to promote foraging activity. Hedgehogs should not be fed raw meat or eggs, which may harbor *Salmonella* species. Milk can cause diarrhea. Avoid nuts, seeds, and large items or hard foods such as raw carrots, as these can become lodged in the roof of the mouth. Hedgehogs may be slow to accept novel foods; therefore, make any dietary changes carefully. Provide fresh water at all times. Many hedgehogs learn to drink from water bottles.

Breeding and Neonatal Care

African hedgehogs are polyestrous and breed throughout the year in captivity. The estrus cycle for *A. albiventris* empirically seems to be similar to that of other hedgehog species, for which the estrus cycle has been reported to be 3 to 17 days of estrus followed by 1 to 5 days of diestrus.[55] Some indirect evidence suggests that ovulation is induced.[5,55] Sterile matings with pseudopregnancy may occur. Although the gestation period is 34 to 37 days, delayed implantation can occur and extend the apparent gestation period to 40 days.[55] Female hedgehogs should be at least 6 months of age before breeding. Pregnancy is most easily determined by weighing the female every few days; a gain of 50 g or more within 2 to 3 weeks of being placed with a male is suggestive of pregnancy.[58] At 30 days, a general swelling of the abdomen or mammary enlargement may be detected. Novice hedgehog breeders should give the female strict privacy from other hedgehogs and people from about 5 days before delivery through 5 to 14 days after delivery to help prevent infanticide. Providing a large cage and an additional hiding place for the female as a refuge from her litter may reduce stress.[28] Male hedgehogs must not be allowed near the neonates because cannibalism (by either parent) often results.

Hedgehogs are born hairless, with closed eyes and ears. At birth, the spines are buried within a layer of skin; within the first few hours, the spines are exposed by an inflating and subsequent deflating of the skin with fluid and removal of the covering by the mother. These first spines are white, but they are replaced by darker spines over the first 3 days of life. Colostral transfer is believed to occur early in lactation.

Normal pups (or "hoglets") stay close to their dam and littermates when resting. In cases of lactation failure or abandonment by the female, fostering of the pups to another dam with similarly aged pups is usually successful. Weaning generally occurs at 5 to 6 weeks, and the young may be moved to separate cages at 8 weeks.[28]

If a surrogate dam is unavailable, a milk replacer may be fed. Based on the composition of European hedgehog milk, a canine milk replacer with added lactase (Lactaid; McNeil-PPC, Ft. Washington, PA) seems to be the most logical formula.[35,55] Hand-rearing of hedgehogs is often associated with high mortality. Feed neonates as much as they will consume every 2 to 4 hours for about 3 weeks. Stimulate neonates to eliminate after each feeding by massaging the ventrum and perineal area with a cloth or swab moistened in warm water.

BASIC PROCEDURES AND PREVENTATIVE MEDICINE

Restraint and Examination

Even very tame hedgehogs often roll up when an examination or other procedure is attempted. Hedgehogs do bite, but infrequently. Patience and a quiet room with subdued light may help calm wary hedgehogs. High-pitched sounds, such as the jingling of instruments, should be avoided. A small towel and light gloves may facilitate handing. Placing a shy animal in a dish of shallow water may also allow auscultation or scruffing. Once uncurled, hedgehogs may be restrained by holding the spined skin as one would hold the scruff of other species; grab the hedgehog just behind the ears at the junction of the haired skin and mantle. Scruffing can provide enough access to perform cardiothoracic auscultation, abdominal palpation, or cephalic blood collection, but may require sedation to perform adequately (Fig. 28.6).

A superficial examination (e.g., evaluation of ventrum) may be performed as the animal moves about within a transparent container, but a thorough examination usually requires chemical restraint (see "Anesthetic and Surgical Considerations" below). Inhalant anesthesia with isoflurane is most frequently used.

Healthy hedgehogs should be active and inquisitive or curled up in a tight ball. Hydration may be assessed by eyelid turgor and skin tent. Body temperature is lower than that of most mammals (Table 28.1). The pinnal margins should be free of crusting or ragged edges. The teeth should be white and the gingiva a uniform pink. Inspect



Fig. 28.6 (A–B) Scruffing is a useful maneuver in sedated or very docile hedgehogs.

TABLE 28.1 Biologic and Physiologic Data for African Pygmy Hedgehogs[23,35,44,55,58]

Average body weight	Captive: male, 400–600 g; female, 300–400 g
Life span (in captivity)	Average 4–6 years, may live to 8 years
Body temperature	95.7°F–98.6°F (35.4°C–37.0°C)
Adult dental formula	2 (I3/2: C1/1: P3/2: M3/3) = 36; variations have been reported
Gastrointestinal transit time	12–16 hours
Heart rate	180–280 beats/min
Respiratory rate	25–50 breaths/min
Age at sexual maturity	Male: 6–8 months; female: 2–6 months
Reproductive life span	Female, 2–3 years; male, throughout life
Gestation	34–37 days
Milk composition	Protein, 16 g/100 g; carbohydrate, trace; fat, 25.5 g/100 g
Litter size	3–4 (range 1–7)
Birth weight	10–18 g
Eyes open	14–18 days
Deciduous teeth eruption	Begins on day 18; all deciduous teeth erupted by 9 weeks
Permanent teeth eruption	Begins at 7–9 weeks
Age at weaning	4–6 weeks (start eating solids at 3 weeks)

TABLE 28.2 Hematologic Values of African Pygmy Hedgehogs[26,46]

Measurement	Mean ± SD (Range)[26]	Mean ± SD (Range)[46]
Pack cell volume, %	36 ± 7 (22–64)	42.0 ± 0.9 (33.5–47.0)
Red blood cells, x10^6/μL	6 ± 2 (3–16)	5.0 ± 0.1 (4.3–6.0)
Hemoglobin, g/dL	12 ± 2.8 (7–21.1)	13.1 ± 0.3 (10.7–14.9)
Mean corpuscular volume, fL	67 ± 9 (41–94)	87.8 ± 1.8 (76.3–99.8)
Mean corpuscular hemoglobin, pg	22 ± 4 (11–31)	27.1 ± 0.7 (22.5–31.4)
Mean corpuscular hemoglobin concentration, g/dL	34 ± 5 (17–48)	30.9 ± 0.5 (27.7–35.2)
Platelets, x10^3/μL	226 ± 108 (60–347)	
White blood cells, x10^3/μL	11 ± 6 (3–43)	15.0 ± 0.7 (11.5–21.7)
Neutrophils, x10^3/μL	5.1 ± 5.2 (0.6–37.4)	9.5 ± 0.5 (6.1–14.6)
Lymphocytes, x10^3/μL	4 ± 2.2 (0.9–13.1)	5.2 ± 0.4 (3.3–8.9)
Monocytes, x10^3/μL	0.3 ± 0.3 (0–1.6)	0.2 ± 0.1 (0–0.8)
Eosinophils, x10^3/μL	1.2 ± 0.9 (0–5.1)	0.2 ± 0 (0–0.3)
Basophils, x10^3/μL	0.4 ± 0.3 (0–1.5)	0.1 ± 0 (0–0.2)

the oral cavity and tongue for ulcers, foreign material, and masses. The nose is normally moist and active. Normal lymph nodes are difficult to palpate, but lymph nodes may become enlarged in cases of neoplasia or infection. Respiration is normally silent except in the defensive or aggressive animal, in which forceful expulsion of air through the nose creates a loud hissing sound. The abdominal contour as the animal rests in the hand of the clinician should be flat. Palpate the abdomen for organomegaly, masses, or fluid waves. Be careful not to mistake the large, paired seminal vesicles present in reproductively active males for an abdominal mass; they are located dorsal to the bladder and can extend cranially to the level of the kidneys (Fig. 28.3). Check the prepuce or vulva for inflammation, discharge, or adherent debris. Testicles may be palpable lateral to the anus in the para-anal recess. Normal stools are very dark brown, and the consistency varies from very soft to pellet-like. Healthy, untroubled hedgehogs walk with the ventrum raised clear off the table, but weak or wary hedgehogs tend to crouch. Inspect the toes for encircling fibers (Fig. 28.5) and overgrown nails. The skin in the spiny areas may have a mildly dry or flaky appearance, but excessive flaking, quill loss, erythema, and crusting are abnormal.

Clinical Techniques

Collecting sufficiently large volumes of blood from hedgehogs can be difficult. The jugular veins may be used for venipuncture, although locating the vessels may be challenging because of their short neck. The femoral, lateral saphenous, or cephalic veins may be used for injections or to collect small samples (often less than 0.5 mL). The cranial vena cava may be used, but there is a greater risk of cardiac puncture because of the relatively cranial position of the heart; use of short needles and general anesthesia are mandatory if this route is used. The technique for caval venipuncture is similar to that used in ferrets. Reference ranges for hematologic and

TABLE 28.3 Serum Biochemical Values of African Pygmy Hedgehogs.[26,46]

Measurement	Mean ± SD (Range)[26]	Mean ± SD (Range)[46]
Alkaline phosphatase, U/L	51 ± 21 (8–92)	22.4 ± 1.0 (18.2–25.5)
Alanine aminotransferase, U/L	53 ± 24 (16–134)	22.8 ± 1.4 (15.2–28.8)
Amylase, U/L	510 ± 170 (244–858)	
Aspartate aminotransferase, U/L	34 ± 22 (8–137)	33.5 ± 3.5 (19.0–65.6)
Bilirubin, total, mg/dL	0.3 ± 0.3 (0–1.3)	—
Blood urea nitrogen, mg/dL	27 ± 9 (13–54)	47.1 ± 2.3 (34.3–57.3)
Calcium, mg/dL	8.8 ± 1.4 (5.2–11.3)	9.7 ± 0.3 (8.6–11.4)
Chloride, mEq/L	109 ± 10 (92–128)	
Cholesterol, mg/dL	131 ± 25 (86–189)	132.5 ± 5.3 (100–150)
Creatine kinase, U/L	863 ± 413 (333–1964)	
Creatinine, mg/dL	0.4 ± 0.2 (0–0.8)	0.7 ± 0.1 (0.5–1.0)
Gamma-glutamyl transferase, U/L	4 ± 1 (0–12)	
Glucose, mg/dL	89 ± 30	86.1 ± 4.7 (60–125)
Lactate dehydrogenase, U/L	441 ± 258 (57–820)	
Phosphorus, mg/dL	5.3 ± 1.9 (2.4–12)	—
Potassium, mEq/L	4.9 ± 1 (3.2–7.2)	—
Protein, total, g/dL	5.8 ± 0.7 (4–7.7)	6.0 ± 0.2 (4.6–6.9)
Albumin, g/dL	2.9 ± 0.4 (1.8–4.2)	3.4 ± 0.2 (2.7–3.9)
Globulin, g/dL	2.7 ± 0.5 (1.6–3.9)	2.6 ± 0.2 (1.9–3.6)
Sodium, mEq/L	141 ± 9 (120–165)	
Triglycerides, mg/dL	38 ± 22 (10–96)	37.8 ± 2.3 (30.8–46.2)



Fig. 28.7 Use of paper tape on a hedgehog to displace the mantle dorsally to minimize artifacts in the lung fields from the keratinaceous spines during lateral radiographic positioning.

serum biochemical values are presented in Tables 28.2 and 28.3. A urine sample may be collected by floor-collection, cystocentesis, or catheterization; however, reference values are not available. Subcutaneous injections can be given in the spiny or furred areas; the furred area is more elastic and vascular, but it is less accessible in a balled-up hedgehog. The junction of furred and spined skin midbody can also be used for subcutaneous fluid administration. Intramuscular injections may be given in the epaxials, triceps, quadriceps, gluteal, or orbicularis muscles. Maintaining an intravenous catheter in all but extremely weak hedgehogs is difficult because the catheter tends to become dislodged if the animal curls. A femoral or tibial intraosseous catheter may be placed as a substitute for vascular access. A 22- or 25-gauge needle or 1-inch spinal needle is used and secured with tape; a tibial crest catheter remains accessible even when the animal is in a curled position.[39]

Oral medication may be difficult to impossible to administer to some animals. Some animals accept pleasant-tasting medications via a syringe. Many hedgehogs will consume mealworms that have been injected with medication; for those that do not, medications may be mixed with a favorite food. Some medication odors may initiate anting behavior.

Radiographs are usually performed under heavy sedation or general anesthesia to allow for proper patient positioning, unless the patient is too weak to roll up. Extend the legs and body for both the lateral and ventrodorsal views. Radiographic detail is greatly diminished by the presence of the spines. For the lateral view, the elasticity of the mantle makes it possible to pull the spines away from most of the chest and abdomen with either tape or a toothed hair clip (Fig. 28.7). Radiographic vertebral heart size scores have been reported for African pygmy hedgehogs. Mean vertebral heart size score measured by using left lateral radiographs was 8.16 ± 0.48 v (vertebral bodies).[6]

Ultrasonography is a useful modality in hedgehogs and can help discern uterine and urinary bladder pathology in cases of hematuria, among other indications. Echocardiographic parameters under isoflurane anesthesia have been reported for African pygmy hedgehogs; normal parameters are presented in Table 28.4. Computed tomography is useful for imaging a variety of anatomic locations in hedgehogs but is most helpful when examining dental, otic, and skeletal disorders, or if detail of the thoracic cavity is needed.

TABLE 28.4 Echocardiographic Measurements Obtained From 13 Clinically Healthy African Pygmy Hedgehogs[6]

Parameter	Values[a]
IVSd, cm	0.15 ± 0.01 (0.13–0.17)
LVIDd, cm	0.74 ± 0.05 (0.67–0.84)
LVIDs, cm	0.58 ± 0.03 (0.54–0.65)
LVFWd, cm	0.16 ± 0.01 (0.14–0.18)
FS, %	21.45 ± 2.50 (17.40–26.80)
LA, cm	0.56 ± 0.04 (0.51–0.62)
AO, cm	0.36 ± 0.02 (0.31–0.40)
LA/AO ratio	1.55 ± 0.16 (1.37–1.92)

[a]Values are mean ± SD (range in parentheses). All animals were maintained under isoflurane anesthesia for measurements.
AO, Aortic diameter during diastole; *FS,* fractional shortening; *IVSd,* interventricular septal thickness in diastole; *LA,* left atrium internal dimension; *LVFWd,* left ventricular free wall thickness in diastole; *LVIDd,* left ventricular internal dimension in diastole; *LVIDs,* left ventricular internal dimension in systole.

Normal electrocardiographic values have been published for this species.[6] Mean ± SD values for R-wave amplitude and QRS duration were 0.22 ± 0.11 mv and 0.03 ± 0.0 sec, respectively.[6]

When weak or debilitated hedgehogs are hospitalized, provide cage temperatures of 80°F to 85°F (27°C–29°C). Hedgehogs may shun unfamiliar food items, and having the owner bring food the animal is accustomed to may enhance voluntary feeding in the hospital. Providing live invertebrates may also stimulate appetite. Feed anorectic animals a protein-rich, high-calorie carnivorous or insectivorous diet via syringe. Holding a shy hedgehog on its back and using a plastic teat cannula on the end of the syringe may facilitate syringe-feedings because the patient will often uncurl enough to place a small syringe near its mouth. For ongoing assisted feeding, a pharyngostomy or esophagostomy tube may be placed, although this can be difficult in obese patients.[39] An esophagostomy tube was used in a hedgehog with oral trauma, although it refused to eat unaided while the tube remained in place.[2]

Preventative Medicine

Because hedgehogs have a somewhat short life span and often hide signs of illness, semiannual examinations are recommended. Hedgehogs are prone to several dental disorders, including periodontal disease. A palatable pet enzymatic dentifrice may be placed on a crunchy treat daily to help prevent this. Tartar-control treats made for dogs and cats may also help prevent the accumulation of calculus. An accurate gram scale to monitor weight allows early detection of obesity or weight loss. Advise owners of the risks associated with cold temperatures, which include metabolic derangement and immunocompromise. Nails must be trimmed to prevent ingrowth. Currently, there are no vaccines for pet hedgehogs. Because hedgehogs are not typically maintained in mixed-sex groups, elective castration or ovariohysterectomy is not usually needed to prevent unwanted offspring.

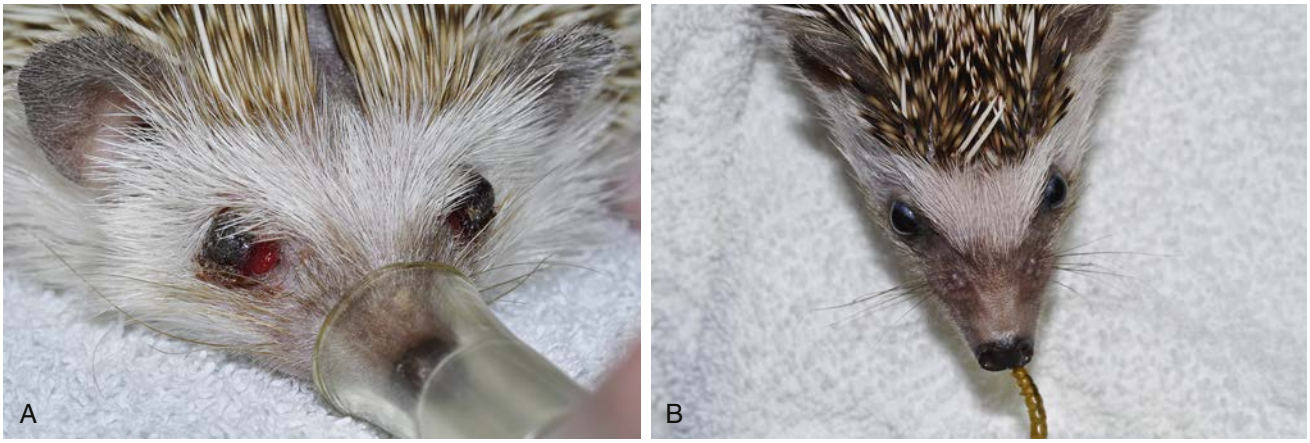


Fig. 28.8 (A) A hedgehog presented for bilateral proptosed eyes and corneal desiccation. (B) A photograph illustrates the shallow orbits of African pygmy hedgehogs, which may predispose them to ocular trauma.

COMMON DISEASES

Common Presentations

Nonspecific signs of lethargy, weakness, and anorexia frequently are the only historical and physical findings, even in hedgehogs with severe systemic disease. Examples include advanced meningeal lymphoma without neurologic signs, debilitating acariasis without evident pruritus, severe gastric ulceration without gastrointestinal signs, and extensive pneumonia without respiratory signs. Hedgehogs with advanced neoplasia, hepatic disease, or renal failure often have nonspecific signs at presentation. The frequent presentation of hedgehogs with nonspecific signs emphasizes the importance of diagnostic testing, for which heavy sedation or general anesthesia is usually required.

Ocular Disorders

Hedgehogs are prone to corneal ulcers and other ocular injuries. Diagnosis and treatment are similar to that for other species, although treatment may be difficult if owners are unable to administer topical medication. Blind hedgehogs seem to navigate their captive environments with minimal detriment to their quality of life.

Ocular proptosis is a relatively common presenting complaint (Fig. 28.8A). In a case series in eight hedgehogs, the ocular sequelae to proptosis were severe and resulted in enucleation or euthanasia in all cases.[60] Moderate to marked orbital inflammation was present in each case; sinusitis, neoplasia, and fungal elements were not observed.[60] Two of the animals had concurrent neurologic disease, which may have resulted in ocular trauma; no known trauma occurred in the other cases. Hedgehogs have a shallow orbit (Fig. 28.8B) that may predispose them to proptosis, especially if excessive fat accumulation or orbital inflammation is present. In hedgehogs with a unilateral proptosis, tarsorrhaphy may be indicated as a prophylactic measure for the remaining eye.[60]

Oral and Dental Disorders

Dental disease is common; calculus, gingivitis, and periodontitis may occur. On examination, reddened and swollen gingiva, calculus, gingival recession, and loose teeth may be present. Signs include decreased appetite, ptyalism, halitosis, and pawing at the mouth. Perform dental radiographs, extractions, cleaning, and antibiotic administration as in other species. Tooth fractures and dental abscesses also occur. A mandibular abscess with extensive osteomyelitis and cellulitis due to *Actinomyces* species infection has been reported.[40]

Excessive tooth wear may occur with advancing age, and animals with this condition should be fed a predominantly moist diet. Hedgehogs are susceptible to wedging of hard items (e.g., peanuts) against the palate; signs are similar to those seen with dental disease.

Respiratory Disorders

Predisposing factors for upper and lower respiratory tract infection include suboptimal environmental temperature; aromatic, dusty or unsanitary bedding; malnutrition; concurrent disease; and other causes of immunocompromise. Signs include nasal discharge, increased respiratory noise, dyspnea, lethargy, inappetence, and sudden death. As in other species, diagnostic testing includes radiographs, hematologic testing, and culture of lower respiratory tract samples. Treatment includes systemic antibiotics, nebulization, supportive care, and correction of husbandry problems. Additional differential diagnoses for dyspnea include pulmonary neoplasia and cardiac disease.[10]

Cardiovascular and Hematologic Disorders

Cardiomyopathy is the most commonly reported cardiovascular disorder in pet hedgehogs, and necropsy findings from several cases have been described.[50] Affected hedgehogs are typically 3 years of age or older, although the disease may occur in animals as young as 1 year of age. Signs include dyspnea, tachypnea, decreased activity, weight loss, heart murmur, ascites, cyanosis, and acute death.[10] Radiographs typically demonstrate varying degrees of cardiac enlargement, pulmonary edema, pleural effusion, hepatic congestion, and abdominal fluid.[10] Reported histologic lesions of the myocardium have included fibrosis, edema, degeneration, and necrosis, with myofibrillar atrophy, hypertrophy, and disarray.[50] Histologic lesions may be confined to either ventricle (more commonly the left), but in some cases both ventricles are affected. Pulmonary and renal infarcts may occur in some affected animals. The cause of cardiomyopathy in hedgehogs is not known, but there may be a genetic or dietary component. Valvular endocardiosis leading to congestive heart failure has been reported.[22]

If cardiac disease is suspected, obtain full-body imaging, and a full cardiovascular examination including an electrocardiogram and an echocardiogram. A complete blood count and biochemical profile are useful to screen for concurrent problems and serve as a reference for monitoring the effects of therapeutic agents. Therapy with cardiovascular drugs commonly used in veterinary medicine (e.g., diuretics, angiotensin-converting enzyme inhibitors, pimobendan) may be helpful initially, but the long-term prognosis for hedgehogs with congestive heart failure is poor. In one case of dilated cardiomyopathy, treatment with furosemide, enalapril, pimobendan, and L-carnitine was successful in improving clinical signs and cardiac contractility.[10]

Myocardial mineralization or calcinosis has been described as a necropsy finding in pet hedgehogs with concurrent diseases.[3,7] The clinical significance of this lesion is not known.

Splenic extramedullary hematopoiesis, the clinical significance of which is not known, has been noted at necropsy in several hedgehogs with cardiomyopathy.[50] Saddle thrombus and pulmonary fibrin thromboemboli were described in a hedgehog with a very large uterine polyp.[3] Congenital erythropoietic porphyria was reported in a 6-month-old male inbred pet African hedgehog.[61] The animal exhibited pink-colored urine and teeth, hepatomegaly, and, under ultraviolet light, fluorescence of the urine, teeth, feet, and spines. The animal behaved normally despite high levels of porphyrins in the urine and feces; it is not known whether the animal was anemic or how long it lived.

Gastrointestinal and Hepatic Disorders

Enteritis may be caused by *Salmonella* species or other bacteria. Diagnosis should be confirmed with fecal culture, using a *Salmonella*-enriching medium. Although treatment is indicated in animals with clinical signs of disease, advise owners of the zoonotic potential and the risks of creating antibiotic resistance.

Fatal cryptosporidiosis of the ileum, jejunum, and colon was reported in a juvenile hedgehog.[18] Juvenile African pygmy hedgehogs were experimentally infected with *Cryptosporidium erinacei* isolated from an infected European hedgehog; the prepatent period was 4 to 5 days after infection, and clinical signs during shedding were not observed.[34] Gastrointestinal parasites are uncommon in pet hedgehogs. However, fecal flotation and wet mount are recommended in newly acquired animals and in those with enteritis.

Pyloric and intestinal obstructions can occur. Presurgical diagnosis of acute gastrointestinal obstruction may be complicated by the fact that marked gaseous dilation of the gastrointestinal tract can be a nonspecific finding in ill hedgehogs. Gastroesophageal intussusception was diagnosed in a hedgehog by using a contrast esophagram and esophagoscopy; the gastric cardia was everted into a severely dilated, distal portion of the esophagus, and the animal had severe esophagitis.[38]

Diarrhea can be associated with some commercial diets or inappropriate foods such as milk. Stressed animals may have bright green diarrhea. Changing the brand of pellets and eliminating inappropriate food items may resolve the condition. Gastrointestinal neoplasia, particularly lymphosarcoma, is relatively common.[52] Other differential diagnoses for gastrointestinal signs include dietary change, toxins, hepatic disease, and malnutrition.

Hepatic lipidosis is relatively common in hedgehogs. Hepatic lipidosis may be a sequela of numerous disease processes and clinical signs include lethargy, inappetence, and icterus. Obese hedgehogs may also have subclinical hepatic lipidosis present on ultrasound or CT imaging findings. Diarrhea or signs of hepatic encephalopathy may also be present. Treatment for clinical hepatic lipidosis in hedgehogs is similar to that in other species.

Chylous ascites was diagnosed in a hedgehog with biliary cirrhosis.[57] Fatal multifocal hepatic necrosis caused by human herpes simplex virus 1 was reported in a hedgehog.[4] The owner of the animal reported that several family members suffered from cold sores, and it seems likely that the animal contracted the infection from a person in the household.

Urinary Disorders

Cystitis and urolithiasis can occur in pet hedgehogs.[29] Signs may include changes in urine color, stranguria, pollakiuria, inappetence, and lethargy. Urinalysis with culture and diagnostic imaging should be obtained. Renal disease is also common and in many cases may be secondary to systemic disease. Nephritis, tubular nephrosis, glomerulosclerosis, infarcts, polycystic kidneys, and glomerulonephropathy have been reported.[15] As in other species, signs associated with renal diseases tend to be nonspecific, although polyuria or polydipsia may be observed. Treatment consists of correcting the underlying cause if possible, fluid therapy, and supportive care.

Reproductive Disorders

Hemorrhagic vulvar discharge is a very common presenting complaint in female hedgehogs and is often caused by uterine neoplasia or endometrial polyps.[3,49] In the authors' experience, uterine neoplasia is common in adult female hedgehogs. In one report, 28 proliferative uterine lesions were diagnosed in 15 hedgehogs 3 to 5 years of age.[43] Lesions were associated with vaginal bleeding in all cases, hematuria in 85% of cases, and weight loss in 58% of cases. Lesions were multiple in 53% of the hedgehogs. Lesions identified included adenosarcomas, endometrial stromal sarcomas, and endometrial polyps.[43] Ovariohysterectomy is the recommended treatment, and mean survival time after ovariohysterectomy was 303 days (n = 10) in one report.[43]

Pyometra and metritis also occur. Dystocia is treated as in other small mammals.[58] Premature births occasionally occur, and the prognosis for young without a sucking reflex is poor.[58] Agalactia may be suspected if neonates lose condition within 72 hours after birth. Diagnosis may be confirmed by attempting to express the mammary glands[58]; however, this procedure usually requires anesthesia and may cause the dam to abandon or cannibalize her young. Possible causes of agalactia include malnutrition of the dam, stress, lack of oxytocin, inadequate mammary development in young females, and mastitis. Supportive care for weak neonates includes warming to normal body temperature over 1 to 3 hours, fluid support, and caloric support once normothermia has been achieved.[58]

Musculoskeletal Disorders

Fractures can occur when a limb becomes entrapped in a rodent wheel or wire cage. Splinting may be performed for distal limb fractures but requires anesthesia. Surgical correction may also be

performed, but any fixation device must be able to withstand the strong rolling-up mechanism. Lameness may be caused by overgrown toenails, arthritis, pododermatitis, constriction of a foot or digit by fibrous foreign material (Fig. 28.5), or neurologic disease.

Neurologic Disorders

Causes of neurologic disease with ataxia include torpor, demyelination ("wobbly hedgehog syndrome" [WHS]), intervertebral disk disease (IVDD), trauma, toxins, infarcts, malnutrition, and neoplasia. Although WHS is a tempting diagnosis for any animal presented for neurologic signs, hedgehogs with a variety of systemic diseases, including neoplasia not associated with the central nervous system, may be presented for ataxia.

Intervertebral disk disease affecting the cervical or lumbar vertebrae is not uncommon in hedgehogs > 4 years of age.[53] Signs included chronic progressive ataxia, lameness, proprioceptive deficits, and bladder atony with urine retention. Radiographic findings may include spondylosis, disk-space narrowing, and disk mineralization. Multiple disks were frequently affected, and degeneration of the nucleus pulposus and annulus fibrosus, dorsal extrusion of disk material, and mineralization of the nucleus pulposus were identified on necropsy.[53] Temporary improvement with corticosteroids has been described in two cases of hedgehog IVDD.[53]

Wobbly hedgehog syndrome (WHS), also known as *demyelinating paralysis*, has been increasingly reported since the mid-1990s in captive African hedgehogs, and a similar disease has been described in European hedgehogs.[19] One of the earliest indications of WHS is the inability to "close the hood" (roll into a ball). Hedgehogs often present with mild ataxia and lack of coordination, becoming off balance and stumbling, tripping, or wobbling. In the early stages of WHS, clinical signs are usually relapsing and remitting.[19] Over several months, the signs become progressively more severe and may include falling to one side, tremors, exophthalmos, scoliosis, seizures, muscle atrophy, and self-mutilation.[19] The paralysis ascends from hind limbs to forelimbs in about 70% of the cases. The disease ultimately leads to complete paralysis.

The onset of WHS commonly occurs in animals under 2 years of age but can occur at any age. In contrast, IVDD typically occurs in older animals. In 60% of WHS cases in one study, the hedgehogs were immobilized within 9 months after the onset of ataxia.[19] In 90% of cases, immobility occurred by 15 months after the onset of ataxia. The progression of WHS is generally accompanied by severe weight loss. However, in most cases there is no apparent loss of appetite until the terminal stages of the disease, when most hedgehogs become dysphagic.[19] Death usually occurs within 18 to 25 months after the onset of clinical signs.

The diagnosis of WHS can only be determined postmortem. Gross lesions are not evident, but histopathologic lesions reveal vacuolization of the white matter of the cerebrum, cerebellum, brainstem, and spinal cord as well as associated neurogenic muscle atrophy.[19] Vacuolization may be most severe in the cerebellum and caudal brainstem.[31] Inflammation of the central nervous system is not associated with WHS. To date, there is no histologic evidence of a viral or autoimmune cause. The cause of this syndrome is unknown, but pedigree analyses from numerous animals suggests a familial tendency to develop the disease. Although no evidence of an infectious agent has been observed, the familial tendency of WHS does not rule out a transmissible component.[19] Numerous treatments for this idiopathic neurodegenerative disease have been attempted, including steroids, vitamin supplementation, antimicrobial therapy, and homeopathic therapies, with little or no success. Although treatments may briefly halt progression of clinical signs, none have stopped disease progression. Supportive care and hand-feeding can initially be performed; euthanasia is recommended when the hedgehog becomes significantly immobilized and its quality of life is compromised. Differential diagnosis is important, however, because brain tumors, intervertebral disk disease, and hepatic encephalopathy are other causes of progressive paralysis.[19]

Hedgehogs experiencing cold or sometimes excessively high temperatures may enter a state of torpor or dormancy. In this state, the animal remains sensitive to touch, but the response is greatly diminished. Heart and respiratory rates are decreased, and these animals may have increased susceptibility to infection. Dormancy can last for several weeks, during which the animal may have periods of activity with ataxia.[28] If a hedgehog housed at inappropriate temperatures is presented nonresponsive, torpor should be ruled out, because the prognosis is good. Provide a quiet, warm environment and fluid therapy and monitor the animal to see whether it becomes more alert over the next several hours. As in other species, head tilt or circling may be caused by otitis media/interna or primary neurologic disease.

Dermatologic Disorders

Dermatologic disorders are considered the most common disorder affecting captive African pygmy hedgehogs, with acariasis being extremely common.[16] *Caparinia tripilis* is probably the most common mite infesting pet hedgehogs. Both male and female Caparinia tripilis mites have three long setae on the third pair of legs.[32] Using the mnemonic "three-on-three" can aid remembrance of this specific anatomic feature. Some hedgehogs have subclinical mite infections, which may account for the high prevalence of mites in the pet population. Infested bedding or fomites from pet stores may be another source. Signs of acariasis include seborrhea, quill loss, hyperkeratosis, and white or brownish crusts (mite droppings) at the base of the quills and around the eyes. Hedgehogs can scratch themselves with their hind limbs or rub against stationary objects, but many individuals do not demonstrate obvious signs of pruritus, even with obvious gross disease. Acariasis also causes nonspecific signs such as lethargy and decreased appetite. Diagnosis is confirmed by a skin scraping. Treatment consists of ivermectin (0.3–0.4 mg/kg orally or subcutaneously [SC] every 10–14 days × 3–5 treatments) or selamectin (20–30 mg/kg topically every 21–28 days). In some cases, ivermectin alone may not be effective in treating mite infestations. A spot-on product for cats containing 1% moxidectin and 10% imidacloprid was also effective in treating *Caparinia* infestations.[33] All bedding must be removed and cage furnishings disinfected or discarded. During the treatment period, the cage is lined with paper that is changed daily. All hedgehogs in the home should be treated concurrently.

Pinnal dermatitis is common in pet hedgehogs; skin crusts, accumulated secretions, and a ragged pinnal margin may be observed (Fig. 28.9). Dermatophytes and acariasis are important



Fig. 28.9 A hedgehog with pinnal dermatitis.

rule-outs for this condition; other possibilities are nutritional deficiencies, dry skin from inappropriate husbandry, or nonspecific seborrhea.

Bacterial or yeast otitis externa also occurs; these infections are often secondary to acariasis or another cause of chronic inflammation. Signs include purulent discharge, odor, and sensitivity of the face and ear. Otic cytology, skin scrapings, cleansing, and topical antimicrobial/antiinflammatory therapy are performed as for dogs.

Ear mites (*Notoedres cati*) are occasionally seen and can cause crusting lesions around the ears. Signs include accumulation of waxy otic debris and otic pruritus. Diagnosis is confirmed by identifying mites in the ear canal or in swabbed material. Ear mites in hedgehogs may be treated as in cats. Pet hedgehogs may be infested with fleas; shampoo and powder products that are safe for kittens appear to be safe for hedgehogs.

Fungal organisms most often identified as infecting hedgehog skin include *Trichophyton erinacei, Trichophyton mentagrophytes,* and *Microsporum* species. These dermatophytes can cause a crusting, usually nonpruritic dermatitis, especially around the face and pinnae. Yeast, probably a secondary problem, may also be identified in cases of dermatitis. Infections may be secondary to other dermatopathies, such as acariasis or trauma. Diagnosis is confirmed by culturing spines from the affected areas in dermatophyte testing media. Treatment consists of topical antifungal agents like enilconazole or clotrimazole administered as sprays or shampoos, or oral agents like terbinafine or itraconazole. Lyme sulfur dips may also be used. Other hedgehogs in the home may be subclinically infected, and treatment of all animals may be indicated. Cases of *Trichophyton* infections in people have originated from contact with infected hedgehogs.[59]

Skin neoplasia has been reported in hedgehogs. Papilloma, squamous cell carcinoma,[9,25] epitheliotropic T-cell lymphoma,[8] and sebaceous gland carcinoma[42] have been described. Extraskeletal osteosarcoma has also been reported in the skin of a hedgehog.[48] Pruritus may occur with the development of new spines, as is seen in young hedgehogs.

Neoplasia

Neoplasms in African hedgehogs are extremely common, and a wide variety of tumors and disseminated neoplastic processes affecting virtually every body system have been reported. Several reviews are available detailing the specifics of numerous reported cases.[20,21,47]

In a survey of 66 hedgehog samples submitted for histopathology, 35 animals (53%) had neoplastic disease.[52] The major body systems in which the tumors were found were integumentary (43%), hemolymphatic (23%), and alimentary (20%). The most commonly diagnosed tumors were mammary gland tumor (23%), lymphosarcoma (17%), and oral squamous cell carcinoma (14%). Eight percent of hedgehogs had more than one type of tumor. The occurrence of tumors was unrelated to sex, and the median age at time of tumor diagnosis was 3.5 years (range 2–5.5 years). More than 80% of the tumors in the survey were malignant.

Oral squamous cell carcinoma is one of the most commonly reported neoplasias in African pygmy hedgehogs.[16,47,52,] Cases of oral squamous cell carcinoma usually present as swelling of the maxillary or mandibular gingiva (Fig. 28.10); affected animals may have loose or lost teeth, swollen gingivae, or gingivitis, and the tumor is often locally infiltrative.[52] Peripheral odontogenic fibromas were reported in a hedgehog presented for bilateral, maxillary, round, pedunculated masses; surgical removal appeared to be curative.[62]

Myelogenous leukemias are rarely reported in hedgehogs. Eosinophilic leukemia was reported in five hedgehogs with nonspecific clinical signs. An eosinophilia was present in one case and postmortem findings included gross splenic abnormalities and infiltration of neoplastic eosinophils in multiple organs, including the bone marrow.[13,24,41] The prognosis for eosinophilic leukemia appears grave, because all five hedgehogs died; in most of these cases, the disease course was rapid, and animals died soon after diagnosis.

Other frequently reported neoplasias are mammary gland tumors and alimentary lymphosarcomas. [42,51,54,] Adrenocortical carcinomas were reported in three hedgehogs.[30] Uterine tumors are relatively common, as described above.[16,43] In addition to the presence of masses, clinical signs of neoplasia may include weight loss, anorexia, lethargy, neurologic signs, diarrhea, dyspnea and ascites.

Diagnosis of neoplasia is based on biopsy (needle, incisional, or excisional) or necropsy and histopathology. Diagnostic imaging for evidence of invasion or metastasis and a complete blood count and biochemical analysis may be useful in determining long-term prognosis. Treatment generally includes surgical excision and supportive care, although different treatment modalities may be helpful. Prognosis and management depend on type and stage of the neoplastic process.

A hedgehog diagnosed with a metastatic C-cell carcinoma was treated with radiation therapy after surgical removal of the mass; no adverse effects of the therapy were observed, and the animal remained clinically healthy with no signs of recurrence or metastasis several months later at the time of publication.[36]

Because African pygmy hedgehogs appear particularly prone to neoplasia, semiannual examinations of adult animals are recommended and should include an appropriate workup for neoplasia in suspect cases. Despite the high incidence of neoplasia in this species, it should be emphasized that not every mass in pet hedgehogs is neoplastic. For example, dental abscesses, bone cysts, papillomas, and uterine polyps have been described.[7,40,49]

Nutritional Disorders

Obesity in captive hedgehogs is very common. Healthy hedgehogs should be able to roll up completely, without any fat

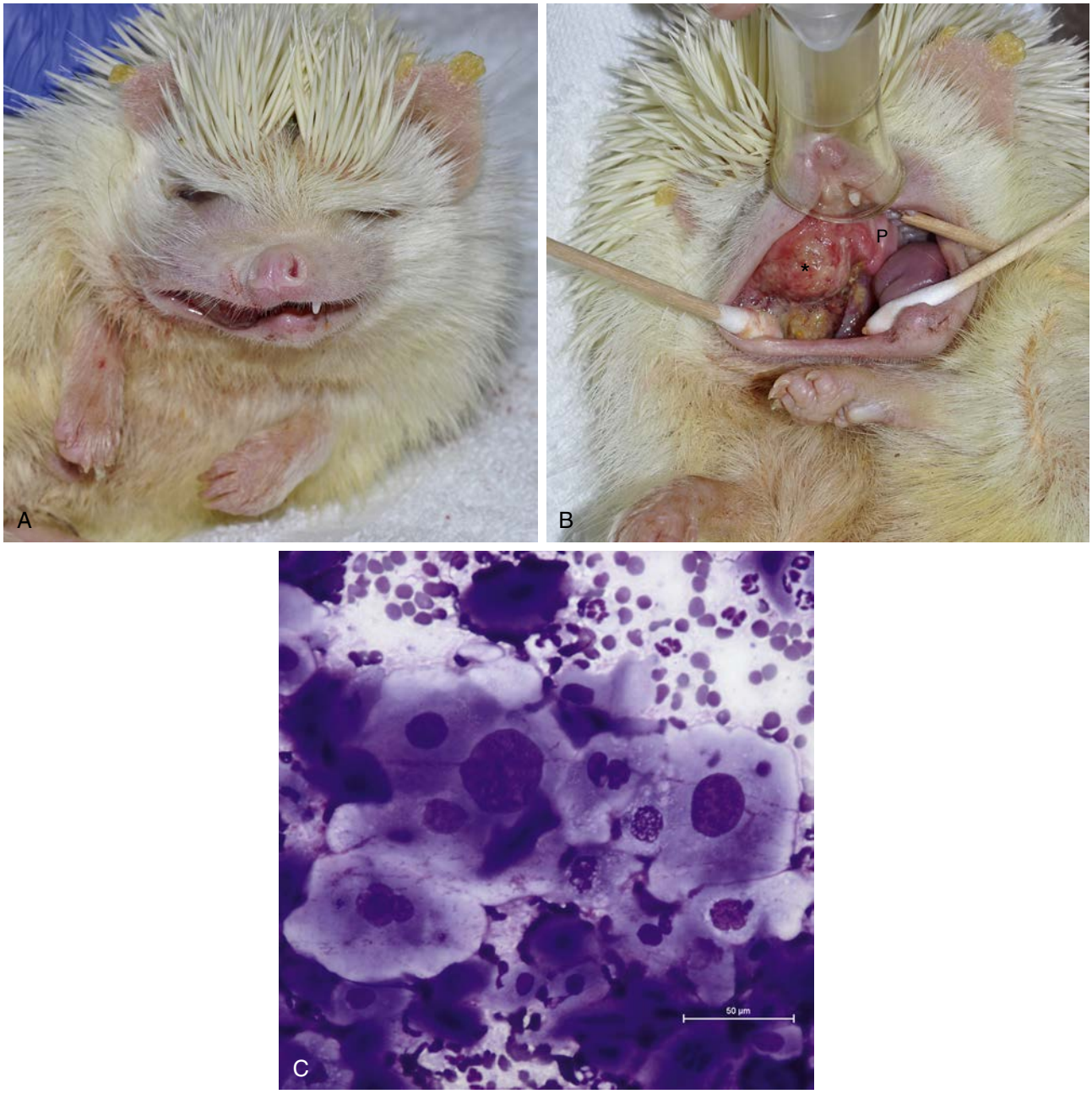


Fig. 28.10 (A) Hedgehog presented for dysphagia and oral swelling; note distortion of right maxilla and lateral deviation of the adjacent right nostril. (B) Intraoral view of the locally invasive mass (asterisk) destroying the hard palate *(p)*; fine-needle aspiration was performed while the patient was under anesthesia. (C) Fine-needle aspiration revealed oral squamous cell carcinoma. Individualized, mature, pleomorphic squamous epithelial cells are arranged in dense groups in a background of mild neutrophilic inflammation and hemorrhage. Wright's-Giemsa, magnification ×400. (Patient images courtesy Dr. C. Mans. Photomicrograph provided by Dr. K. R. Friedrichs.)

deposits protruding. Obese hedgehogs may have large axillary fat deposits or a decreased ability to roll up. Treatment includes eliminating high-fat foods, rationing the main diet, and increasing exercise. Hiding food in the substrate or disseminating it throughout the enclosure can help promote foraging and exercise. Weight reduction should be gradual to prevent hepatic lipidosis, and owners should monitor their pet's weight with an accurate scale. Hedgehogs, particularly those whose diet consists mainly of non-gut-loaded invertebrates, may have problems associated with calcium deficiency. Vitamin excess or deficiency may also occur with unbalanced diets.

ANESTHETIC AND SURGICAL CONSIDERATIONS

Anesthesia is often required for a thorough physical examination, restraint for imaging and other diagnostic testing, and surgical procedures. A several-hour fast is recommended before anesthesia. After a period of preoxygenation, isoflurane alone is commonly used for the induction and maintenance of anesthesia. A large anesthetic mask used for dogs works well as an induction chamber for small hedgehogs and limits waste gas exposure (Fig. 28.11). For larger individuals, use a small



Fig. 28.11 Induction of inhalant anesthesia in a hedgehog using a face-mask designed for large dogs.

anesthetic induction chamber. Tracheal intubation is indicated for longer or oral procedures and is accomplished with a 1.0- to 2.0-mm endotracheal tube. Intubation is difficult due to the small size of the oropharynx, but a rigid endoscope or small laryngoscope blade may provide visibility of the glottis.

Useful anesthetic monitoring equipment in hedgehogs includes Doppler, pulse oximetry, electrocardiography, capnography, and noninvasive blood pressure measurement. Electrocardiography clamps may be attached to the patient by using needles to prevent skin trauma.

There is little research investigating safe and effective anesthetic and analgesic agents in hedgehogs. Injectable agents may be used but may result in prolonged recoveries compared with inhalant anesthesia alone. In the authors' experience, midazolam (0.5 mg/kg intramuscularly [IM], SC) in combination with butorphanol (0.5 mg/kg IM, SC) may result in sufficient sedation to permit scruffing for further examination, and low doses of ketamine (3–5 mg/kg IM, SC) can be added if deeper sedation is required. A combination of alfaxalone (3 mg/kg)-midazolam (1 mg/kg) or ketamine (30 mg/kg)-midazolam (1 mg/kg) administered SC in the mantle provides heavy sedation, which is partially reversible with flumazenil (0.05 mg/kg) SC.[20a]

There is little information available regarding the use of analgesic agents in hedgehogs.In a recent study, a single dose of buprenorphine administered at 0.03 and 0.05 mg/kg SC provided analgesia for 36 and 48 hours, respectively, without apparent adverse effects.[12] Commonly reported agents used for analgesia in hedgehogs include opioids and meloxicam.[1,23,27]

When removal of spines is necessary, they may be clipped at the skin surface or removed with steady traction at the base. Lacerations and other wounds are occasionally seen. Hedgehogs often bite cage mates below the spined skin on the hind legs. Hedgehogs may self-mutilate traumatic or surgical wounds; therefore implement prompt primary closure with subcuticular sutures whenever possible. Bandages and dilute chlorhexidine baths are well tolerated. If the cutaneous muscle is damaged, it must be closed in a separate layer. Contraction of the "rolling-up" musculature can cause wound dehiscence. Elizabethan collars are not practical in this species.

Because hedgehogs are generally housed individually, castrations and ovariohysterectomies are generally performed to remove diseased organs rather than for population control. Perform castration through a para-anal skin incision over each testicle. Ovariohysterectomy is similar to the procedure in other mammals, although the short uterine horns are curled and the broad ligament is more narrow than in other species (Fig. 28.12).

EUTHANASIA

There are no specific euthanasia guidelines for pet hedgehogs, and the approach should follow current recommendations for other small mammals.[37] Animals should always be anesthetized or unconscious before administration of euthanasia agents. Barbiturate agents (e.g., commercial pentobarbital solutions) are commonly used and may be administered intravenously (e.g., cranial vena cava), intracardiac, or by other nonintravascular routes (e.g., intraperitoneal). Saturated potassium chloride solutions may also be used intravenously or intracardiac, but only in deeply anesthetized animals.

ZOONOSES

Several strains of *Salmonella* occur commonly in hedgehogs, particularly *Salmonella enterica* serovar Tilene, *Salmonella typhimurium,* and *Salmonella enteritidis;* in many cases hedgehogs are asymptomatic carriers.[56] Many cases of transmission from pet hedgehogs to people have been documented, particularly in young children living in homes with hedgehogs. In many cases, the children had no direct contact with the hedgehogs.[56] Hedgehogs' messy droppings and propensity to walk in their feces may facilitate dissemination of *Salmonella* in the household. As with reptiles, it should be assumed that all pet hedgehogs can carry and transmit this pathogen, and animals should be handled accordingly (e.g., wash hands after handling, do not allow animals or fomites to contact food or food preparation areas, keep cages clean, etc.). Subclinically infected animals may shed intermittently, so fecal culture results should not be used to rule out the carrier state. Treatment aimed at eliminating the carrier state is unlikely to be successful and should not be attempted because resistance may result.

Several cases of human dermatophytosis transmitted from pet hedgehogs have been documented.[56,59] In addition, some people are extremely sensitive to contact with African hedgehog spines and develop a transient but markedly pruritic urticaria within minutes after handling a hedgehog.[14] One person reportedly developed a more persistent papular eruption after the urticaria.

To prevent introduction of infectious diseases found in wild African pygmy hedgehogs to the United States, importation of African hedgehogs was banned by the USDA in 1991.[56] Rabies has not been reported in captive African hedgehogs, but the profuse salivation that occurs during self-anointing is occasionally mistaken as a sign of rabies.

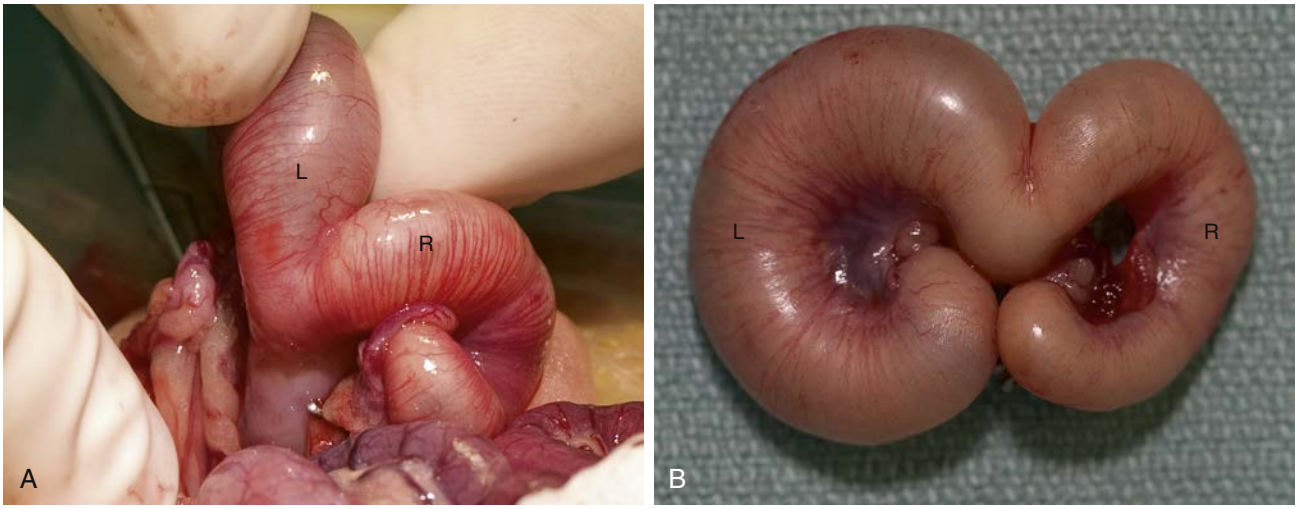


Fig. 28.12 (A) Ovariohysterectomy procedure in a hedgehog presented for hematuria; an enlarged fluid-filled left uterine horn was noted on ultrasonography. (B) Removed uterus and ovaries from the same hedgehog, demonstrating the curled uterine horns. *L,* left uterine horn; *R,* right uterine horn. (Photos courtesy Grayson Doss)

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Skunks

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BIOLOGY AND ANATOMY

Taxonomy and Natural History

Striped skunks (*Mephitis mephitis*) are crepuscular and nocturnal mammals belonging to the family Mephitidae, within the order Carnivora.[11] Thirteen subspecies of striped skunks have been recognized in North America.[15] Until recently, skunks belonged to the family Mustelidae, together with ferrets, otters, and badgers. However, because of differences in the anatomy of the cranium and dentition, they have now been classified under their own family, Mephitidae.[12]

Striped skunks are native to North America, covering a territory that extends from central Mexico to Canada.[11] In the wild, striped skunks adapt to a variety of environments, such as grass areas, woodlands, cultivated areas, and urban areas.[11] Skunks are generally solitary animals, but they can live in small groups of a male and several females, sharing the same den. Their territory covers an area between 0.5 to 12 square kilometers (0.2–4.6 square miles).[11]

During the winter, skunks do not hibernate but have periods of inactivity. This largely depends on the geographic area and the temperatures during the winter, with longer periods of inactivity in the northern areas because of food shortages and low temperatures.[35]

Striped skunks became domesticated in the nineteenth century in North America.[31] Whereas in the past they were kept for their ability to kill pest rodents and for their fur, these days skunks are popular as pets and as part of zoological collections. In several states, it is illegal to keep skunks as pets because of rabies transmission concerns (see Zoonosis below), and owners and veterinarians should be aware of local restrictions and regulations.

Anatomy and Physiology

Striped skunks are medium-size mammals, well known for their black and white coat and the strong smell of the scent glands. They have a small triangular head with a larger body and a long tail. Biologic data are summarized in Table 29.1.

Skunks have small ears and black eyes, which lack the nictitating membrane. Their eyesight is poor, and instead, they have a very well–developed sense of smell. Their feet are plantigrade with bare soles and five digits each.[11,15] The nails of the front feet are long and curved, and they are used for digging. Striped skunks have 7 cervical, 15 thoracic, 6 lumbar, and 3 fused sacral vertebrae and 15 pairs of ribs.[29] Skunk dentition consists of a total of 34 teeth (Table 29.1). The gastrointestinal tract consists of a simple stomach and a short intestinal tract with no cecum.

Males skunks have an os penis, a prostate, and two testicles positioned in scrotal sacs on each side of the penis. They are polygamous and in the wild breed with several females. Female skunks have a bicornuate uterus and five to seven pairs of mammary glands.[27] Males and females can be distinguished by the anogenital distance, which is shorter in females.

TABLE 29.1 Biological Reference Data of Captive Striped Skunks

Parameter	Range
Body weight	2.5–5.5 kg
Life span	8–12 years
Adult dental formula	I3/3, C 1/1, P3/3, M1/2
Heart rate	140–190 beats/min
Respiratory rate	25–50 breaths/min
Body temperature	98.8°F–102°F (37.1°–38.9°C)
Age at sexual maturity	10–12 months
Gestation	59–77 days
Litter size	5–7 (up to 12)
Birth weight	30 grams (25–40 grams)
Eyes open	3–4 weeks
Age at weaning	6–8 weeks

Striped skunks present the characteristic black and white coats, with a white stripe extending from the head and branching out in two stripes around the shoulders and continuing along the flanks to the tail. They also present a white marking between the eyes along the nose. Different color mutations are bred in captivity, such as albino, lavender, champagne, and brown. The stripes are generally paler but still visible, except in the albino skunks.

Striped skunks have one perianal scent gland on each side of the anus. They use the sphincter muscles to express the glands and eject the musk via papillae protruding through the anus.[15] The musk is an oily yellow liquid, containing a mixture of sulfur-containing chemicals, which has a pungent offensive odor.[15] It is reported that it takes up to 10 days for a skunk to fill up glands after emptying. Skunks have functional scent glands by 1 week of age, but the scent is more gas than liquid at this age.[11] Spraying is a normal defense mechanism for this species. The main warning signs are raising of the tail, stomping of the feet, teeth grinding, and growling.

Behavior

Skunks are intelligent, inquisitive, and very active animals. In captivity, they are solitary animals but tend to build a close relationship with the owner and adapt to the owner's daily routine. Skunks are generally considered friendly animals when young, but they can become less social with age. When stressed, scared, or nervous, skunks can bite or spray. Neutering or spaying is strongly recommended, in addition to proper socialization and gentle handling to reduce the incidence of biting and aggression.[29] Well-socialized skunks are very tame and interactive with their owners, and overall they are considered very interesting animals.

HUSBANDRY

Housing

Skunks are generally kept free range indoors. However, when the owner is not at home, skunks should be kept in either a large cage, dog crate, or in a skunk-proofed room. When skunks are allowed to roam free, the house should be proofed to avoid climbing, escaping, digging, and chewing of electric cables. Locks can be used for cupboards, whereas child safety gates can be added to prevent access to specific areas. Provide a sleeping area by using either a cardboard or plastic box or a carrier/kennel containing fleece blankets or other bedding materials. Skunks can also be trained to use a litter box. Provide a variety of toys to prevent boredom and encourage exercise. Small hard rubber toys, cardboard boxes, and tubes with hidden pelleted food can be used.[24] Skunks can get along with other pets such as cats and dogs, but they should not be left unsupervised.

Diet

Striped skunks are considered opportunistic omnivores.[11] In the wild, their diet consists primarily of insects such as beetles, crickets, and earthworms. They can also eat snails, frogs, mice, and bird eggs. The rest of their diet is composed of fruits, vegetables, grains, and carrion. Skunks use their claws to search for insects and dig for food items.

The diet of pet skunks should consist of a variety of food items, but the calorie content needs to be carefully considered because they can easily become obese. The diet should consist of two-thirds protein source (e.g., low-fat dog food), one-third vegetables, and a small amount of fruit. Feed adult skunks twice daily and only offer the quantity of food that they can consume in 5 to 15 minutes.[49] Young and pregnant animals need higher levels of fat and protein. Food can be offered in a bowl or hidden around the house or cage to promote exercise and environmental enrichment. Provide water in a bowl available at all times.

Breeding and Neonatal Care

Striped skunks become sexually mature at 10 to 12 months of age. Females are induced ovulators, and ovulation occurs within about 42 hours after mating.[15] The breeding season is spring (February–April), and females go into estrus once a year for a week and half.[11] If they lose the litter, a second pregnancy might occur. Pregnancy generally lasts 59 to 77 days.

Skunks are generally born around May to June, and the litter size usually consists of five to seven kits. Newborn skunk kits are blind, deaf, and naked and weigh approximately 30 grams (Fig. 29.1). Kits already present the characteristic stripes on the skin even before the fur grows in (Fig. 29.1). The eruption of teeth occurs between 34 to 52 days.[50] Skunks are weaned at around 6 to 8 weeks of age. Male skunks do not play a role in raising the kits.

Orphaned kits can be raised using puppy milk replacement products such as Esbilac (PetAg, Inc, Hampshire, IL). Offer milk replacement every 2 hours for the first few days. The formula should be diluted initially with an electrolyte solution; the strength is gradually increased over the next 24 hours. As a guideline, feed 0.5 to 1.0 mL of milk per 10 grams of body weight. Take care during feeding to prevent aspiration pneumonia, and stimulate the genital area after each meal for urination and defecation. Record the body weight once or twice daily.

BASIC PROCEDURES AND PREVENTATIVE MEDICINE

Restraint

Skunks that are used to being handled by owners are generally amenable pets; however, if scared or in pain, they can inflict painful bites. The handling techniques used for cats are



Fig. 29.1 Striped skunk kits (A) at birth and (B) at 4 weeks of age. (Courtesy Exeter Exotics)



Fig. 29.2 Handling of a pet skunk. One hand should be placed around the shoulders, while the other hand support the rest of the body.



Fig. 29.3 Intravenous catheter placed in the cephalic vein of a skunk. (Courtesy Elisabetta Mancinelli)

generally considered suitable for skunks as well. For restraint, place one hand around the shoulders while the other hand supports the rest of the body (Fig. 29.2). If the animal is nervous, or during blood collection or injections, a skunk can be gently restrained by scruffing. Sedation should be considered if manual restraint is insufficient or the patient is not tolerant to manual restraint (see Anesthetic and Surgical Considerations below).

Clinical Techniques

Oral medication can be given by gently raising the head and inserting the liquid medication just behind the canine teeth, as in cats. Administer subcutaneous injections in the scruff of the neck, whereas intramuscular injections can be given in the lumbar extensor and the quadriceps muscles. The cephalic and saphenous veins can be used for intravenous injection and placement of an intravenous catheter (Fig. 29.3). In skunks that require intravenous fluid and drug administration in which an intravenous catheter cannot be successfully placed, intraosseous catheters can be placed in the tibia or femur.

Collect blood samples from the cephalic or jugular veins in conscious and docile animals. With the skunk under sedation, other venipuncture sites can be used, such as the cranial vena cava, the lateral saphenous vein, and the femoral vein. Hematologic and biochemical reference values are listed in Tables 29.2 and 29.3.

Sedation is required for proper positioning for radiography (Figs. 29.4 and 29.5) and computed tomography. Ultrasonography can be performed while the animal is conscious for short procedures, but otherwise, sedation is advisable.

TABLE 29.2 Hematologic Reference Values for Striped Skunks[23]

Analyte	Mean ± SD
Hematocrit, %	43 ± 6.5
Red blood cell count, × $10^6/\mu L$	8 ± 0.7
Hemoglobin, g/dL	13.4 ± 1.1
Mean corpuscular volume, fL	53 ± 2.6
Mean corpuscular hemoglobin, pg	17 ± 0.4
Mean corpuscular hemoglobin concentration, g/dL	31.8 ± 1.2
Platelets, × $10^3/\mu L$	312 ± 120
White blood cell count, × $10^3/\mu L$	6.9 ± 2.9
Neutrophils, × $10^3/\mu L$	3.5 ± 1.9
Lymphocytes, ×$10^3/\mu L$	2.6 ± 1.5
Monocytes, × $10^3/\mu L$)	0.24 ± 0.17
Eosinophils, × $10^3/\mu L$	0.38 ± 0.44

TABLE 29.3 Biochemical Reference Values for Striped Skunks[23]

Analyte	Mean ± SD
Alanine aminotransferase, U/L	134 ± 141
Albumin, g/dL	3.2 ± 0.7
Alkaline phosphatase, U/L	53 ± 48
Amylase, U/L	199 ± 100
Aspartate aminotransferase, U/L	83 ± 42
Bilirubin, total, mg/dL	0.2 ± 0.2
Blood urea nitrogen, mg/dL	25 ± 15
Calcium, mg/dL	9.6 ± 1
Chloride, mEq/L	113 ± 5
Cholesterol, mg/dL	166 ± 70
Creatine kinase, U/L	481 ± 309
Creatinine, mg/dL	0.8 ± 0.4
Gamma-glutamyl transferase, U/L	4 ± 4
Globulin, g/dL	3.5 ± 1
Glucose, mg/dL	106 ± 39
Lactate dehydrogenase, U/L	870 ± 810
Lipase, U/L	520 ± 438
Magnesium, mg/dL	1.86 ± 0.55
Phosphorus, mg/dL	5.6 ± 2.4
Potassium, mEq/L	5 ± 0.5
Protein, total, g/dL	6.6 ± 1.1
Sodium, mEq/L	151 ± 6
Triglycerides, mg/dL	82 ± 59

Preventive Medicine

Vaccinate skunks against canine distemper and rabies, where indicated. Vaccination against canine distemper virus can be given by using either inactivated distemper vaccines or modified live virus distemper vaccine. Give 3 vaccinations subcutaneously 3 to 4 weeks apart, with the initial vaccine at 6 to 8 weeks, and then booster annually. In countries where rabies vaccination is required, start administering killed rabies vaccines to skunks at 16 weeks of age. However, complete immunity cannot be guaranteed, and, because the use of rabies vaccines in skunks is off-label, vaccination is not legally recognized. Other vaccines, such as feline panleukopenia virus and leptospirosis, are not routinely administered in pet skunks.



Fig. 29.4 Dorsal-ventral radiograph of a healthy skunk. The enlarged scent glands are also visible. (Courtesy John Chitty)



Fig. 29.5 Lateral radiograph of a healthy skunk. The enlarged scent glands are also visible. (Courtesy John Chitty)

Skunks may be infested with external parasites such as fleas, lice, ticks, and mites. Drugs available for the treatment and prevention of ectoparasites in cats can be safely used at the same doses in skunks. Treat for gastrointestinal parasites based on test results of fecal parasite tests. The prevalence of the ascarid roundworm *Baylisascaris columnaris* (Fig. 29.6) has been reported as 25% in pet skunks in Europe.[10] Because this roundworm is associated with neural larva migrans, which is



Fig. 29.6 Fecal flotation in a pet skunk. *Baylisascaris columnaris* eggs are present. An average egg size is 73 × 63 μm. (Courtesy Nikola Pantchev)



Fig. 29.7 The nails of pet skunks should be regularly clipped.

a dangerous zoonotic disease in people, all pet skunks should be checked regularly by fecal examinations and treated with anthelmintics.

Spaying and neutering should be performed by 6 months of age. This is done to prevent aggression and complications related to extended estrus, (estrogen toxiciosis) in female skunks because they are induced ovulators.[24]

Skunks can easily become obese and should be weighed regularly. Common signs of obesity are a round-shaped body and fat pads under the eyes. Check teeth and gingiva regularly to monitor for dental diseases. Dental disease can be prevented by regular tooth brushing and chew toys for small dogs. Check nails regularly, especially if skunks do not have a chance of digging. Clip the nails using normal cat and dog nail clippers (Fig. 29.7).

COMMON DISORDERS

Ocular Disorders

Ophthalmologic disorders are rarely reported in striped skunks. Fatty deposits can be seen in obese animals.[41] Skunks infected with canine distemper virus may develop scleral inflammation, conjunctivitis, and mucopurulent ocular discharge as in other related species such as ferrets.[41]

Oral and Dental Disorders

Dental disease is common in skunks. Similar to dogs and cats, periodontal disease may develop as a result of poor diet.[24] Affected animals may exhibit dysorexia, change in eating habits, drooling, halitosis, pawing at the mouth, and facial swelling.[41] Treat dental disease as is done in dogs and cats.

Cardiac and Respiratory Disorders

Cardiac disease is not uncommon in skunks. A recent survey described a prevalence of 12% in a population of 95 skunks.[3] Myocardial fibrosis was the most common presentation, followed by myxomatous valve degeneration, hypertrophic cardiomyopathy, dilated cardiomyopathy, and valvular endocardiosis. The mean age of the affected animals was 5.5 years. The main clinical signs were heart murmur and increased respiratory effort at the early stage of the disease.[3] With the progression of the disease, weakness, lethargy, reduced appetite, weight loss, exercise intolerance, posterior paralysis, tachypnea, and abnormal lung sounds were also observed. Diagnosis of cardiac disease is made by radiographic evaluation and echocardiography. Therapy reported is generally extrapolated from cats and dogs (Table 29.4). Obesity has been described as a risk factor for cardiac disease in pet skunks from the age of 2 years.[22] *Trypanosoma cruzi* and dirofilariosis can also lead to cardiac disease.[22]

Canine distemper virus infection is an important cause of respiratory disease in unvaccinated animals. Canine distemper is caused by a paramyxovirus, and skunks are highly susceptible. It can be transmitted to skunks by direct contact with infected animals or by droplets from respiratory excretions resulting from coughing or sneezing. The main acute clinical signs are fever, oculonasal discharge, conjunctivitis, labored breathing, lethargy, anorexia, diarrhea, and vomiting. Ataxia and depression can also develop in the late stage of the disease. Diagnosis can be made by polymerase chain reaction (PCR) testing of nasal secretions or biopsy. Prognosis is generally poor. All skunks at risk of exposure should be vaccinated against canine distemper.[49]

Gastrointestinal and Hepatic Disorders

Skunks are susceptible to Aleutian disease, an infection caused by a parvovirus that mainly affects mink.[24,38] The same clinical signs manifesting in mink may be seen in affected skunks and include melena, fever, wasting, hepatomegaly, splenomegaly, and eventually neurologic signs.[46] Serologic testing and PCR testing of tissue samples can be done for diagnosis. No specific treatment is available, and the prognosis is generally poor.

TABLE 29.4 Drugs Commonly Used in Skunks

Drug	Dosage
Antibiotics	
Amoxicillin/clavulanic acid	12.5–20 mg/kg PO every 12 h
Clindamycin	11 mg/kg PO every 12 h
Enrofloxacin	10 mg/kg PO, SC every 24 h
Antiparasitics	
Fenbendazole	50 mg/kg PO every 24 h for 5 days
Ivermectin	0.4 mg/kg SC repeat after 14 days
Praziquantel	10 mg/kg PO, SC
Pyrantel pamoate	4.4 mg/kg PO repeat after 14 days
Sulfadimethoxine	50 mg/kg PO once, then 25 mg/kg every 24 h
Anesthetics and Sedatives	
Medetomidine, ketamine, butorphanol	Sedation: (M) 0.05–0.1 mg/kg, (K) 5 mg/kg, (B) 0.2 mg/kg IM
Dexmedetomidine, butorphanol, alfaxalone	Sedation: (D) 0.02 mg/kg, (B) 0.3 mg/kg, (A) 4 mg/kg
Medetomidine, ketamine, propofol	Premedication: (M) 0.1 mg/kg, (K) 5 mg/kg IM Induction: (P) 1–2 mg/kg IV
Midazolam, buprenorphine	Premedication: (M) 0.25 mg/kg, (B) 0.03 mg/kg IM
Ketamine	Sedation: 10–15 mg/kg IM
Analgesics	
Buprenorphine	0.01–0.03 mg/kg every 8–12 h IM, SC
Butorphanol	0.3 mg/kg IM, SC
Carprofen	2 mg/kg PO every 12 h or 4 mg/kg PO every 24 h
Fentanyl	Loading dose: 2–5 μg/kg followed by a CRI at 2–10 μg/kg per hour
Meloxicam	0.3 mg/kg PO every 24 h
Tramadol	5–12.5 mg/kg PO every 12 h
Miscellaneous	
Digoxin	0.005–0.01 mg/kg PO every 12–24 h
Enalapril	0.25–0.5 mg/kg PO every 24 h
Furosemide	1–4 mg/kg PO every 8–24 h
Pimobendan	0.25–0.5 mg/kg PO every 12–24 h

CRI, Constant rate infusion; *IM,* intramuscular; *IV,* intravenous; *PO,* by mouth; *SC,* subcutaneous.

Supportive treatment and systemic antibiotics, along with corticosteroid treatment, may be helpful to relieve clinical signs in other mustelids.[46]

Endoparasites, such as coccidia, may cause diarrhea, weight loss, anorexia, and dehydration in skunks.[41] *Isospora spilogales* and *Isospora sengeri* are the main coccidia species reported in wild spotted skunks.[32] Treatment with sulfadimethoxine for 7 to 10 days has been effective in achieving remission of clinical signs.

Baylisascariasis is common in captive and wild skunks. Although animals are generally asymptomatic, fecal examination is highly recommended in newly acquired animals and in those with signs of enteritis.[10]

Rectal prolapse and perineal herniation have been reported as complications after scent gland removal in skunks. Damage of the anal sphincter during sacculectomy can lead to rectal prolapse.[6] A case of bilateral perineal hernias has been seen in a 1-year-old intact female striped skunk that was evaluated for chronic intermittent constipation after sacculectomy at an early age. Colopexy and cystopexy, followed by unilateral perineal herniorrhaphy, achieved long-term resolution of clinical signs without recurrence.[48]

Liver disease has been reported in skunks and can have metabolic or infectious causes. Hepatic lipidosis is relatively common in obese striped skunks, which become anorectic.[24] Other potential causes of hepatic lipidosis are nutritional imbalances, starvation, toxicosis, and pregnancy. Clinical signs may include lethargy, inappetence, and weight loss. Base the diagnosis on results of serum biochemical analysis, diagnostic imaging, and hepatic cytology or biopsy. Treatment for hepatic lipidosis in skunks is similar to that in other species.

Several cases of adenovirus-induced hepatitis have been reported in wild skunks from Canada.[25,28] Currently there are no reports of adenovirus (e.g., canine adenovirus 1)–induced hepatitis in captive skunks, and routine vaccination is not recommended. Liver necrosis has been reported in a skunk affected by systemic sarcocystosis and concurrent canine distemper. The protozoa were found in multiple tissues and were associated with necrosis and inflammation of lungs, brain, liver, and nasal epithelium.[4] Canine distemper virus infection also can cause gastrointestinal signs, including vomiting and diarrhea.

Urinary Tract Disorders

Bacterial cystitis may be diagnosed in skunks showing stranguria, pollakiuria, and lethargy. Diagnosis is based on results of urinalysis, bacteriology, and diagnostic imaging. Treatment consists of antimicrobials, based on results of culture and sensitivity testing, and anti-inflammatory and analgesic drugs. Functional urinary retention with no obvious mechanical cause has been reported in a 5-year-old spayed pet skunk. Successful treatment was achieved by injections of botulinum-A toxin at the trigone of the bladder under ultrasound guidance.[36]

Leptospirosis has been reported in wild skunks, and a high number of wild skunks are seropositive. Clinical cases and seroprevalence have not been reported in captive skunks, and it is unlikely to play a significant role because of the low risk of exposure of indoor-housed skunks.

Reproductive Disorders

Postpartum diseases such as uterine prolapse (Fig. 29.8) and endometritis have been reported in captive striped skunks.[8] A partial uterine prolapse occurred in a 2-year-old striped skunk 2 days after a normal pregnancy and delivery. Blood testing showed mild hypocalcemia. Treatment included ovariohysterectomy and supportive care.[8] A case of endometritis occurred in a 4-year-old striped skunk after a prolonged delivery. The animal underwent ovariohysterectomy and received supportive care.[8] In both reported cases, similar clinical signs were observed, including depression, lethargy, inappetence, poor lactation, and neglect of the offspring.[8] Antepartum vaginal prolapse has also been anecdotally reported in a pet skunk.

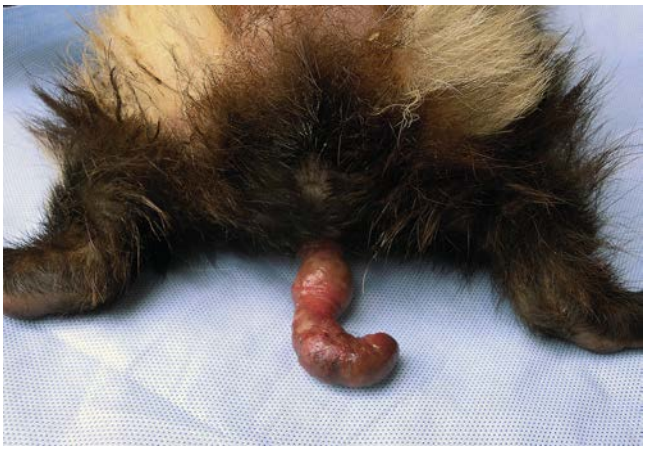


Fig. 29.8 Postpartum partial uterine prolapse in a pet skunk. (Courtesy Dario d'Ovidio)

Musculoskeletal Disorders

Pathologic fractures associated with lameness and lethargy are common in skunks affected by calcium or vitamin D_3 deficiency.[45] Diets deficient in calcium, vitamin D_3, or both may lead to secondary nutritional hyperparathyroidism.[21] Radiographic examination may show generalized reduced bone density. Biochemical evaluation should also be performed to confirm the diagnosis. However, normocalcemia does not rule out secondary nutritional hyperparathyroidism. Treat fractures by immobilization with splinting or surgical intervention, while simultaneously addressing the underlying cause. Improve the diet by feeding a diet that provides sufficient levels of calcium and vitamin D_3.

Lameness has been reported as a result of osteoarthritis and suppurative polyarthritis.[17] Mycoplasma has also been reported as possible cause of suppurative polyarthritis in skunks.[17] Other causes of lameness include pododermatitis, trauma, and neoplasia.

Neurologic Disorders

Intravertebral disk herniation affects skunks most commonly at 3 to 6 years of age.[30] The main clinical signs are pelvic limb weakness, discomfort, ataxia, paresis, and proprioceptive deficit. The clinical signs are generally progressive. A diagnosis can be made by neurologic examination revealing upper or lower motor neuron disease and diagnostic imaging, with similar findings as described in dogs and cats.[30] Conservative treatment may be unsuccessful, and surgical treatment may be necessary. Surgical removal of the extruded disk material by hemilaminectomy, facetectomy, and dorsal laminectomy has been reported.[30] The prognosis is considered favorable with surgical treatment, and only minor residual neurologic deficits have been reported after surgery.[30]

Cauda equina compression has been reported in a 6-year-old male skunk showing progressive bilateral pelvic limb ataxia and paralysis of the left hind limb. Laminectomy was successfully performed for treatment of lumbosacral stenosis.[18]

Seizures have been described in skunks as a result of hypoglycemia and hypocalcemia.[21,24] Rabies should be a main differential for skunks with abnormal behavior and central nervous system signs (see Zoonosis section).



Fig. 29.9 Alopecia and dermatitis in a skunk secondary to conspecific aggression. (Courtesy Dario d'Ovidio)

Skunks can act as an intermediate host for *Toxoplasma* species. Infection can be transmitted through ingestion of sporulated oocysts. The main clinical signs are fever, splenomegaly, lymphadenomegaly, pneumonia, hepatitis, myocarditis, encephalitis, and hydrocephalus. Diagnosis can be made by serologic testing. Treatment can be attempted with antiprotozoal drugs.[41]

Nutritional Disorders

Obesity is a common health concern in captive striped skunks.[24] This condition is common in animals fed excessive amounts of food or high-fat cat food and in those lacking physical activity.[11] Skunks are omnivores and will readily eat almost anything offered. Therefore regulation of the quantity and quality of food is crucial to prevent obesity. Treatment includes offering low-fat foods, appropriate portion size, rationing the main diet, and increasing exercise. Calcium and vitamin D_3 supplementation is highly recommended unless a complete diet (e.g., commercial dog food) is fed predominately to prevent secondary nutritional hyperparathyroidism.[21,24]

Integumentary Disorders

Dermatologic disorders have mainly been reported in wild skunks. Filarial dermatitis has been observed in several wild striped skunks from Kansas and Colorado.[16,43] The animals showed a severe diffuse dermatitis characterized by extensive alopecic areas, thickened skin, and multiple, scattered cutaneous abscesses on the dorsal aspect of the head, neck, and trunk. The parasite and the parasite ova were found in the skin at histologic evaluation.[16,43] Lice infestation (*Neotrichodectes mephitis*) is common in wild skunks and may be associated with dermatitis.[24,29] Fleas and ticks can cause severe anemia in young wild skunks and act as carriers for several tickborne diseases. Aleutian disease is the only reported viral disease causing dermatologic signs such as periocular erythema.[1] Noninfectious skin diseases, such as alopecia can be associated with nutritional deficiencies, inappropriate husbandry (e.g., fighting, Fig. 29.9) and metabolic diseases.[9,13] Bilateral alopecia and organomegaly due to idiopathic amyloidosis have been reported in a captive skunks.[13]

Neoplastic Disorders

Neoplasms in captive striped skunks are reported mainly in ageing animals and include pulmonary carcinoma, adenocarcinoma and adenoma, interstitial cell tumor, spindle cell



Fig. 29.10 General anesthesia in a juvenile skunk for sacculectomy. Note the intravenous catheter in the right cephalic vein, the lumbosacral area prepped for administration of epidural anesthesia, and placement of a blood pressure cuff and endotracheal intubation.

sarcoma, pheochromocytoma, renal adenocarcinoma, biliary cystadenoma squamous cell carcinoma and lymphoma, primary diffuse malignant mesothelioma, and retroperitoneal teratoma.[26,33,34,37,47] Predominant clinical signs associated with neoplasia are weight loss, anorexia, lethargy, diarrhea, dyspnea, ascites and abdominal enlargement, neurologic signs, and lymph node enlargement. Diagnosis of neoplastic disease follows guidelines established for dogs and cats. Prognosis and treatment depend on the type and stage of the neoplastic process.

ZOONOSES

Rabies is the most important zoonotic disease transmitted by wild skunks. In a recent survey in the southwestern United States, most human and domestic animal exposures were primarily as a result of wild skunk interactions (58% and 50%, respectively).[7] However, the zoonotic risk due to the transmission from pet skunks is very low, and animals bred for the pet trade that live indoors and are vaccinated are unlikely to become infected.[24] In cases of a skunk biting a person, public health authorities may require euthanasia of the skunk and subsequent rabies testing.

Skunks are considered the primary definitive hosts of the roundworm *Baylisascaris columnaris*.[44] Although *B. columnaris* is less pathogenic than *Baylisascaris procyonis*, the raccoon roundworm, this nematode is considered a potential cause of visceral, ocular, or neural larva migrans in mammals, including people, when sufficient quantities of infective eggs are ingested.[2,20] *Baylisascaris* eggs can be easily identified by fecal flotation (Fig. 29.6), whereas identifying parasites at species level requires molecular techniques (e.g., PCR).[10] Treat affected animals with fenbendazole.

Cryptosporidium parvum infection was diagnosed in an asymptomatic wild striped skunk from New York.[39] Also, a case of human cryptosporidiosis caused by a skunk genotype was reported in a 25-year-old woman from a rural area of southwest England.[42] Although unreported in pet skunks, this parasite should be considered in pet animals because of the zoonotic threat for owners.

A few strains of Salmonella (*Salmonella kumasi*, *Salmonella infantis*, *Salmonella montevideo*, and a subtype IV strain) have been found in fecal samples from wild skunks in California.[19] *Campylobacter jejuni* has been isolated in wild striped skunks in Canada.[51] However, these bacteria have not been reported in captive skunks to date, and further studies shall determine whether skunks transmit salmonellosis and campylobacteriosis directly to people. Various *Leptospira* species have been detected in wild skunks from the northern United States.[40] No information is available on the prevalence of *Leptospira* in pet skunks.

Herpes simplex virus has been isolated from eight pet skunks in California affected with fatal encephalitis. It was suggested that the eight cases were examples of an anthropozoonosis, the agent apparently being transmitted naturally from people to the skunks.[14]

ANESTHETIC AND SURGICAL CONSIDERATIONS

Chemical restraint of skunks is necessary for many clinical procedures such as thorough physical examination in nervous or stressed animals, blood collection, diagnostic imaging, and surgery. A fasting period of 6 to 12 hours is recommended before general anesthesia. Always provide thermal support and fluid therapy during surgery.

For procedural sedation, a combination with medetomidine (0.05–0.1 mg/kg), ketamine (5 mg/kg), and butorphanol (0.2 mg/kg) administered intramuscularly has been used by one of the authors (L.B.) for sedation. The combination of dexmedetomidine (0.02 mg/kg), butorphanol (0.3 mg/kg), and alfaxalone (4 mg/kg), administered intramuscularly was used in two pet skunks undergoing a dermatologic examination, including skin biopsy. After administration of atipamezole, the skunk recovered rapidly.[9]

Premedication with alpha-2 agonists, benzodiazepines, opioids, or dissociative agents followed by induction and maintenance with isoflurane or sevofluorane is routinely used for general anesthesia in skunks. Midazolam (0.25 mg/kg intramuscularly [IM]) combined with buprenorphine (0.03 mg/kg IM) followed by isoflurane administration has been safely used for ovariohysterectomy.[8] Skunks can be easily intubated with a 2.5- to 3.5-mm endotracheal tube[8,18] (Fig. 29.10) after application of a local anesthetic agent to prevent laryngospasm.

Always consider a preoperative multimodal analgesic regimen before surgery. Analgesic drugs that are used in skunks are butorphanol, buprenorphine, fentanyl, meloxicam, and carprofen (see Table 29.4).[8,9,18,30]

Common surgical procedures include ovariohysterectomy and orchiectomy (Fig. 29.11). The techniques are similar to those described in cats and dogs. Both prescrotal and scrotal approaches to orchiectomy have been anecdotally reported in captive skunks. Sacculectomy, removal of the perianal scent glands, is frequently performed in skunks. The surgical procedure can be performed as in ferrets[5,24] (Fig. 29.12). During this surgical procedure, damage of the anal sphincter may occur, leading to rectal prolapse.[6]

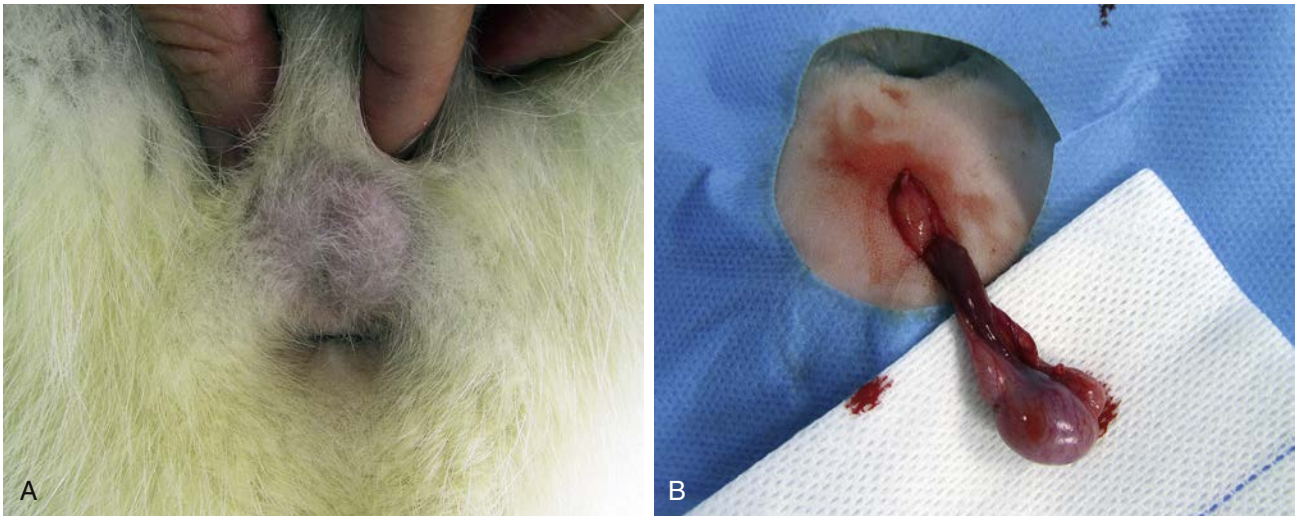


Fig. 29.11 Prescrotal castration of a skunk. (A) Before surgery and (B) during surgery. (Courtesy Elisabetta Mancinelli)



Fig. 29.12 Saculectomy procedure in a skunk. (A) Identification of the papilla of the right perianal scent gland. (B–C) The papilla is ligated or clamped, and the gland is removed by sharp and blunt dissection through the anus. (Courtesy Grayson Doss)

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30

General Principles of Surgical Techniques

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The natural history of rabbits and rodents has a significant impact on their ability to survive surgical procedures. These animals generally are shy and fearful prey species, and, when they experience fear, pain, and stress, they may die for no apparent medical reason. Patients may appear to recover normally from anesthesia and surgery, surviving to discharge, only to die 2 or 3 days later at home. However, the more human contact the animal is used to receiving, the better it appears to bear the stresses of illness and surgery. Animals that are frequently held, played with, and cuddled are more likely to survive than those that are kept in a cage and never handled. Unlike rabbits and rodents, ferrets are carnivores and are more like dogs and cats in their ability to tolerate anesthesia and surgery.

Pet rabbits and rodents that are stressed may stop eating. They ferment cellulose in the cecum, and if they become anorectic, life-threatening complications can occur. Some patients struggle violently with restraint, injuring themselves. Some become so stressed that their levels of circulating catecholamines become very high, which can negatively affect anesthesia, resulting in acute death. This concern underscores the need for preemptive and appropriate preoperative and postoperative analgesic, anxiolytic, and tranquilizing agents. If an animal seems stressed by the hospital environment, and surgery is not urgent, it may be best to hospitalize it for a day or more, allowing the animal to adjust to the new environment before surgery. Generally, performing multiple short anesthetic events is better than combining several procedures during a long anesthesia.

PRESURGICAL CONSIDERATIONS

Patient Support

Although many surgical procedures in exotic companion mammals are analogous to those performed in dogs and cats, the small size of these patients makes surgery more challenging. As surgical patients, companion exotic mammals are especially prone to complications such as hypovolemia from blood loss, hypothermia, and renal and respiratory compromise.

Preoperative Testing

A preoperative database ideally should include a complete blood count, plasma or serum biochemical analysis, urinalysis, and appropriate radiographs, especially to evaluate the lungs, because many species are especially prone to asymptomatic respiratory diseases, as well as to renal compromise. Rats and mice frequently have subclinical *mycoplasma* pneumonia. Renal disease is common in older rodents and rabbits. At the very least, a preoperative database should include a packed cell volume, serum total

protein, urine specific gravity, and blood urea nitrogen estimate (azotemia test strip) or blood urea nitrogen/creatinine analysis.

Preoperative Fasting

Rabbits and rodents physiologically are unable to vomit, so a prolonged fast is not necessary. Small mammals with a negative energy balance are at greater risk for postoperative complications.[4] They also have relatively low hepatic glycogen stores and are prone to developing hypoglycemia during a prolonged fast.[2,6] A prolonged fast has not been shown to decrease the volume of abdominal contents in these hindgut cellulose-fermenting species. A 1- to 2-hour fast is typically recommended to allow the patient to clear its mouth of food material, reducing the risk of carrying food into the trachea during intubation. Ferrets have a short gastrointestinal transit time (approximately 3–4 hours), so a prolonged fast is not recommended. A fast of 1 hour will allow the stomach to empty, reducing the risk of aspiration pneumonia. Because of the high incidence of insulinomas in ferrets, a preoperative blood glucose level is important to measure as part of the preoperative database.

Thermal Support

Most companion small mammals have a large body surface area/volume ratio, predisposing to the development of hypothermia during anesthesia and surgery. A temperature-monitoring probe is ideal for continuous evaluation of core body temperature. The body temperature of a rat can drop 18°F (10°C) after 20 minutes of anesthesia.[3] Hypothermia decreases the metabolism and excretion of many anesthetic drugs. A short operative time accomplished by having all the necessary equipment ready and accessible will help to minimize hypothermia. Forced warm air blankets are commonly used but can be difficult to position. Combining a warm air blanket around the patient with a warming device under the patient seems to better combat hypothermia than any single device. Because these patients have a higher body temperature, set a circulating warm-water blanket under the patient at 104°F (40°C). Drape the patient as quickly as possible to hold in heat.

When performing abdominal surgery, fill the cavity with warm (101°–103°F; 39°–40°C) saline solution before closing and allow it to dwell for several minutes. Repeat this process until the temperature begins to rise to reverse the downward trend. If the body temperature drops below 96°F (35.5°C) during surgery, do this warm saline lavage before continuing the surgical procedure and then again before closing.

Hemodynamic Support

Seemingly small amounts of hemorrhage can be disastrous in small patients. Ideally, have blood from a conspecific available for transfusion when more than minimal blood loss is anticipated. Strict attention to hemostasis is vital. The average cotton-tipped applicator holds approximately 0.1 mL of blood when completely soaked. The reported total blood volume of small mammals is approximately 57 mL/kg of body weight.[3,4] Loss of 10% to 15% of total blood volume is usually safe. With loss of 15% to 20% of the total blood volume, most mammals experience hypovolemic shock and release large amounts of catecholamines. Life-threatening consequences occur with loss of 20% to 30% of the total blood volume.[3,4] Loss of more than five cotton-tipped applicators full of blood in a 50-g mouse is equivalent to more than 20% of the blood volume and is potentially dangerous.[2] Approximately 1.2, 1.4, 4.0, and 4.5 mL of blood is equivalent to more than 20% of the blood volume in the average-sized gerbil, hamster, rat, and guinea pig, respectively.[2–4]

Crystalloid or colloid fluids or whole blood from a conspecific can be used in patients experiencing severe blood loss. In ferrets, no blood types or transfusion reactions have been described, making it safe to transfuse without a cross-match in this species.

Parenteral fluid administration is recommended for most surgical procedures. Vascular access can be difficult to obtain in small patients; however, vascular access through an intravenous catheter or an intraosseous cannula allows one to administer fluids during anesthesia and also provides a route by which emergency drugs can be administered if necessary. If maintaining vascular access is possible after surgery, continue administering fluids until the patient is eating and drinking normally. The standard recommendation for intravenous fluid support during anesthesia and surgery is 10 mL/kg per hour. A single dose of 10 mL/kg of subcutaneous 4% dextrose has been recommended for short procedures in healthy small mammals.[6] Fluids administered subcutaneously or intraperitoneally are slowly absorbed and are not appropriate for treatment of severely ill, dehydrated, or shocky patients.

INSTRUMENTATION

In general, ophthalmic instruments are not suited for surgery in small patients. The short length of the instruments makes them difficult to control and to manipulate tissues within a body cavity. Microsurgical instruments are constructed so that only the tips are miniaturized.[1] The tips of the instruments should extend beyond the fingers far enough to use within the patient's body cavity. The handles should be rounded to facilitate the required rolling action between the thumb and first two fingers. Rounded handles are most important for the needle holders, where a curved needle must be rolled through the tissue by rolling the needle holder in the fingers. Many prefer needle holders without a clasp or box lock, because the motion that occurs when the lock is set and released may cause the needle to tear tissues. Hold a microsurgical instrument as if you were holding a pen. An across-the-palm grip is inappropriate and limits the function of these precision instruments (Fig 30.1).

A microsurgical pack minimally should consist of a microsurgical needle holder, scissor, and thumb forceps. Many microsurgeons use jeweler's forceps as microsurgical forceps. These are significantly less expensive and serve the purpose, but they are not ideal. Ring-tipped microsurgical forceps are of a standard length, counterbalanced, and delicate, but the tips have rings that distribute the pressure over a wider surface, making them less traumatic but allowing the surgeon to hold the fine strand of suture for knot tying. After experience has been gained, other microsurgical instruments may be added to the pack.

Retractors

Spring-loaded eyelid retractors do not work well in small mammals because the tension cannot be adjusted to fit the



Fig. 30.1 (A) Ophthalmic instruments (right) are short, with flat finger grips, compared with microsurgical instruments, which are standard length and have rounded grips (left). (B) Instruments should be held like a pen. Microsurgical instruments are long enough to extend beyond the fingers into a body cavity and balance in the hand, requiring very little muscle action and thus reducing fatigue and tremor.

individual patient. Heiss and Alm self-retaining retractors work well as abdominal and tissue retractors. The Lone Star Retractor® system (Cooper Surgical, Trumball, CT consists of elastic stays with tissue hooks on the ends and a plastic frame (Fig 30.2). Depending on the model, all components are fully autoclavable and durable. Place the stay hooks in the tissue and insert the elastic stays into the notches of the frame to retract tissue.

Hemostatic Aids

Hemostatic clips are very useful and available in various sizes, with small and medium being the most applicable for small mammal surgery. A right-angled applier is also available, which is very helpful when placing clips deep into a cavity (Fig 30.3).

Sterile cotton-tipped applicators are useful to absorb fluids, as well as for gentle tissue dissection and manipulation. Moisten the applicators when using them for tissue manipulation and dissection but use them dry to absorb fluids. Absorbable gelatin sponge and other absorbable hemostatic agents are valuable for controlling hemorrhage. Surgicel® (Ethicon, Inc., Sommerville, NJ) is oxidized regenerated cellulose, resembling cloth. It is a hemostatic aid that adheres nicely to moist tissues but is not capable of absorbing much fluid. Gelatin sponges are thick and absorb more fluid than oxidized regenerated cellulose but are prone to falling off.

Suction and Irrigation

Ophthalmic bulb syringes work well for tissue irrigation in small mammals, but a syringe with a needle attached is also

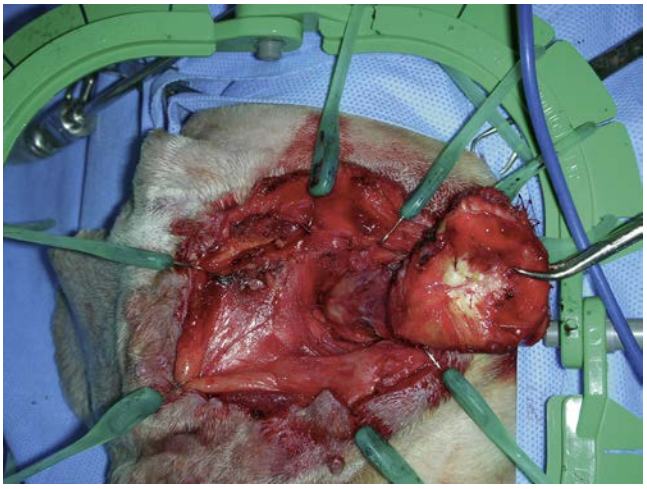


Fig. 30.2 The Lone Star Retractor is autoclavable. The tissue hooks on elastic stays are used to gently retract tissues during surgery. The hooks are placed into the tissue and the stays, under gentle tension, are wedged into the notches on the plastic frame.

applicable. To minimize the risk of inadvertently damaging tissue, break the needle tip off by bending the needle repeatedly at the hub. Fine Barron suction tips have a release hole, providing two degrees of suction. For small mammal patients, leave the hole open to provide suction that will not traumatize tissues. If there is a larger volume of fluid, occlude the hole with the index finger to increase the suction. Another option in small patients is to place the corner of gauze over the end so it is not able to suck tissue onto the tip.

Magnification

Some form of magnification is recommended because our inability to visualize small structures limits dexterity and manipulation. The need for magnification has nothing to do with one's visual acuity. With magnification, small amounts of hemorrhage appear more significant, and individual vessels are more easily identified for coagulation, minimizing hemorrhage. Binocular loupes are available in various styles, with hobby loupes being the least expensive and simplest but having several disadvantages, including a set focal distance, no focal light source, and the inability to look around the lenses when magnification is not required. In general, the higher the magnification, the closer the lenses must be to the object to be in focus. Anything outside of the specific focal distance of the lenses will not be in focus, resulting in dizziness. Furthermore, if the wearer moves her or his head, everything goes out of focus, exacerbating the dizziness.

A modification of the hobby loupe is marketed with interchangeable lenses and a light-emitting diode (LED) focal light source (MDS, Inc., Brandon, FL). These allow the surgeon to change the degree of magnification and to illuminate body cavities. This type of loupe still has a set focal length, and the surgeon is committed to looking through the lenses. These factors contribute to dizziness and also require the surgeon to bend his or her neck to be able to see through the lenses, resulting in fatigue and neck pain.

Surgical loupes (SurgiTel; General Scientific Corp., Ann Arbor, MI) eliminate most of the problems associated with the



Fig. 30.3 A right-angled Hemoclip applier (A) is very useful for placing clips deep in a body cavity (B).

hobby loupes. They are engineered to be used with a proper neck posture, the lenses do not cover the entire visual field so the surgeon can look over the lenses, they have a focal LED light source, and the lenses have a focal range rather than a set focal distance, which generally allows the entire patient to be in focus during surgery. Similar surgical loupes manufactured by other companies are available.

Focal Light

Overhead lights are not adequate for surgery in small mammals. A focal light provides illumination of a smaller area, allowing better visualization of the tissues and projects into the small body cavity. Various types of lights with or without magnifying loupes are available through various companies. Inexpensive headband-mounted LED lights are another option. SurgiTel loupes are available with different light options that mount onto the frame to illuminate the surgeon's field of view.

A digital video camera with magnification ×3 (SurgiCam HD, General Scientific Corp) that mounts on the loupe frame allows the procedure to be viewed on a monitor, and images and videos of the procedure can be captured onto the computer.

Electronic Hemostatic Devices

Electrocautery

Electrocautery refers to the use of electricity to heat metal until it is red hot to coagulate tissues. Because the heat causes damage to adjacent tissue, it is of limited value. Ophthalmic-type cautery pens are useful to cauterize small vessels in small exotic mammals if electrosurgery is not available. They have a fine wire tip and are battery operated.

Electrosurgery

Electrosurgery uses high-frequency alternating current to generate energy. There are two electrodes (an active electrode and an indifferent electrode or ground) with concentration of current density at the tip of the smaller (active) electrode. The patient is within the electrical circuit. Burns can result if the ground plate contacts only a small area of the patient, because the current concentrates where it exits the patient. The Surgitron Dual Frequency 120 (Ellman International, Inc., Hewlett, NY) uses radiofrequency current that is received by the indifferent electrode acting as an antenna. The area of contact between the patient and the indifferent electrode is irrelevant because the wavelength is in the radiofrequency range (4.0 MHz).

The bipolar forceps are primarily used for hemostasis. The same current generator is used but the patient is not part of the electrical circuit. The current only affects tissue within the forceps. Bipolar forceps are most useful for hemostasis within body cavities. Bipolar mode is standard on most electrosurgical units, including the Surgitron.

Carbon Dioxide Laser

The carbon dioxide (CO_2) laser (Aesculight, Bothell, WA) has been popular in surgery on small mammals. It produces a beam of light energy at a wavelength that is highly absorbed by water molecules, making it ideal for cutting with a focal beam or vaporizing tissue with a diffused beam. The CO_2 laser seals vessels less than 0.6 mm in diameter, so many incisions are bloodless, resulting in less bruising and postoperative swelling because the lymphatic vessels are also sealed. Incisions made with the CO_2 laser are reportedly less painful than those made with a blade or electrosurgical units because the laser beam seals nerve endings. When used appropriately, the amount of lateral heat damage is said to be minimal[6]; however, when used incorrectly, lasers can cause significant thermal damage.

The CO_2 laser can be used to cut tissue, including skin, and can also be used to fulgurate or destroy tissue, such as a tumor. When used to cut tissue, it should be used on a high power setting, and the tip should be as close to the tissue as possible without touching it. A smaller tip will create a smaller spot and will cut better with less lateral heat compared with a wider tip. A wider beam will create more heat, which is beneficial for coagulating vessels. Proper safety training for all personnel is important when using surgical lasers.

Vessel Sealing Devices

LigaSure™ (Medtronic, Minneapolis, MN) is a vessel/tissue sealing system that is commonly used in veterinary surgery. The ForceTriad™ combines the tissue sealing technology with monopolar and bipolar electrosurgery. Although the specific technology is proprietary, the LigaSure™ is a type of bipolar cautery. The generator senses the electrical impedance of the tissues within the tips and delivers the amount of current needed to melt the elastin and collagen; it then allows the elastin and collagen to re-form, creating a permanent seal in a single application. It is approved by the Food and Drug Administration to seal vessels up to 7 mm in diameter and generates less than 1 mm of lateral heat. A variety of handpieces are available, including one for a 5-mm cannula for minimally invasive surgery and one for delicate dissection during open surgeries.

PATIENT PREPARATION

Standard aseptic technique is essential with small mammals. Because of their caging, they are usually in proximity to their urine and feces, predisposing them to perioperative infection. For surgical preparation, minimize the area where fur is clipped to help control heat loss. Chinchilla and rabbit skin is particularly fragile and can be easily damaged during clipping; the fur is very fine and epilates easily. A No. 50 clipper blade (Oster Professional Products, McMinnville, TN) is ideal for fine, thin fur in these patients with thin skin. The teeth of the No. 50 blade are closer than those of No. 40, making it more difficult for the patient's skin to get caught between the teeth and be cut. Flatten the skin in front of the clipper blade, move slowly over the skin, and clean and lubricate the blade frequently.

Historically, isopropyl alcohol has not been recommended for skin preparation because of concerns that the evaporative cooling would have a prolonged detrimental effect on body temperature. In a recent study in mice comparing the use of povidone iodine alone, alcohol alone, or povidone iodine alternating with alcohol, saline solution, or warmed saline solution, alcohol alone or in combination with povidone iodine caused an initial dramatic drop in surface and core temperature.[7] However, with alcohol alone, body temperature rebounded to the level of the controls within minutes. When alcohol or saline solution was alternated with povidone iodine, this did not occur. Using warm saline solution did not alter this effect. All povidone iodine treatment groups had the coldest core temperature, which persisted. The authors theorized that the evaporative cooling ends when the alcohol is gone, whereas saline solution evaporates slowly and continues to have a negative impact on body temperature, and that residual povidone iodine continues to cause evaporative cooling. The authors concluded that although alcohol is not appropriate as a stand-alone surgical skin preparation, alcohol is a good alternative to saline solution as a skin wipe when used in combination with povidone iodine for rodent aseptic preparation. In another study, an alcohol-based skin preparation was compared with chlorhexidine in reducing surface bacteria in dogs.[5] Results indicated that the alcohol-based skin preparation applied once and allowed to dry was equally as effective as chlorhexidine when used according to manufacturer instructions. This may be a better method in rodent skin preparation because it is only applied once, so it is faster, and no other agent is applied that might prolong evaporative cooling, exacerbating patient hypothermia. If electrosurgery or a CO_2 laser is used, the alcohol can ignite, so it is essential that all alcohol has evaporated before using these instruments.

Scrubbing the patient's skin is not necessary. Scrubbing can irritate the skin, predisposing to postoperative infections. According to the instructions for use, chlorhexidine preparation solution should be applied and left for 2 minutes before wiping it off. No need has been established in any species for alternating between the chlorhexidine preparation solution and saline or alcohol. A newer skin preparation product, ChloraPrep One Step (BD Medical, Franklin Lakes, NJ), a combination of 2% chlorhexidine and 70% isopropyl alcohol, is applied to the skin for 30 seconds and left to dry for 30 seconds, after which the skin is ready for incision.

Clear plastic drapes allow respiration to be monitored during the procedure and may also hold in heat better than other drapes. For small patients, place the four-quarter drapes around the patient rather than the proposed incision, then place the plastic drape over the patient to cover the entire table and create a sterile field. For larger patients such as ferrets and rabbits, use large plastic drapes or standard draping techniques.

SUTURES, NEEDLES, AND CLOSURE

In general, the sutures and needles used in the average veterinary practice are too large for use in small mammals. It is best to use the smallest-size suture and needle to accomplish the desired task. Suture sizes 4-0 to 7-0 are most commonly used in small mammal species. Absorbable materials degraded by hydrolysis (e.g., polyglactin 910) rather than proteolysis (e.g., catgut) are recommended to prevent severe tissue reaction. Suture that is present for many months, such as polydioxanone and polyglyconate, is not usually needed. Soft, absorbable, braided materials are rapidly absorbed and are less irritating to subcutaneous tissues than stiffer monofilament materials. Some surgeons recommend stainless steel for cutaneous sutures; however, this material is very stiff, and the cut ends often cause irritation, actually stimulating rather than preventing self-mutilation. Skin closure is best accomplished with an intradermal or subcuticular technique; this can be time-consuming. Skin staples are quickly applied, and most companion exotic mammals will not bother them. Cyanoacrylate tissue adhesive can be used to close

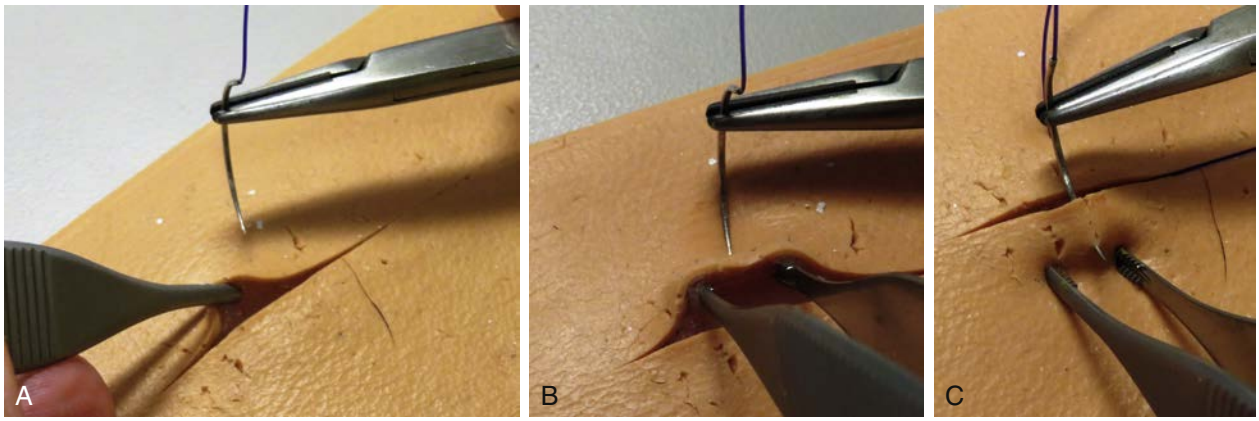


Fig. 30.4 Use forceps to provide counterpressure when passing a needle through the skin, rather than holding the skin edge. Pinching the skin (A) causes irritation that can lead to self-mutilation. Insert the forceps into the incision and pass the needle between the tips (B). Then pass the needle into the incision, use the forceps on the outside for counterpressure, and exit the needle between the tips of the forceps (C).

small incisions; however, excessive amounts of the adhesive will often attract the patient's attention, and it will try to groom it off, potentially resulting in dehiscence.

Cutting needles are mainly used for skin. Atraumatic taper-point needles are recommended for soft tissues. When a cutting needle is used on soft tissues, it cuts the tissue and predisposes the suture tearing through the tissue. A reverse-cutting needle is slightly less likely to promote tearing through tissue.

Gentle tissue handling is important to help minimize the risk of self mutilation. If the patient demonstrates a tendency toward self-mutilation, anxiolytic medications may help modulate the behavior, allowing appropriate recovery and healing. This treatment may be needed for only a day or two until the patient becomes accustomed to the surgical wound. Most patients that have proper postoperative analgesia do not bother their surgical site. Guinea pigs, chinchillas, and degus appear less likely to bother surgical incisions than are rabbits and other species of rodents. Pinching the skin with forceps during suture placement can cause bruising and irritation, predisposing to self-mutilation. In placing sutures, use forceps to provide counterpressure and guide the tissues without pinching (Fig 30.4). Ferrets appear to be particularly prone to developing ecchymosis around surgical incisions.

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31

Soft Tissue Surgery: Ferrets

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PREOPERATIVE CONSIDERATIONS IN FERRETS

Cardiac disease is common in middle-aged and older ferrets; therefore evaluate cardiac function before surgery by obtaining thoracic radiographs as well as performing echocardiography and electrocardiography as indicated. In addition, evaluate a complete blood count (CBC) and plasma biochemical analysis. Hypoglycemia can be present because of concurrent insulinoma. Regardless of whether the ferret exhibits hypoglycemia, always evaluate and palpate the pancreas for nodules during abdominal surgeries; if nodules are encountered, resect the abnormal tissue (see Pancreatic Surgery below).

SURGERY OF CUTANEOUS NEOPLASIA

Ferrets are commonly presented with a variety of cutaneous neoplasms, most of which are not malignant (see Chapter 9). Consequently, wide surgical margins generally are not required. Preoperative treatment with corticosteroids and antihistamines may decrease mast cell tumor size and inflammation; however, this is not performed by the authors.

Despite the generally benign nature of most ferret cutaneous neoplasms, do not omit appropriate preoperative workup for potential neoplastic disease. Depending on the case and presentation, consider hematologic testing, plasma biochemical analysis, abdominal ultrasonography, and thoracic radiography. When appropriate, further diagnostic tests may include bone marrow aspiration as well as regional lymph node aspiration or biopsy, computed tomography, or magnetic resonance imaging. Perform fine-needle aspiration (FNA) of the mass, and submit samples for cytologic evaluation to plan appropriate surgical margins and discuss the possible prognosis with owners before surgery. Although cytologic examination may not provide a definitive diagnosis, a general cell type as well as distinction between malignant and benign processes can often be appreciated.[1,25] To prevent tumor seeding, plan approaches such that the needle tract of the FNA is through areas slated for removal. Full histologic analysis is recommended for all excised tumors.

Surgery of cutaneous and subcutaneous neoplasia in ferrets is similar to that in other species. Scalpel, laser, and radiosurgical techniques have been described.[25] Regardless of the technique used, pay close attention to gentle tissue handling and rapid hemostasis. Cryosurgery has also been used to ablate superficial tumors; if this technique is chosen, use two freeze/thaw cycles.[16] Because of the extensive tissue necrosis that occurs adjacent to a mass ablated by cryosurgery, closure is usually not performed. For the same reason, obtain a definitive diagnosis before cryosurgical treatment.

Postoperative care for cutaneous mass resection, including pain control, is similar to that for other species. Because ferrets

are not amenable to Elizabethan collars, avoid skin sutures in general and perform subcuticular closure with 4-0 absorbable suture material.

EXPLORATORY LAPAROTOMY

When performing a complete exploratory laparotomy, begin the ventral midline incision at the xiphoid and extend it to the pubis in female ferrets and immediately cranial to the prepuce or paraprepucially, if needed, in males. Ferrets have relatively thin skin and little subcutaneous tissue; therefore use a light touch with the scalpel blade. The linea alba of ferrets is a wide, thin structure that is easily identified (Fig 31.1). Be extremely cautious in penetrating the abdominal cavity or extending the incision to avoid damaging dilated or enlarged organs (most commonly the spleen). Also, use caution in extending the incision in the linea cranially to avoid penetration of the diaphragm. To help gain exposure to the abdominal cavity, use small Balfour retractors with moistened gauze sponges or a commercially available self-retaining retractor (Lone Star Retractor; CooperSurgical, Inc., Trumbull, CT). Remember that hypothermia is a major intraoperative complication, especially when a large abdominal incision is required; therefore monitor body temperature and be prepared to use multiple methods of thermal support (see Chapter 30). After completing the procedure, close the linea in a simple continuous or interrupted pattern using 3-0 or 4-0 absorbable monofilament or polyfilament suture material—for example, polydioxanone (PDS) or polyglactin 910 (Vicryl) (Ethicon, Johnson and Johnson Healthcare, Piscataway, NJ). Close subcutaneous tissues with fine absorbable suture material. A subcuticular pattern may be used to complete the closure. Alternatively, skin sutures may be used but are not recommended. Instead, cyanoacrylic tissue glue may be used by applying the material to apposing skin edges. Do not place tissue glue within the subcutaneous tissues where it is likely to elicit a foreign-body reaction.

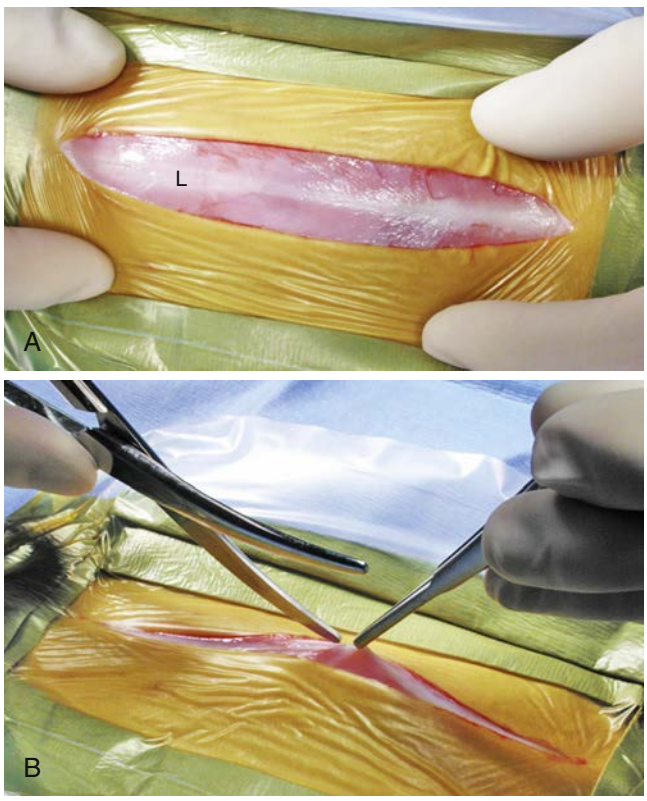


Fig. 31.1 Approach to ferret exploratory laparotomy. (A) Note the wide linea alba *(L)* and minimal subcutaneous fat. Adherent plastic sheeting is applied to the ventral abdominal skin to keep the ferret dry and warm during the surgical procedure. (B) Extending the incision in the linea alba with fine scissors. Note that the abdominal wall is elevated to prevent damage to the underlying abdominal organs.

SURGERY OF THE DIGESTIVE TRACT

Salivary Mucocele Resection

Ferrets have five pairs of salivary glands: parotid, mandibular, sublingual, molar (buccal), and zygomatic.[14] Although mucoceles are uncommon, they have been reported in ferrets (see Chapter 3).[21,27] The zygomatic and molar (buccal) glands are most commonly affected. Aspiration may provide temporary relief from the swelling; however, treatment should involve marsupialization or surgical removal of the involved gland or glands. A thorough knowledge of the regional anatomy is required so that all of the involved glandular material is removed. As described in dogs, the zygomatic arch can be partially resected to facilitate exposure of the zygomatic gland. The prognosis appears to be good after surgical removal of the affected gland.[21,27]

Mucoliths are common in the parotid salivary gland of ferrets. Although these are generally asymptomatic, affected ferrets are used as models in studies of human salivary mucoliths.[43,44]

Gastrointestinal Surgery

Common indications for gastrointestinal (GI) surgery include removal of foreign bodies and intestinal/gastric biopsy. Biopsy of the stomach and intestines is indicated in cases of chronic diarrhea, vomiting, or weight loss or the presence of a gastric or intestinal mass. Inflammatory bowel disease (especially lymphoplasmacytic gastroenteritis) is commonly diagnosed at one author's (V.J.) practice. Surgical GI biopsy samples are obtained as in dogs and cats. After thoroughly exploring the abdomen, isolate the affected area of stomach or intestine with moistened gauze. Collect multiple samples, starting with the stomach, which is the least contaminated area. First, remove the stomach contents by aspiration. Milk the contents in the intestinal lumen away from the biopsy site. Place a full-thickness, 3-0 or 4-0 monofilament stay suture in the stomach or antimesenteric wall of the intestines perpendicular to the long axis of the intestines. Perform a wedge biopsy with a scalpel or with scissors and then close the enterotomy/gastrotomy site with a continuous or interrupted appositional pattern of 3-0 or 4-0 absorbable suture material. After closure, check the suture line for possible leakage.

One of the most common surgeries performed in young ferrets is removal of ingested foreign material from the stomach or small intestine. Foam rubber sponges, rubber objects, and cork are the most common foreign bodies.[29] Foreign bodies in the proximal duodenum may be milked into the stomach for removal (Fig. 31.2). Trichobezoars may result from normal or

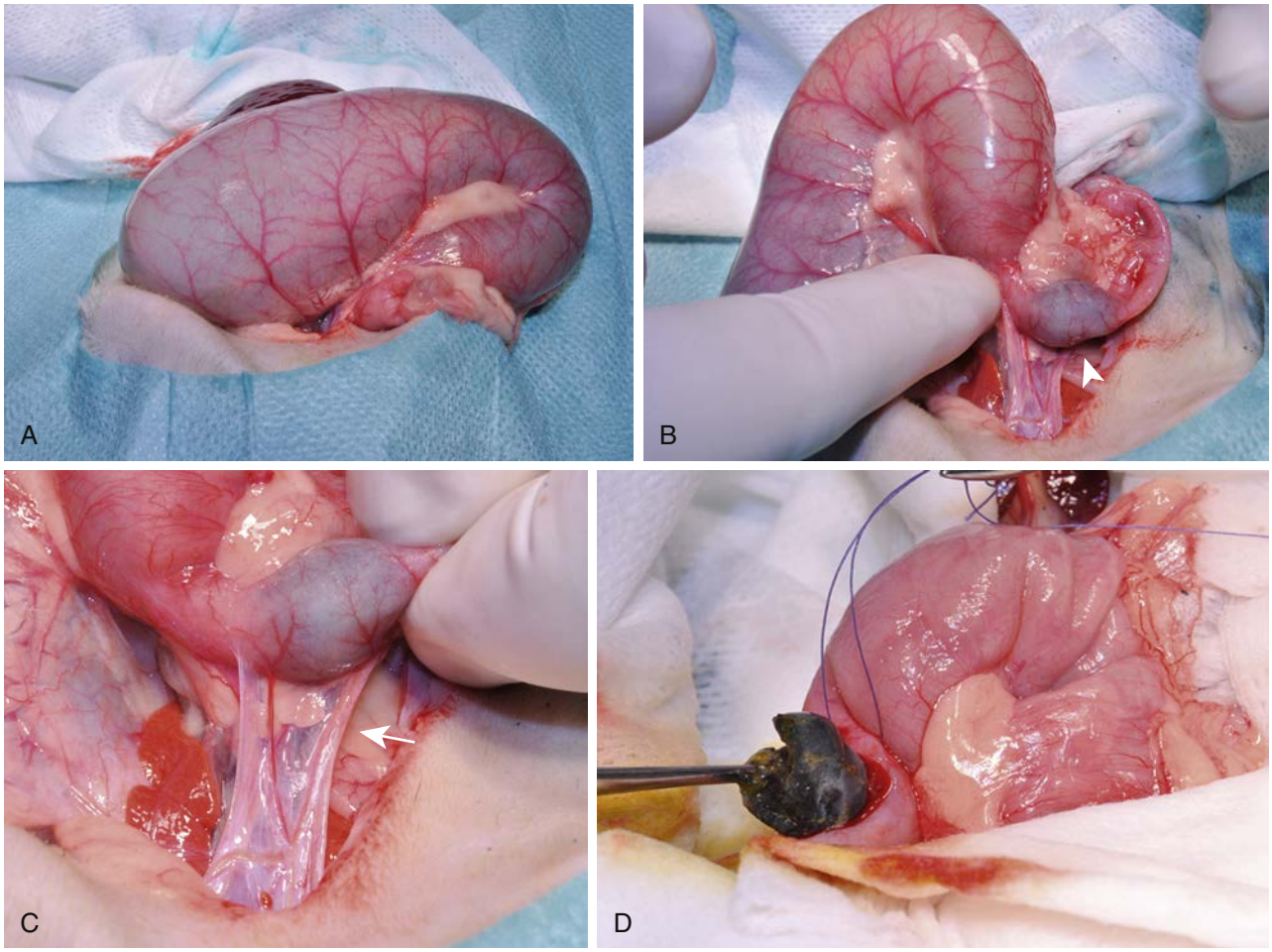


Fig. 31.2 Gastrotomy in a ferret. (A) Exteriorization of the stomach into the surgical wound. Note fluid distension of the stomach. (B) Foreign material *(arrowhead)* identified in the lumen of the proximal duodenum. (C) Detailed view of the location of obstruction close to the duodenal papilla; the *arrow* indicates the biliary and pancreatic ducts. (D) The foreign body is gently milked into the stomach, after which the stomach wall is incised at the greater curvature and the foreign body is removed. The gastrotomy site is closed in two layers with an inverting suture pattern using absorbable suture material. (Photographs courtesy Vladimir Jekl and Karel Hauptman, with permission.)

excessive grooming behavior, particularly in older ferrets, and tend to lodge in the stomach.[29]

Although vomiting is not as frequent in ferrets with GI foreign bodies as in other domestic species,[29] clinical signs in ferrets are similar to those of other small animal patients with GI obstruction (see Chapter 3 for a description of clinical signs, physical examination, and diagnostic tests). Foreign bodies in the intestinal tract may also be discovered during exploratory laparotomy in ferrets that have no clinical signs attributable to intestinal obstruction.

As with other species, surgery to relieve an intestinal foreign-body obstruction is considered an emergency procedure and should be performed as soon as the ferret is rehydrated and stabilized. If GI perforation has occurred, peritoneal effusion is often present. If so, sample the fluid and evaluate it for the presence of bacteria, as well as decreased glucose levels or higher lactate levels relative to the peripheral blood, and submit the sample for bacterial culture and sensitivity testing.

Although esophageal foreign bodies are rare in ferrets, they have been reported.[8,29] Treat these as in other small animal species. If possible, remove the foreign body by endoscopy or by advancing it into the stomach for retrieval by gastrotomy. An esophagostomy may be performed through a right lateral thoracotomy, median sternotomy, or midline cervical approach, but this procedure can be complicated by postoperative leakage or stricture formation.[8]

Most intestinal foreign bodies can be retrieved during an exploratory laparotomy. The ferret's intestine lacks a distinct ileum; instead, the jejunoileum extends from the duodenojejunal flexure to the ascending colon.[14] Ferrets also lack a cecum. Evaluate the entire intestinal tract because multiple foreign bodies may be present, and perform gastrotomy, enterotomy, or resection and anastomosis as in other small animals. Because the ferret's intestinal tissue is very thin and fragile, gentle tissue handling is needed to prevent iatrogenic damage to the intestines. Gastrotomy incisions may be closed in one or two layers by using a simple interrupted or continuous suture pattern with 4-0 or 5-0 monofilament absorbable suture material. When performing an enterotomy, make the incision with a No. 15 scalpel blade longitudinally in healthy tissue proximal or distal to the obstruction and then extend the incision with fine scissors. The enterotomy site is closed by using 4-0 or 5-0 monofilament

suture material in a transverse simple interrupted pattern. The luminal diameter of the jejunum is very small, so handle tissue carefully to minimize the risk of intestinal stricture formation.

Resection and anastomosis is performed as described for other small animal species. Instead of using Doyen clamps to prevent contamination, use sterile bobby pins, which cause less tissue trauma. As with other species, use full-thickness simple interrupted sutures with an absorbable small-gauge suture.

Water can be offered as soon as 2 hours after surgery. If the ferret is awake and alert, offer small amounts of food 2 to 4 hours after surgery. Continue intravenous (IV) fluid therapy until the ferret is eating well. Overall, the prognosis is very good, but possible complications are intestinal leakage and peritonitis, as well as stricture formation with possible reobstruction.

Liver Biopsy/Lobectomy

In ferrets, ultrasound-guided FNAs or biopsies are most commonly performed to diagnose suspected liver disease. However, a liver biopsy may be performed during an exploratory laparotomy. If all liver lobes have a similar appearance and palpate similarly, perform a random liver biopsy. If a section of liver is protruding, use a guillotine suture technique by placing a preformed encircling ligature of 4-0 monofilament absorbable suture material around the protruding section of liver (Fig. 31.3). Tighten the ligature until it has crushed through the hepatic parenchyma. After completing several throws in the knot, excise the sample 1 to 2 mm distal to the ligature with Metzenbaum scissors or a scalpel blade. Take care to avoid crushing the sample and destroying the architecture by using forceps. Similarly, partial or total lobectomy can be performed. Take care to avoid ligation of the common bile duct.

If a specific area of the liver is of interest, the tissue sample can be obtained by the transfixion method or with a 6-mm skin biopsy punch. For the transfixion method, place a ligature through the liver lobe approximately 8 to 10 mm from its edge. Tighten the ligature to crush through the parenchyma of half of the desired biopsy specimen. Make an additional throw at a right angle to the first ligature, tightening the ligature to crush the parenchyma for the second half of the specimen. Vascular clips (hemoclips) may be used to crush the parenchyma in the shape of an inverted V. Remove the sample 1 to 2 mm distal to the crushed area with a scalpel blade or Metzenbaum scissors. If the area of interest does not lie near the edge of the liver lobe, a 6-mm biopsy punch can be used. Push the biopsy punch through the liver parenchyma on the ventral surface in the desired area, making sure not to penetrate the opposite surface of the liver. Use extra caution if the biopsy site is close to the hilum so that no more than one-half the thickness of the liver lobe is penetrated. Remove the biopsy punch and separate the biopsy sample from the liver with scissors, taking care not to crush the sample. Control bleeding either by filling the defect with gelatin sponge hemostatic material and applying digital pressure for 3 to 5 minutes or by suturing the liver capsule with a fine absorbable monofilament suture material in a cruciate pattern.

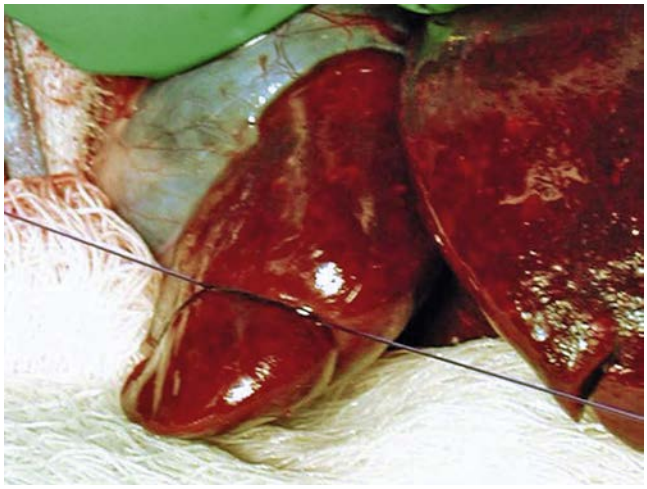


Fig. 31.3 The guillotine liver biopsy technique is performed by placing a ligature around the area of interest at the edge of a liver lobe and slowly tightening the ligature. The biopsy specimen is then divided approximately 2 mm distal to the encircling ligature.

Gallbladder Surgery

Choleliths are rare in domestic species and may be found occasionally in ferrets. Gallbladder rupture, cholecystitis, and extrahepatic bile duct obstruction have been described in ferrets presented with anorexia, general weakness, and progressive weight loss (see Chapter 3). Choleliths have also been found incidentally in ferrets during exploratory abdominal surgery for other conditions.[21]

The biliary system of ferrets is similar to that of other domestic animals (Fig 31.4A). The gallbladder empties into the cystic duct, which joins the central hepatic duct to become the common bile duct. The main pancreatic duct joins the common bile duct before it empties into the duodenum at the major duodenal papilla, which is generally located 2 to 3 cm distal to the pylorus.[32]

Choleliths can be located in the gallbladder or they can obstruct the common bile duct as choledocholiths (Fig 31.4B). Therefore thoroughly examine the biliary tree during exploratory abdominal surgery for gallstones. If the obstruction is located in the common bile duct, attempt to retropulse the stones by gently milking them backward into the gallbladder with your fingertips. Alternatively, make an incision in the antimesenteric border of the duodenum at the level of the major duodenal papilla, cannulate the common bile duct with a 25-gauge catheter, and flush the stones into the gallbladder. Check the common bile duct for patency by flushing the duct with a 3.5-Fr catheter. If the duct is patent, perform a standard cholecystectomy (as in other domestic species) to prevent recurrent cholecystitis.[23] Submit sections of the gallbladder for bacterial culture and histopathologic examination and submit gallstones for crystallographic analysis.

SURGERY OF THE ENDOCRINE SYSTEM

Surgery of the Adrenal Gland

Adrenal neoplasia is common in ferrets. Cortical hyperplasia, adenomas, and carcinomas that secrete estrogen and other steroid hormones are the most common tumor types (see Chapter 7).[2,21,37] Other types of adrenal gland neoplasia, such as spindle

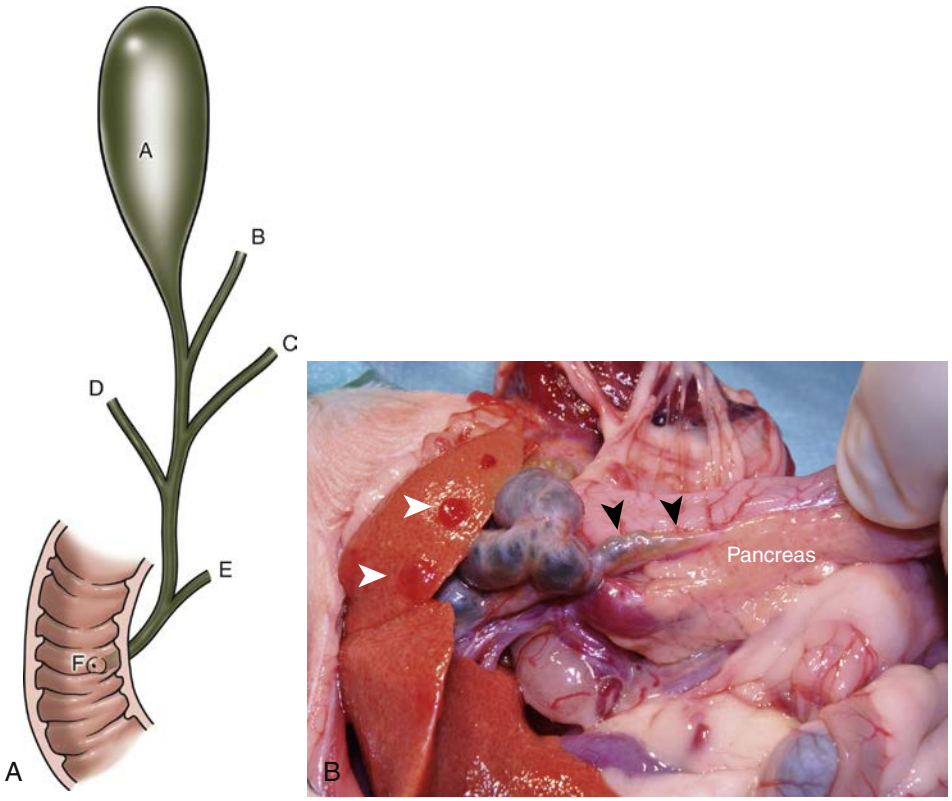


Fig. 31.4 (A) The biliary tree and gall bladder. *A*, Gallbladder and cystic duct; *B*, central hepatic duct; *C*, left hepatic duct; *D*, right hepatic duct; *E*, main pancreatic duct; *F*, major duodenal papilla of common bile duct entering the duodenum approximately 2.75 cm distal to the pylorus. (B) Intraoperative view of a ferret with cholecystitis, biliary stones, and hemangiosarcoma. The common bile duct *(black arrowheads)* and cystic bile duct are grossly distended. Lesions of hemangiosarcoma are seen within the liver parenchyma *(white arrowheads)*. (Photograph courtesy Vladimir Jekl and Karel Hauptman, with permission).

cell tumors, pheochromocytomas, teratomas, and myelolipoma, have been reported with a much lower frequency.[20]

Instead of secreting excess cortisol, affected adrenal glands produce estrogens and androgens.[36,46] Refer to Chapter 7 for a complete description of adrenal disease in ferrets. Physical examination may reveal a mass palpable cranial to the left kidney. The cranial aspect of the right kidney is generally not accessible to palpation. Abdominal ultrasonography is used to identify an enlarged adrenal gland or glands and to determine whether the disease is unilateral or bilateral. Color-flow Doppler scanning can be used to determine the extent of caudal vena cava invasion when a right adrenal gland is affected. Ultrasonography also screens for the presence of other disease processes in abdominal organs.

Medical management for adrenal disease in ferrets is discussed in Chapter 7. If surgery is elected, it is performed through a standard midline approach. The left adrenal gland is often embedded in fat and is located cranial and medial to the left kidney (Fig. 31.5). The right adrenal gland lies craniomedial to the right kidney and adjacent to the caudal vena cava. Normal adrenal glands are whitish pink, 2 to 3 mm wide, and 6 to 8 mm long.[30] Remember that not all diseased adrenal glands are enlarged, and the glands should always be palpated for abnormal texture. If the entire left adrenal gland is not visible, use mosquito hemostats and cotton-tipped applicators to carefully dissect the thin layer of peritoneum and fat surrounding

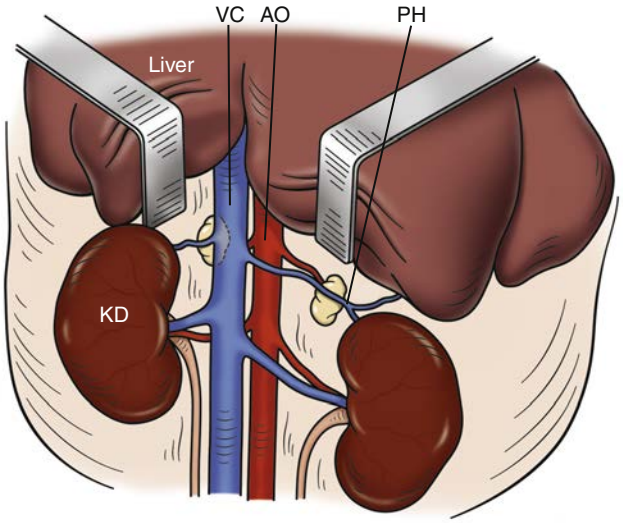


Fig. 31.5 Normal adrenal anatomy. The hepatorenal ligament has been incised to allow retraction of the caudate liver lobe and visualization of the right adrenal gland. The right adrenal gland is adhered to the wall of the caudal vena cava *(VC)*. If neoplastic, it often extends dorsally along the vessel wall (indicated by *dashes*). *AO,* Aorta; *KD,* kidney; *PH,* phrenicoabdominal vein.

the gland to free it. To expose the right adrenal gland, the hepatorenal ligament (which attaches the caudate lobe of the liver to the right kidney) must be incised. Yellow-brown discoloration,

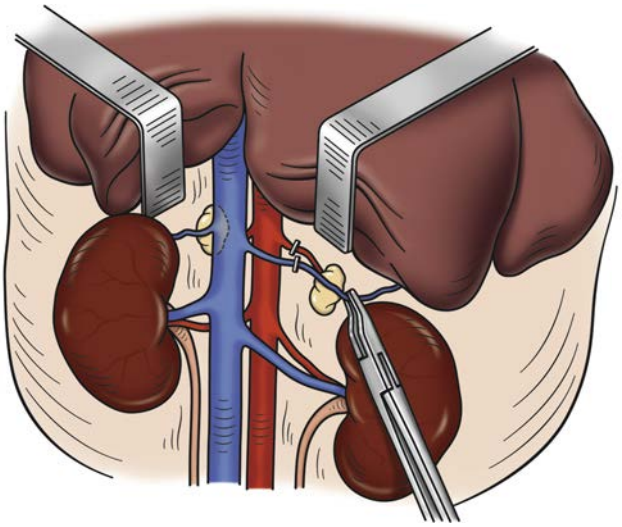


Fig. 31.6 Left adrenalectomy is usually simple because of the distance of the gland from the caudal vena cava. Hemostatic clips are useful for ligating the phrenicoabdominal vein as it courses from lateral to medial over the ventral surface of the gland.

an overly firm or gritty texture, and the presence of cysts or enlargement are all indications of a diseased adrenal gland. Manipulation of either adrenal gland may cause a significant tachycardia and increased blood pressure because of catecholamine release. Esmolol (0.25–0.5 mg/kg slow IV bolus) may be used to control this effect.

Left adrenalectomy is usually easily accomplished, taking care not to disrupt the capsule of the gland. Control hemorrhage of large vessels with cautery, ligation, a vessel-sealing device, or hemostatic clips (Fig. 31.6). The phrenicoabdominal (adrenolumbar) vein is first encountered at the craniolateral aspect of the gland as it courses over the gland's ventral surface and is ligated with suture or small hemostatic clips. After dissecting the caudal, lateral, and cranial aspects of the gland, lift it by grasping tissue along its lateral aspect. Examine the area where the phrenicoabdominal vein enters the vena cava for soft tissue invasion. If no invasion is detected, ligate the vein with hemoclips or suture and remove the gland.

Right adrenalectomy is more difficult because of adherence of the gland to the wall of the vena cava and the greater potential for vascular invasion. At surgery, have magnifying loupes, microsurgical instruments, and vascular clamps available. Begin dissecting around the gland as described for left adrenalectomy. If the tumor is small and extends lateral to the cava, it often can be almost completely freed from the wall of the cava with gentle dissection. However, it may be impossible to determine whether either ligation or resection might disrupt the vena cava. If in doubt, place a vascular clamp (described below) before resection. Small hemostatic clips or small suture ligations may be placed between the gland and the cava before the gland is resected.

If the gland cannot be freed from the vena cava because of tumor invasion or if it is located mostly on the dorsal aspect of the vessel, this technique will often be unsuccessful for complete removal. In these cases, place a small (neonatal) atraumatic vascular clamp on the vena cava for either partial or total occlusion of the vessel (Fig. 31.7). Next, remove the gland with a portion of the caval wall and suture the defect with 9-0 or 10-0 suture in a simple continuous pattern. If only a small defect is created, a simple interrupted pattern can be used. Limit the time of venous occlusion to 20 minutes, as all ferrets that underwent vena cava occlusion for that amount of time during a study were reported to have survived.[7] In addition to decreasing renal perfusion, prolonged occlusion of the vena cava may promote emboli formation. Before releasing the clamp, place a piece of gelatin sponge over the suture line. Mild oozing is usually observed from the incision line, and gentle pressure can be applied to the area with a cotton-tipped applicator. If hemorrhage is severe, replace the clamp and identify and suture the area of bleeding.

With extensive vascular invasion of the vena cava, resection and anastomosis of the cava may be necessary. Some have reported successful outcomes with complete ligation of the vena cava[48]; presumably these ferrets had enough collateral circulation to allow survival. However, renal compromise is common after ligation of the vena cava, and renal failure has been reported in 30% of ferrets in which this procedure has been performed.[19]

Before surgery, venography is sometimes used to determine the extent of collateral circulation, mostly via the paravertebral venous plexus.[7] If collateral circulation is evaluated before surgery and is deemed sufficient, ligation of the caudal vena cava is presumed less likely to impair renal function. However, additional factors may be involved in post-adrenalectomy renal compromise in ferrets.[19]

Cryosurgery, laser surgery, and ultrasonic and radiosurgical ablation of the right adrenal gland have been reported anecdotally. A disadvantage of these techniques is that the tissue is not available for histopathologic evaluation. In addition, it may be difficult to evaluate how completely the adrenal gland has been destroyed.

Bilateral gland involvement has been reported in 16% to 68% of ferrets with adrenocortical disease.[35,47] In one study, 32% of ferrets with unilateral adrenal disease presented an average of 11 months after the first surgery with disease of the contralateral gland.[48] Subtotal adrenalectomy, with complete removal of one gland and partial removal of the other, is one option for bilateral disease[48]; however, this is not recommended by the authors and by other authors[42] because there is a high possibility of tumor metastases and recurrence of abnormal adrenal tissue and clinical signs of disease. Moreover, postoperative adhesions and rapid increase in size of the remaining adrenal tumor make a second surgery difficult. Complete bilateral adrenalectomy is performed with good success. Monitor electrolyte levels after surgery for evidence of mineralocorticoid deficiency. After total bilateral adrenalectomy, most ferrets initially require glucocorticoid and mineralocorticoid therapy, and some may require it for life. Ameroid constrictors, cellophane bands, and hydraulic occluders, which are used in other animal species to gradually occlude the vena cava for adaptation purposes weeks before a definitive surgery is performed, are unlikely to be needed in the ferret.[25]

Intraoperative and postoperative complications include hypothermia, tachycardia, hypotension, hemorrhage, glucocorticoid and mineralocorticoid deficiency, and renal failure. If recovery from surgery is slow or the ferret appears depressed, collect a blood sample to measure the packed cell volume and blood glucose and electrolyte concentrations, assess the pulse

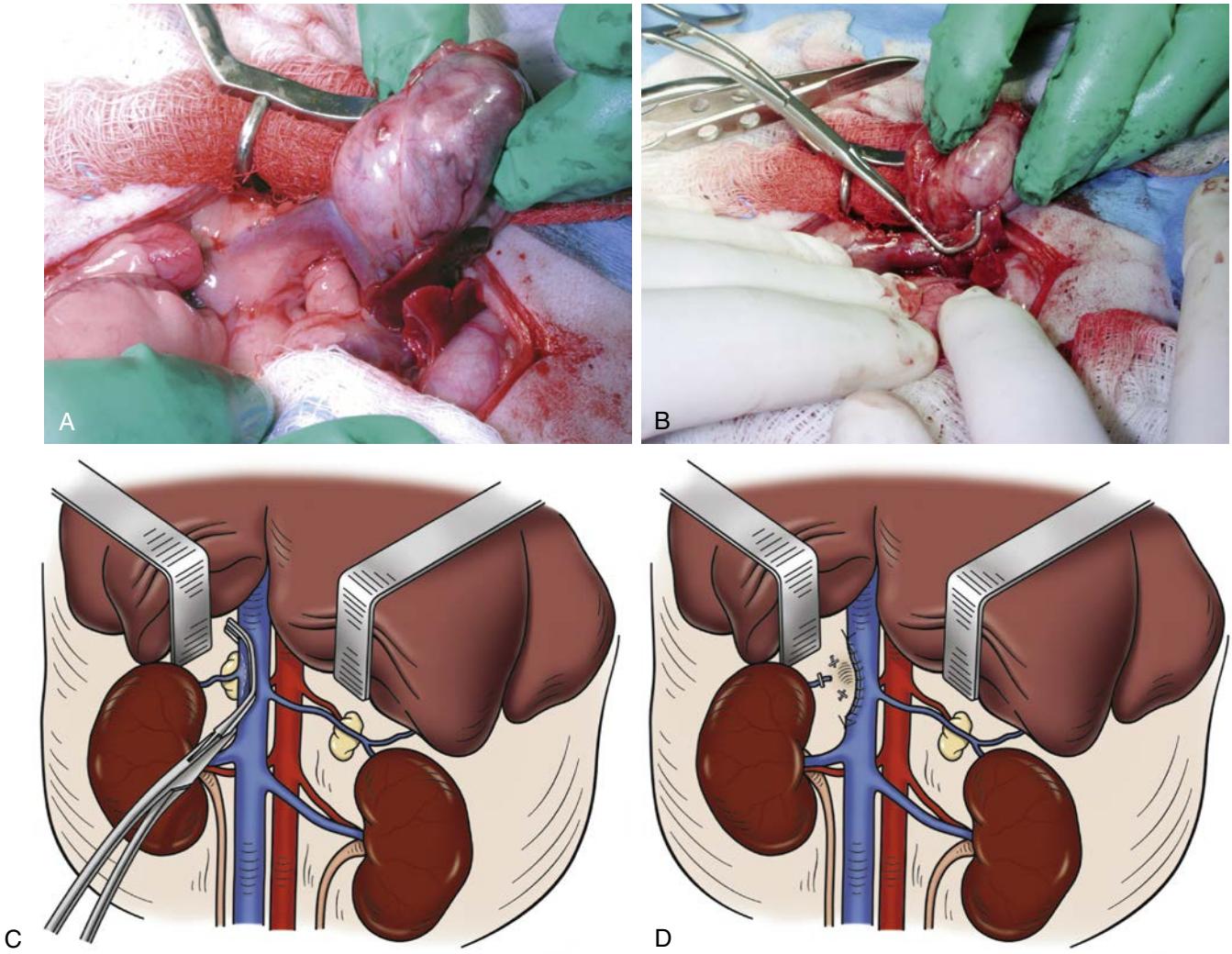


Fig. 31.7 (A) Large right adrenal mass attached to the caudal vena cava. (B) Neonatal Satinsky clamp is applied to the vena cava around the base of the mass to result in partial occlusion of the caudal vena cava. (C) Application of the Satinsky clamp. The wall of the caudal vena cava can be incised at this point to remove tumor that is invading the vessel, or it can be resected with the adherent right adrenal mass. (D) Closure of the vena cava with a simple continuous suture pattern. The lumen of the vena cava has been preserved. Hemoclips have been used to ligate small vessels and the phrenicoabdominal vein.

quality, and measure the systolic blood pressure. Continue IV crystalloid therapy, supplementing fluids with dextrose as required. If hypotension is refractory to crystalloid therapy, consider a colloid (e.g., hetastarch) delivered by bolus (5 mL/kg) or continuous-rate infusion (CRI) (20 mL/kg per day). Vasopressors, such as dopamine, are a last resort. Monitor body temperature until it remains within the normal range without external thermal support.

If hypoadrenocorticism is suspected, administer dexamethasone initially at a dose of 0.5 mg/kg or begin therapy with a physiologic dosage of prednisone (0.2 mg/kg per day). If hyperkalemia and hyponatremia are present, consider supplementation with a mineralocorticoid.

In most cases, postoperative recovery is uneventful, and the ferret is fed as soon as it is fully awake. Prostatic or vulvar enlargement usually regresses within days; however, complete hair regrowth may take 1 to 6 months.[51] Marked postoperative bruising around the incision is common in ferrets. Caution owners about this before surgery so that they will not be alarmed when they take the animal home. This bruising generally disappears 5 to 6 days after surgery and does not seem to cause undue discomfort. Also, alert owners that at 33 to 40 days after surgery, the ferret may develop a blue tint to the skin, which results from new hair growth under the skin and not bruising.

Histopathologic analysis of abnormal adrenal tissue usually reveals hyperplasia, adenoma, or adenocarcinoma. Two or even all three of these states of diseased tissue may be found within the same adrenal gland. Metastasis of carcinomas is rare but does occur.

Pancreatic Surgery

Insulin-secreting pancreatic islet cell tumors (also known as *pancreatic beta-cell tumors* or *insulinomas*) are among the most common neoplastic diseases of ferrets (see Chapter 7). Ferrets typically are presented between 3 and 7 years of age but can be affected as early as 2 years of age.[9,13] Refer to Chapter 7 for a clinical discussion of insulinomas. Surgery is a recommended treatment for ferrets assuming that other health concerns are not prohibitive.[9,49] Although not curative, surgical treatment

allows for evaluation of concurrent disease and usually results in a prolonged medication-free and disease-free interval and increased survival time.[13,49]

The preoperative workup for insulinoma surgery is similar to that listed for adrenal surgery. Pharmacologic control of clinical signs (e.g., with glucocorticoid therapy) is more important than establishing normoglycemia (see Chapter 7). During surgery, maintain patients on a CRI of 2.5% to 5% dextrose and monitor glucose levels frequently during and after surgery.[26] If available, a CRI of glucagon may be administered at a rate of 15 ng/kg per minute (6.8 ng/lb per minute).[3]

The anatomy of the ferret's pancreas is similar to that of cats. The common pancreatic duct empties along with the bile duct into the duodenum at the major duodenal papilla. An accessory pancreatic duct is also occasionally present. The blood supply to the pancreas comes from three sources: the right limb is supplied by the cranial and caudal pancreaticoduodenal vessels, and the left limb is supplied primarily by a branch from the splenic artery.

At surgery, assess any adrenal gland abnormalities, enlarged lymph nodes, or evidence of abnormalities of the liver or spleen. Evaluate each limb of the pancreas by visually inspecting and gently palpating the ventral and dorsal surfaces. The body of the pancreas can be inspected only on its ventral surface. Insulin-secreting tumors can appear as visible masses that are discolored or as small nodules (usually less than 1 mm in diameter) that are not visible initially but are firm on palpation (Fig. 31.8A–B). Magnification loupes are ideal for locating small nodules. Multiple nodules involving more than one lobe of the pancreas are common. Partial pancreatectomy, when possible, is recommended and has been reported to increase survival times.[49] Create a window on either side of the pancreatic limb to be removed and free the limb from the surrounding omentum or mesoduodenum. Tighten 4-0 PDS, Vicryl, or Monocryl (poliglecaprone 25) (Ethicon, Johnson and Johnson Healthcare) suture around the base of the limb, allowing a margin of at least 3 to 5 mm from the last visible nodule. Transect the pancreatic limb distal to the ligature and close the rent in the omentum or mesoduodenum with small sutures in a simple continuous pattern. Take care during dissection to avoid the pancreaticoduodenal vessels; damage to these vessels can result in necrosis of the duodenum. A cotton-tipped applicator can often be used to bluntly free the pancreas from these vessels. Preserve the body of the pancreas to avoid damaging the pancreatic duct. Some nodules in this central area cannot be safely resected. If the nodules can be accessed without risking damage to the common bile duct, the nodules can be gently teased away from the surrounding pancreatic tissue (nodulectomy) (Fig. 31.8C–E) If more than one limb is affected, often a partial pancreatectomy is performed on the limb that contains most of the masses (usually the left pancreatic limb) (Figs. 31.8 and 31.9). Nodules on the remaining limb may be removed by nodulectomy. Use a mosquito hemostat and cotton-tipped applicators to bluntly free the nodules from the surrounding tissue. Hemorrhage is usually minimal and does not require suturing. The mesenteric lymph nodes in ferrets with GI inflammation are often enlarged and usually reactive, not neoplastic. If enlarged lymph nodes are detected and lymphoma or other disease is suspected, submit biopsy samples for histopathologic evaluation.

Maintain an IV catheter after surgery and monitor the blood glucose concentration during recovery. Hyperglycemia can occur 2 to 12 hours after surgery; however, the blood glucose level generally normalizes within a few days. Occasionally, an insufficient amount of abnormal pancreatic tissue has been removed, or a suspected tumor is not found, causing persistent hypoglycemia. Postoperative pancreatitis is uncommon, and food and water may be offered

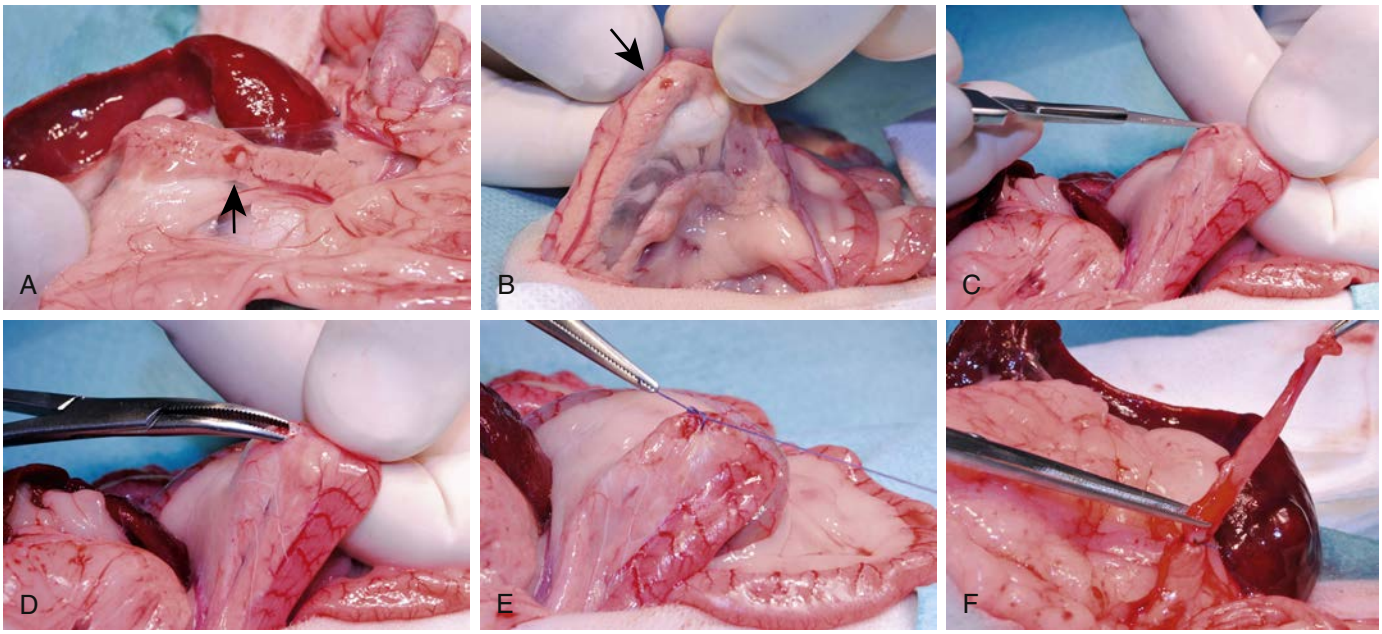


Fig. 31.8 Pancreatic nodulectomy. (A, B) Insulinoma is often red *(black arrow)* and is found in either the left or right pancreatic limb. (C–E) Nodulectomy of the tumor—incision of the mesentery (C), blunt dissection (D), and ligation (E). (F) Partial pancreatectomy. The surrounding mesentery has been dissected free from the left limb of the pancreas, and the pancreas was ligated proximal to the mass using guillotine suture. (Photographs courtesy Vladimir Jekl and Karel Hauptman, with permission.)

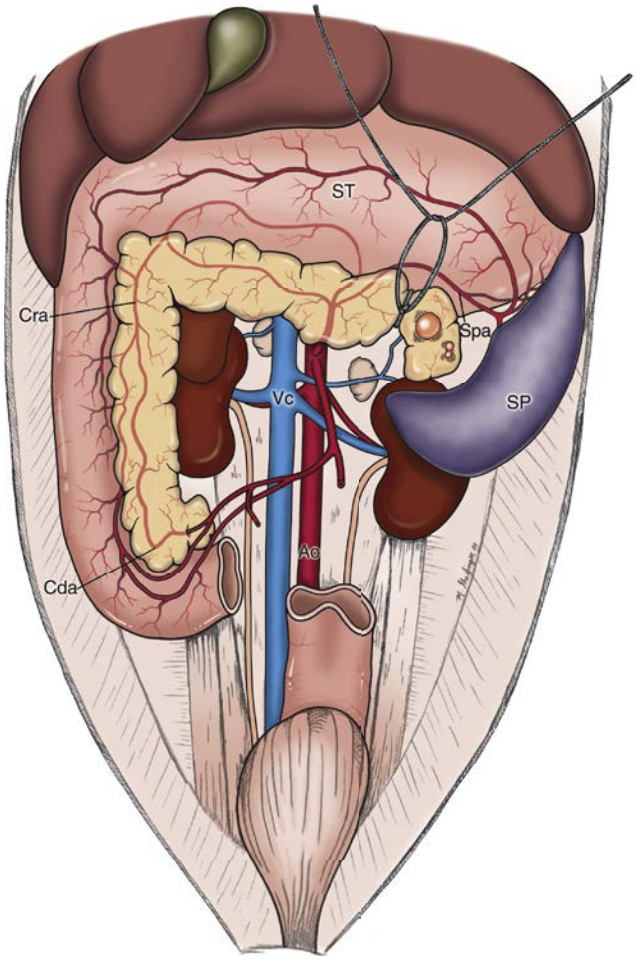


Fig. 31.9 Diagram of guillotine suture for partial pancreatectomy with normal pancreatic anatomy. Note the shared blood supply of the pancreas with the spleen and duodenum. *Vc,* vena cava; *Ao,* aorta; *SP,* spleen; *ST,* stomach; *Spa,* splenic artery; *Cra,* cranial pancreaticoduodenal artery; *Cda,* caudal pancreaticoduodenal artery.

within 2 hours after surgery. Rarely, diabetes mellitus requiring insulin supplementation develops after insulinoma resection. Reevaluate the blood glucose concentration every 6 hours for 24 hours after surgery while the ferret is hospitalized, then at 10 to 14 days and every 3 to 4 months thereafter.

Histopathologic analysis may reveal hyperplasia, adenoma, or adenocarcinoma, but these findings do not dictate prognosis. Recurrence of disease and clinical signs is common. Prognosis is affected by the duration of clinical signs and the presence of local invasion at surgery.[13] The longer the duration of clinical signs before surgery, the worse the prognosis. Prognosis is not affected by the number of nodules present or by persistence of hypoglycemia after surgery.[9,13] Mean disease-free intervals after surgery are reported to be 284 to 365 days.[13] If hypoglycemia recurs, ferrets can be successfully managed medically with frequent feedings and prednisone, diazoxide, or both for extended periods; alternatively, a second surgery may be performed. Average survival times of ferrets treated surgically are reported to be 563 to 668 days.[9,13,49]

Splenectomy

Splenomegaly is a common finding on abdominal exploration. The condition is usually benign and represents extramedullary hematopoiesis.[5] Neoplastic conditions associated with splenomegaly may include lymphosarcoma and occasionally hemangiosarcoma, adrenal adenocarcinoma, or insulinoma.[5,50,51] Cardiomyopathy, Aleutian disease, and eosinophilic gastritis have also been reported as causes of splenic enlargement. Splenic sequestration of red blood cells, seen with isoflurane and sevoflurane anesthesia, can result in both splenomegaly and a significant reduction in the hematocrit and plasma protein concentration.[22]

Ferrets with splenomegaly should be evaluated for underlying disease conditions. If abnormal echogenicity is noted on ultrasonography, ultrasound-guided FNA or core needle biopsy can help determine whether primary splenic disease is present. Before splenic biopsy, determine clotting ability by evaluating the CBC, platelet count, prothrombin time, and partial thromboplastin time if possible.

Splenectomy is indicated for primary splenic or metastatic neoplasia, large hematomas, or severe splenic enlargement that interferes with abdominal visceral function. Because the spleen is a major site of erythropoiesis in ferrets, splenectomy should not be undertaken lightly, and the potential consequences of surgery must be considered carefully.

The approach to the spleen is comparable to that described for exploratory laparotomy. Splenic biopsy techniques are the same as for liver biopsy. Small absorbable suture material (e.g., 4-0 PDS) can be placed in a cruciate or mattress pattern to control hemorrhage. Sutures tend to hold better in the spleen than in the liver because of the relatively thick splenic capsule. Hemoclips may also be used. Although partial splenectomy is rarely indicated, it can be performed for benign processes that result in excessive splenic enlargement. For this procedure, ligate and divide the vessels supplying the portion of spleen to be removed. Place a clamp across the area to be resected, and close it to crush the tissue. Place a thoracoabdominal stapling device (TA-30; U.S. Surgical Corporation, Norwalk, CT) in the crushed area after the clamp is removed. After the staples are fired, transect the spleen distal to the stapler and release the stapler. Control any subsequent hemorrhage with hemoclips or mattress sutures. As an alternative to a stapling device, place mattress sutures through the spleen proximal to the crushing clamp to control hemorrhage. Before removing the clamp, close the splenic capsule in a simple continuous pattern.

Total splenectomy involves ligating all vessels supplying the spleen. Individually, double-ligate the splenic artery and vein, being careful to avoid damaging the vascular supply to the pancreas. Ligate the short gastric vessels close to the spleen to avoid damaging blood supply to the stomach. Vascular sealing devices and small hemoclips can be used instead of suture material to control hemorrhage; however, stapling devices used in other small animals (e.g., Autosuture LDS; U.S. Surgical Corporation) are too large for use in ferrets. An accessory spleen can sometimes be present and appears to be clinically insignificant.

SURGERY OF THE UROGENITAL SYSTEM

Nephrectomy

Nephrectomy is indicated in cases of unresolved hydronephrosis, chronic bacterial nephritis, large renal cysts, and neoplasia.

The kidneys of ferrets, like those of other domestic species, are located in the retroperitoneal space. For nephrectomy, the surgical approach is through a ventral midline incision. Isolate the involved kidney with moistened sponges and open the peritoneum over the kidney to access the retroperitoneal space. Grasp the kidney and apply gentle traction while using cotton-tipped applicators to isolate the renal vessels and ureter. If possible, individually isolate the renal artery and vein and ligate them close to the abdominal aorta and caudal vena cava by using clips or ligatures. The vessels may be double-ligated with hemostatic clips or fine 4-0 or 5-0 suture material. Dissect the ureter along its retroperitoneal course to the level of the urinary bladder. Then ligate and transect the ureter as close to the urinary bladder as possible without damaging the nerves that run in the lateral ligament of the bladder. Leaving the ureter intact can predispose to vesicoureteral reflux and recurrent lower urinary tract infections.[25] Lavage the abdominal cavity and close it routinely.

Cystotomy

Like other domestic species, ferrets can suffer from cystic and urethral calculi, and the history and clinical signs of urolithiasis in ferrets are also similar (see Chapter 4). Surgery to remove calculi is indicated to relieve clinical signs and for quantitative crystallographic stone analysis.

Cystotomy in ferrets is similar to the procedure performed in other small animal species through a caudal midline abdominal incision in females, with the incision extended to the prepreputial area in males. The wall of the ferret's urinary bladder is relatively thin, so take care when applying traction to stay sutures to prevent tearing. After making an incision in the bladder wall, remove the calculi and thoroughly inspect and lavage the bladder. Flush the urethra with a small, soft catheter to ensure that no calculi remain. Submit the calculi for stone analysis and submit a crushed specimen of the calculi and a small section of the bladder wall for bacterial culture and sensitivity testing. The cystotomy incision is closed with fine (5-0) synthetic absorbable suture material in either a simple interrupted or a simple continuous pattern. Check the bladder for leakage by using a syringe and a 25-gauge needle to infuse sterile saline solution. If leakage is observed, add a continuous inverting suture layer over the initial sutures. Postoperative radiographs of the bladder and urethra are recommended to ensure removal of all calculi.

Perineal Urethrostomy

Because of urethral calculi, distal strictures, or neoplasia, a perineal urethrostomy is occasionally indicated in a ferret. The anatomy of the ferret's penis and urethra most closely resembles that of dogs. The site of the urethrostomy should be located caudal to the os penis, proximal to the site of obstruction, and ventral to the anus. Magnification with surgical loupes greatly simplifies the procedure. Place the ferret either in dorsal recumbency with the pelvic area elevated or in ventral recumbency within a perineal stand (Fig. 31.10). Aseptically prepare the perineal region and caudal abdomen. If possible, place a urethral catheter in the anesthetized ferret before surgery. Make a skin incision approximately 1 cm ventral to the anus. This exposes the urethra and cavernous tissue. If a urethral catheter is present, palpate the catheter and make a 1-cm longitudinal incision along the ventral aspect of the urethra. If a urethral catheter cannot be placed, make the incision ventrally, taking care not to stray laterally and incise the cavernous tissue. Open the urethra and place a larger urethral catheter proximally to assist in locating the lumen and mucosa. Use simple interrupted sutures of 5-0 or 6-0 synthetic absorbable suture material to close the urethral mucosa to the skin. Remove the sutures after 10 to 14 days.

Paraurethral/Prostatic Cysts

Prostatic disease in ferrets is usually associated with adrenal gland neoplasia. Ferrets are presented with a history of stranguria and, potentially, urinary obstruction. Alopecia, pruritus, and other clinical signs associated with hyperadrenocorticism

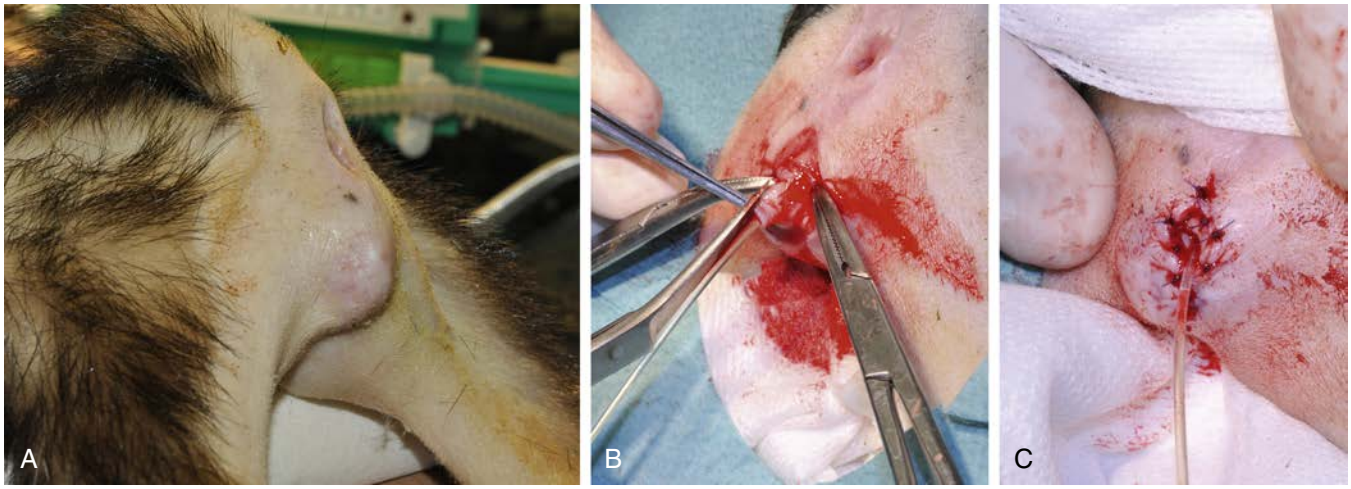


Fig. 31.10 Urethrostomy in a ferret with preputial gland adenocarcinoma. (A) Ferret is positioned in ventral recumbency with its back slightly elevated. The preputial mass is located ventral to the anus. (B) The urethra is catheterized and incised longitudinally to allow urethroplasty with skin. (C) The urethra is then sutured with skin in an "aves-through" method. (Photographs courtesy Vladimir Jekl and Karel Hauptman, with permission.)

may also be observed. Differential diagnoses for stranguria include urinary calculi, infection, penile or preputial lesions, neoplasia of the urinary tract or prostate, and prostatic cysts or hyperplasia.[37] Refer to Chapter 4 for further discussion of paraurethral and prostatic cysts.

If the bladder is distended and cannot be expressed, pass a urinary catheter after the ferret is anesthetized. If urethral catheterization is unsuccessful, perform cystocentesis under anesthesia with a 25-gauge needle. Because of the communication between the prostate and the bladder, cystocentesis will significantly reduce the contents of a cystic prostate and often allow urine outflow to be reestablished (Fig. 31.11).

Medical management is usually successful in treating urinary obstruction due to prostatic hypertrophy and cystic prostatic disease. Several drugs are useful in rapidly reducing both prostatic size and the secretions of prostatic cysts (see Chapter 7).

If medical therapy is not successful, abdominal exploration and adrenalectomy may be indicated. At surgery, aspirate the prostatic or paraprostatic cyst with a small-gauge needle. The fluid contained within the cyst is often green and viscous; submit a sample for bacterial culture and sensitivity testing. Because multiple cysts may be present, aspirate multiple sites. If the cysts are small, aspiration may be the only treatment required. For larger cysts (i.e., >2 cm in diameter), remove a portion of the cyst wall for biopsy and allow complete drainage of all cavitations. Restrict dissection of the prostate to the ventral two-thirds of the gland. Trauma to the dorsolateral aspect, between 10:00 and 2:00, should be avoided at all costs to spare the neurovascular structures supplying the prostate in this region.[33] The cyst can then be omentalized. Theoretically, omentalization provides continued drainage of the cyst, aids in adhesion formation, and enhances immune function to fight against infection. Place a portion of the omentum into the cyst cavity and suture it to the cyst wall with 4-0 absorbable suture.[4] Place three to four sutures, being careful to avoid disrupting the blood supply to the omentum. Express the bladder to check for leakage of urine from the cyst. If leakage is observed, place more omentum into the cyst and partially close the opening into the cyst with suture. If leakage is still seen, a transurethral catheter or tube cystostomy will have to be maintained for 1 to 2 days after surgery until the rents have sealed. The prostate usually decreases in size and cysts regress within 1 to 2 days after adrenalectomy.

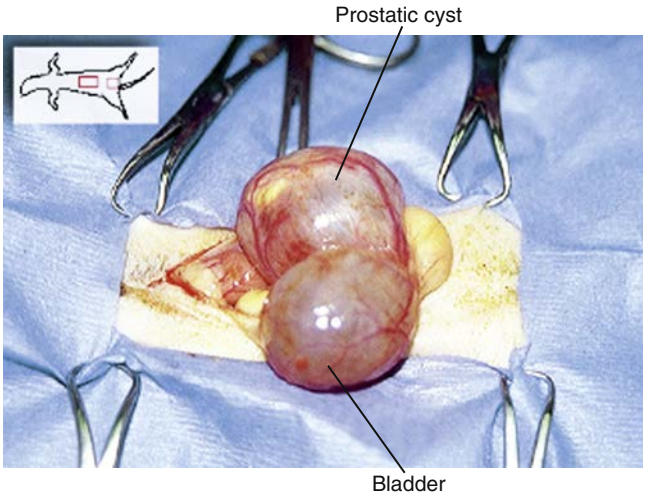


Fig. 31.11 Prostatic cyst in a male ferret with adrenal disease. Generally, the prostatic cyst communicates with the bladder, and cystocentesis of either structure often reduces the obstruction and reestablishes urethral patency.

Ovariohysterectomy

Because most pet ferrets in the United States are spayed at breeding farms before they are 8 weeks of age, ovariohysterectomy is not a common procedure in U.S. veterinary practices. Intact female ferrets remain in estrus with high circulating estrogen levels until they are stimulated to ovulate through breeding or artificial stimulation. Spaying of intact pet ferrets is recommended to prevent life-threatening bone marrow suppression caused by estrogen. For ovariohysterectomy, make a ventral midline incision about 1 cm caudal to the umbilicus. The ferret's uterus is bicornuate and can be found just dorsal to the bladder. Because of the large amount of body fat in female ferrets, the ovarian vessels may be difficult to locate (Fig 31.12). Depending on the amount of fat, use 4-0 absorbable suture material to ligate the ovarian ligament and ovarian vessels separately or as one unit. To prevent retention of ovarian remnants, do not penetrate the ovarian bursa. Use a transfixing suture pattern to ligate the uterus and uterine vessels at the level of the cervix or distal aspect of the uterine body. Close the abdominal wall routinely in two layers with 3-0 or 4-0 absorbable suture.

Ovariectomy alone is not recommended due because of the risk of adrenal gland disease and sex hormonal dysbalance, which can negatively affect the uterus.[18] Alternatively, treatment with a GnRH agonist (e.g., deslorelin acetate implant) can be considered (see Chapter 7).

Ovarian and Uterine Neoplasia

In a retrospective study of 4774 ferrets (1968–1997), only 2.3% of 639 tumors recorded involved the reproductive system.[20] Within the reproductive system, the ovary is the organ most frequently affected by neoplastic proliferation, with ovarian leiomyoma being the most common tumor reported. Ovarian leiomyomas are well-defined, unilateral or bilateral tumors that may reach 1 to 8 cm in diameter; however, they are generally much smaller. A high number of ovarian tumors have been seen by Jekl and Hauptman[18] in ferrets referred after incomplete ovariectomies. Ovarian tumors can be found incidentally during clinical examination or in ferrets presented with hormonal alopecia, chronic weight loss, and signs of estrus because of elevated sex hormones. Uterine leiomyoma, uterine leiomyosarcoma, and malignant mixed Muellerian tumor involving the uterus have been reported.[15,20,38] Elevated estradiol or progesterone levels may be also associated with hydrometra, cystic endometrial hyperplasia, or other uterine disorders.

Abdominal palpation and ultrasonography are recommended diagnostic imaging modalities. Hormonal analysis can show increased levels of sex hormones. Despite increased level of estradiol, signs of bone marrow suppression are not common findings in ferrets with ovarian tumors.[17] Rule out adrenal gland disease by adrenal gland ultrasonography and decreased postoperative levels of sex hormones.

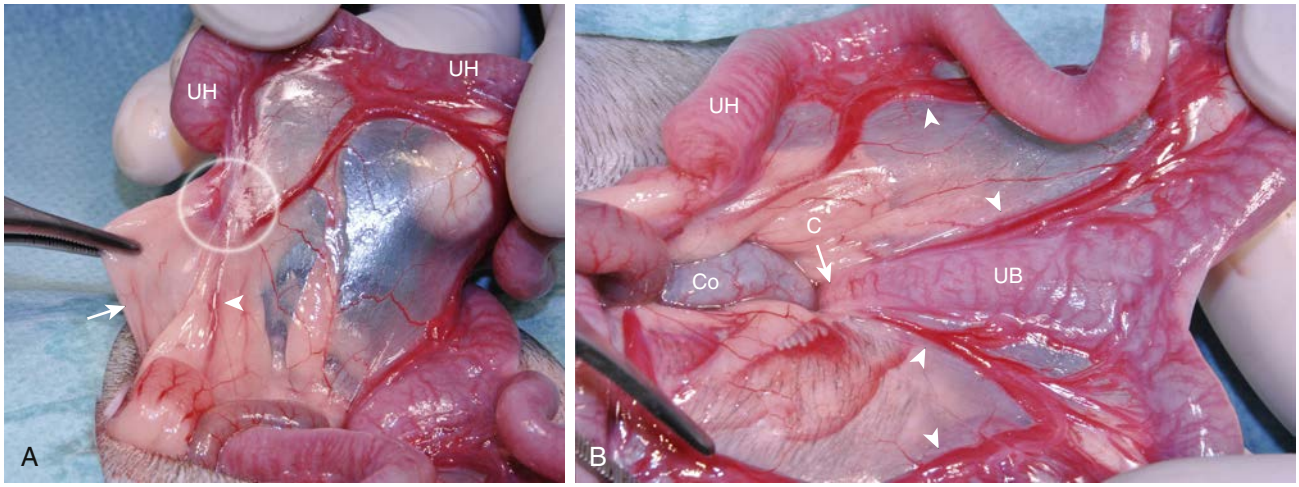


Fig. 31.12 Perioperative photographs of a ferret reproductive organs. (A) Ovaries are located in the dorsal abdomen caudal to both kidneys. The ovary *(encircled)* is attached to the abdominal wall by the ligamentum suspensorium ovarii *(arrow)*. Blood supply is provided by the ovarian artery that, with the ovarian vein, is embedded in fat *(arrowhead)*. (B) Uterine horns *(UH)* and uterine body *(UB)* are thickened due to pseudopregnancy. Vascularization is provided by uterine veins and arteries *(arrowheads)*. Uterine cervix *(C)* is more whitish than surrounding tissue. The colon *(Co)* is located close to the uterine body. (Photographs courtesy Vladimir Jekl, with permission.)

Ovarian Remnant

In a spayed female ferret, clinical signs of estrus (e.g., a swollen vulva) are usually caused by adrenal neoplasia. Occasionally, these signs result from an ovarian remnant or an ovarian tumor. Signs typically occur in ferrets younger than 2 years of age, which is generally younger than in ferrets with adrenal disease. Before abdominal exploratory surgery, evaluate the ferret for anemia and thrombocytopenia, which can result from estrogen toxicity. At surgery, the remnant is typically found immediately caudal to the kidneys.[21] However, perform a thorough exploration, because more than one remnant may be present, and ovarian remnants can be found in any part of the abdominal cavity. Submit the resected tissue for histopathologic examination to verify that it is ovarian and to look for neoplasia. Vulvar swelling should resolve after removal of the remnant.

Pyometra

Because most ferrets are spayed at an early age in the United States, pyometra is uncommon. Clinical signs suggestive of pyometra include vulvar discharge, lethargy, and anorexia. Polyuria and polydipsia are not commonly reported. Radiographs and ultrasound scans are usually diagnostic. The treatment for pyometra is ovariohysterectomy combined with fluid and antibiotic therapy. Before surgery, submit a blood sample for a CBC to evaluate for bone marrow suppression associated with hyperestrogenism. Ovariohysterectomy is routine with special care to prevent contamination. Lavage the uterine stump before abdominal closure. Treat with a broad-spectrum antibiotic to cover the organisms associated with pyometra in ferrets, including *Staphylococcus, Streptococcus*, and *Corynebacterium* species and *Escherichia coli*.[18] Stump pyometra may occur with ovarian remnants or adrenal gland disease. In these cases, remove the remnant or adrenal gland in addition to resecting the stump.

Hydrometra

Hydrometra associated with hormonally active ovarian tumors is one of the most frequently diagnosed uterine diseases of ferrets, and it is especially common after incomplete ovariectomy.[17,18] High levels of estrogen are presumed to influence the development of hydrometra. At a later stage of development, the originally sterile uterus may become infected, thus producing pyometra. Hydrometra and cystic endometrial hyperplasia have been described in ferrets with segmental atresia of the uterus, adrenal gland disease, and congenital defects.[18] Uterine torsion has also been seen by the author (V.J.) associated with hydrometra and ovarian neoplasia.

Therefore ovariohysterectomy is the preferred means of neutering female ferrets. If signs of estrus appear in a ferret after neutering, thoroughly investigate the possible causes and institute appropriate therapy.

Castration

Ferrets are usually castrated to reduce aggressive behavior and the musky odor, to prevent breeding, and to decrease the risk of cryptorchidism and testicular tumors. Castration at an early age, as routinely performed by ferret facilities in the United States, is associated with an earlier onset of adrenal disease.[40] Delayed castration and use of GnRH receptor agonists in the interim may be considered in young male ferrets to mitigate testosterone-related signs (see Chapter 7).[39]

Castration can be performed as it is in cats, with an incision in the scrotum over each testicle. Use an open or closed technique and ligate the spermatic cord closed with an overhand tie, open with a "self-tie" technique (i.e., tying the vas deferens to the vessels), or ligated with 4-0 absorbable suture. Leave the incisions open to heal by second intention. Alternatively, make a prescrotal incision and exteriorize both testicles through the same incision. With this technique, close the subcutaneous

tissue with 4-0 or 5-0 absorbable suture, and close the incision with either intradermal or skin sutures.

Cryptorchid testicles are approached via an inguinal or abdominal approach based on location of the testicles. Cryptorchid testicles can be found between the inguinal canal and the caudal pole of the kidney or by following the ductus deferens.[18] The spermatic cord and testicular artery and vein are ligated separately, and the testicle is excised.

Preputial Masses

Approximately 75% of preputial gland neoplasms (i.e., tumors of the apocrine glands of the prepuce) are malignant, exhibiting aggressive infiltration of local tissues, metastasis to local lymph nodes, and occasionally pulmonary metastasis.[31,45] Moreover, these tumors tend to recur at the excision site.

Ferrets are usually presented with acute onset of preputial swelling or a mass (Fig. 31.10). Preputial tumors are firm on palpation and can reach more than 4 cm in diameter.[18] As part of the overall health screening, perform thoracic radiography and abdominal ultrasonography to look for metastasis and to evaluate the adrenal glands. Adrenal gland disease has been proposed to play a role in the developed of ferret preputial tumors.[6]

Remove adenomas by marginal excision and reconstruct the preputial orifice by using 5-0 suture material. Because complete surgical excision of malignant preputial tumors is difficult, and because of their aggressive nature, remove masses in the preputial region and submit them for histopathologic examination as soon as possible. Surgical excision with wide surgical margins (≥5 mm, but preferably >1 cm) is recommended with partial, or preferably complete (V.J.), penile amputation and diversion of urine flow by perineal urethrostomy (Fig. 31.10).[45] Rotational or advancement grafts may be used if needed. Subsequent radiation therapy and/or chemotherapy may be required, but risk of recurrence remains high.[28]

MISCELLANEOUS SURGICAL PROCEDURES

Anal Sacculectomy

In the United States, anal sacculectomy (descenting) is mainly performed in conjunction with early neutering at ferret breeding farms; however, it may be done at any age. In countries other than the United States, routine anal sacculectomy may be prohibited by governmental regulations. Medical reasons for anal sacculectomy include chronic abscessation and neoplasia.

The anal sac openings are located at the anocutaneous junction at the 4:00 and 8:00 positions. Magnification is of great assistance in locating the anal sac openings and throughout the surgical procedure. Identify the opening of the anal sac and grasp it with fine mosquito forceps. Incise the skin 1 to 2 mm around the anal sac opening with a No. 15 scalpel blade. Use a scraping motion with the blade to remove glandular tissue, skin, and subcutaneous tissue surrounding the duct and sac. Dissection of the gland is initially difficult because of the close association of the surrounding tissue; however, after a few millimeters, a tissue plane exposing the yellow surface of the anal sac will become evident. Continue to dissect the anal sphincter muscle from the anal sac until the entire sac is freed. Ligate or clamp the duct and remove the intact sac. If any of the anal sac tissue remains after surgery, fistulous tracts may develop. If bleeding is observed that does not stop quickly with digital pressure, small blood vessels may need to be ligated or coagulated. Lavage the defect, and either close the opening with a single subcuticular suture using 5-0 synthetic absorbable suture material or leave it open to heal by second intention.

Remnants of anal sacs may be encountered from incomplete resection performed in young ferrets. These remnants may still be secretory, creating a typical strong ferret odor. Alternatively, to reduce body odor, use a GnRH agonist (see Chapter 7).[39]

Minimally Invasive Surgery

Laparoscopy and thoracoscopy are becoming increasingly more common in small animals, including exotic species. Laparoscopy has several advantages over traditional surgery, such as less postoperative pain, a quicker return to activity, less hemorrhage, and reduced tissue trauma.[10] Illumination and magnification provided by the telescope lead to superior visualization of abdominal organs, allowing smaller lesions to be seen more easily. Laparoscopy has a steep learning curve, which may lead to increased surgery and anesthesia time until proficiency is achieved. Because the necessary abdominal insufflation restricts movement of the diaphragm, intubation and ventilation are required, which is often easily accomplished in ferrets. Lift laparoscopy, which involves creating a pneumoperitoneum without insufflation, can be performed without intubation but may not allow the same degree of visualization. Pediatric laparoscopic equipment is readily available, with the 2.7-mm rigid telescope most appropriate for use in ferrets.[41] Refer to Chapter 35 for a detailed discussion of the basic laparoscopy equipment necessary for exotic animals.[11,24] Abdominal exploratory for examination and biopsy of the liver is the most common indication for laparoscopy in ferrets, with examination and biopsy of the kidneys, pancreas, and bladder also possible. Ovariohysterectomy and adrenalectomy may also be accomplished laparoscopically; however, obesity in ferrets makes conversion to an open procedure common, as large amounts of fat obscure organs and obstruct visualization.[12,34]

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Soft Tissue Surgery: Rabbits

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GENERAL PRINCIPLES

Many small animal surgical technique descriptions are based on procedures defined in dogs and cats. However, because of the species-specific anatomy and physiology, additional intrinsic challenges are associated with surgery in rabbits. Risks of anesthetic complications are often higher in rabbits than in dogs and cats.[2] Lack of knowledge and experience with the species on the part of the owners can also lead to unrealistic expectations and complications. Some preoperative clinical signs or postoperative sequelae, such as anorexia, often have minimal impact to surgical recovery and overall prognosis in dogs but can indicate or lead to potential life-threatening problems in rabbits. Postoperative complications like ileus and adhesion formation are also relatively common in rabbits.

General Presurgical Considerations

Before general anesthesia or surgery, each patient should undergo a complete physical examination. A complete blood count and biochemical panel is recommended in most nonelective surgeries. The coagulation status of the patient should be assessed if significant operative bleeding is anticipated and should be prioritized in patients with preexisting liver disease or anemia. Even in apparently clinically normal rabbits, subclinical azotemia and anemia are common. Radiographs are recommended, especially in geriatric rabbits (> 6 years), because silent but significant comorbidities

such as subclinical thoracic masses or other disorders can be found.[43] Stabilizing sick rabbits as much as possible before general anesthesia and surgery is essential to optimizing outcome. Because of their inability to vomit, rabbits do not need to be fasted for hours before general anesthesia, and therefore they do not experience the same risks of aspiration as other species. Monitoring and correcting the body temperature is important; hypothermia is common in debilitated rabbits, but they are also prone to hyperthermia because they do not pant or sweat effectively. [30] Sedation before any stressful intervention is important. In the perioperative period, multimodal pain management using a combination of systemic and local anesthetic drugs that target different steps of the body's pain transmission pathway is essential (see Chapter 37). Perioperative antibiotics are also administered as indicated following same guidelines as in dogs and cats, and with additional consideration for impacts of specific classes of antibiotics in this species.

General Surgical Principles

The surgical site is prepared routinely, with some exceptions. Rabbit skin is very thin and the fur is dense; therefore, clip the fur very carefully to prevent skin damage. A No. 50 clipper blade is ideal. Aseptically prepare the skin in the surgical site with chlorhexidine scrub alternating with alcohol or sterile saline solution.[28] Using excessive amounts of sterile saline solution, alcohol, and chlorhexidine may result in hypothermia.

Because of the elasticity of rabbit skin, the skin incision can be shorter than the body wall incision during abdominal surgeries; however, plan the incision carefully to ensure that a reduced incision length does not compromise operative approach or procedural visualization. Handle the organs gently and examine them in situ without unnecessary manipulation. Always prevent drying of the surface of delicate visceral organs with regular lavage with warm sterile saline solution and by using moistened gauze squares. Rehydrate the gauze squares with additional saline before removing them to avoid visceral surface trauma that could promote postoperative adhesion formation.

General Postoperative Considerations

Fluid therapy, pain management, and nutritional support are essential to reduce the chance of postoperative complications. Pain management usually involves the use of nonsteroidal antiinflammatory drugs or opioids, or both (see Chapter 37). Prokinetics (e.g., metoclopramide, cisapride) and H2-antagonists (e.g., ranitidine) can be used to reduce the incidence of gastric ulcerations and increase gastrointestinal motility.[54] The use of Elizabethan collars to prevent self-trauma to surgical wounds is stressful for rabbits and prevents cecotrophy, which is important for normal gastrointestinal function. If a collar is necessary, preferably use a soft collar. After surgery, monitor the rabbit's appetite, fecal and urine output, heart rate, respiratory rate, and temperature.

SURGERY OF THE INTEGUMENTARY SYSTEM

Removal of Perineal Skin Folds and Inguinal Pouches

Perineal dermatitis that results from urine scald or chronic diarrhea is common. Obesity, urinary tract disease, gastrointestinal disease, and spinal cord disease are often underlying contributing factors. Long-term correction of dermatitis depends on preventing urine contamination of the perineal tissues. In obese rabbits, a large fold of skin and fat may partially cover the genital area, interfering with urination. Alternatively, the rabbit may be unable to rotate its pelvis during urination or defecation to direct the stream of urine caudally, resulting in soiling the skin of the perineum and legs. Several adjunct and salvage procedures can be used to correct these problems[28,38]; however, every effort should be made to correct the underlying cause of the problem before surgery is undertaken.[38] Rabbits have two deep hairless pouches on either side of the genital orifice that contain the inguinal scent glands.[28] Each gland consists of a superficial pale spherical lobe and an adjacent deeper-lying dark brown lobe. Ducts of the gland open into the deep part of the hairless pouch, which fills with plugs of waxy exudates.[51] If the pouches are a contributing source of moisture and bacterial overgrowth, the pouches and adjacent scent glands can be removed in addition to removing extra skin folds.[28]

With the rabbit placed in dorsal recumbency, make a crescent-shaped incison inmmediately around the genital area at the skin fold that is to be removed. If the scent glands need to be removed as well, make two additional incisons over the inguinal pouches extending to the previous incision. Dissect the skin of the pouch and identify and remove the scent glands. Appose the edges of the skin over the pouches and close with an intradermal or simple interrupted pattern. Stretch the skin fold around the genital area to determine how much skin needs to be removed. Remove the excess skin once the edges are apposed without causing too much tension to prevent everting of the urethral opening. Close the skin in an intradermal simple interrupted pattern.[48] After surgery, ensure the rabbit is housed on clean bedding. Administer pain medications and antibiotics as needed if residual bacterial dermatitis is present. Monitor the wound for 3 to 7 days after surgery for uncomplicated procedures.

SURGERY OF THE EYE

Enucleation

Ocular conditions that result in irreversibly blind, painful eyes may require surgical treatment. A blind, painful eye may be associated with exophthalmos from orbital or retrobulbar disease and is especially associated with extension of dental disease. Other possible causes are corneal disease (especially perforated ulcers), full-thickness globe lacerations with extrusion of intraocular contents, chronic uveitis, intraocular tumors, and uncontrolled glaucoma (which may be primary or, more commonly, secondary to other conditions).[15] However, consultation with a veterinary ophthalmologist is warranted before enucleation is chosen as a treatment option.

The rabbit orbit communicates with the contralateral orbit through the optic foramen, an opening of about 5 mm. Within the orbit lies the retrobulbar venous plexus (orbital sinus), which communicates with major veins and the intracranial cavernous sinus. The orbital lacrimal gland is situated caudodorsal to the eyeball.[19] The accessory lacrimal glands (retroorbital, orbital, intraorbital lobes) extend along the caudal and ventral orbital margins and protrude medially into the orbit, with a single excretory duct opening into the lateral edge of the conjunctival sac.[19] The glands of the third eyelid lie against the convex surface of the cartilage (superficial gland or nictitans gland) and rostromedially in the orbit (deep gland or Harderian gland).[19]

With the patient in lateral recumbency, position the head and secure it to the underlying table with the aid of tape and a vacuum beanbag or other padding or supports. Clip the hair in at least a 2- to 3-cm margin around the eyelids. Irrigate the eyeball, conjunctiva, and fornix with dilute (half-strength aqueous) povidone-iodine solution and rinse with sterile saline solution.[15] Do not use povidone-iodine scrub, chlorhexidine scrub, or alcohol even if the prepared eye is being removed, as these could inadvertently damage the other eye.[15]

Because of concern for blood loss, a subconjunctival enucleation instead of transpalpebral eye removal is preferred in most cases because this approach allows dissection closer to the globe and is more likely to avoid larger vascular structures.[15] To facilitate maximal exposure, place an eyelid speculum to retract the eyelids and perform a lateral canthotomy. While grasping the bulbar conjunctiva near the limbus, dissect the conjuntiva to the level of the sclera with tenotomy scissors. Carefully extend the dissection 360 degrees around the globe to avoid possible iatrogenic traction injuries, including the oculocardiac reflex, or damage to the optic chiasm and contralateral optic nerve fibers, which could potentially blind the other eye. Transect the extraocular muscle attachments at their insertions on the globe. Clamp the optic nerve and associated vasculature with a mosquito hemostat a few millimeters posterior to the globe without placing excessive tension on the globe and nerve (a hemoclip or transfixing suture can be placed but is not necessary), and transect these distal to this clamp. Remove the globe from the orbit, transecting any remaining periocular tissue attachments. The orbital venous plexus/sinus integrity is protected to avoid exsanguination; if hemorrhage occurs, several minutes of digital pressure through gauze sponges may be necessary to achieve hemostasis. Remove the eyelid speculum and excise the eyelid margins and palpebral conjunctiva full thickness (≈3 mm back) with tenotomy scissors. Before excision, clamp the third eyelid and associated glands at its base below the gland(s) to reduce hemorrhage, because the glands are intimately associated with and surrounded by the orbital venous plexus. Vascular clips can be placed to reduce intraoperative hemorrhage. Flush the orbit with saline solution pulsed from a syringe and use gentle suction as needed. Close the deepest apposable subcutaneous tissue first, with absorbable 4-0 to 6-0 suture in a simple continuous pattern, and then the skin, with nonabsorbable 4-0 to 6-0 suture in a simple interrupted, cruciate, or simple continuous pattern.[15]

Administer pain medications, and monitor the wound for 3 to 7 days after surgery for uncomplicated procedures. Use antibiotics only when indicated. Hemorrhage, most commonly because of damage to the venous sinus, is one of the most common complications. Infection and abscess formation, as well as orbital cyst formation, can also occur. Wound dehiscence may occur secondary to self-trauma (scratching or rubbing), infection, or poor surgical technique.[15,19]

SURGERY OF THE EAR

Bacterial otitis media and externa are common in rabbits and often refractory to medical management. Several surgical techniques haven been described.[9–11,18,45] Partial ear canal ablation (PECA) or total ear canal ablation (TECA), with or without lateral bulla osteotomy (LBO), is often performed; the choice of procedure depends on the location and extent of disease in the bulla or ear canal in each patient. Unlike TECA procedures commonly performed in dogs, in which the dissection is initiated at the otic canal opening and removes all of the external ear canal cartilage, a PECA leaves the pinna and more distal canal intact. Whereas a TECA may be indicated in rabbits with neoplasms of the ear canal[13] or rarely those with very extensive infectious disease, in our experience, the risks of damage to pinna vascular supply and potential pinna necrosis may be higher with TECA than with PECA. Ventral bulla osteotomy should be performed only when the bullae alone is affected.[13] Resection of the lateral wall of the ear canal is less commonly indicated in rabbits because of anatomic and pathologic characteristics.[13]

The rabbit external ear canal does not exhibit separate vertical and horizontal ear canals as observed in dogs. Instead, multiple cartilaginous plates form the single vertical ear canal. The most proximal (deep) cartilage is the annular cartilage (synonym: cartilaginous acoustic meatus), which forms a ring and arises from the bony acoustic meatus of the bulla. Distal to the annular cartilage are the scutiform and auricular cartilages that form the distal part of the ear canal and the pinna. The tragus, which is the proximal portion of the auricular cartilage, connects to the annular cartilage. The auricular arteries and veins run along the center and margins of the dorsal/medial surface of the pinna.[13] In lop-eared rabbits, the ear pinna and the most distal part of the ear canal are turned ventrally, compressing the ear canal. These anatomic differences predispose lop-eared rabbits to otitis media and externa. The tympanic membrane of rabbits is elliptical and consists of distinct portions, the larger pars tensa located ventrally and the smaller pars flaccida located dorsally.[37] The tympanic bulla is thicker on the lateral and rostral aspects of the bullae and thinner on the ventral, medial, and caudal sides.[11] The facial nerve enters the facial canal on the medial aspect of the bulla and exits the skull immediately caudal to the bulla, through the stylomastoid foramen coursing along the ventral surface of the tympanic bullae.[11] The close proximity of the nerve to the ear canal and bulla can lead to facial nerve paralysis in some cases of severe otitis media.[11]

Partial Ear Canal Ablation

Place the rabbit in lateral recumbency. Make a vertical incision over the proximal ear canal and isolate the canal from the surrounding soft tissue by using blunt and sharp dissection (Fig. 32.1). Transect the canal transversely approximately 2 cm from the external opening, just proximal to the blind-ended tributary canal present in most rabbits. After transection, suture the more distal canal that remains associated with the pinna with absorbable suture in a circumferential or interrupted pattern in such a manner that the otic canal walls are tightly apposed, obstructing the canal lumen, such that ceruminous discharge or other external contaminants cannot leak from the residual canal into the subcutaneous tissues, which would increase risks of postoperative infection/abscessation. Continue dissecting the proximal portion along the external aspect of the cartilaginous canal to the level of the bony acoustic meatus, taking care to stay close to the canal to avoid accidentally injuring the facial nerve, which courses caudal and ventral to the base of the ear canal. Once the canal is isolated, transect it at the level of the bony acoustic meatus and remove it en bloc.[18] Most often, after completion of the PECA, an LBO is performed to provide sufficient access so that all debris can be removed from the middle ear.[13] Copiously lavage the bulla and subcutaneous tissues, using gentle suction to remove debris. If only a PECA is performed, most commonly the surgical site is closed in a routine fashion, using 4–0 or smaller absorbable suture material for the subcutaneous tissue and 4-0 or smaller nonabsorbable suture material for the skin.[13] However, in cases of gross contamination, clinicians may alternatively elect to leave the incision open and manage the site as an open wound.

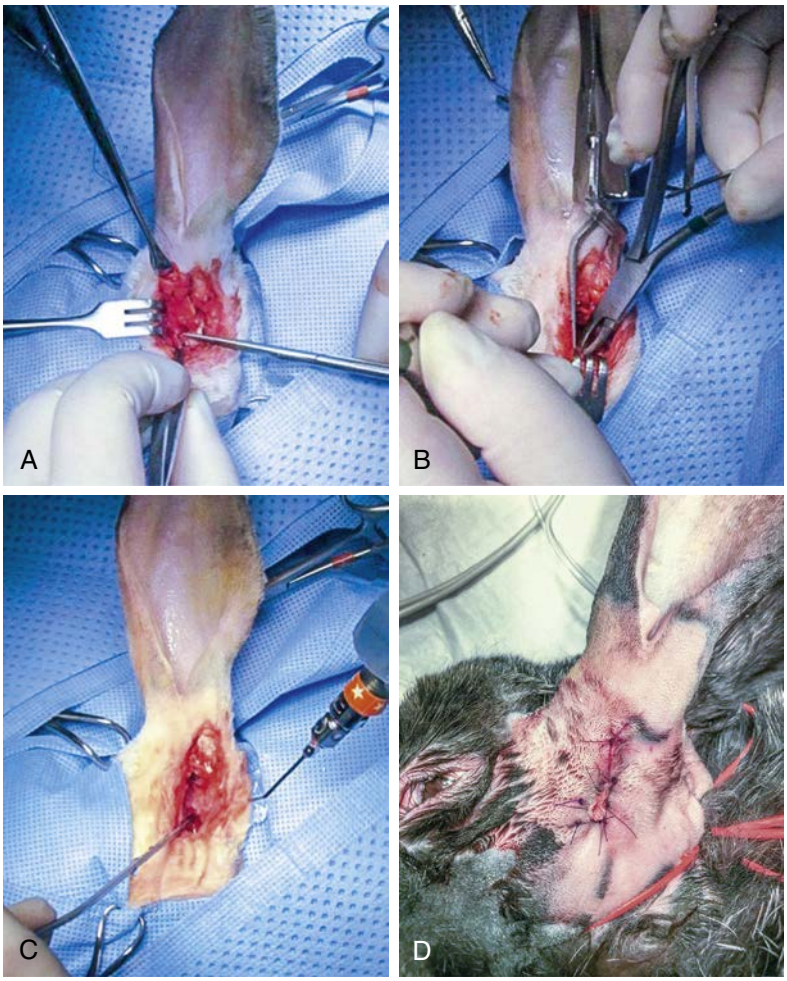


Fig. 32.1 Partial ear canal ablation and lateral bulla osteotomy in a rabbit. (A) A vertical incision is made over the proximal ear canal, and the canal is isolated from the surrounding soft tissue using a combination of blunt and sharp dissection. The proximal canal is transected transversely approximately 2 cm from the ear opening first and then at the level of the bony acoustic meatus. (B) Purulent debris is removed from the bulla and a lateral bulla osteotomy is performed with fine rongeurs. (C) The bulla and subcutaneous tissues are copiously lavaged and the surgical site is closed routinely with 4–0 or smaller absorbable suture material for the subcutaneous tissue and 4–0 or smaller non-absorbable suture material for the skin. (D) In cases of gross contamination, clinicians may alternatively elect to leave the incision open by creating a stoma over the bulla and managing the site as an open wound, packed with umbilical cord tape in the immediate postoperative period and allowing it to heal by second intention,

Total Ear Canal Ablation

With the rabbit in lateral recumbency, make a T-shaped incision over the ear canal. The vertical portion of the incision extends from the midpoint of the horizontal incision down the lateral aspect of the canal. Continue the horizontal incision circumferentially around the external ear canal opening and isolate the ear canal from the surrounding tissue by blunt and sharp dissection, taking care to stay close to the cartilage to avoid accidentally injuring the pinna vasculature or the facial nerve. Remove the external ear canal in its entirety, including the communicating but blind-ended tributary that parallels the canal. Failure to remove all of the canal will leave secretory epithelium in the subcutaneous tissues, placing the patient at higher risk for subsequent development of draining tracts. At the level of the bony acoustic duct, excise the entire cartilaginous canal as for a PECA procedure.[10] As in the case of the PECA, most often after completion of the TECA, a LBO is performed.[13] Close the surgical site in a routine fashion, as with the PECA.[13]

Lateral Bulla Osteotomy

Remove the lateral wall of the acoustic meatus by using small rongeurs or a pneumatic burr to provide adequate access and drainage of the bulla, taking care to avoid the facial nerve that exits the stylomastoid foramen immediately caudal to the acoustic meatus. Carefully curette the bulla to remove any debris, as well as any secretory epithelium, taking care to avoid the oval and round windows on the dorsal medial aspect of the bulla. Submit samples from the bulla and ear canal for bacterial culture and histopathologic examination as indicated. Lavage the site copiously with saline solution and suction gently to remove debris.[18] Some authors suggest packing with antibiotic-impregnated beads because of the high risk of recurrence or abscess formation in cases with severe otitis media.[11] Close the surgical site routinely, using 4-0 or smaller absorbable suture material for the subcutaneous tissue and 4-0 or smaller nonabsorbable suture material for the skin.[18] Some authors suggest creating a stoma over the surgical site in the bulla in severe cases, carefully suturing the skin to the deeper tissues to allow healing by secondary intention.[45] However, suture placement into the deeper subcutaneous tissues may increase risk of traumatizing local neurovascular structures with attendant complications, or may trap infectious material in the folded subcutaneous tissues. In these cases, if flushing is required during the postoperative period, do this very gently with a small catheter to prevent further neurologic deficits.

Ventral Bulla Osteotomy

Position the rabbit in dorsal recumbency with the neck fully extended. Because of the presence of a prominent semicircular mandibular angle in rabbits, the bulla cannot be directly palpated until the overlying muscles are partially dissected. Make a 3- to 5-cm skin incision parallel and medial to the mandible. Continue the incision through the platysma muscle medial to the mandibular salivary gland.[10] Dissect the digastricus muscle from the hyoglossal and styloglosssal muscles, taking care to avoid the hypoglossal nerve coursing lateral to the hyoglossal muscle. Palpate the bulla between the jugular process of the skull and mandibular angle and expose the ventral surface with a Freer periosteal elevator. Enter the bulla with a Steinman pin and hand chuck, and extend the osteotomy site with rongeurs or a pneumatic burr. Carefully curette the bulla to remove any debris, as well as the epithelium lining the middle ear. Collect samples for culture and histopathologic examination as needed, then lavage with sterile saline solution. The same considerations mentioned for the LBO regarding the use of impregnated beads apply in the ventral bulla osteotomy.[10] Close the surgical site routinely, using 4-0 or smaller absorbable suture material for the muscle and subcutaneous tissue and 4-0 or smaller nonabsorbable suture material for the skin.[10]

Postoperative Considerations

After surgery, administer pain medications and, if indicated, systemic antimicrobial therapy. Institute eye lubrication to reduce the risk of exposure keratitis if facial nerve paralysis is present. If the surgical site is left open, gently flush the wound with saline daily until healed. [45] Sutures can be removed at 10 to 14 days after surgery in most cases, even if a temporary stoma over the bulla has been created.

Temporary or permanent vestibular disease (head tilt, rolling, circling, nystagmus) and facial nerve paralysis (lack of palpebral reflex, ipsilateral drooling, facial drooping or contraction) can occur after ear surgery, especially with surgery of the bulla.[9,10,13,45] Owners should be fully educated about the risk of these possible complications. Other possible complications are incisional dehiscence, infection, and partial or complete necrosis of the cartilage or pinna.

SURGERY OF THE ABDOMINAL CAVITY

Exploratory Laparotomy

Exploratory laparotomy is used to diagnose and treat abdominal disease. Abdominal explorations in rabbits may be elected for a wide range of reasons, including acute abdominal pain due to gastrointestinal obstruction, urinary tract blockage, peritonitis, and visceral organ torsion, among other indications.[20,28,29] Abdominal exploratory surgery may be contraindicated if the patient is not systemically stable. However, surgery often cannot be delayed in cases of active bleeding causing life-threatening blood loss, or in cases of septic peritonitis. In these patients, every attempt should be made to stabilize them before general anesthesia, but the timing of surgery is often a judgment call.[20]

Place the patient in dorsal recumbency. Prepare the skin for the longest possible incision, from the caudal half of the thorax to the pelvis, including the inguinal area, to allow the extension of the incision in both directions, if necessary. A Lone-Star Retractor (Cooper Surgical, Trumbull, CT), Balfour retractor, or other visceral retractors can be used to improve exposure of the abdomen (Fig. 32.2).

A ventral midline approach usually is used because it provides excellent bilateral exposure of the peritoneal cavity, and an incision through the linea alba is less painful than a more lateral incision through muscle. The length of the incision is variable: an incision from the xiphoid process to the umbilicus allows for examination of the liver and the stomach. An incision

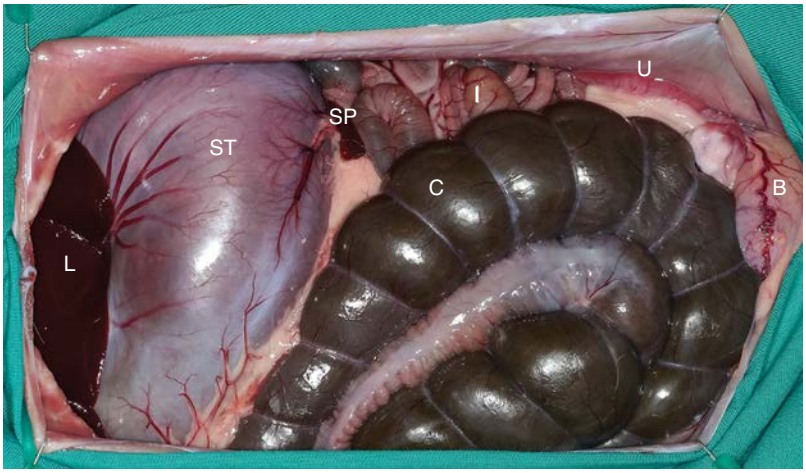


Fig. 32.2 Exploratory laparotomy in the rabbit showing, from left to right, liver *(L)*, stomach *(ST)*, spleen *(SP)*, intestines *(I)* and cecum *(C)*, uterus *(U)*, and bladder *(B)*.

from the umbilicus to the pelvis is useful to assess the bladder and the reproductive tract. Paramedian, flank, and paracostal approaches are infrequently used because they do not provide access to the contralateral side.[28] After making the skin incision, cauterize the cutaneous blood vessels to provide hemostasis and minimize blood loss, and identify the linea alba. Tent the abdominal muscles with forceps away from the viscera and make a small incision in the abdominal cavity through the linea with a scalpel blade. Place the forceps or a finger through the incision, parallel to the line alba, lifting it away and protecting the viscera while the incision is extended cranially, caudally, or both. Place an abdominal retractor and moisten the exposed organs with saline solution regularly during surgery. If peritonitis is present or if the abdominal cavity was contaminated during the procedure, lavage the abdomen copiously with warm saline solution and then suction before closure. Examine the abdominal cavity systematically and perform any necessary interventions. Close the body wall layer with a 4-0 or 3-0 monofilament, slowly absorbable suture material in a simple interrupted or continuous pattern.[40,47] Fast-absorbing suture materials such as chromic gut or polyglicaprone 25 (Monocryl; Johnson and Johnson, Somerville, NJ) are not appropriate for the holding layer of body wall reconstructions because of their relatively rapid loss of in vivo tensile strength.[53] Gut suture also causes the most severe inflammatory reaction compared with other routinely used sutures.[28] Because the primary holding layer of the abdominal wall is the fascia, always incorporate an appropriate amount of fascia in the suture bites. Including the peritoneum in the sutures is controversial. Results of an experimental study in rabbits suggested that direct appositional closure of the peritoneum could reduce adhesion formation,[77] but the real clinical importance in rabbits undergoing laparotomy is unknown. Close the subcutaneous tissue with continuous or interrupted sutures with 4-0 absorbable suture material and close the skin with continuous intradermal (subcuticular) sutures using the same suture material. The use of an Aberdeen knot is preferred by some for ending the suture and to bury the knot under the skin.[28] External skin sutures are rarely indicated, combined with tissue glue if needed. Always apply tissue glue to the external skin and not the subcutaneous tissues to minimize the risk of postoperative foreign body reaction to the glue and possible fistula formation.

Described complications after abdominal surgery are heat loss, anorexia, gastrointestinal stasis, adhesion formation, inadvertent organ penetration, peritonitis, abscessation, wound infection, seroma development, and abdominal wall dehiscence.[20] Peritoneal adhesion formation can interfere with gut motility or bladder function, cause ureteral obstruction, and cause discomfort or pain. Successful long-term treatment of adhesions is difficult. Surgical breakdown can be attempted, but recurrence is common; when possible, conservative management is preferred, but if evidence of obstruction is present, surgery may be indicated. Preventing adhesion formation is critical; always handle the organs gently using atraumatic methods and keep organs moist by using repeating irrigation and wet surgical sponges. Avoid wiping or scrubbing at delicate viscera with sponges, maintain sterile technique, aggressively manage infectious material within the peritoneum, control leakage from hollow organs or abscesses, and avoid any form of chemical irritation (powder from gloves, urine contamination, etc.); these factors will increase risks of adhesion formation.

Inguinal Hernias

Hernias are commonly classified by anatomic location, etiology, reducibility, and contents.[61] Indirect hernias occur when abdominal viscera herniates through the inguinal canal by passing through the lumen of the vaginal process, whereas direct hernias occur when viscera herniate into the inguinal canal adjacent to the normal evagination of the vaginal process. Congenital hernias are developmental and are present since birth, although they may remain undiagnosed until later in life, whereas acquired hernias occur secondary to trauma, failure to heal after prior surgery, or from pathologic changes in collagen formation and metabolism that weaken tissues at the normal neurovascular lacunae.[21] Hernias are reducible if contents of the hernia can be replaced into the cavity and irreducible or incarcerated if contents cannot be replaced. Compromise of the vascular supply to incarcerated hernia contents can lead to tissue

necrosis; these hernias are further classified as strangulated. Incarcerated or strangulated hernia contents may necessitate organ amputation (spleen) or resection and anastomosis (intestines). In rabbits, reports on inguinal herniation are limited to a small case series and a few individual case reports.[26,55,65,72] Inguinal hernias in rabbits commonly involve herniation of the urinary bladder; both direct and indirect types of hernias are described. Males have wide-open inguinal rings throughout life, which may predispose these animals to development of indirect inguinal and scrotal hernias.

For surgical repair, place the patient in dorsal recumbency and make a skin incision in the affected inguinal region and, in the case of scrotal hernias, extend the incision caudally over the distended scrotum.[26,55,72] (Fig. 32.3) Carefully dissect through the subcutaneous tissues to identify the urinary bladder, inguinal ring, pudendal vessels, genitofemoral nerve, and, in males, the vaginal tunic. If a direct hernia is present, incise the hernial sac and retract it away from its contents. The herniated urinary bladder may be decompressed by passing a catheter retrograde through the urethra, or alternatively via cystocentesis, while collecting a sample for urinalysis. Once decompressed, replace the herniated portion of the bladder into the abdominal cavity through the inguinal ring. If the bladder is not easily reduced through the ring, or if other viscera have herniated as well, a concurrent midline caudal abdominal approach is made to assist in repositioning the viscera within the abdomen. If necessary, the inguinal ring opening may be enlarged by sharp incision, taking care not to damage the hernia contents or normal neurovascular structures. A cystopexy can be performed if elected by securing the bladder to the left lateral abdominal wall. After the hernia contents are reduced, excise the redundant hernial sac and oversew the remaining tissue in a simple continuous pattern with 4-0 polydioxanone. Close both inguinal rings and the abdominal wall with 3-0 to 4-0 nonabsorbable suture in a simple interrupted or horizontal mattress pattern. If the rabbit is an intact male, perform an open castration, and suture the tunica closed near the inguinal ring with 3-0 to 4-0 polydioxanone suture (PDS II; Johnson and Johnson) in a simple interrupted pattern. A total scrotal ablation can be performed on the enlarged scrotum to remove redundant tissue.[55]

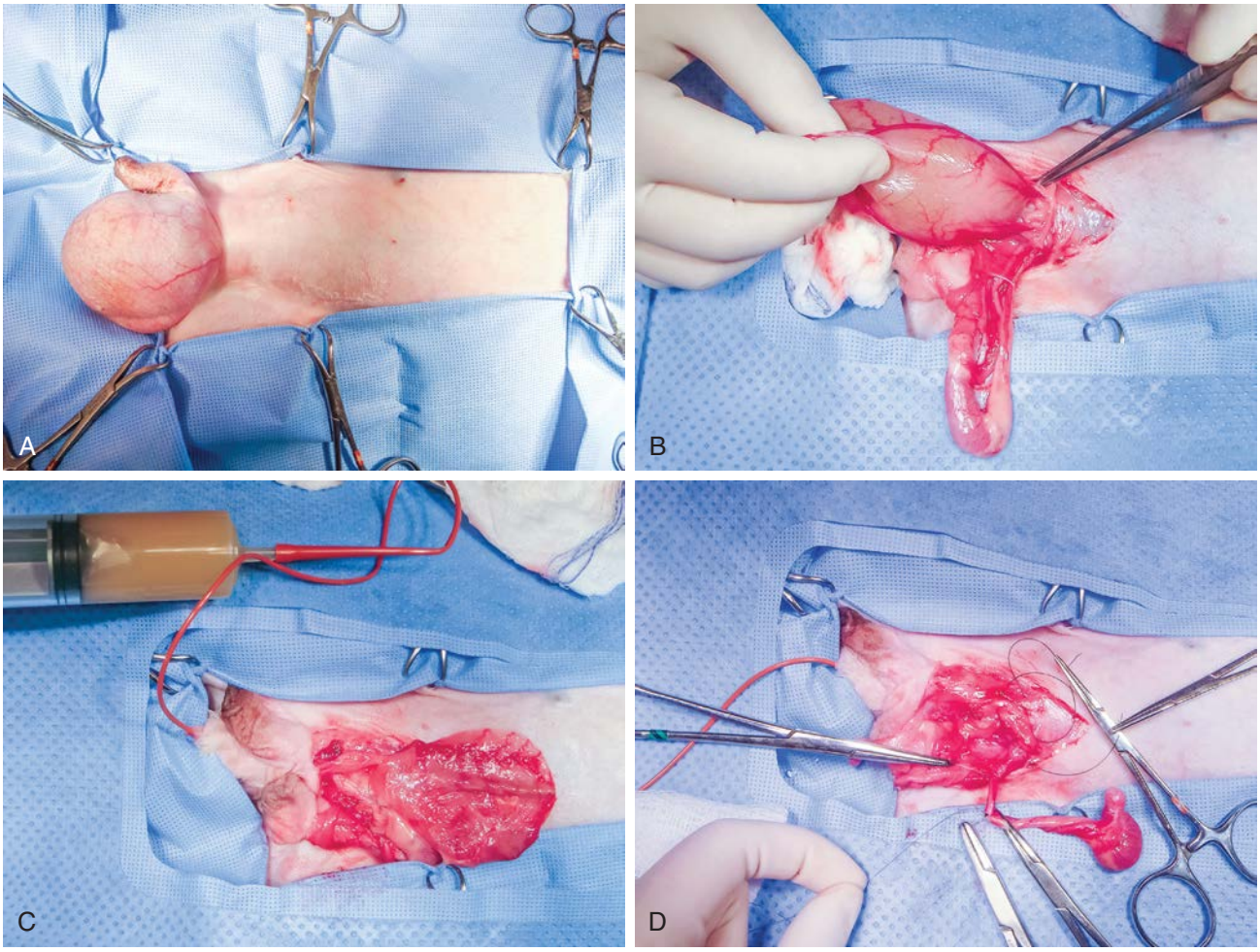


Fig. 32.3 Inguinal scrotal hernia surgery in the rabbit. (A) Inguinal scrotal hernia resulting in an enlarged left hemiscrotal sac. (B) Dissection is performed through the subcutaneous tissue to identify the urinary bladder, inguinal ring, and vaginal tunic containing the spermatic cord. (C) The herniated urinary bladder is decompressed by passing a catheter retrograde through the urethra. (D) The herniated portion of the urinary bladder is replaced into the abdominal cavity through the inguinal ring. An open castration with closure of the inguinal rings and reconstruction of the abdominal wall is performed.

Close the subcutaneous tissues with 3-0 to 4-0 poliglecaprone 25 (Monocryl; Johnson and Johnson) in a simple continuous pattern for the subcutaneous and intradermal layers; use 4-0 nylon in an interrupted pattern if skin sutures are desired.

After surgery, strict cage rest is necessary to prevent breakdown of the inguinal ring reconstruction.[72] Most hernia repairs are clean procedures and do not require antibiotic therapy. The prognosis of uncomplicated, freely reducible inguinal hernias is good unless visceral perforation and leakage of luminal contents from herniated organs occurs. If wound contamination occurs or is suspected, aggressive wound management, bacterial culture, and targeted antimicrobial therapy are important, because surgical site infection is a demonstrated predictor of both recurrence and reoperation.[36] Common postoperative complications are hematoma, seroma, abscessation, inguinal repair breakdown, and hernia recurrence.[72] Always discuss inguinal repair breakdown and hernia recurrence with owners and emphasize the importance of restricting activity to minimize risk.

SURGERY OF THE DIGESTIVE SYSTEM

Surgery of the Stomach

Gastric surgeries are performed in rabbits to remove foreign objects (commonly hairballs) and, less commonly, to treat or diagnose gastric neoplasms or ulcerations that are life threatening or nonresponsive to medical treatment.[14,62] In cases of small intestinal obstruction, the stomach is usually very distended and filled with gas and ingesta, which should be reduced via an orogastric tube before surgery.[35] Generally, gastrotomy is safer and easier to perform than enterotomy because of the small diameter and thin walls of the small intestine in rabbits. Therefore, if possible, small-intestinal foreign objects should be carefully milked back to the stomach and removed via gastrotomy.[34] Complications such as peritonitis, stricture, and obstruction are less common after gastrotomy compared with entrotomy.[28]

For gastrotomy, make a standard midline cranial abdominal approach from the xiphoid process to the umbilicus. Inspect the abdominal organs, locate all foreign objects, evaluate the stomach, and identify any other abnormalities before making a gastric incision. Isolate the stomach from the abdomen with wet, warm laparotomy sponges. If possible, make the gastric incision at a hypovascular area, between the lesser and greater curvatures of the stomach; place stay sutures 1 to 2 cm apart from the ends of the planned incision (Fig. 32.4). Make a full-thickness stab incision through the stomach wall and place the end of the suction tube at the opening to occlude it. Extend the initial incision and use suction to empty the stomach. Remove the foreign object or excise the mass or ulceration and submit tissue for biopsy. Palpate the pylorus to check patency. Close the stomach wall in two layers with 3-0 or 4-0 absorbable, monofilament suture material with a tapered needle. Both the mucosal/submucosal and seromuscularis layers can be closed with a continuous appositional suture pattern. As an alternative, use a 2-layer closure including the serosa, muscularis, and submucosa in the

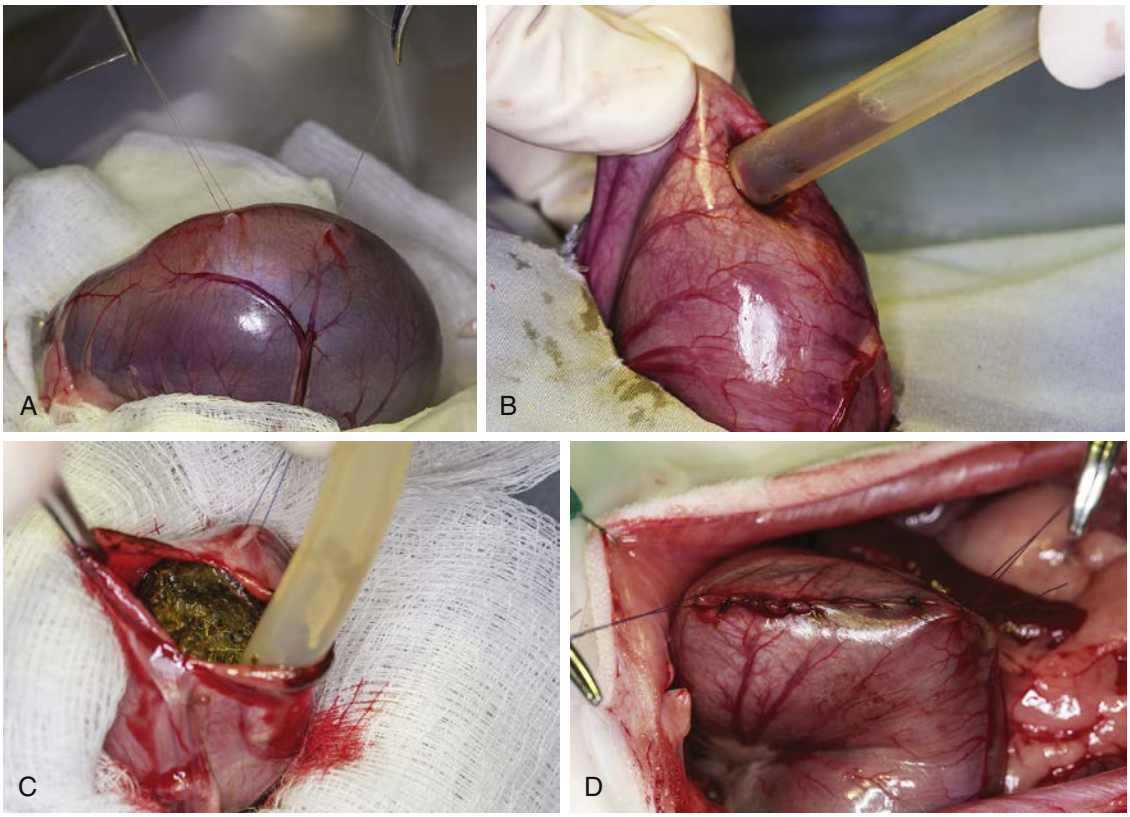


Fig. 32.4 Gastrotomy in the rabbit. (A) Stay sutures are placed in the stomach wall 1 to 2 cm apart from the ends of the planned incision. (B) Suction is used to remove fluid and gas from the stomach. (C) The stab incision is extended and the stomach is emptied. (D) The stomach is closed using a simple continuous pattern.

first layer of closure in a Cushing pattern and then incorporate the serosal and muscularis layers in an inverting pattern (e.g., Cushing or Lembert pattern). Take care to maintain even suture tension between bites, regardless of pattern elected. Lavage the gastrotomy site before removing the laparotomy sponges and replacing the stomach within the abdomen, then copiously lavage the abdominal cavity with warm saline solution. Replace contaminated instruments and gloves with sterile ones and close the abdomen routinely as described for abdominal exploratory surgery.

Postoperative supportive care includes analgesics, fluids, and prokinetic therapy. Antibiotics are indicated if infection is present or abdominal contamination occurs. Fasting is not necessary: feeding small amount of high-fiber herbivore food is recommended 2 hours after recovery to maintain the normal intestinal flora and encourage normal gut motility.[35] Leakage, dehiscence, perforation, peritonitis, ileus, adhesions, shock, and death are possible complications of gastrointestinal surgeries.[20]

Enterotomy and Intestinal Biopsy

The most common indication for enterotomy in rabbits is to remove foreign objects. Intestinal biopsy is performed to collect samples in the diagnosis of neoplasms and other intestinal wall abnormalities.[20,57]

The surgical approach is as described above for exploratory laporatomy. If an intestinal foreign body is found, milk it back to the stomach if possible and then perform gastrotomy. If not possible, milk the object toward the large intestine; once in the large intestine, the rabbit usually can pass the object without any problems. If the object cannot be moved in either direction, perform an enterotomy to remove it. After locating the foreign object or intestinal lesion, exteriorize the abnormal intestine from the abdominal cavity, isolating it from surrounding viscera with moistened gauze sponges. Gently milk the intestinal contents orally and aborally away from the identified segment. To reduce risk of contamination, have an assistant use their index and third fingers to occlude the lumen of the intestine on either side of the segment. Alternatively, small and gentle atraumatic clamps can be used. Make the intestinal incision at the antimesenteric border with a No. 11 or No. 15 scalpel blade at a healthy portion of the intestine, aborad to the obstruction. Extend the incision with the blade or with sharp tissue scissors (Fig. 32.5). The incision should be long enough to remove the object without tearing the tissue. Intestinal biopsy is done by using a 2-mm biopsy punch or by performing a small enterotomy and excising a small segment of the intestinal wall at the enterotomy site. After removing the object or biopsy, clean the intestinal lumen with a swab to reduce contamination. Close the incision with a monofilament absorbable suture (5-0 to 6-0) with a taper needle in a simple interrupted or continuous pattern. If possible, a longitudinal incision is closed transversely to minimize narrowing of small intestinal luminal diameter. If this method is used, place one simple interrupted suture initially at the middle of the wound to transpose the incision to a transverse orientation, placing remaining sutures to either side of the first one. When placing the sutures, the needle may be angled slightly so that the serosal surface of the intestine is engaged farther from the edge than the mucosa; this may help to reposition the everting

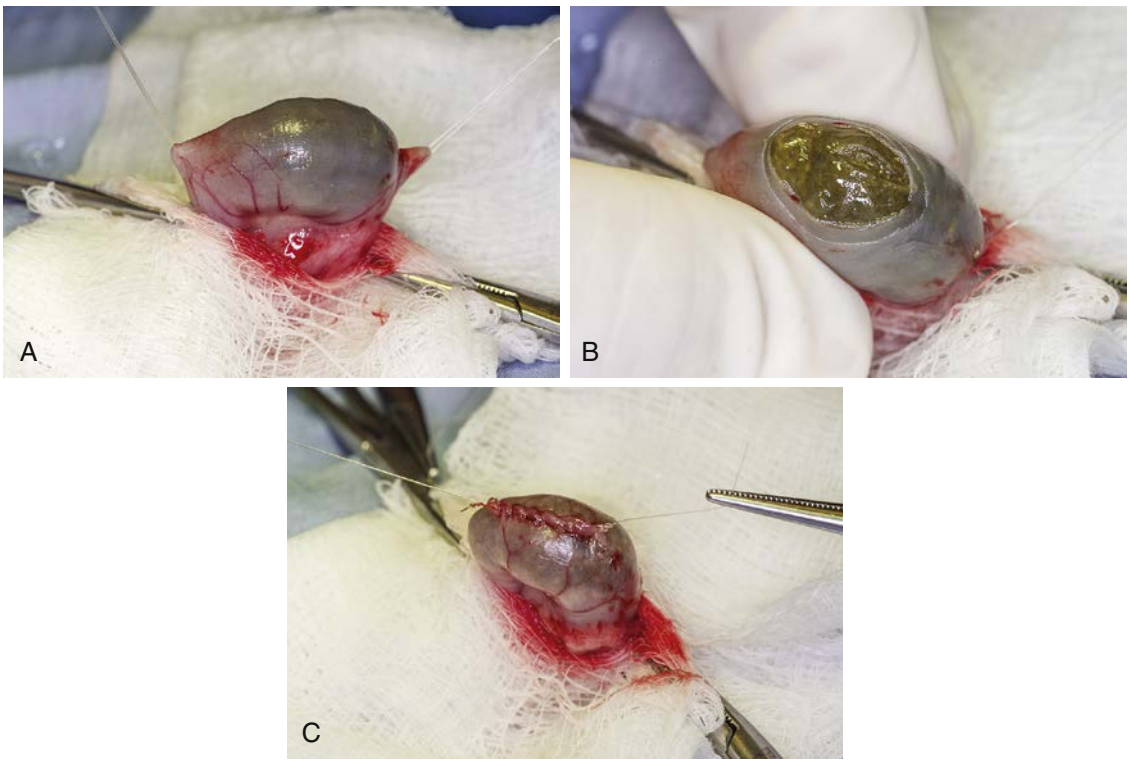


Fig. 32.5 Enterotomy in the rabbit. (A) Stay sutures are used to manipulate the intestine. (B) The incision is made in the antimesenteric side to expose the hairball blocking the intestine. (C) The incision is closed using a simple continuous pattern and the intestine is filled with saline solution to check for leakage.

mucosa into the lumen of the intestine, but if angled too much or with bites that are too large, this may result in tissue inversion and loss of luminal diameter. Alternatively, it may be difficult to find balance between gaping of the incision and the increased risk for fine suture under tension to cut through the wall and result in leakage from around the suture bites. Gently tie the sutures with sufficient tension to provide good apposition but to prevent them from cutting through the intestinal layers. The use of crushing or overtly inverting sutures is not recommended. After closing the enterotomy site, while maintaining obstruction of the lumen orad and aborad to the incision, inject 1 to 2 mL of warm saline solution into the lumen of the intestine with a 25-gauge needle, and check the enterotomy closure for leakage while applying gentle digital pressure. If leakage occurs, place additional sutures. Because of the small size of the omentum in rabbits, omentalization of the surgical site is usually not possible.[28] Lavage the abdomen and suction to remove all free fluid, replace contaminated instruments and gloves, and close the abdomen routinely.

Small-Intestinal Resection and Anastomosis

Intestinal resection is performed to remove an abnormal intestinal segment because of intussusception, perforation, stricture, neoplasm, abscess, and ischemia. Any bowel segment of questionable viability should be resected.[20]

The surgical approach is as described above for enterotomy. If a diseased portion of the intestine is identified, exteriorize and isolate the section, keeping tissues moist. Assess the viability of the intestine and determine the portion that needs to be resected. Ligate and transect the mesenteric vessels that support the intestinal segment to be removed. Gently milk intestinal contents orally and aborally from the segment. Artery forceps can be used to occlude the lumen of the diseased segment, because this portion will be removed. Occlude the lumen of the healthy intestine with a gentle, atraumatic, temporary method, such as with the fingers of an assistant. Sharply transect the intestine between the forceps and the fingers of the assistant. To increase the diameter of the lumen, a short oblique incision is recommended, ensuring that the antimesenteric border is shorter than the mesenteric one. If there is a large difference between the lumen diameters of the two ends, performing an obliquely oriented incision (45–60 degrees) on the narrower bowel segment and a more transverse incision (90 degrees) on the wider bowel segment will help to manage the disparity. Using this method, the oblique incision will widen the lumen of the smaller segment and reduce the luminal diameter disparity between the two ends. Close the anastomosis with 5-0 to 6-0 monofilament, absorbable suture material with a taper needle. It may be helpful to place the first suture at the mesenteric border and the second at 180 degrees from this at the antimesenteric border. After placing the first two sutures, close one side with simple interrupted or simple continuous sutures, then flip the intestine over and close the other side in a similar manner (Fig. 32.5C). If the suture tags are temporarily left long, hemostats can be applied to the tags and used to carefully stretch the incision into a more linear, two-sided orientation during closure, with care taken not to apply so much tension on the anchoring sutures that they pull through the tissue. This orientation makes it easier to space suture bites for a surgeon without technical assistance at surgery. Place the sutures through all layers of the intestinal wall and gently oppose the edges. The use of crushing or overtly inverting sutures is not recommended.

After closure, inspect the sutures and trim suture tags. Fill the lumen of the intestine with warm saline to test for leakage and lumen patency. Close the mesenteric rent with simple continuous sutures using 6-0 monofilament suture material, while taking care not to damage the arcadial vessels around the defect. Lavage the abdomen and gently suction residual fluid, then replace contaminated instruments and gloves and close the abdomen routinely.

SURGERY OF THE PERINEUM, RECTUM, AND ANUS

Resection of Anorectal Masses

Anorectal papillomas are benign, well-differentiated epithelial tumors that arise from the rectal squamous columnar epithelium at the mococutaneous junction of the rectum and anus. The cause remains unknown. Small papillomas will remain within the rectum, whereas larger ones often protrude through the anus.[50]

With the rabbit in dorsal or sternal recumbency, evert the rectal mucosa by placing stay sutures circumferentially around the anus or in the rectal mucosa and use gentle traction to expose the papilloma. Papillomas are often friable with a tendency to bleed, and mucosal attachments vary from stalk-like to broad-based. Excise the papilloma either with sharp dissection of the mucosal/submucosal layer or by using laser or electro/radiosurgery, taking care to avoid penetrating the muscularis layer of the rectum, and ensuring that the entire mass is excised to prevent recurrence. Appose the mucosa in a simple interrupted or simple continuous pattern with 5-0 to 6-0 absorbable suture material on a taper needle.[38]

Resection of small papillomas via a mucosal eversion technique usually does not require hospitalization for postoperative care. Because of the amount of mucosal eversion required to perform resection of large papillomas, pain management with opioid drugs is required. Some straining in the immediate postoperative period is possible, secondary to inflammation and edema, but this is usually self-limiting, and specific therapy is not required.

SURGERY OF THE LIVER

The rabbit liver is composed of a right hepatic lobe, single caudate and quadrate lobes, and a left hepatic lobe separated into lateral and medial parts.[67] The quadrate lobe is narrow and contains the gallbladder fossa. The caudate process of the caudate lobe is highly developed and extends over the right kidney.[67]

Liver disease in rabbits often requires liver biopsy or lobectomy for diagnostic or treatment purposes. Biopsy is indicated to confirm a specific diagnosis such as diffuse or unresectable suspected neoplasia, hepatitis, or hepatic lipidosis,[49] whereas lobectomy is indicated to remove the part of the liver affected by

neoplasia, abscess, or a torsion and may be both therapeutic and diagnostic.[32] Because liver disease is associated with reduced production of clotting factors and dysregulation of coagulation pathways, biopsy may result in hemorrhage that is difficult or impossible to control during surgery. Therefore, assessing the coagulation status of a rabbit with severe liver disease before surgery is important; if a coagulopathy is identified, postpone the intervention if possible. Other contraindications to liver biopsy are moderate to severe anemia or thrombocytopenia, decreased renal function, and poor overall health status for general anesthesia. Contraindications for liver lobectomy include diffuse, disseminated, or metastatic neoplastic disease.[20]

Rabbits do not have a single liver-specific enzyme, but measuring the serum concentrations of liver-associated enzymes, bilirubin, bile acids, and total protein can be useful in defining liver disease (see Chapter 39).[49] In a retrospective study in rabbits with liver lobe torsion, anemia and increased levels of alanine aminotransferase, alkaline phosphatase, and aspartate amino-transferase were the most common hematologic and biochemical abnormalities.[32] Rabbits also commonly had increases in serum urea nitrogen and creatinine levels, suggesting perfusion alterations with prerenal or renal impacts.[32] Diagnostic imaging, especially ultrasonography, is important in diagnosing abnormalities of the liver or biliary system. In the study of rabbits with liver lobe torsion, abdominal radiographs revealed nonspecific findings, whereas abdominal ultrasound confirmed the diagnosis in all cases in which it was performed.[32] Before liver surgery, prophylactic antibiotic therapy targeting aerobic and anaerobic bacteria (e.g., enrofloxacin combined with metronidazole) is recommended.[54] If hepatic function is compromised, the anesthetic protocol should be adjusted accordingly.

Liver Biopsy

The surgical approach is as for exploratory laparotomy. Use retractors to expose the abdominal contents, then systemically examine the abdominal organs. Reflect the omentum and the stomach caudally and inspect the whole liver. Identify the area of interest for biopsy; if the abnormality is diffuse through the liver, choose a marginal area for sampling to reduce the chance of hemorrhage. Always gently handle the biopsy sample to minimize crushing artifact that may impair histologic interpretation and diagnosis.

A skin biopsy punch can be used to take small liver samples. Use Metzenbaum or smaller iris scissors to transect the sample if needed, taking care not to crush it. Place an absorbable gelatin sponge in the biopsy defect to encourage clot formation. If hemorrhage from the sample is excessive, place interrupted capsular sutures with monofilament absorbable suture in a horizontal mattress pattern; however, the capsule does not hold suture well, and suture material may tear through.

Guillotine suture biopsy is useful to sample or remove peripheral liver lesions. A loop of absorbable suture material is placed around a peripheral segment of liver tissue and carefully tightened (see Fig 32.7B), cutting through the liver tissue and ligating the blood vessels and small biliary ducts. Once a ligature has been placed, the isolated hepatic tissue can be excised by transecting the tissue distal to the ligature but leaving a small cuff of liver tissue to prevent the ligature from slipping off.

Total Lobectomy

Torsion of a liver lobe (usually the caudate or the right lateral lobe) is a well-described emergency presentation diagnosed in rabbits.[22,23,66,68,69,75,76,78] The recommended treatment of a liver lobe torsion, whether acute or chronic, is total lobectomy of the affected lobe(s) (Fig. 32.6). When performing total lobectomy, the vessels and bile ducts at the base of the lobe are ligated. Methods of ligation include ligation with monofilament, absorbable suture material with or without the Surgitie instrument (Surgitie Loop with Polysorb Suture; Covidien, Mansfield, MA), vascular clips (e.g., Hemoclips; Teleflex, Wayne, PA), surgical stapling devices, or sealing systems (LigaSure; Medtronic, Minneapolis, MN). Because the blood vessels are very short and broad, double ligation or stapling is recommended. Once ligatures have been securely placed, transect the hepatic tissue distally and remove the lobe.

The most common complication during and after hepatic surgery in rabbits is intraabdominal bleeding. This might result from ligatures slipping off friable hepatic tissue. Take care to ensure a stump of tissue remains distal to the ligature when encircling sutures are used for biopsy or partial hepatectomy.[20] Monitor the patient for signs of bleeding for 24 to 48 hours after surgery.[23]

SURGERY OF THE KIDNEY AND URETER

Urinary tract surgery in rabbits is challenging because of the small size of the patients. Urolithiasis is a common occurrence because of the unique calcium metabolism of rabbits and their high calcium excretion in the urine.[60]

Before surgery, perform diagnostic tests as indicated; generally tests include urinalysis and urine bacterial culture.[33] Radiographs are very useful to diagnose kidney and bladder stones; both plain and contrast radiographs[32] can be used along with ultrasonography.[5] Cystoscopy and laparoscopy may also be used.[33]

Start fluid therapy at maintenance rates (100 mL/kg per day), with increases as necessary to correct any azotemia or dehydration. Closely monitor urine production, body weight, and cardiovascular function to prevent volume overloading, especially at higher fluid rates. Intravenous fluid therapy during surgery at up to 10 mL/kg per hour should be used, again with careful monitoring to prevent fluid overload.[28] For renal procedures, a more cranial abdominal incisional is helpful to provide adequate exposure, with a midline incision initially from just caudal to the sternum down to umbilicus or more caudally, depending on the surgical goals.

Nephroureterectomy

Nephroureterectomy, the surgical removal of a kidney and ureter, is indicated if there is extensive, irreversible renal disease that could worsen the status of the patient if the kidney is left in place. Indications for nephrectomy are severe, irreversible renal trauma, focal neoplasia, abscess, end-stage hydronephrosis, unilateral pyelonephritis that is not responsive to attempts at drainage and antibiotic therapy, urine leakage, or uncontrollable hemorrhage.[20,28,63]

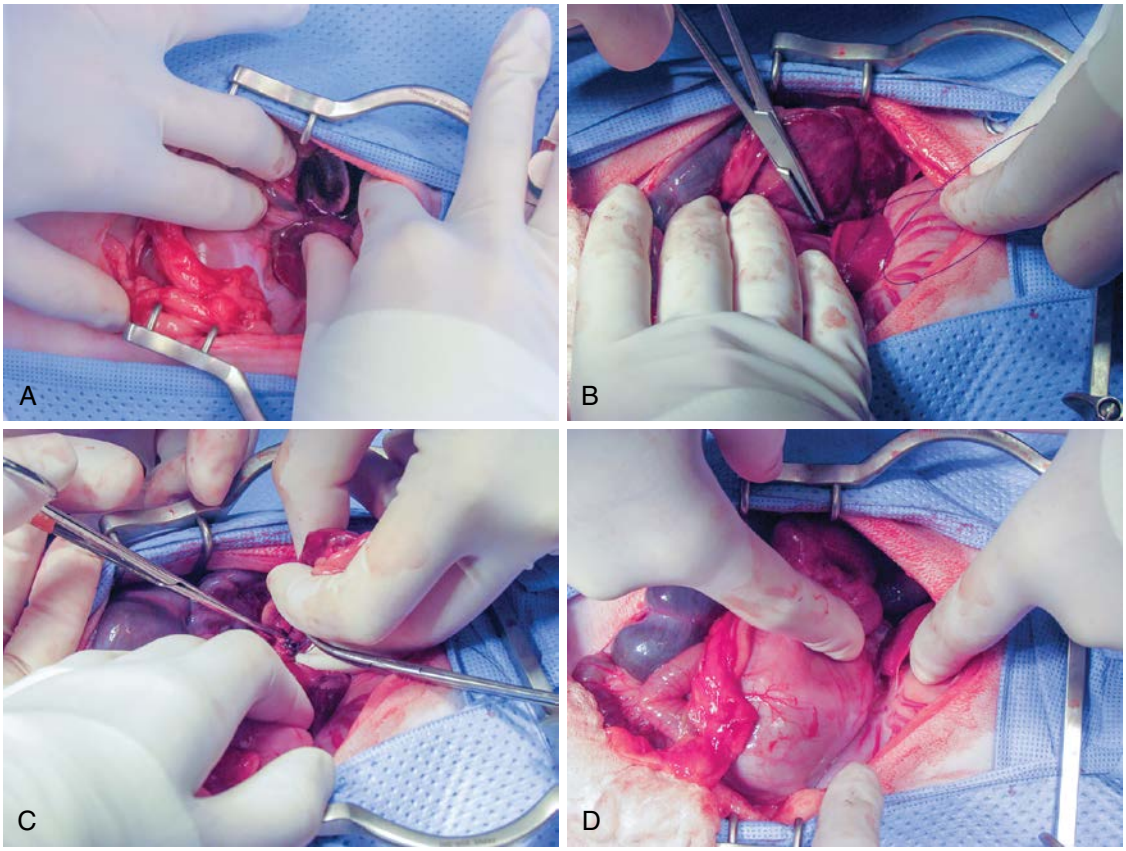


Fig. 32.6 Total liver lobectomy in the rabbit. (A) The liver lobe affected (right liver lobe) is identified. (B) The vessels and bile ducts at the base of the lobe are double ligated with monofilament, absorbable suture material. (C) Once ligatures have been securely placed, the hepatic tissue is transected distally. (D) The stump is checked for bleeding after removal of the liver lobe.

A contraindication to nephrectomy is significantly impaired function of the contralateral kidney. In general, in the absence of neoplasia, nephrectomy is a salvage procedure that should be avoided whenever possible because of the permanent loss of functional renal mass and concerns of future impact of progressive renal disease in the contralateral kidney. Presurgical diagnostic tests are aimed at establishing that renal function in the contralateral kidney is adequate and confirming that disease in the affected kidney is end-stage and refractory to any other alternative therapies.

Dissect the overlying peritoneum from the region of the affected kidney, which is then gently lifted from the retroperitoneum and rotated medially to identify the hilus, ureter, and the renal artery and vein. The renal vessels and the ureters are individually clamped and ligated with 4-0 absorbable suture material, vascular clips, or vascular sealing technology such as a LigaSure. Follow the ureter and gently detach it from the peritoneum along its length. Ligate the distal end of the ureter at the level of its insertion into the urinary bladder, taking care not to crush or kink the trigone or contralateral ureter; transect the ureter above the ligature and remove it. Peritoneal lavage and closure are routine as for other abdominal procedures.

Prolonged fluid therapy is especially necessary after kidney surgery to promote renal perfusion and diuresis that helps to flush luminal blood clots before they become large and risk luminal obstruction. Antibiotics should be considered if bacterial infection is suspected or contamination during surgery has occurred. Monitoring urine output and urinalysis in the postoperative period is very important.

Complications include bleeding, hematuria, and urine leakage into the abdomen (which may trigger peritonitis). In the near term, urine flow blockage may occur due to blood clots, debris, or missed calculi, and, in the longer term, adhesions and strictures. Fluid diuresis during and after surgery and copious flushing will reduce some of these risks.

SURGERY OF THE BLADDER AND URETHRA

Cystotomy and Cystectomy

Indications for cystotomy are removing large bladder stones, removing urethral stones that can be flushed back into the bladder, repair of bladder rupture, biopsy, removal of focal bladder masses, and investigation of chronic, refractory cystitis that is resistant to medical treatment.[20] Small stones and hypercalciuria ("bladder sludge") may be removed from the bladder with catheterization. Cystectomy is the removal of a portion of the bladder to treat bladder neoplasm, benign inflammatory polyps, bladder wall necrosis, and traumatic injuries. It is performed in a similar approach and manner to a cystotomy. About two-thirds of the bladder wall can be removed without interfering

with the function of the bladder if the trigone is left intact and the ureters are not damaged.[20,28]

For bladder surgery only, a caudal laparotomy approach is used, with a midline incision centered in the caudal third of the abdomen, ending approximately 1 cm cranial to the pelvis. Take care not to enter the bladder inadvertently if it is distended when making the incision. A healthy bladder is very thin walled, but the wall may be thickened if chronically inflamed. Identify the bladder, then gently lift and exteriorize it, placing moistened gauze or surgical sponges around it. Place stay sutures in the bladder wall cranial and caudal to the planned incision site. To reduce contamination of the peritoneal cavity with urine, drain the bladder with a syringe and needle or by gentle suction with a Poole tip suction instrument before making the incision. Make the incision through an avascular portion of the bladder wall. A chronically inflamed bladder wall bleeds easily. Removal of the calculi may be aided by using a surgical spoon or forceps. Calculi may be adhered to the inflamed bladder wall or buried deep within mucosal folds; take care not to damage the bladder wall during calculi removal. Calculi also may be found deep in the neck of the bladder, far from the incision site. If calculi are lodged in the urethra, retrograde flushing into the bladder from the external urethral orifice, using a urinary catheter, should be performed to allow calculus removal via the cystotomy. If multiple small bladder or urethral stones are present, a Foley urethral catheter can be placed before surgery to minimize risks of stone migration and missed calculi.

If a urine sample was not collected before incision into the bladder, collect swab samples of the bladder wall for bacterial culture and sensitivity testing. Collect biopsy samples of the bladder wall for histopathologic examination if indicated. Gently flush the bladder cavity with warm saline solution to remove blood clots or debris. Flush the urethra with saline solution, either retrograde or normograde with a sterile catheter inserted through the bladder incision. Close the bladder wall with 4-0 or 5-0 absorbable monofilament suture material in a simple interrupted or continuous appositional suture pattern placed full thickness through the wall. Ideally, the suture material should not enter the bladder lumen; however, ensuring that the submucosal holding layer of the bladder is adequately engaged by suture during closure is equally if not more important and should be prioritized. Monocryl (Ethicon, Somerville, NJ), while not generally considered a durable suture for closure of anatomic holding layers, is often preferred over polydioxanone (PDS; Ethicon) in patients at risk for urinary calculus formation because of the positive and rapid intrinsic healing characteristics of the urinary bladder and the long persistence of polydioxanone, with the concern that retained luminal suture material could contribute to recurrent urolithiasis. However, consider suture choice in the context of whether severe urinary tract infection is present that may delay bladder healing time or speed suture breakdown.[24] Check the bladder incision for leakage by filling the bladder with sterile saline solution.

Complications include rupture or perforation of the overdistended bladder, especially during the abdominal incision, postoperative incisional dehiscence, and uroabdomen. A chronically inflamed bladder may form adhesions to the surrounding intestine or uterus. Ureters can be damaged if the incision is made into the dorsocaudal aspect of the bladder. Other potential complications include persistent hematuria, obstructive luminal blood clots, and postoperative straining secondary to cystitis. Uroliths in the folds of a collapsed bladder wall or in the bladder neck can be missed; therefore, if uroliths are radiopaque, postoperative radiographs are recommended to confirm and document removal of all stones.

Prescrotal Urethrotomy

Prescrotal urethrotomy is the incision into the urethra of the male rabbit, usually to remove urethral calculi causing blockage.[28] Urethral blockage often is initially a medical not a surgical emergency. Hyperkalemia caused by postrenal obstruction may be present. Appropriate fluid therapy and bladder drainage may be needed to correct electrolyte abnormalities to stabilize the rabbit before anesthesia. The most common location of the blockage is the distal urethra. Forced, manual expression of the bladder is not recommended because of the risk of bladder rupture. In some cases, the urolith can be flushed back to the bladder and a cystotomy can be performed instead of urethrotomy. Postoperative stricture formation is a possible complication after urethrotomy, so cystotomy is preferred if possible.

For urethrotomy, surgically prepare the pubic area and the hemiscrotal sacs, reflecting the scrotum to expose the surgical area. Insert a sterile urinary catheter into the urethra to reach the level of the calculus; measuring the length of the catheter to the skin helps to identify the appropriate location of the skin incision. Make a longitudinal incision in the skin on the ventral or lateral side of the penis at the level of the calculus, locating the position of the calculus in the urethra by digital palpation. Next, make a midline longitudinal incision into the urethra directly over the stone and remove the urolith. Advance the catheter to check the patency of the urethra. Control any hemorrhage by digital pressure. Close the urethra by using 5-0 monofilament, absorbable suture material in a continuous suture pattern. Close the subcutis and the skin and remove the catheter. Alternatively, leave a urinary catheter in place for 24 to 48 hours to decrease risk of urethral obstruction in the immediate postoperative period.

Postoperative complications may include obstruction of the urine flow secondary to tissue swelling and temporary luminal compromise, fibrosis, or necrosis. Urine leakage from the wound into the subcutis can lead to infection, irritation, and stricture formation.

SURGERY OF THE REPRODUCTIVE SYSTEM

Ovariohysterectomy and Ovariectomy

The ovaries lie in the dorsal midabdomen close to the kidneys. The cranial end of the ovaries attaches to the fallopian tubes, receiving blood supply from branches of the circumflex renal artery and branches of the ovarian artery. The fallopian (uterine) tubes open into long, convoluted uterine horns, which end in the cervices. The two cervices are attached to each other, and each connects with the vagina. The uterine horns receive blood supply cranially from branches originating in the uterine artery anastomosis with the ovarian artery and caudally from branches

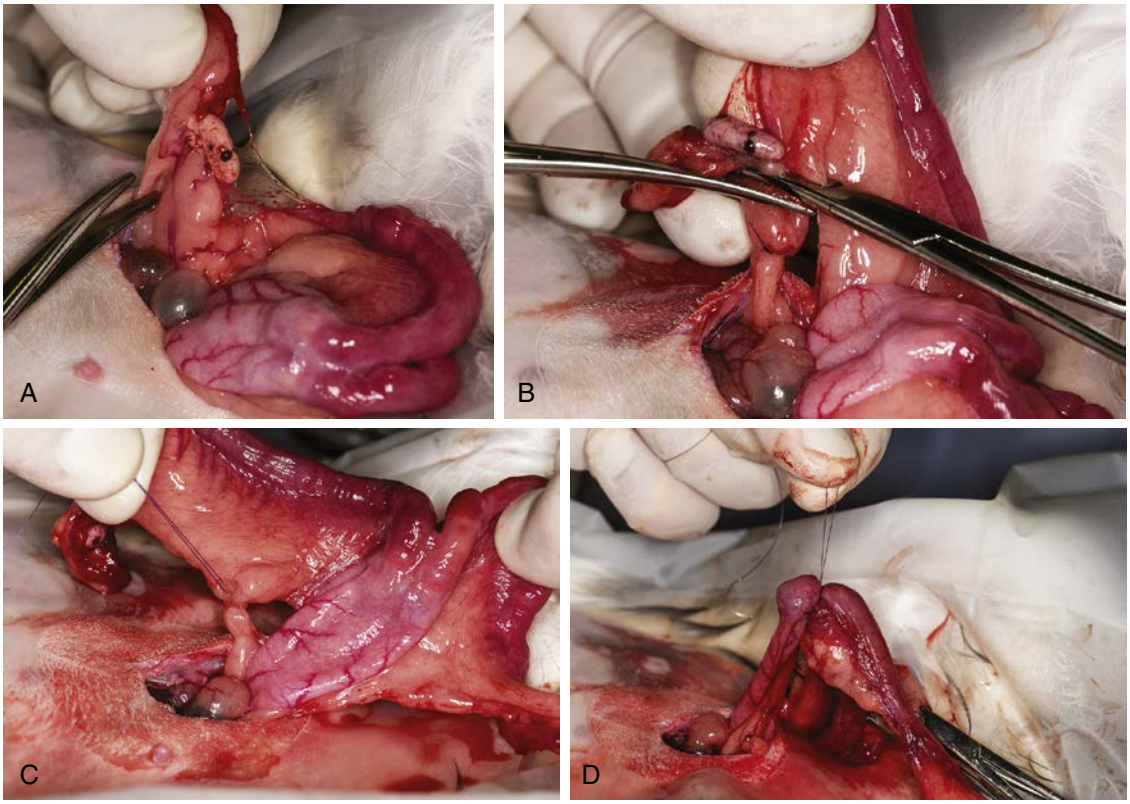


Fig. 32.7 Ovariohysterectomy in the rabbit. (A) The ovarian suspensory ligament can be transected to facilitate the exteriorization of the ovary. (B) The ovarian vascular pedicle is identified and a small fenestration through the mesometrium is made. Then the ovarian vascular pedicle is ligated using standard two- or three-clamp techniques and 3-0 or 4-0 absorbable suture material. (C) The uterine vessels within the mesometrium are identified and a small fenestration through the mesometrium adjacent to the uterine artery is made. Then the mesometrium is ligated with absorbable suture material or vascular clips. (D) The double cervix is clamped together and double ligated as far caudal as possible, using 3-0 or 4-0 synthetic absorbable suture and transected above the second ligature.

from the uterine artery. There is no uterine body. The vagina is long, large, flaccid, unpaired organ. The urinary bladder lays ventral to the vagina, and the urethra opens into the caudoventral vaginal body. The mesometrium is usually filled with fat, especially in overweight rabbits.[31]

Elective ovariohysterectomy is done as a preventive for various conditions, including prevention of pregnancy, false pregnancy, uterine and ovarian neoplasms, hydrometra and pyometra and to reduce the incidence of mammary gland disease or hormonal territorial behavior.[64] Uterine adenocarcinoma is the most common tumor in female rabbits, with an incidence up to 75% in 7-year-old female rabbits.[25,74] Surgery is easier once the rabbit has reached puberty, as the uterus enlarges and the ligaments become slightly looser (between 6 and 9 months); however, surgery is best not delayed too long as significant fat can be laid down around the uterus and ovaries.[28] Ovariohysterectomy may be performed to terminate pregnancy or pseudopregnancy, but if viable young are desired, delay surgery after a doe gives birth until the babies are weaned at 4 to 5 weeks of age.[28] Ovariectomy procedures alone should be limited to young animals between 6 to 12 months of age.[16,28]

Presurgical diagnostic tests are performed based on the animal's age and suspected concurrent diseases. Thoracic radiographs should be evaluated before surgery in older animals, as uterine adenocarcinoma is common and readily metastasizes to the lungs.[28] Contraindications include planned future use as a breeding doe, severe systemic disease, or evidence of metastatic disease.

A standard ventral midline approach to the caudal abdomen is recommended. The initial incision should be approximately 2 to 3 cm long, centered approximately midway between the umbilicus and the pubic symphysis, which usually allows for the complete exteriorization of the uterus while keeping the gastrointestinal tract within the abdomen. If there is a large amount of fat in the mesometrium, the incision may need to be extended. Take care when entering into the abdomen or extending the incision, as the cecum or proximal colon are usually in apposition with the body wall. Carefully locate and exteriorize the uterine horns and follow along to exteriorize the ovaries. The ovarian suspensory ligament can be transected to facilitate exteriorizing the ovary (Fig. 32.7). Identify and double-ligate the ovarian vascular pedicle after making a small fenestration through the mesometrium, using standard two- or three-clamp techniques and 3-0 or 4-0 absorbable monofilament suture material, vascular clips, or vessel-sealing technology (LigaSure). Transect the pedicle above the second ligature and check for hemorrhage before returning the pedicle to the abdomen. Check the ovary

to ensure all ovarian tissue has been removed. Identify the uterine vessels within the mesometrium; the fat may be profuse and visually obscure the vessels. After making a small fenestration through the mesometrium adjacent to the uterine artery, ligate the artery with absorbable suture material or vascular clips. Clamp the double cervix together and double ligate it as far caudally as possible with 3-0 or 4-0 synthetic absorbable suture and transect it above the second ligature. If the uterine horns or the cervices appear diseased, all tissue should be removed and the transection performed at the cranial vagina. Because the vagina is not sterile and sometimes filled with urine, take particular care to close the lumen after transection. Laparoscopic and laparoscopic-assisted approaches to ovariectomy and ovariohysterectomy have also been described in rabbits.[17,59]

Complications in the immediate postoperative period include gastrointestinal stasis, wound healing complications, and self-inflicted wound trauma. Longer-term problems include adhesion formation and colonic extraluminal obstruction.[27] Transection and ligation of the vagina can result in urine leakage into the abdomen and could cause local peritonitis and adhesions.[31]

Orchiectomy (Castration)

The testes descend to the hemiscrotal sacs as early as 10 weeks of age.[31] The testes are elongated with prominent epididymis in the caudal pole. The inguinal canal remains open throughout life, and the testicles freely move from the hemiscrotal sacs in to the abdominal cavity.

The indications for castration of male rabbits are to prevent breeding, prevent testicular neoplasia, and to reduce aggression, sexual behavior, and urine marking, particularly if done before full sexual development.[1,46,64,71] Rabbits can be castrated as soon as testicles are palpable within the hemiscrotal sacs, which can be as early as 10 weeks of age.[28]

For any castration approach, place the rabbit in dorsal recumbency and clip the prescrotal area, hemiscrotal sacs, and prepuce, taking care not to traumatize the delicate skin. A local anesthetic can be injected subcutaneously at the incision site, and testicular blocks are performed. If the testes are withdrawn into the abdomen before surgery, gentle manual pressure on either side of the caudal abdomen should cause each testicle to return to the scrotum.

The surgical approach may be scrotal, prescrotal, or abdominal.[7,52] Although the scrotal approach is technically easier, it requires two incisions, the scrotal skin is easily irritated during surgical preparation, and contamination of the wounds through cage bedding is possible. The prescrotal approach requires a single incision and may have less postoperative complications than a scrotal approach.[17a] Sterile preparation of the surgical site is also easier compared with the scrotal approach. The abdominal approach requires entering the abdominal cavity, with the associated increase in operative morbidity, and should be reserved for repair of inguinal or hemiscrotal herniation or treatment of true cryptorchism.[7] Regardless of approach, orchiectomy in rabbits should always be performed closed or in an open-to-closed manner to prevent herniation of the intestine or urinary bladder through the open inguinal canals.

Scrotal Approach

For the closed technique, make a 1- to 2-cm scrotal skin incision on the ventral aspect of the testicle without incising the vaginal tunic. Free the testicle from the scrotal skin with blunt dissection. Exteriorize the testicle completely after carefully tearing the attachment between the caudal end of the vaginal tunic and the scrotal skin. Clamp the spermatic cord twice with hemostats, distal to the inguinal canal. Ligate each clamped site firmly in the crushed tissue with 3-0 or 4-0 synthetic monofilament absorbable suture, thus ligating the vessels and vas deferens within the vaginal tunic and closing the inguinal canal. Transect the vessels, vas deferens, and vaginal tunic above the ligature and remove the testicle; then, check the ligatures for hemorrhage. Repeat the procedure in the other testicle.[7] For the open-to-closed technique, make a 1- to 2-cm scrotal skin incision on the ventral aspect of the testicle, through the scrotal skin, incising the vaginal tunic (Fig. 32.8). Exteriorize the testicle and identify the vascular cord and ductus deferens. Detach the caudal attachment of the tail of the epididymis from the scrotum and clamp the vaginal tunic with hemostats. Separate and ligate the vascular cord and ductus deferens with two ligatures each using 3-0 or 4-0 absorbable monofilament sutures or vascular clips and transect them above the sutures. Check the ligatures for hemorrhage and replace the stump within the vaginal tunic. Close the vaginal tunic with a ligature using 3-0 or 4-0 absorbable monofilament sutures. No skin sutures are required and are better avoided because they may stimulate self-trauma in the case of the rabbit; tissue glue may be used if necessary.[7]

Prescrotal Approach

Make a 1- to 2-cm single midline prescrotal incision. Bluntly dissect the subcutaneous tissue and inguinal fascia and identify the spermatic cord caudal to where it enters the abdomen through the inguinal canal. This can be difficult in mature rabbits with abundant subcutaneous fat. Massaging the testicles back and forth from the hemiscrotal sac to the abdomen can help to visually identify the spermatic cord as the testicle passes through the transparent vaginal tunica. For the closed technique, gently retract the spermatic cord caudally while the testicle is pushed out through the incision and exteriorized with blunt dissection. Free the vaginal tunic from the parietal attachments of the scrotum, which inverts the scrotal sac. Ligate the spermatic cord containing ductus deferens and blood vessels as described in the scrotal approach, transecting it distally and checking for hemorrhage. Use a hemostat to replace the inverted scrotal sac. Repeat the procedure on the other side and close the incision routinely.[7]

For the open-to-closed technique, exteriorize the spermatic cord and place a loose suture around it to secure it. Incise the vaginal tunic with blunt scissors to prevent iatrogenic damage to the vessels of the spermatic cord. Exteriorize the testicle through the incision, and gently dissect the ligament between the hemiscrotal sac and the tail of the epididymis and free the testicle from the hemiscrotal sac. Invert the hemiscrotal sac again and replace it with forceps, and suture the spermatic cord and vessels as described in the scrotal approach. The remaining suture used to pass around the vaginal process is tied securely

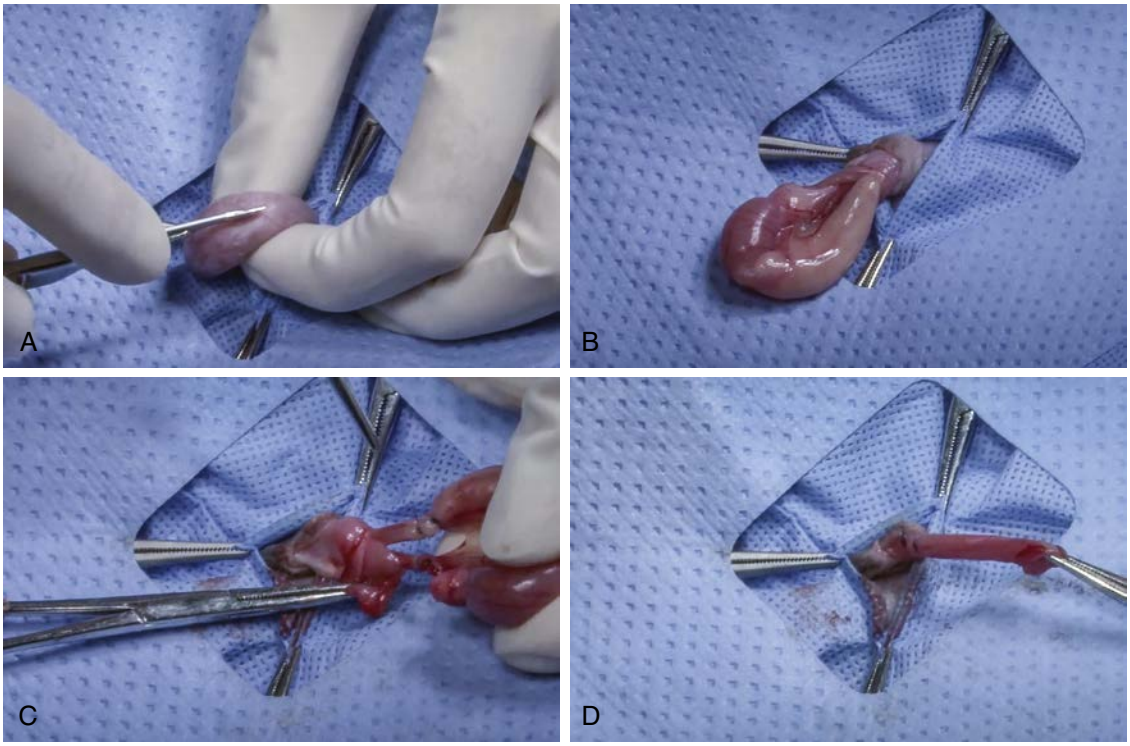


Fig. 32.8 Scrotal castration in the rabbit. (A) For the open-to-closed technique make a 1- to 2-cm scrotal skin incision on the ventral aspect of the testicle incising the vaginal tunic. (B) Exteriorize the testis and identify the vascular cord and ductus deferens. (C) Detach the caudal attachment of the tail of the epididymis from the scrotum and clamp the vaginal tunic with hemostats. Then separate and ligate the vascular cord and ductus deferens with two ligatures each using 3-0 or 4-0 absorbable monofilament sutures or vascular clips and transect them above the sutures. (D) Check the ligatures for hemorrhage and replace the stump within the vaginal tunic. Close the vaginal tunic with a ligature around it using 3-0 or 4-0 absorbable monofilament sutures. Tissue glue may be used if necessary to appose the skin incision.

proximal to the incision to close the vaginal process. Repeat the procedure on the other side, and close the skin incision routinely.[7]

Possible complications of castration are postoperative swelling and edema of the scrotal sacs, infection of the surgical site, and herniation of the abdominal organs if the inguinal ring is not closed effectively during the open-to-close technique. If herniation occurs, strangulation of the organ (e.g., intestine) can lead to infarction, obstruction, and shock if the condition is not recognized and treated promptly.[31]

SURGERY OF THE THORACIC CAVITY

The thoracic cavity of rabbit is much smaller in relation to the abdominal cavity than in dogs and cats, making surgical interventions challenging.[39] Indications for thoracotomy in rabbits are removal of thoracic masses (e.g., thymoma) and foreign objects and lung lobectomy in the case of primary lung neoplasms, lung abscesses, or lung lobe torsion.[20]

In addition to routine blood tests and orthogonal radiographs, presurgical diagnostic tests for thoracic and lower respiratory disorders may include advanced diagnostic imaging (especially computed tomography), fine-needle aspiration and cytologic examination, bacterial culture and susceptibility testing, bronchoalveolar lavage, and tracheoscopsy and/or bronchoscopy. Intermediate positive-pressure ventilation (IPPV) is required for thoracotomy procedures. To ventilate the patient during the thoracotomy, an endotracheal tube must be placed and sealed and either manual or mechanical ventilation performed.[12] Often specialized surgical instrumentation is needed for successful thoracic interventions.

Thymoma Removal Via Median Sternotomy

The thymus is found in the mediastinum, cranioventral to the heart, and in rabbits it does not involute but persists for life.[41] Thymomas are the most common mediastinal tumors in rabbits (see Chapter 20).[56] On radiographs, a thymoma appears as a large soft tissue mass in the cranial thorax dorsally displacing the trachea. Thymomas are usually histologically benign, rarely metastasize, but have a tendency to recur after incomplete removal. Thymomas are usually not considered classically invasive but can be adhered to the pericardium.[28,42] Thymic carcinomas with metastatic tendency are rare.[73] The perioperative mortality rate in rabbits after surgical removal of thymomas can be high, and radiation therapy is an alternative therapy. In one case series, five of nine (55%) rabbits died within 3 days of surgery, with a wide range of survival times reported, from 0 to 955 days (median 3 days).[42]

Midline sternotomy is recommended for thymoma removal to allow access to both sides of the thoracic cavity.[12] Place the

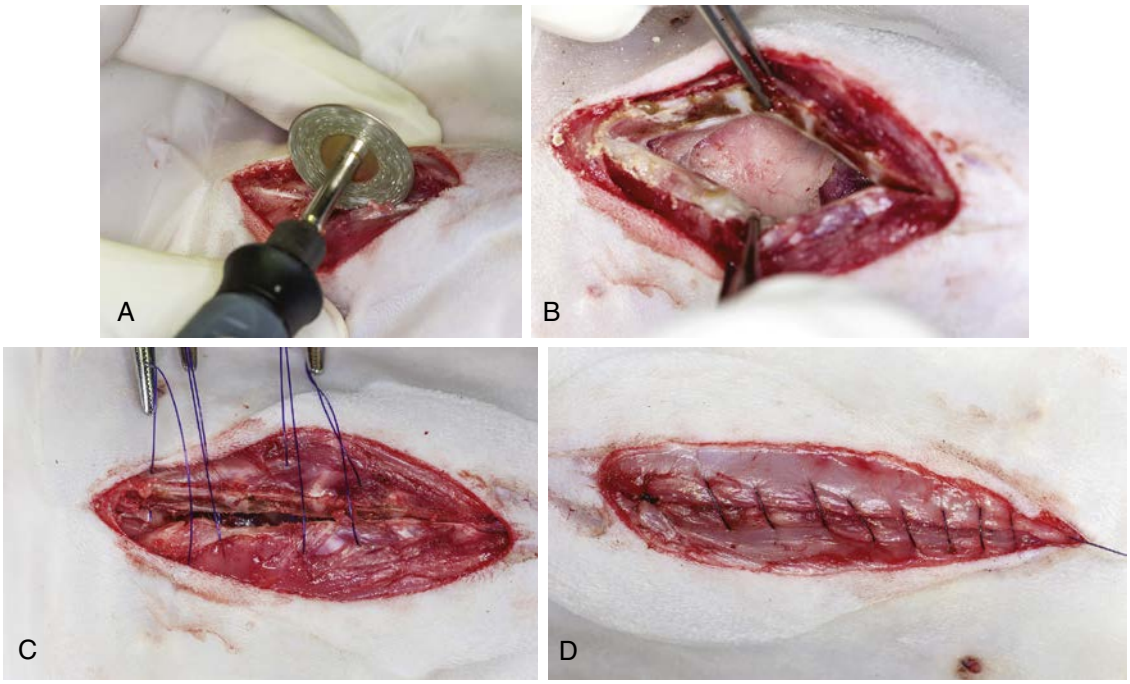


Fig. 32.9 Thoracotomy in the rabbit. (A) A midline skin incision is made, and the exposed sternum is cut on midline with a cutting disk attached to a rotary tool. (B) Large amounts of fat can be found in the thorax, even in rabbits in normal body condition. (C) Appose the sternabrae with simple interrupted sutures by using preplaced monofilament suture placed circumferentially around the sternabrae. (D) Closure of the median sternotomy wound.

rabbit in dorsal recumbency and shave and aseptically prepare the skin from the neck to the cranial portion of the abdomen. Make a midline skin incision from 2 to 3 cm cranial to the manubrium to the xiphoid process (Fig. 32.9). Remaining on midline will allow dissection between muscle layers. If necessary, separate the sternocephalicus and sternohyoideus muscles to expose the manubrium. Cut the exposed sternum along the midline with an oscillating saw or diamond-cutting disk attached to a rotary tool. After accessing the thoracic cavity, start IPPV, being careful to prevent overinflation of the lungs. After osteotomizing the first few sternebrae, place moistened surgical sponges along the edges of the sternotomy site and use a retractor to stabilize the thorax and facilitate the careful transection of the remaining sternebrae. Ideally, a sternebra at each end of the sternotomy (two total) should be left intact to stabilize the thorax during recovery. If additional access is desired, a minimum of one total sternebra at either the cranial or caudal end may be left intact. If the goal of the sternotomy is to explore the caudal half of the thorax, then the manubrium should be left intact and the last sternebrae can be cut. Identify the thymic mass and bluntly dissect it from the surrounding tissue. Large amounts of fat can be found in the thorax, even in rabbits in normal body condition. At the thoracic inlet, exercise caution when dissecting the mass from the jugular and subclavian veins and from the carotid and subclavian arteries. After removing the mass, flush the thorax with warm saline solution and suction to remove any blood clots and debris.

An indwelling thoracic drain is placed if ongoing fluid or air accumulation into the thorax is expected. Appose the sternebrae with simple interrupted sutures using preplaced monofilament material placed circumferentially around the sternabrae. Close the muscle, subcutaneous, and skin layers routinely. Remove the excess air from the thoracic cavity and inflate the lungs using the chest drain, or leave a temporary, small red rubber tube in the chest during closure for immediate post-op evacuation. The tube is left in place until the rabbit is awake and there is no loss of negative pressure for at least two of the subsequent checks.

Patients must be closely observed in the postoperative period. After thoracic surgery, the rabbit should receive supplemental oxygen and must be closely observed. Radiographs may be needed to assess for persistent pleural fluid, pneumothorax, atelectasis, or postoperative aspiration pneumonia. The chest drain is used to remove air and fluid as needed after surgery. Manage postoperative pain with nonsteroidal antiinflammatory drugs, opioid drugs, and local anesthetic drugs diluted with saline solution and instilled into the thoracic cavity while the chest drain is in place (e.g., constant-rate infusion). Administer antibiotics, fluid therapy, and supportive feeding as needed.

This a stressful surgery for rabbits. Most complications occur during and up until 10 days after surgery. The most common complication after thoracotomy is acute perioperative death.[42] This may be related to pain, stress, hemorrhage, or anesthetic complications.

SURGERY OF THE UPPER RESPIRATORY SYSTEM

Rhinotomy and Rhinostomy

Disease of the upper airways, specifically chronic rhinitis, is common in rabbits and is particularly debilitating in this

obligate nasal-breathing species. Because of the close anatomic relationship of dental structures with the nasal and paranasal cavities, severe or end-stage dental disease can indirectly affect nasal structures. Diagnostic imaging provides information about the extent of the disease and guides the surgical approach. Surgical treatment might be indicated in severe cases of chronic rhinitis and usually involves rhinotomy or rhinostomy (see also Chapter 15). Rhinotomy provides access to the nasal cavity through bone incision (osteotomy), with the intention to reconstruct and close immediately after surgery. Rhinostomy is used to describe the same, but with the intent of second-intention closure or purposely leaving it permanently open.

The nasal cavities of rabbits are separated by the longitudinal septum and contain the paired dorsal, middle, and ventral nasal conchae, also called nasal turbinates owing to the presence of highly convoluted cartilaginous membranes covered by mucosa, and the third and fourth endoturbinates.[58] The paranasal cavities of rabbits are represented by the paired dorsal conchal, sphenoidal, and maxillary sinus.[8] The maxillary sinus is the largest, ventral to the dorsal conchal sinus, lateral to the nasal cavity, and divided into a dorsal and a ventral recess that connect caudally by a large opening. The maxillary sinus is connected to the dorsal conchal sinus through a large opening in the rostral part of the dorsal maxillary recess and to the nasal cavity with a common slit-like opening with the dorsal conchal sinus. The dorsal conchal sinus is situated dorsally in the middle third of the nasal cavity. The sphenoidal sinus is the most caudally located, and connects to the middle nasal meatus through a slit-like rostral opening.[8] The dome of the alveolar bulla (the reserve crown and apices of the third premolar and the three molar teeth) is caudoventrally adjacent to the orbital fossa and craniomedially adjacent to the lacrimal bone. Cranially, the alveolar bulla is in close proximity to the maxillary sinus.[4] The surgical procedure can be unilateral or bilateral, depending on the specific case presentation and severity and extent of disease.

For the dorsal approach to the dorsal conchal sinus, position the rabbit in ventral recumbency with the nose pointing down. Identify the surgical site just caudal to the midpoint of the imaginary midline from the level of the medial canthi to the rostral margin of the nasal bone.[31] Incise the skin over the surgical site in the posterior rostral plane and, using a trephine or a dental bur, create an opening into the sinus, which can be enlarged as needed. The size of the opening depends on the surgical goal (rhinoscopy, flushing, or extensive debridement) and outcome desired (rhinotomy or rhinostomy). Collect samples for cytologic examination and bacterial culture. Irrigate the sinus with saline solution combined with suction. Use a surgical probe to explore the surgical site atraumatically. If any necrotic bone is encountered, it should be removed. A temporary catheter can be placed in the sinus through a separate incision and sutured to the skin at different positions for continuous flushing of the recess, but the sinus needs to drain into the medial meatus for this to be effective. If a bone flap is created for the opening, it may or may not be replaced. The skin is closed (rhinotomy) or left open (rhinostomy) as indicated.[6,9,44]

For the lateral approach to the maxillary recesses (lateral rhinostomy or pararhinotomy), place the rabbit in lateral recumbency on a tilted table with the head lowest. Approach the dorsal recess dorsal to an imaginary line from the medial canthus to the commissure of the nose, rostral to the rim of the bony orbit. The ventral recess is approached rostral to the facial tuberosity and just above the line of the diastema to avoid the infraorbital neurovascular bundle located dorsally.[31] Incise the skin over the surgical site in the posterior rostral plane and, using a threphine or a dental bur, create an opening into the recess, which can be enlarged as needed (Fig. 32.10). Collect samples for cytologic examination and bacterial culture. If any necrotic bone is encountered, it should be removed. If an antrostomy is performed creating a permanent opening with the middle meatus or the integrity of the sinuses has been disrupted, a catheter should be able to be passed through the sinus into the nasal meatus, indicating permanent drainage pathway from the maxillary sinus into the nasal meatus.[70] The skin is closed routinely or left open to create a stoma in the surgical site.[6,9,79] If a catheter is left in the recesses, flushing is continued for a few days until no inflammatory material is flushed.[44]

For the ventral approach to the nasopharynx, in lateral or sternal recumbency, intraorally incise the oral mucosa midline on the hard palate through the palatine fissure.[3] Rigid endoscopy can be particularly useful in this approach for evaluation of the cranial nasopharynx. Collect samples, remove purulent material and close the mucosa as described in the previous approaches.

SURGERY OF THE LOWER RESPIRATORY SYSTEM

Lung Lobectomy Via Lateral Intercostal Thoracotomy

Lateral intercostal thoracotomy is performed to remove lateralized thoracic abscesses, a torsed lung lobe, or a primary lung neoplasm. For this procedure, place the rabbit in lateral recumbency, with the affected side facing the surgeon, and prepare the area for surgery similarly to median sternotomy. The exact surgical approach will be determined by the specific lesion location, but most approaches are centered around the fifth intercostal space, which allows good exploration of the thoracic cavity and access to the pulmonary hilus. Make a dorsoventral skin incision at the caudodorsal border of the scapula. Incise the latissimus dorsi muscle from ventral to dorsal. Identify the thoracic inlet and the first rib by palpation beneath the latissimus dorsi muscle. Separate the serratus ventralis muscle and transect the scalenus muscle along the fifth rib. Transect the intercostal muscles and spread the ribs with a retractor. Start IPPV immediately after accessing the thoracic cavity. For lung lobectomy, lift the affected lung lobe from the thoracic cavity and ligate the very short bronchus and vessels with absorbable suture material or with vascular clips. Remove the lobe and check the bronchus for air leakage by filling the thoracic cavity with warmed sterile saline solution and watching for bubbles from the transected bronchus during several cycles of respiration. Remove the saline solution from the thorax with suction. Place a thoracic drain to allow evacuation of excess air and fluid from the chest after closure and during recovery. Close the thoracic wall by bringing

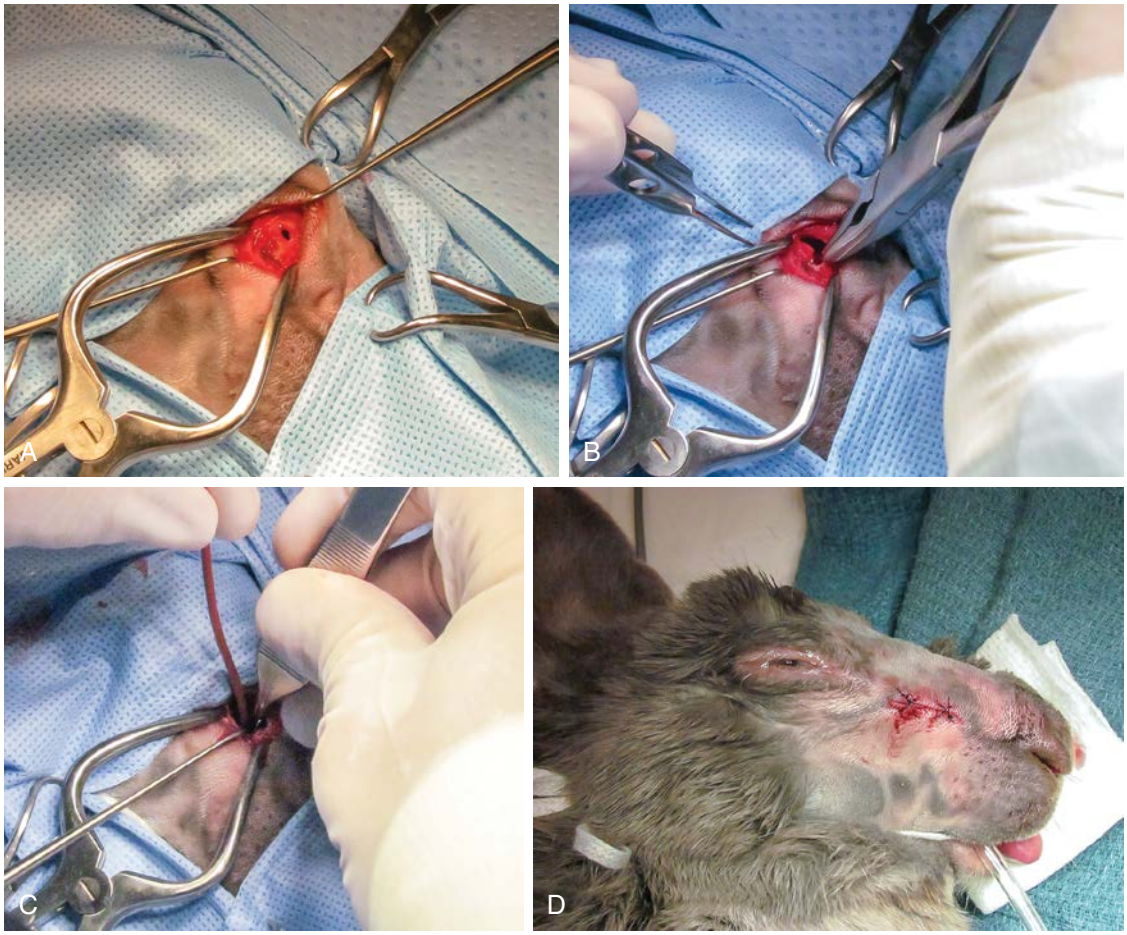


Fig. 32.10 Lateral rhinotomy or pararhinotomy in the rabbit. (A) The skin is incised over the surgical site in the posterior rostral plane and, using a threphine or a dental bur, an opening into the recess is created that can be enlarged as needed. (B) If any necrotic bone is encountered, it should be removed and the recess is flushed copiously. (C) If an antrostomy is performed into the nasal meatus, a catheter can be used to check the patency. (D) The skin closed primarily or left open to heal by secondary intention.

the ribs back into position (but not overlapped) using preplaced absorbable monofilament sutures encircling the ribs cranially and caudally from the wound. Reconstruct the muscles with long-acting absorbable suture. Postoperative care is similar to that for median sternotomy.

Thoracostomy Tube (Chest Drain Placement)

A chest drain facilitates the removal of air and fluid from the pleural space, eliminating the need for needle-guided thoracocentesis after surgery. It can be placed in a closed technique for air or fluid removal before surgical intervention or in an open technique during any thoracotomy procedure. Advantages to placing thoracostomy tubes during surgery include the ability to protect intrathoracic structures, as well as to guide the tube to its desired location.[28]

For this procedure, make a stab incision at the level of the tenth to twelfth intercostal space at the dorsal side of the chest. Advance the tip of the drain with the trocar cranially, creating a subcutaneous tunnel to the level of approximately the eighth intercostal space. Gently advance the trocar through the eighth intercostal space, perpendicular to the thoracic wall, avoiding the caudal edge of the eighth rib. Only a short portion of the trocar is advanced into the thorax to prevent any injuries of intrathoracic organs. Push the drain on the trocar forward to cover the sharp end. Both the trochar and the drain are then flattened to allow advancement parallel to the thoracic wall and fed into the level of the second rib. After reaching the desired position, pull the trocar back while the drain is held in position. Immediately occlude the drain with a clamp and a connector with a three-way stopcock. Remove the clamp and drain the excess air from the chest with a 3- to 6-mL syringe. We suggest no more than 3-mL negative pressure when using a syringe. Close the three-way tap and seal the ports. Suture the chest drain to the chest wall with a Chinese finger-trap around the tube, cover the site of insertion with a dressing, and lightly bandage the tube to the chest.

Animals in which a thoracostomy tube has been placed must be monitored at all times to ensure leakage of air does not occur and result in a life-threatening pneumothorax. Check the connections regularly to ensure that a closed system is maintained. A soft Elizabethan collar can be considered if necessary to prevent interference with the tube.[28] Specific thoracic complications are related to the surgical procedure performed but can include wound infection or dehiscence, atelectasis, pneumonia,

pyothorax, pneumothorax, re-expansion pulmonary injury, traumatic pulmonary injury, phrenic nerve irritation, Horner's syndrome, or cardiac arrhythmias. Disadvantages are prolonged surgical time, prolonged hospitalization and increased cost, and the intense, regular maintenance required.[20,28]

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33

Soft Tissue Surgery: Rodents

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Techniques of soft tissue surgery of companion rodents follow the basic principles of those for other companion mammals, with some modifications based on the size and species of rodent. General surgical principles and instrumentation are discussed in Chapter 30. This chapter will review common surgical techniques used in both large rodents (e.g., guinea pig, chinchilla, degu) and small rodents (e.g., rat, mice, hamster, gerbil) commonly presented for veterinary care.

SURGERY OF THE FEMALE REPRODUCTIVE TRACT

Ovariectomy and Ovariohysterectomy

Indications for neutering female rodents are controlling reproduction; preventing and treating dystocia; treating cystic ovaries, uterine prolapse, uterine torsion, mucometra, pyometra, and uterine or ovarian masses; reducing the risk of mammary and pituitary tumors; and suppressing anxiety.[6] In laboratory rats, ovariectomy before 7 months of age has been shown to significantly decrease the risk of development of mammary neoplasia.[13,20] In addition, ovariectomized female rats have a significantly lower incidence of pituitary tumors and a higher survival rate to day 630 than intact female rats. However, ovariectomy also predisposes rats to osteopenia.[13] In some rodent species, ovariectomy performed at any age may have a behavioral benefit. Evidence shows that compared with intact rats, those ovariectomized at a young age (3 months), at adulthood (6 months), and at an advanced age (18 months) demonstrate significantly decreased episodes of behavior consistent with anxiety.[6]

In most species, ovariectomy at a young age is effective at preventing uterine disease. Therefore, unless uterine pathology is present at the time of surgery, ovariectomy is preferred over ovariohysterectomy. Because of the common occurrence of ovarian disease in companion rodents, particularly guinea pigs, routine juvenile ovariectomy should be considered as a preventive measure. Ovariectomy is easier to perform and causes less morbidity in young, healthy animals with normal ovaries than in older animals with possible ovarian pathology.

In guinea pigs with cystic ovaries, ovariohysterectomy is the treatment of choice because uterine disease secondary to ovarian cysts is common, although the mechanism has not been established (Fig. 33.1).[2] In a recent study of 23 guinea pigs with uterine pathology, 18 of 19 animals in which an ovary was examined also had cystic rete ovarii.[31] Nonneoplastic uterine lesions described were endometrial hyperplasia, endometrial hemorrhage secondary to uterine prolapse, pyometra, polyp, and mucometra, and neoplastic uterine lesions included leiomyoma, adenoma, leiomyosarcoma, and choriocarcinoma.[31]

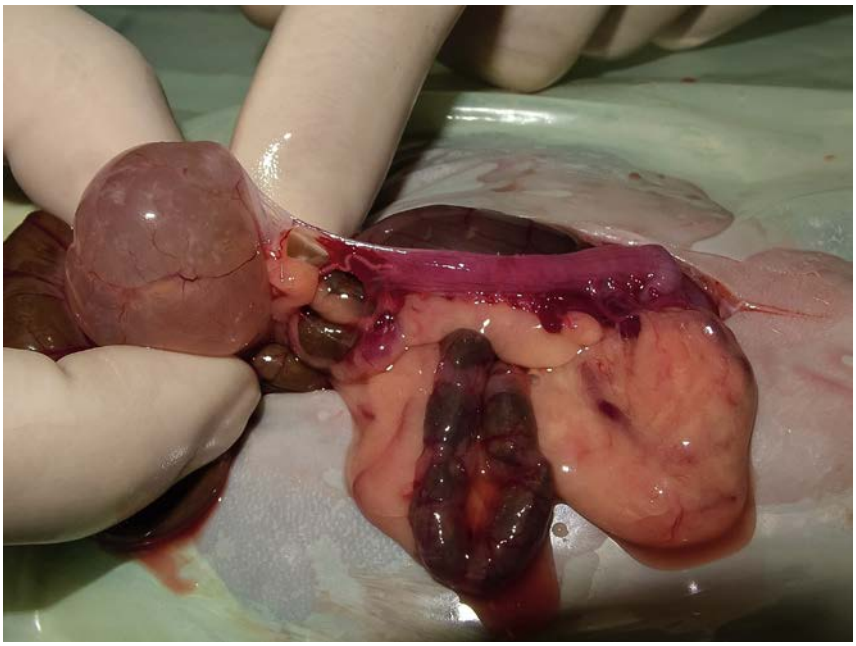


Fig. 33.1 Large ovarian cyst in a guinea pig.

The anatomy of the female rodent reproductive tract varies by species. The ovaries are located caudolateral to the kidneys and deep to the abdominal viscera.[14] In guinea pigs, the ovaries measure approximately 3 to 6 mm by 2 to 4 mm by 2 to 3 mm[10]; the oviduct lies in close proximity to the dorsal aspect of the ovary, encircling it before joining the uterine horn.[14] The suspensory ligament is quite short in some species. The ovarian artery and vein, which are branches of the renal vessels, split into an ovarian branch and a uterine branch.[21] A single artery and vein run medial to each ovary and uterine horn.[11] Rodents have a duplex uterus with either one cervix (e.g., guinea pig, hamster) or two cervices (e.g., chinchilla, rat, mouse); in some rodent species, the caudal cervices may fuse into one distal cervical canal or may appear to fuse externally.[5,10,18] In guinea pigs, the horns join to form a uterine body, which is divided internally by a well-developed intercornual ligament but with a single cervical os. The mesovarium, mesometrium, and broad ligaments are established sites of fat storage in guinea pigs and chinchillas, adding to the difficulty of ovariohysterectomy in these species.

Ovariectomy and ovariohysterectomy can be performed through either a ventral midline approach or a dorsolateral (flank) approach, each of which is described here.[24] One advantage of the flank approach is that the gastrointestinal tract does not have to be manipulated. In addition, the incisions are dorsal, so they are not subject to the weight of the viscera. There is also less morbidity because the incisions are smaller, the procedure can be performed relatively quickly, and—in the author's clinical experience—postsurgical pain may be less. The primary disadvantage of the flank approach, however, is that it can be more difficult to access the uterus if ovariohysterectomy is necessary.[26]

Ventral Midline Ovariectomy and Ovariohysterectomy

The ventral midline approach for ovariohysterectomy as described here for a guinea pig also applies to other rodent species, with modifications. With the animal anesthetized, gently express the urinary bladder. Shave and surgically prepare the ventral abdomen from the xiphoid to the pubis. Make a 2- to 3-cm incision midway between the umbilicus and pubis. Undermine the skin to expose the linea alba, which is covered by little subcutaneous tissue. When incising the linea and entering the abdominal cavity, avoid traumatizing the bladder and, in hindgut fermenters, the thin-walled cecum.

Because the ovaries are positioned deep in the abdomen, the viscera must be retracted to gain exposure. Use a blunt instrument or a finger to move the cecum and bladder to the side on which you are standing, allowing visibility of the uterine horn on the opposite side. Grasp the uterus gently with forceps, exteriorize it, and trace it cranially to locate the ipsilateral ovary. The short mesovarium, which originates in the area of the caudal pole of the kidney, can make it relatively difficult to access the ovaries. Drain any ovarian cysts to improve ventilation during anesthesia and facilitate ovariectomy. The broad ligaments contain a large amount of fat, which can make identifying the ovarian vessels difficult. It may be necessary to extend the incision cranially to avoid tearing the friable, fat-filled ovarian ligament. Carefully transect the suspensory ligament to facilitate exteriorization of the ovary.

Use gentle blunt dissection to create an opening in the mesovarium and place two hemostatic clips or one or two absorbable synthetic ligatures on the vessels supplying the ovary. Alternatively, the vessels can be sealed and transected with a bipolar forceps, a carbon dioxide (CO_2) laser, a harmonic device, or a LigaSure tissue-sealing device (Medtronic, Minneapolis, MN) (Fig. 33.2). Transect the mesovarium and vessels distal to the ligatures. Remove the entire oviduct encircling the ovary, because ovarian remnants can develop into cystic masses.[14] Repeat the procedure on the opposite side. Then, bluntly dissect the broad ligament to the level of the uterine body. Ligate the uterine vessels with the uterine body unless they appear particularly large,

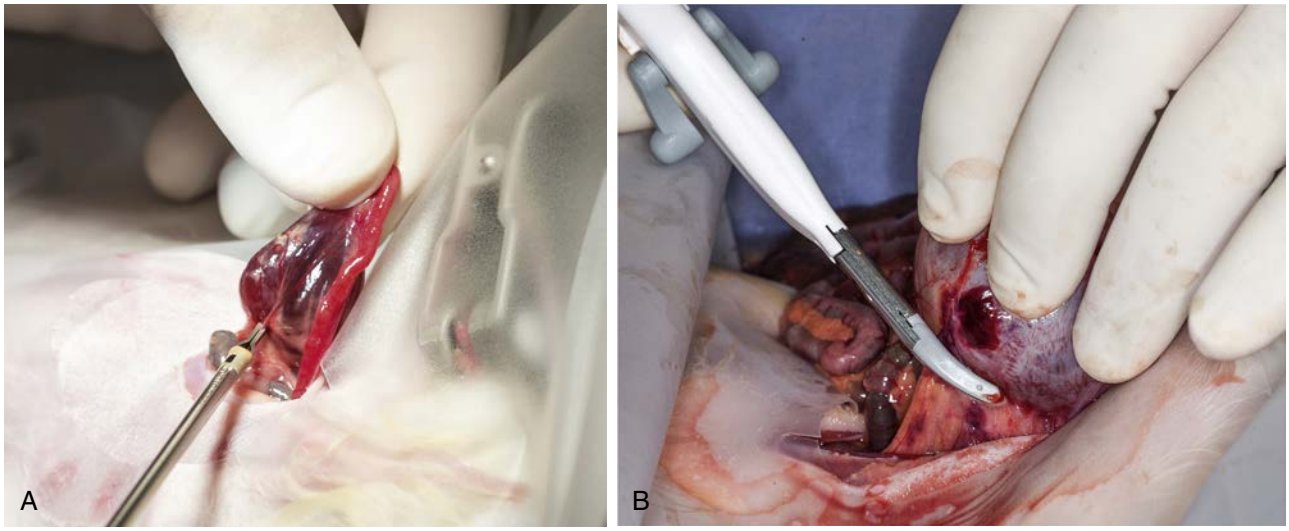


Fig. 33.2 Ovariohysterectomy to remove ovarian cysts by using bipolar forceps in a hamster (A) and a LigaSure tissue sealing device in a guinea pig (B).

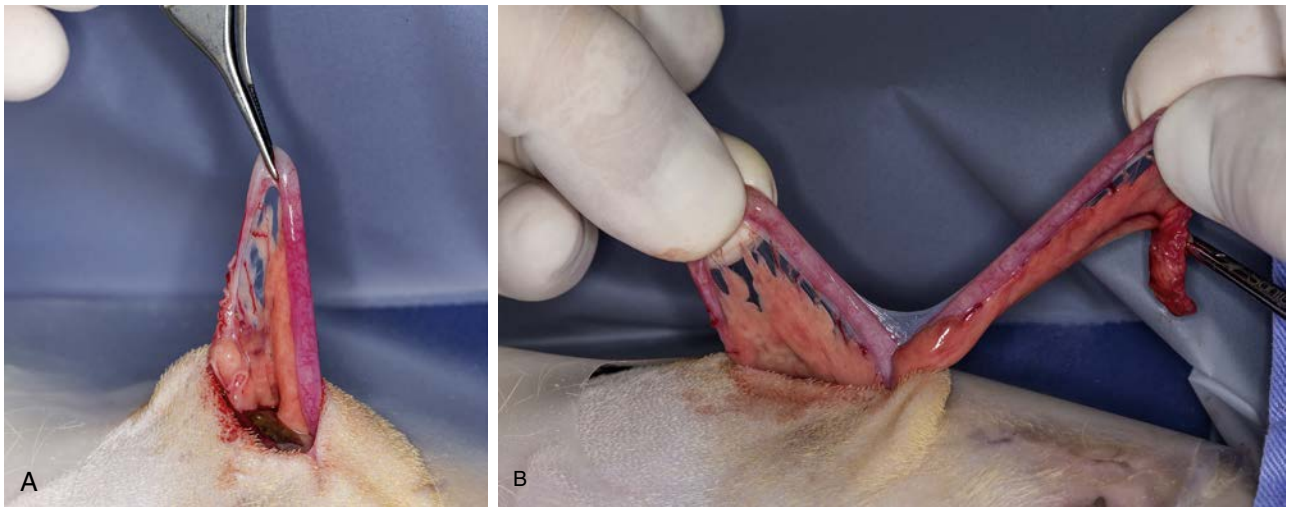


Fig. 33.3 Ovariohysterectomy via a dorsolateral (flank) approach in a guinea pig. (A) The left ovary and uterine horn are elevated through the incision. (B) Both uterine horns are elevated.

in which case ligate them separately. The uterus may be ligated with an encircling or a transfixation ligature. Remove the ovaries and uterus en bloc. Close the abdominal cavity with 4-0 monofilament absorbable suture in a simple continuous pattern in the linea alba and 5-0 absorbable suture for the subcutaneous or subcuticular closure. Use tissue adhesive, if necessary, to appose skin edges.

The procedure for ovariohysterectomy is similar in other small rodents. However, because gerbils and dwarf hamsters of both sexes have a midventral sebaceous gland located near the umbilicus, make a paramedian incision that avoids the gland in these species.

Dorsolateral (Flank) Ovariectomy and Ovariohysterectomy

Shave and surgically prepare both flanks and the abdominal skin in case a ventral midline celiotomy is necessary because of complications or unexpected uterine pathology.

To perform an ovariectomy in a rat or guinea pig–size rodent, make a 1- to 2-cm incision on each side ventral to the erector spinae muscle and approximately 1 cm caudal to the last rib. Bluntly penetrate the muscle with a hemostat and enlarge the opening to approximately 1 cm. Press the ovary to the incision by applying pressure on the abdomen, then grasp the ovary with forceps (Fig. 33.3, A). Drain fluid as necessary from large ovarian cysts in guinea pigs. Exteriorize the ovary and use a hemostatic clip or ligature to ligate the ovarian vessels. Take care to remove the entire oviduct surrounding the ovary. Experienced surgeons can remove both ovaries and uterine horns through one side, especially in young animals. However, if necessary, the approach can be repeated on the opposite side. In small rodents (i.e., rats, mice, hamsters, and gerbils), a dorsal midline incision can be made through the loose skin of the back and pulled from one side to the other, allowing removal of both ovaries through one dorsal skin incision with bilateral muscle incisions.

A dorsolateral approach can also be used for ovariohysterectomy. However, be aware that it is technically more difficult to remove the uterus by this approach, especially in older or obese rats or if uterine pathology is present. Exteriorize the ovary and



Fig. 33.4 This guinea pig was presented for uterine prolapse the morning after farrowing.

use suture or hemostatic clips to ligate the ovarian vessels, then transect between the ligatures. Retract the ovary and associated uterine horn out of the opening in the dorsal body wall. Continue until the uterine body and contralateral uterine horn are identified (Fig. 33.3, B). Trace that horn to the contralateral ovary, and repeat the process. Exteriorize both ovaries and uterine horns before ligating the uterus and transecting it distal to the ligature. In some cases, after removing the first ovary, it is easier to ligate and transect the uterus and then retract and remove the contralateral ovary. Close the opening in the body wall with 4-0 to 6-0 synthetic absorbable suture and appose the skin edges with tissue adhesive or an intradermal suture pattern.

Treatment of Uterine Prolapse

Uterine prolapse is seen commonly in guinea pigs and is usually associated with parturition.[2] In most cases, a tissue mass is seen protruding from the vulva after delivery of young (Fig. 33.4). Most often, the owner discovers live young at the time the prolapse is noticed. Depending on how long the uterus has been prolapsed, the sow may be stable or debilitated at presentation. Before administering anesthesia for surgery, stabilize the patient medically. Consider epidural anesthesia for patients that are not stable enough to undergo general anesthesia. Clean and assess the prolapsed uterus, which is usually contaminated by a substrate. If the uterus appears to be viable, clean and reduce the prolapse. At this stage, a solution of concentrated sugar or 50% dextrose, applied topically to the prolapsed tissue, usually helps reduce edema and facilitates replacement.

If the reproductive viability of the sow is to be preserved, reduce the prolapsed uterine horn into its proper location within the abdomen. Using an appropriately-sized blunt probe or moistened cotton-tipped applicator, gently push the horn to approximately midabdomen. After the horn is reduced, monitor the sow closely for further prolapse. If this occurs, perform an emergency ovariohysterectomy. A purse-string suture is not recommended because the prolapsed uterus might be retained in the vagina and cause potentially fatal urinary obstruction.

In most cases of uterine prolapse, ovariohysterectomy is the preferred definitive treatment. Prognosis is fair to good if the patient is alert and active at presentation.

Cesarean Section

Dystocia is relatively common in guinea pigs and chinchillas and also occurs in degus because of the relatively large fetal size.[33] Guinea pigs, in particular, are prone to dystocia if first bred after 8 to 12 months of age (see Chapter 21).

Dystocia in guinea pigs and chinchillas can be surgically treated by either cesarean section or ovariohysterectomy of the intact gravid uterus. For either procedure, make a ventral midline abdominal incision and exteriorize the gravid uterus, ensuring that the skin incision avoids the enlarged mammary glands and associated blood vessels. For cesarean section only, isolate the uterus with moistened sponges before carefully making a longitudinal incision in a relatively avascular area. Deliver the neonates to an assistant, and close the incision with a simple continuous pattern, using 4-0 to 6-0 monofilament absorbable suture on a small atraumatic needle. Irrigate the abdomen with warm saline before closing. To aid uterine involution, oxytocin can be administered after delivering the fetuses.

Ovariohysterectomy of the intact gravid uterus is similar in technique to that used for routine ovariohysterectomy described above. After ligating and transecting the ovarian pedicles, clamp the uterine vessels and uterine body and transect and remove the gravid uterus. Pass the uterus to an assistant, who will open it and deliver the neonates while the surgeon ligates the uterine vessels and uterine body. It may be necessary to ligate the enlarged uterine vessels separately and then transfix the uterus.

If the uterus is exceptionally large or contains a large amount of blood and the sow is anemic, the en bloc technique is not recommended. In the case of an ovariohysterectomy, first perform a cesarean section and allow the uterus to involute before removal. This allows most of the blood in the uterus to return to the sow's circulation. To speed involution, administer oxytocin intravenously, intramuscularly, or directly into a uterine artery.

SURGERY OF THE MALE REPRODUCTIVE TRACT

Orchidectomy

The primary indication for orchidectomy in rodents is to prevent breeding, because generally it is easier to castrate males than to spay females. Orchidectomy is also helpful in decreasing the risk of urethral blockage due to urethral plugs. Urethral plugs, which are high-protein, rubber-like, vacuolized masses adherent to the urethral mucosa, have been described in male rats, gerbils, golden hamsters, mice, and guinea pigs as a normal finding; however, they may rarely cause urethral obstruction in rats.[16,17] The size of urethral plugs decreases by 99% after orchidectomy.[3] Because castration virtually eliminates the risk of a urethral plug causing obstruction in rodents, some authors recommend routine orchidectomy at a young age for rats. Orchidectomy is also the treatment for testicular tumors, such as Leydig cell tumors, which occur especially commonly in rats. Prostatic and testicular tumors are also reported in gerbils.[29] There is no evidence that orchidectomy ameliorates aggression in rodents. In most species, orchidectomy is recommended before puberty because, once sexual behaviors manifest, they become learned behaviors that are not necessarily affected by the loss of hormones.[1]



Fig. 33.5 The genitalia of a male hamster.

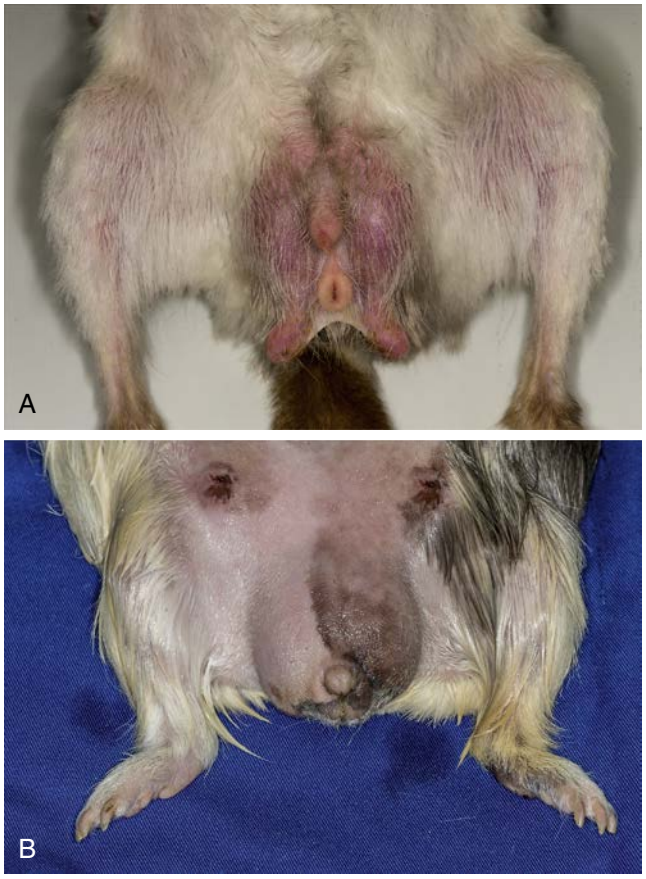


Fig. 33.6 The genitalia of a male chinchilla (A) and a male guinea pig (B).

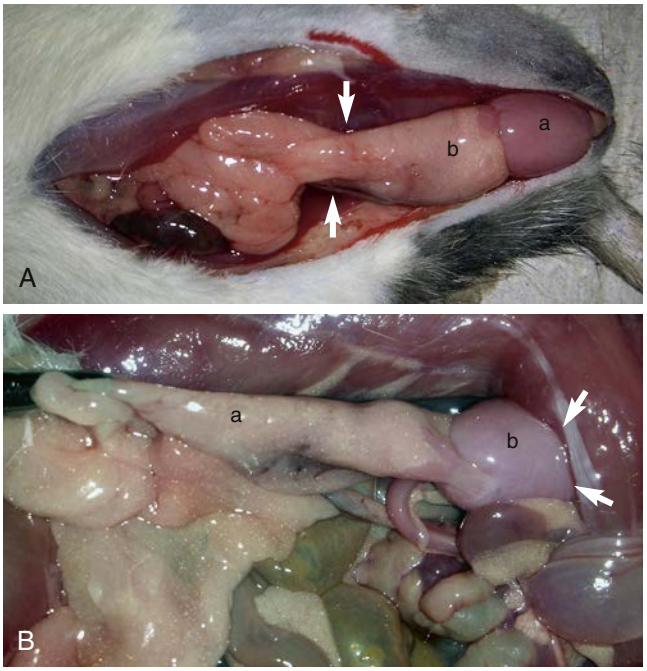


Fig. 33.7 (A) In this rat, the testicle (a) is visible with a large fat pad attached to the head of the epididymis (b) and extending cranially through the inguinal canal (arrows) and into the abdomen. The body wall, inguinal canal, scrotum, and vaginal tunic have been incised to show the normal location of the epididymal fat. (B) The fat (a) is being retracted cranially within the abdomen, pulling the testicle (b) through the inguinal canal (arrows) into the abdomen. In this image about half of the testicle is within the abdomen.

The testicles of most rodents are comparatively large and are located caudoventrally. Myomorphic rodents have well-defined scrotal sacs caudal to the penis (Fig. 33.5). By contrast, hystricomorphic rodents do not have well-developed scrotums; instead, their testicles are located bilateral to the penis in the inguinal region (Fig. 33.6). The testicles usually descend during the first 1 to 2 weeks of life. The inguinal canals remain open, and a functional cremaster muscle allows the testicles to migrate into and out of the abdominal cavity. The testicles can easily be pushed back into the scrotum with gentle, rolling, caudoventral pressure just cranial to the pubis. Epididymal (testicular) fat extends bilaterally into the abdominal cavity near the kidneys and may be responsible for preventing intestinal herniation (Fig. 33.7).[14] Together with the testicular artery and vein, this fat passes through the inguinal canal into the scrotum. According to some authors, preservation of this fat may decrease risk of visceral herniation after open or closed orchidectomy in small rodents; however, this risk has not been clearly documented.[1] Because of their anatomy, inguinal hernias are very rare in these rodents, and visceral herniation after orchidectomy has not been reported. The author removes the epididymal (testicular) fat during castration and ligates the vaginal tunic as proximal as possible to prevent herniation. To date, no cases of postcastration scrotal herniation have been encountered by the author with this approach.

Orchidectomy can be performed via abdominal, prescrotal, bilateral inguinal, or scrotal incisions, each of which is described here. During the procedure, the vaginal tunic can either be left intact (i.e., the closed technique), opened to facilitate manipulation of the testicles and then closed by ligation (i.e., the open-closed technique), or left open. The author recommends the abdominal or prescrotal approach combined with an open-closed technique because the protocol is simple and has low rates of complication.

Once the patient is anesthetized, inject each testicle with lidocaine or bupivacaine for local anesthesia to minimize pain during manipulation (see Chapter 37). Although this does not

provide long-term postoperative analgesia, local blocks may lower the percentage of inhalant gas necessary to maintain anesthesia. With the patient in dorsal recumbency, shave the fur on the caudal half of the abdomen around the scrotum, penis, and inner thighs and aseptically prepare the area.

Orchidectomy Via the Abdominal Approach

Even in adult rodents, the inguinal canal is large enough for the testicles to move freely into the abdominal cavity; therefore, they can be removed through a small abdominal incision. Empty the bladder before surgery by applying gentle pressure. Make a 1-cm skin incision between the umbilicus and penis and perform a routine caudal midline celiotomy. Apply gentle pressure to the scrotum and push the testicles into the abdominal cavity. Identify the testicles or yellow epididymal fat bilateral to the bladder and gently exteriorize the testicles. Carefully separate the ligament of the tail of the epididymis from the internal surface of the vaginal tunic (Fig. 33.8). Ligate the vessels and vasa deferens and remove the testicles and epididymal fat. Repeat the procedure with the contralateral testicle and close the abdomen routinely.

Orchidectomy Via a Prescrotal Incision

If the testicles are in the abdomen, return them to the scrotum by applying gentle caudoventral pressure. Make a caudal midline skin incision cranial to the prepuce, being careful to avoid the comparatively large penis. Use Metzenbaum scissors to bluntly dissect the subcutaneous tissue toward the scrotum. Isolate the spermatic cord with forceps, and gently pull it cranially. At the same time, bluntly separate the parietal tunic from the internal wall of the scrotum. Because of the presence of the fat pad, the spermatic cord is thick and not easy to ligate. Therefore the fat pad can be removed using the open-closed technique. Open the vaginal tunic with a distal incision, exteriorize the testicle and fat pad, and then ligate the spermatic cord close to the external inguinal ring, proximal to the incision (Fig. 33.9).

Orchidectomy Via a Scrotal Incision

Palpate both testes, being careful not to confuse the body of the penis with a testicle. The penis can feel similar to a testicle under the skin, especially if one testicle is retracted into the abdomen. The testes are wider and rounder than the body of the penis, and the penis, which is located on the midline, cannot be pushed back into the abdomen as the testicles can. Isolate the penis and scrotum and make a single transverse 0.5- to 1.0-cm incision at the caudal tip of the scrotum. Alternatively, two incisions can be made in a dorsal-to-ventral orientation, one on each side of the scrotum at the tail of the epididymis. Make the incision as far dorsally as possible to minimize postoperative contamination by cage substrate. The testicles can be removed with either a closed or an open technique.

For the closed technique, grasp the tunic and remove the testicle from the scrotum, leaving the tunic intact. The tunic is tightly adherent to subcutaneous tissues, so carefully dissect it circumferentially. The tunic is also tightly adherent to the tip of the scrotum by the ligament of the tail of the epididymis, must



Fig. 33.8 Orchidectomy via the abdominal approach in a guinea pig. The ligament of the tail of the epididymis is gently separated from the internal surface of the vaginal tunic.

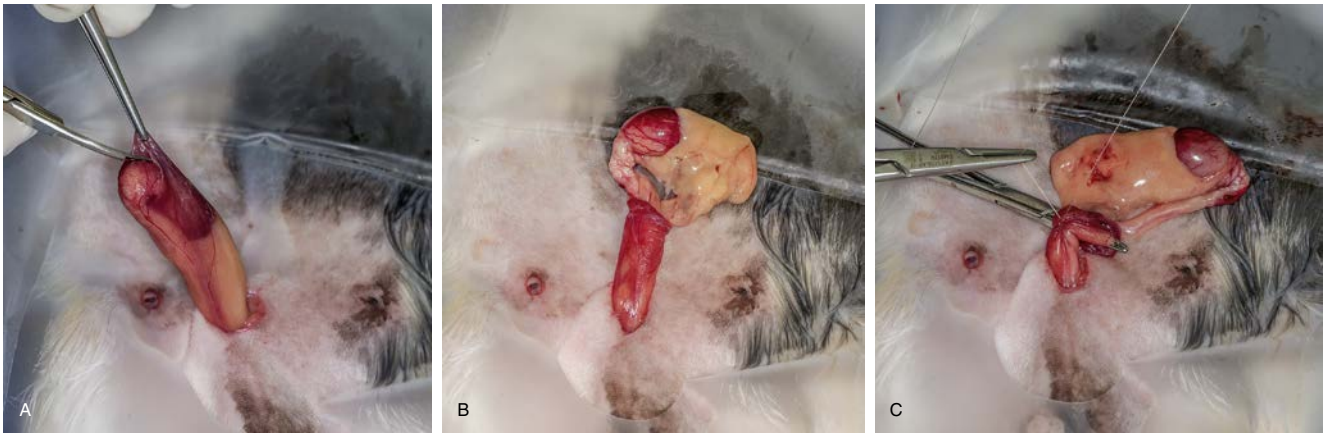


Fig. 33.9 Orchidectomy via a prescrotal incision in a guinea pig. (A) The vaginal tunic is opened with scissors to (B) expose the testicle and fad pad. (C) The spermatic cord is ligated close to the inguinal canal.

be broken down to exteriorize the testicle. After the testicle has been removed from the scrotum, use a dry gauze sponge to apply caudal traction and strip the fascial attachments until the narrow portion of the cord is exposed. Clamping the cord is not recommended in small rodents because it may tear the tunic and testicular vessels. Rather, place a single encircling absorbable ligature of 4-0 to 6-0 suture immediately distal to the epididymal fat (i.e., between the fat and the head of the epididymis), and transect the cord distal to the ligature.

Alternatively, with the open technique, extend the incision through the tunic on both sides to allow the testicles to be exteriorized. Manually rupture the ligament of the tail of the epididymis, freeing the testicle from the tunic and scrotum. Replace the everted scrotum to its normal position. Apply caudal retraction to the testicle to expose the spermatic cord. Ligate the cord as close to the testicle as possible, using a single ligature between the head of the epididymis and the fat. Leave the epididymal fat intact and transect it distal to the ligature. Replace the fat in the inguinal canal. The tunic may be left open or ligated closed, which should be done as proximal as possible (open-closed technique), thereby blocking the inguinal canal. The skin incision may be left open to heal by second intention or it may be closed with tissue adhesive or intradermal sutures.

Orchidectomy Via Bilateral Inguinal Incisions

This technique involves making bilateral skin incisions at the cranial aspect of the spermatic cord, near the inguinal canal.[4] The theoretical advantage of the inguinal approach is that it is close to the external inguinal ring, allowing the cord to be occluded either by direct ligation within the tunic or by placing a suture across the external inguinal ring. The inguinal skin is also relatively thicker, facilitating placement of intradermal sutures. A disadvantage of this approach is that the incisions are normally in contact with the substrate during normal ambulation, which could predispose to postoperative infection.[4]

Make 1-cm incisions in the skin, approximately 0.5 to 1.0 cm lateral to the penis on each side. Do not incise too close to the prepuce, because the support for the penis can be damaged.[22] Gently grasp the spermatic cord within the tunic, and carefully free the tunic from its attachments circumferentially to place a ligature. At this point, an open-closed or open orchidectomy can be performed. Although a closed technique can be performed using the inguinal approach, the scrotal skin is adherent to the vaginal tunic, making it difficult to free the testicle through the more cranial incision.

Using the open-closed technique, the tunic is opened to facilitate removal of the testicles but is ligated closed proximal to the opening. Preplace a ligature, using 4-0 to 6-0 suture, around the cord and incise the tunic distal to the ligature. Identify the epididymal fat and push it proximal to the suture before tying the ligature, thus ensuring that the spermatic cord is occluded within the tunic at the junction of the epididymal fat and the head of the epididymis. The goal is to block the inguinal canal with the epididymal fat, and the epididymal head can easily be detached from the testis and left within the tunic. Exteriorize the testicle through the incision in the tunic and detach the scrotal skin from the ligament of the tail of the epididymis. Replace the scrotum with the attached tunic into its normal position and ligate the exposed spermatic cord distal to the first ligature. Transect the spermatic cord and remove the testicle.

The open technique is performed in a similar manner, but a ligature is not placed around the vaginal tunic containing the spermatic cord. Using this technique, incise the tunic and exteriorize the testicle while taking care to avoid pulling the epididymal fat out of the inguinal canal.[4] Detach the ligament of the tail of the epididymis from the scrotum and replace the scrotal skin with the attached vaginal tunic to its normal position. Ligate the open spermatic cord, making sure that the fat is replaced into the inguinal canal.

Regardless of the prescrotal, scrotal, or inguinal technique used, close the incisions with intradermal sutures or cyanoacrylate tissue adhesive.

Postoperative Care

After surgery, keep the cage substrate clean and change it at least twice daily for 1 week. Generally, sexual activity should decrease within 1 to 2 weeks after orchidectomy. However, in mature rodents that have bred before orchidectomy, mounting and intromission usually persist for several weeks. Viable sperm can remain in the ductus deferens, so castrated males should not be in contact with females for 6 to 8 weeks after surgery to avoid unwanted pregnancy.

Complications associated with orchidectomy include hematoma, self-trauma, and infection.[24] In the author's experience, the incidence of wound infections in guinea pigs is higher with scrotal incisions than with prescrotal or abdominal incisions.

Penile Prolapse

Penile prolapse seems to occur in hystricomorphic rodents more commonly than in other small mammals. It can be seen after orchidectomy and may be related to nerve damage.[2] When prolapsed, the penis is subject to trauma and contamination. With long-term exposure, the mucosa of the penis will thicken and become more resistant to trauma; however, most owners are concerned with chronic prolapse.

Preputial damage with lateral deviation of the penis into the subcutaneous tissues was reported as a complication of orchidectomy in a degu.[22] An attempt to maintain the penis within the prepuce by suturing the base of the penis to the base of the prepuce was unsuccessful. Eventually, the tip of the penis was sutured to the edge of the preputial orifice with four interrupted polydioxanone sutures, taking care to avoid the urethra, without the need to scarify the tissue. The penis remained adherent to the prepuce for 2 years after surgery. This technique is simple and easy to perform, and it maintains the penis in its normal position within the prepuce. Therefore the author recommends this procedure for rodents with penile prolapse.

SURGERY OF THE MAMMARY GLAND

In guinea pigs, benign and malignant mammary tumors are described in both female and male guinea pigs.[27] Tumors tend to develop in animals older than 3 years of age, and both benign and malignant tumors have been shown to be estrogen

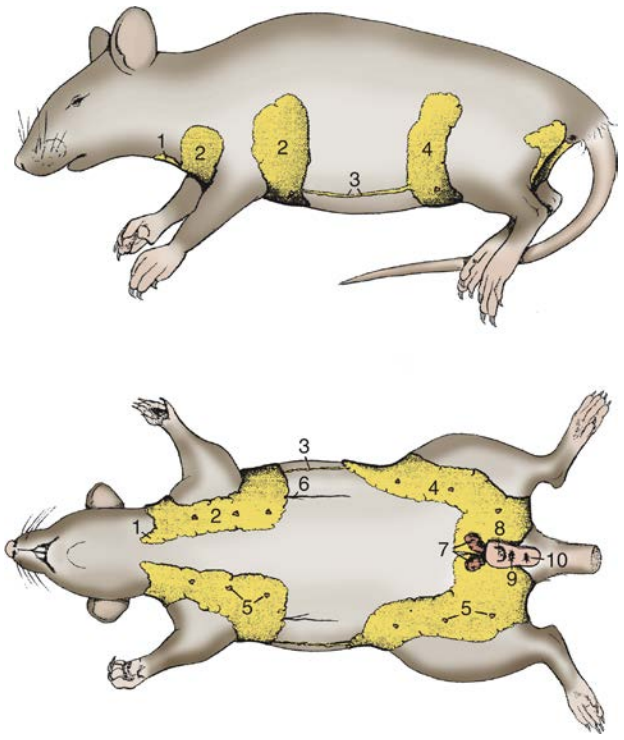


Fig. 33.10 Mammary tissue is extensive in rats, and tumors can develop in any location. 1-4, Mammary glands; 1, cervical gland; 2, thoracic gland; 3, abdominal gland; 4, inguinal gland; 5, mammae papillae; 6, superficial cranial epigastric vein (subcutaneous abdominal vein); 7, preputial gland; 8, prepuce; 9, opening of vagina; 10, anus. (From Popesko P, Rajtovd V, Horák J. *Atlas of the Anatomy of Small Laboratory Animals. Vol. 1. Rabbit and Guinea Pig; Vol. 2: Rat, Mouse and Golden Hamster*. Bratislava: Príroda Publishing, 1990 [Czechoslovak edition].)

receptor-positive.[27] Although malignant tumors are usually locally invasive and rarely metastasize, pulmonary metastasis can occur.[27] The benefit of ovariectomy for decreasing the risk of mammary gland tumors has not been studied in guinea pigs; however, this may be a consideration to decrease estrogen levels. [27]

To date, there are no published reports of mammary neoplasia in chinchillas or degus, although mammary tumors in chinchillas have been described in an exotic animal pathology database.[2]

Mammary tumors in mice generally carry a poor prognosis because these are commonly malignant and associated with mouse mammary tumor virus.[9] Surgery can be difficult and has not been shown to prolong survival in mice. Similarly, ovariectomy has no protective effect.

In rats, the distribution of mammary tissue is extensive (Fig 33.10) (see also Chapter 25). Mammary gland tumors are usually benign mammary fibroadenomas, which do not metastasize but can become quite large (see Fig. 25.22). Tumors are uncommon in rats younger than 1 year of age.[13] Because rat mammary gland tumors are hormone-sensitive, prophylactic ovariectomy before 5 to 7 months of age is associated with significantly lower incidence of mammary tumors.[7,27,29] Therefore, ovariectomy in young rats is recommended to prevent tumor development. Currently there is no evidence that ovariectomy after 7 months of age in rats with mammary gland tumors is effective in preventing recurrence or further mammary tumor development. In one study, 3 rats that underwent ovariohysterectomy concurrently with mammary tumor excision, or 7 months after, developed subsequent mammary tumors within 13 months.[32]

In hamsters, mammary tissue is confined to the ventral thorax and abdomen. Mammary gland neoplasia is rare, and most tumors are benign.[29] Mammary tissue is similarly confined to the ventral thorax and abdomen in gerbils, and mammary gland neoplasia appears to be rare in this species, although usually malignant.[29]

Because malignancy is possible, ensure that a preoperative biopsy or fine-needle aspirate for cytology is performed first. Next, treat any animals with ulcerated or infected mammary masses with antibiotics, analgesics, and anti-inflammatory drugs for several days to reduce inflammation before surgery and allow the gross tumor margins to be assessed more accurately.

Surgical treatment consists of excising the tumor and associated mammary gland, and—in some cases—performing ovariectomy. Neutering will not prevent further development of preexisting mammary tumors, but it will prevent uterine diseases and decrease the influence of estrogen hormones on existing tumors. The benefit of a mastectomy over a lumpectomy has not been studied in small rodents; however, mastectomy is recommended.

For benign lesions, perform a regional or partial mammectomy to remove benign mammary masses within mammary tissue that is grossly normal, usually preserving the skin over the tumor. Because of the extensive nature of mammary tissue in rats and mice, total mastectomy is not practical. Use electrosurgical or laser dissection and tissue-sealing devices to excise the mammary tissue on the affected side. Bluntly dissect around the mass, ligating vessels as they are encountered. Submit the resected mass for histologic evaluation. Replace tumor-contaminated gloves and instruments before wound closure. To help reduce dead space, tack the skin and subcutaneous tissues to the body wall. However, be aware that tacking can cause irritation and stimulate postoperative chewing of the incision site. If bilateral mammary tumors are present (whether benign or malignant), two unilateral mastectomies should be staggered 2 to 4 weeks apart, allowing one side to heal and the skin to expand before the other gland is removed.

If a mass is diagnosed as malignant, stage the disease before surgery when practical, depending on the size or species of animal and the financial considerations of the owner. Staging in most animals includes thoracic radiographs, routine blood tests, urinalysis, abdominal ultrasound, and evaluation of regional lymph nodes. Wider excision is recommended for malignant mammary tumors. If the mass is ulcerated or known to be malignant, the skin overlying the tumor should also be removed. This involves making a fusiform incision around the involved mammary gland(s), leaving 0.5 to 1.0 cm of healthy tissue surrounding the mass. Continue the incision through the subcutaneous tissue to the fascia of the external abdominal wall. Resect the fat surrounding the mammary gland and the inguinal lymph node. If the tumor has invaded deeper tissue,

excise the fascia as well. If it has invaded the abdominal musculature, a portion of the abdominal wall must also be excised. Plan carefully to allow for adequate closure because tissue is not abundant in this area. Locate and remove the inguinal or axillary lymph nodes. Replace tumor-contaminated gloves and close the wound as previously described. When excised tissue is submitted for histologic evaluation, request that the pathologist evaluate the margins of the submitted tissue for evidence of tumor. If the margins are clean, ask the pathologist to measure the distance from the tumor to the cut surface.

SURGERY OF THE ALIMENTARY TRACT

Cheek Pouch Prolapse in Hamsters

Impaction of a hamster's cheek pouch can occur when excessive amounts of inappropriate food (e.g., very large or very small seeds, dry grains) or bedding materials (e.g., cotton, paper) are stored in the pouches. Inappropriate bedding materials may desiccate and adhere to the epithelium where the hamster is unable to remove them. Such retained material can result in abscess formation. Additionally, if the hamster tries too hard to remove the adherent material, the pouch(es) may prolapse (see Fig. 26.7).

If the prolapse is acute, sedate the hamster and remove the adherent material from the mucosa. If the mucosa is healthy, replace the pouch in its anatomically correct position. Then, insert a 1-mL syringe case or cotton-tipped applicator into the pouch and use 4-0 or 5-0 monofilament nonabsorbable suture to place a single, full-thickness, percutaneous mattress suture into the pouch. A stent is not necessary because the suture is not tightened enough to cause skin necrosis. The hamster should be able to eat immediately after the procedure, and the suture should be removed in 14 days.

If the mucosa is severely damaged or infected, it should be excised. If necessary, place an atraumatic hemostat at the base of the prolapsed pouch and transect the tissue distal to the clamp. After removing the clamp, place a single layer of fine monofilament, rapidly absorbable sutures in a simple continuous pattern. After surgery, withhold a normal diet because the animal will attempt to pack it into the pouch, which could result in incisional dehiscence. Instead, syringe-feed with a formula diet for 10 days and remove any bedding materials that could be packed into the pouch.

Cheek pouch neoplasia often goes undetected until the mass prolapses with the pouch. In this case, amputate as above and also remove the skin over the mass.

Gastrotomy

Gastric surgery is rarely performed in rodents; however, it may be performed in guinea pigs to remove foreign objects, such as hairballs. Large gastric trichobezoars, which result in clinical problems, have been reported in long-haired Peruvian guinea pigs.[1,28] The compacted nature of such bezoars makes them unlikely to be broken down and passed by medical management alone.

If a gastrotomy is necessary, perform a ventral midline celiotomy from the xiphoid to the pubis, allowing sufficient space for a large foreign body to be removed easily. Explore all abdominal organs before making an incision in the stomach. Palpate the gastric contents to confirm the location of the foreign object or mass. If the object is in the small intestine near the stomach, attempt to milk it back to the stomach. Isolate the stomach with warm saline solution–moistened gauze, and place stay sutures 1 to 2 cm from the ends of the planned incision. Make the incision in a relatively avascular area of the stomach, midway between the lesser and greater curvatures. If the stomach is distended with gas and fluid, use suction to empty it and minimize contamination of the abdominal cavity. Remove the foreign object, mass, or lesion. Irrigate the stomach, being careful to minimize abdominal contamination, and then palpate the pylorus to confirm patency. Close the stomach in two layers, using 4-0 to 6-0 monofilament absorbable suture on an atraumatic needle in a simple continuous pattern oversewn with an inverting pattern. Replace the contaminated instruments and gloves with sterile ones, irrigate the abdomen with warm sterile saline solution, and close routinely.

Intestinal Prolapse

Intestinal prolapse occurs most often in hamsters, is less frequent in chinchillas, and is rare in other rodents. Rectal prolapse or intussusception of the small intestine or colon can result from the excessive straining seen with proliferative ileitis, neoplasia, intestinal parasitism, or diet-induced diarrhea.

Rodents with rectal prolapse or intestinal intussusception are usually critically ill and should be treated with fluids, dextrose, and antibiotics before emergency surgery. It is important to ascertain what segment of the bowel is prolapsed before surgery. If there is an orifice at the end of the tissue, the tissue can be assumed to be a section of the bowel. If the tissue is solid, it may be a protruding rectal mass or polyp. Once you have determined that the exposed tissue is a portion of the bowel, gently pass a small, blunt-ended probe (e.g., a lubricated tomcat catheter or mini cotton-tipped applicator) alongside it. If the probe passes into the pelvic canal, the tissue is an intestinal intussusception. If the probe does not advance, the exposed tissue is a rectal prolapse.

If the tissue is not devitalized, the rectal prolapse can be replaced and maintained in reduction with a purse-string suture or with transanal sutures. Lubricate the tissue well with sterile lubricant and reduce it with a mini cotton-tipped applicator or a soft urinary catheter. Once the tissue has been positioned in its normal intrapelvic location, place a purse-string suture in the anus using 6-0 nonabsorbable suture, snugly but not tightly, over a 5-Fr red rubber catheter or similar tool. Alternatively, because a purse-string suture can potentially damage the sphincter muscles, place two dorsal-ventral, transanal sutures, allowing space for fecal material to pass. Remove the sutures in 3 to 5 days. Treat the medical condition causing the prolapse.

A necrotic rectal prolapse must be amputated, sutured circumferentially, and anastomosed with healthy bowel. Make a full-thickness, 180° incision through the prolapsed tissue where it is healthy. Suture the healthy rectum to the healthy anus with 6–0 monofilament synthetic absorbable sutures in a simple interrupted pattern. Repeat the steps with the second half

of the prolapse. The terminal colon will thus be sutured to the anal mucocutaneous junction with suture knots in the lumen. Dorsal-ventral transanal sutures are not needed.

A small intestinal or colonic intussusception requires abdominal exploration to replace the intestine in its normal location, assess the viability of the tissue and its blood supply, and perform an intestinal resection if necessary. Patients with an intussuscepted bowel have a very poor prognosis because they usually present in a debilitated condition from the primary disease.

Intestinal Resection and Anastomosis

Intestinal resection is performed to remove intestinal tissue damaged by intussusception, stricture, neoplasia, abscessation, or ischemia. Intussusception is seen with some frequency in chinchillas, possibly secondary to enteritis. In these cases, any bowel segment of questionable viability should be resected.

In rodents with small intestinal or colonic intussusception, perform a routine ventral midline celiotomy and identify the abnormal segment. If possible, gently reduce the segment, using a combination of traction on the orad segment and pushing the intussusceptum within the aborad segment. Ligate and transect the mesenteric vessels supporting the intestinal segment to be removed. Milk the intestinal contents orally and aborally away from the abnormal segment. To reduce the risk of contamination, use small atraumatic clamps to occlude the lumen of the healthy intestine cranial and caudal to the abnormal portion. Hemostatic forceps can be used to occlude the lumen of the diseased segment. Use atraumatic forceps or preplaced stay sutures to manipulate the intestine. Transect the intestine between the hemostatic forceps and atraumatic clamps. An oblique incision may increase the luminal diameter. If there is a significant difference between the lumen diameters of the two free intestinal ends, create an oblique incision (45° to 60°) at the narrow end and a perpendicular incision at the wider end. When creating an oblique incision, make the antimesenteric border shorter than the mesenteric border. Close the anastomosis using 6-0 to 8-0 monofilament absorbable suture. Place a sterile cotton-tipped applicator in the intestinal lumen during closure to keep the walls of the intestine apart. Place the first suture at the mesenteric border and the second one on the antimesenteric border. After placing the first two sutures, close the remainder of the intestinal wall using simple interrupted or simple continuous sutures, tying them gently when apposing the edges. After closing one side, remove the cotton-tipped applicator and close the other side. Close the defect in the mesentery with 6-0 absorbable suture. Intestinal plication is no longer recommended because it is time-intensive and is associated with an increased risk of postoperative complications; however, an enteropexy is quick to perform and minimizes the risk of recurrence. Make a 1- to 2-cm incision in the peritoneum and, with 6-0 monofilament absorbable suture, tack the intestine to the incised peritoneum at the site of the anastomosis. Change gloves and instruments after completing the anastomosis, irrigate the abdomen with warm saline solution, and close the abdomen routinely.

Complications

Potential complications of gastrointestinal surgery in rodents include leakage, dehiscence, perforation, peritonitis, stenosis, ileus, adhesions, shock, and death. Postoperative care may include fluid support, analgesia, nutritional support (using a syringe-fed diet), prokinetic medication, and antibiotic therapy. In guinea pigs and chinchillas, free access to fresh hay, regular grooming of long hair, sufficient exercise, and minimizing stress are important to reduce the risk of recurrence.

SURGERY OF THE URINARY TRACT

The most common indication for urinary tract surgery in rodents is urolithiasis, which is relatively common in guinea pigs and chinchillas but less common in other rodent species. Urolithiasis is the primary differential diagnosis for hematuria.[11] Uroliths in guinea pigs are most often composed of calcium carbonate and can be found in the bladder, urethra, and distal ureter.[12] Renal urolithiasis is rare in rodents; however, renal function can be compromised secondary to ureteral, bladder, or urethral obstruction. In male guinea pigs, urinary tract obstruction can occur secondary to plugs of sperm and seminal fluid that may form in the seminal vesicles.

Survey radiographs are indicated in any animal with suspected urolithiasis (see Fig. 21.13). Contrast radiographs (contrast urethrogram or cystogram) may be helpful in larger patients (see Fig. 38.6). Ultrasound scanning is a vital part of the workup for any patient diagnosed with urolithiasis, as it will confirm the location of stones within the urinary system and determine whether they are causing partial or complete obstruction, as well as allow assessment of the bladder wall. Some mineral-dense objects that appear radiographically to be within the urinary tract may be outside it, and renal mineralization often cannot be distinguished from nephrolithiasis on survey radiographs. Ultrasonography will determine the presence of calculi rather than mineralization of the renal pelvis. The recommendation is to remove renal calculi only if they are causing intractable infection or obstruction of urine outflow.

In addition to routine presurgical imaging, perform urinalysis and obtain a urine culture in most cases. Preoperative fluid therapy is especially important if the patient is azotemic. However, take care to monitor and adjust the rate of infusion to prevent overload.

If bacterial infection is suspected or if contamination occurred during surgery, consider administering antibiotics initially and then adjust treatment based on culture and urinalysis results. Monitor urine output and perform urinalysis during the postoperative period. Medical dissolution of stones has not been documented in guinea pigs, and recurrence is common after surgical removal (see also Chapter 21).

The urethra of female guinea pigs is quite large, and large stones often obstruct the urethral papilla because they cannot pass through it (Fig. 33.11). Stones within the bladder do not usually cause signs of obstruction but should be removed because they cause pain and cystitis, predispose to bacterial urinary tract infections, and may migrate into the urethra, causing obstruction.

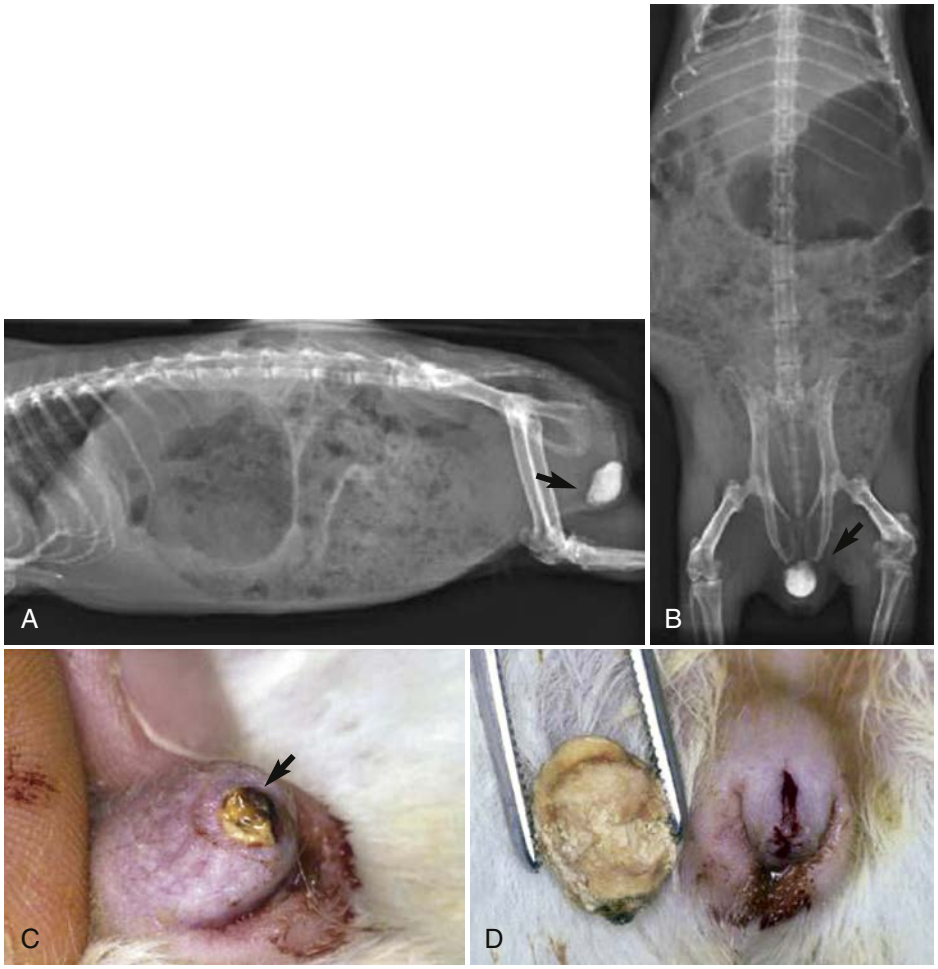


Fig. 33.11 (A) and (B) A radiodense urethral calculus (arrow) located at the urethral papilla is visible on abdominal radiographs of this guinea pig. (C) The stone can be seen at the external orifice of the urethra (arrow). (D) An incision was made over the urethra to allow the stone to be removed. The incision was allowed to heal by secondary intention. (Images courtesy of Dr. Estella Boehmer.)

Cystotomy

The indications for cystotomy are removal of cystic calculi, removal of urethral or ureteral calculi that can be flushed retrograde into the bladder, repair of bladder rupture, bladder biopsy, removal of bladder masses, and investigation of refractory cystitis.

For cystotomy, anesthetize the animal and place it in dorsal recumbency. Make a ventral midline celiotomy incision just cranial to the pubis. Exteriorize the bladder and carefully examine the urinary tract. Isolate the bladder with gauze sponges moistened with saline solution. Place stay sutures in the bladder wall cranial and caudal to the planned incision. If possible, place a retrograde catheter into the urethra to prevent stones from migrating into the urethra during surgery or to flush stones in the urethra back into the bladder. In small rodents, often a small (24- to 26-gauge) intravenous catheter can be passed into the urethra of both males and females; magnification is very helpful for this procedure. In larger rodents such as guinea pigs, a 3.5- to 8-Fr red rubber catheter can be used. Make a 2- to 3-cm incision on the avascular ventral aspect of the bladder, closer to the apex than the neck, which should help avoid damaging the ureters at the trigone. If indicated, trim about 1 mm of bladder wall from one side of the incision and submit the tissue for culture and sensitivity testing and for histologic examination. Use a surgical spoon or a pair of forceps to remove the calculi. Calculi may be adhered to the inflamed bladder wall or be buried deep within a mucosal fold, so take care not to damage the bladder wall during removal. Calculi may also be found deep in the neck of the bladder, far from the incision site and difficult to remove without retrograde passing a urethral catheter or flushing the urethra. After removing the calculi, irrigate the bladder extensively to ensure that all calculi have been removed. Use a small catheter passed from the neck of the bladder into the urethra to confirm the patency of the urethra before closure. Using absorbable, monofilament suture material on a small atraumatic needle, close the cystotomy site in a single-layer simple continuous pattern, making sure the suture material does not enter the bladder lumen. If the bladder wall is thin or fragile, a double-layer closure using an inverting suture pattern is recommended. Check the bladder incision for leakage by filling the bladder with sterile saline solution. Irrigate the abdomen with warm saline solution and close routinely. Submit the calculi for stone analysis and culture and sensitivity testing.

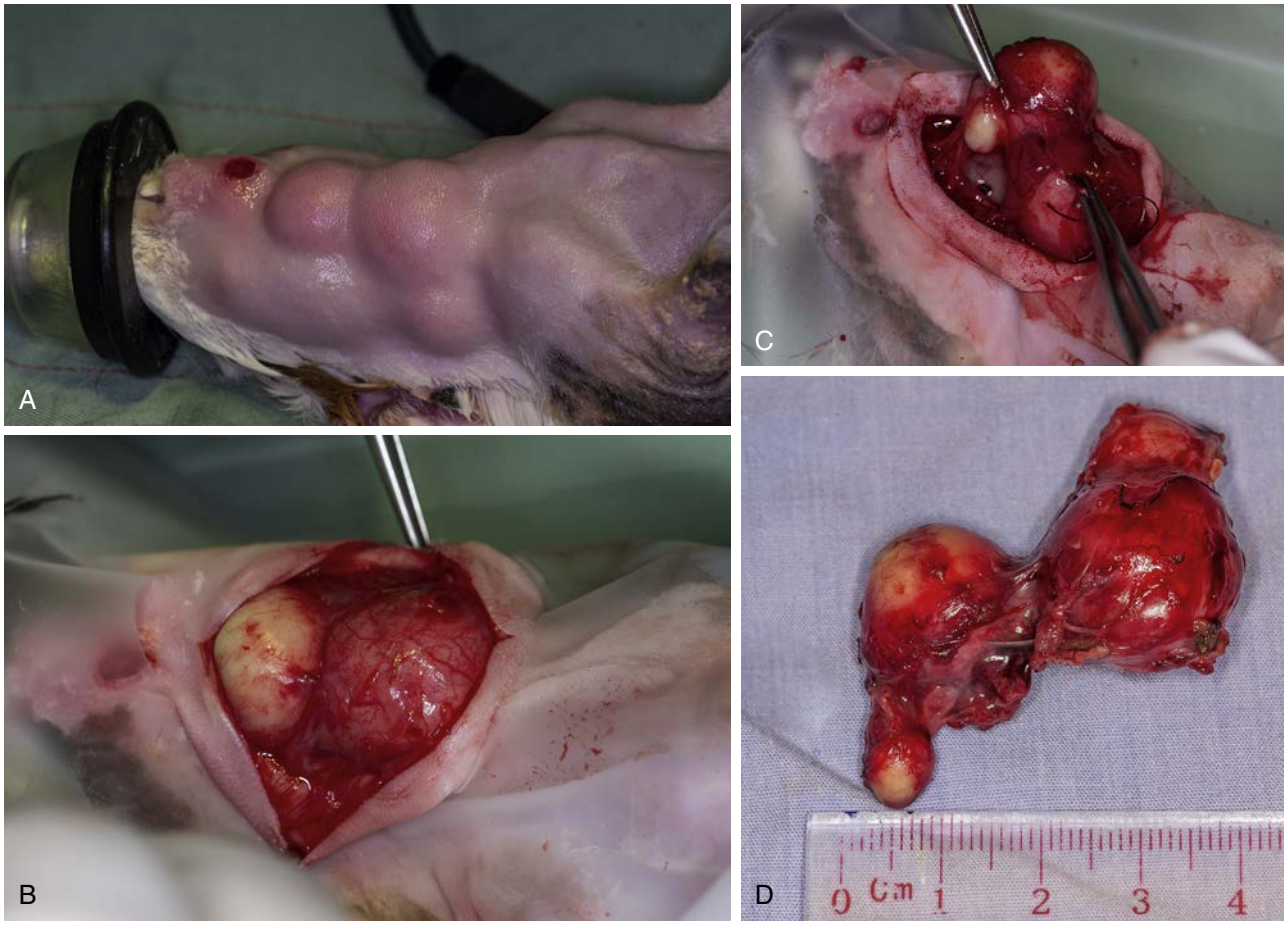


Fig. 33.12 Cervical lymphadenitis in a juvenile guinea pig (A). Multiple abscess were completed excised (B, C, D).

Complications include rupture or perforation of the overdistended bladder, especially during the abdominal incision, and urine leakage from the bladder incision. A chronically inflamed bladder also may have formed adhesions to the surrounding intestine or uterus. Iatrogenic damage of the ureters is more likely if the incision is made into the dorsocaudal aspect of the bladder. Checking for leakage after the bladder has been closed can prevent the risk of postsurgical urine leakage.

SURGICAL TREATMENT OF ABSCESSES

Abscesses in small rodents are usually the result of bite wounds from cage mates, especially in hamsters. Cervical lymphadenitis, a condition known as "lumps" in guinea pigs, is a streptococcal infection of the cervical lymph nodes (Fig. 33.12).[19] Infection may occur secondary to trauma of the oral mucous membrane and it usually results in lymph node abscessation.

Before surgery, drain as much purulent discharge as possible from the abscesses and submit a sample for aerobic and anaerobic culture and sensitivity testing. Immediately start the patient on empirical antibiotic therapy, revising the treatment protocol in response to results of culture and sensitivity testing. The goal of drainage and antibiotic therapy is to reduce the size of the abscess to facilitate surgical excision, but this approach may result in a cure if the abscess is sufficiently small and responsive.

With cervical lymphadenitis, the optimal treatment is complete surgical excision of any affected lymph nodes, not merely lancing and draining the abscess. If excision is not possible, lance, drain, and flush the abscess, leaving the wound open to heal by second intention. Although wound irrigation with topical and systemic antibiotic therapy may resolve the abscess, recurrence is very common. Consider marsupializing the cavity or packing with an antimicrobial wound dressing (Aquacel Ag Hydrofiber Ribbon Dressing; ConvaTec, Bridgewater Township, NJ) to prevent premature closure. Another option is to fill the dead space with antibiotic-impregnated beads after debridement, and then close the subcutaneous tissue and skin routinely over the beads. However, polymethylmethacrylate beads can act as a nidus if not removed; therefore absorbable beads (calcium sulfate) may be preferable.

SURGERY OF CUTANEOUS NEOPLASIA

The most common skin neoplasms in rodents are trichofolliculomas and lipomas in guinea pigs and scent gland tumors in hamsters and gerbils. Cytologic examination of samples collected by fine-needle aspirate is recommended for tentative

diagnosis, including differentiation of neoplasia from abscessation. However, some neoplastic lesions can have a purulent, necrotic core that can be misdiagnosed as a primary abscess. Identifying malignant neoplasms as early as possible is important because the prognosis and surgical management vary with the stage of disease. Benign cystic masses can also become infected, especially if surgery is delayed.

Before surgery, assess skin tension and elasticity and carefully plan the shape of the incision and the method of closure. Shave and prepare the skin generously, especially if there is a possibility that skin flaps will be needed for closure. Hamster skin is quite elastic and abundant, making skin closure relatively easy. However, guinea pig skin tends to be less elastic, making it more difficult to close large surgical wounds.

Treat benign skin masses with total surgical excision followed by histopathologic examination. Use a monopolar electrosurgery unit to make a fusiform incision at a length-to-width ratio of 4:1 around the mass, which should minimize dog-ear formation. Use bipolar forceps or ligatures to control bleeding. Irrigate the wound bed after tumor excision. If necessary after mass excision, create a single-pedicle advancement flap with the pedicle being no less than half the length of the flap, then trim any dog-ear tissue away from the pedicle to maximize blood supply to the flap. Use walking sutures oriented along the long axis of the flap to advance the flap and close the dead space. Use monofilament nonabsorbable suture material in a simple interrupted pattern to close the skin.

For malignant skin masses, plan the resection with a wide margin in all directions. Ideally, excision of infiltrative or aggressive tumors should extend at least one fascial layer below the detectable tumor margins. However, because of the small size of most rodent patients, this often cannot be achieved. Amputation is recommended when tumors are poorly localized on the extremities. Replace any tumor-contaminated gloves and instruments before wound closure.

SURGERY OF THE THORAX

The primary indication for thoracotomy in rodents is resection of a pulmonary abscess or neoplasm. The caseous nature of the purulent material in most rodents often means that even long-term antibiotic therapy is inadequate to resolve pulmonary abscessation. Pulmonary abscesses can be treated by abscess resection or pulmonary lobectomy; however, patients with abscesses are usually systemically ill, which complicates outcomes. Additionally, during manipulation of the lung lobe, purulent material can flow from the affected lobe into the bronchus and then into other lobes. These factors contribute to the poor prognosis for rodents undergoing resection of pulmonary abscesses by pulmonary lobectomy or otherwise. Most pulmonary tumors are slow-growing, and clinical signs do not occur until late in the disease course.

Intermediate positive-pressure ventilation (IPPV) is required for any thoracotomy procedure; however, the difficulty or endotracheal intubation in rodent species makes this challenging.[8,15,30] Rats maintained using a tight-fitting facemask for anesthesia and receiving controlled ventilation had very low mortality after pulmonary lobectomy.[25] During thoracotomy, ventilation was supported at 20 breaths/min, and the degree of lung expansion was directly visualized to ensure sufficient expansion and avoid overinflation. This technique would likely be useful in other rodent species as well.[25]

If thoracotomy is indicated and the patient cannot be intubated per os, a temporary tracheostomy can be used for ventilation during surgery.[2] Make a 1.0- to 1.5-cm skin incision on the ventral cervical midline, bluntly dissect through the subcutaneous tissues, and identify the sternocephalicus muscles. Separate the muscles along the midline, taking care not to damage the thyroid vein. Identify the trachea, and bluntly dissect the peritracheal tissues from the cartilage, preserving the recurrent laryngeal nerves. Place a 3-0 nylon suture around the cartilage ring caudal to the proposed tracheotomy site and create a large loop of suture with long suture tails. Use the suture to pull the trachea to the surface, facilitating tracheostomy tube placement. Make a transverse incision in the trachea that is one-third its diameter and enlarge the incision to one-half the diameter with hemostats (to avoid cutting the recurrent laryngeal nerves). Insert a sterile 1- to 2-mm endotracheal tube into the aborad segment of the trachea. Once the surgery is completed and the patient is awake, remove the tracheostomy tube and allow the surgical site to heal by second intention.

If the thoracic mass is small enough, pulmonary lobectomy can be achieved through a lateral thoracotomy as has been described in laboratory rats.[25] Magnification is very helpful for this type of procedure. Place the patient in lateral recumbency with the affected side facing the surgeon. Aseptically prepare the surgical area and perform an intercostal nerve block with bupivacaine. Use a standard intercostal approach at the fourth to fifth intercostal space. Divide the intercostal muscles, paying attention to hemostasis, and use an arterial forceps to penetrate the intercostal space and enter the thoracic cavity. Spread the hemostat to open the intercostal space, again taking care to avoid vessels. Place a Bennett or Heiss retractor to maintain exposure while the lung lobe is exteriorized. After accessing the thoracic cavity, start gentle IPPV while taking care to prevent overinflation. The inflating pressure should be less than 10 to 20 cm H_2O, and the lung should not turn pale or expand beyond the chest. Identify the hilus, pulmonary artery and vein, and bronchus of the exteriorized lobe. Ideally, the pulmonary artery and vein should be isolated, ligated, and transected individually to minimize the risk of arteriovenous fistulas; however, realistically, it is easier to ligate the artery, vein, and bronchus with a single ligature. Transect distal to the ligature and remove the affected lobe. Inspect the stump for hemorrhage or air leakage. Fill the chest with warm saline solution to observe for bubbles and allow for patient warming, then remove the solution before closure. Place two 4-0 or 5-0, slowly absorbable, monofilament sutures around the ribs adjacent to the thoracotomy to appose the ribs. Tighten the suture to leave a gap between the ribs, approximating the intercostal space. Before tying the sutures, place a thoracostomy tube to maintain negative intrapleural pressure during recovery. A 3.5-Fr red rubber catheter serves this purpose well. Close the muscle, subcutis, and skin layers routinely. Once negative pressure has been maintained for a

couple of hours, remove the tube. A tube within the thoracic cavity can stimulate the production of 1 to 2 mL of effusion per kilogram body weight per day.

For large masses and cranial mediastinal tumors, a ventral midline thoracotomy is preferable to allow access to both sides of the thoracic cavity. Place the patient in dorsal recumbency, shave the skin, and prepare it surgically from the neck to the cranial abdomen. Make a ventral midline incision from 1 cm cranial to the manubrium to the xiphoid process. The approach is analogous to that used for larger animals, with one exception: because the sternebrae are very narrow, it is not feasible to split them longitudinally; instead, the ribs are cut on one side at their attachment to the sternebrae. Use either an oscillating saw or a diamond-cutting disc attached to a rotary tool. Start IPPV after accessing the thoracic cavity, similar to lateral thoracotomy. After performing an osteotomy of the first few ribs, place moistened surgical sponges along the edges of the thoracotomy site and use a retractor to stabilize the thorax and facilitate careful transection of the remaining ribs. When performed to resect a pulmonary abscess, gently lift the affected lung lobe out of the thorax and quickly clamp the hilus to prevent pus from migrating into other lobes. Ligate or clip proximal to the clamp to control the artery, vein, and bronchus, then transect between the clamp and ligature. After removing the affected lobe, inspect the stump for hemorrhage or air leakage. Fill the chest with warm saline solution to observe for bubbles and allow for patient warming, then remove the solution before closure. Place a chest tube as described above to allow control of the pleural space postoperatively. Close the thorax with figure-of-8 sutures (using monofilament absorbable material) that encircle the sternebrae at each rib. A second layer, apposing the muscles ventrally, is placed to provide additional stability. Close the subcutaneous tissues and skin routinely.

Provide the patient with supplemental oxygen after any thoracic surgery. Take radiographs to assess the condition of the lung and to monitor the presence of air in the thoracic cavity. If needed, instill diluted bupivacaine into the thoracic cavity every couple of hours through the chest tube for pain control until the tube is removed. Wear gloves when handling thoracostomy tubes to prevent ascending bacterial infection. Check the connections regularly to ensure that a closed system is maintained and consider using an Elizabethan collar to prevent interference with the tube. Antibiotics, fluid therapy, analgesia, and supportive feeding are recommended as for abdominal surgeries.

Complications most often occur during surgery or within 10 days after surgery, with the most common complication being acute perioperative death. This may be related to pain, stress, or anesthetic complications. However, thoracostomy tubes also cause complications, including infections, pneumothorax (if poorly placed or managed), lung injury (due to excessive suction), phrenic nerve irritation, Horner's syndrome, or cardiac arrhythmias.

ENUCLEATION AND EXENTERATION

Indications for enucleation are diseases that cause painful, irreversibly blinding, or end-stage ocular disease. Murid rodents do not have a third eyelid, and proptosis is common in small rodents, especially hamsters. If treated promptly with lavage, replacement, and tarsorrhaphy, it may be possible to salvage the eye (see Chapter 26); however, when left untreated for longer periods, enucleation is often necessary. When performing any surgery, remember that rodents have a large orbital venous sinus, which surrounds the muscles and Harderian gland, immediately caudal to the globe. In laboratory settings, this site is used for blood collection with a capillary tube. Damage to the sinus during enucleation results in significant hemorrhage, which is the most common complication of this surgical procedure.

Two techniques are described for enucleation of rodents: transconjunctival and transpalpebral approaches.[1,24] Both techniques involve excising the globe, the conjunctiva, and the third eyelid (in species that have one). The difference is whether the eyelid margin and palpebral conjunctiva are removed at the beginning of the procedure along with the globe and bulbar conjunctiva (i.e., transpalpebral) or if they are removed at the end of the procedure, after the globe and its conjunctiva have been removed (i.e., transconjunctival).[1] Because of concerns about blood loss, transconjunctival enucleation is usually preferred because it allows closer dissection to the globe and is more likely to avoid large vascular structures. However, the transconjunctival technique may be less preferable if infection is present in the anterior segment, such as severely infected corneal ulceration. In such cases, the sterile surgical site may be contaminated by the infected ocular surface, and infection could spread to the orbit.

Place the patient in lateral recumbency with the head slightly elevated. Shave the skin at least 1 cm around the eyelid margins. Irrigate the globe, conjunctiva, and fornix with dilute (half-strength aqueous) povidone–iodine solution, and rinse with sterile saline. Do not use povidone–iodine scrub, chlorhexidine scrub, or alcohol.

For transconjunctival enucleation, first perform a lateral canthotomy. Make a circumferential incision about 1 to 2 mm from the limbus in the bulbar conjunctiva. Securely grasp the 2-mm edge of conjunctiva attached to the limbus while the globe is excised. Then, bluntly dissect deep to the conjunctiva through Tenon's fascia to the sclera. Identify and transect the extraocular muscles as close as possible to their insertion on the globe to minimize muscle hemorrhage. Use care in applying traction to the globe, since this pulls on the optic chiasm and can damage the ocular nerve to the contralateral eye. After all the muscles have been transected, the globe will rotate freely within the orbit. At this point, gently lift the globe and ligate, clip, or clamp the optic nerve and associated blood vessels. Incise distal to the clip or ligature, allowing the globe to be removed, and inspect the remnant for hemorrhage. If a clamp was used, a ligature can be more easily placed once the globe is removed. If the sinus has been damaged and hemorrhage is significant, pack a piece of cellulose sponge into the defect and apply gentle pressure for 5 minutes. After the globe has been removed, the conjunctiva must be removed; if not, cysts can form. Using Metzenbaum scissors, excise the upper and lower eyelid margins about 2 mm from the edges to join at the medial canthus. The medial angular vein is superficial and medial to the orbital

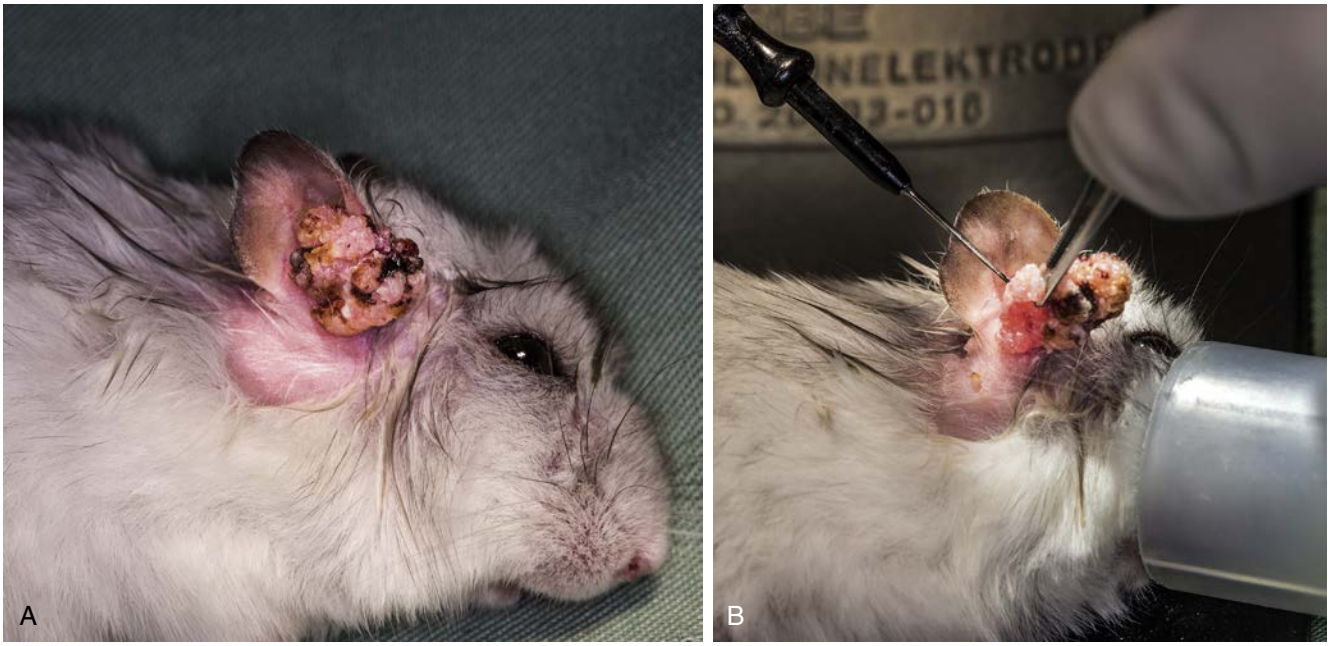


Fig. 33.13 Papilloma in the ear canal of a dwarf hamster (A). The mass was resected using a monopolar knife (B).

rim and is best avoided by meticulous dissection. Inspect for any remaining conjunctival tissue and remove the Harderian gland. Be prepared for hemorrhage. Before removal, the third eyelid and associated glands can be clamped at their base proximal to the glands for reduced hemorrhage. One can partially suture the eyelids closed before removing the third eyelid and Harderian glands to allow the remaining lid margin to be closed quickly to provide pressure for hemostasis. Alternatively, excise the tissue quickly and control the hemorrhage with a gelatin sponge and digital pressure; the sponge can be left in place and will be absorbed. Once hemostasis is achieved, suture the eyelids closed. It is acceptable to place skin sutures in the eyelids because rodents cannot chew them.

The transpalpebral approach is recommended if there is a superficial infectious ocular disease, such as bacterial conjunctivitis, because it can prevent the contamination of periocular structures. Suture the eyelids together with fine nylon suture. Make an incision into the palpebral conjunctiva, but not through it, about 2 mm from the eyelid margins. Dissect down to the sclera rostral to the extraocular muscles without penetrating the conjunctiva. Then, transect the extraocular muscles at their insertion and continue the dissection as described above. With the transpalpebral approach, the conjunctiva and glands are removed with the globe, and any surface infection should be contained within the sutured eyelids. Hemorrhage is controlled and lids are then closed, as per the transconjunctival approach.

Exenteration involves removing all structures within the bony orbit, including the globe, ocular muscles, glands, and nictitans (if present). Exenteration is indicated if there is periocular disease, such as a retrobulbar abscess or neoplasia. Perform a lateral canthotomy, remove the eyelid margins, and excise all tissue within the orbit, staying as close as possible to the bone, and remove the whole sinus together with the eye. Control hemorrhage with hemostatic clips and a gelatin sponge, as needed. Close the eyelids as previously described.

SURGERY OF THE EAR

Dwarf hamsters are often presented with a papilloma in the ear canal, which can grow quite large, block the ear canal, cause earwax to build up, and result in otitis externa (Fig. 33.13). Monopolar or bipolar electrosurgery is used for resection of these masses. In rats, the Zymbal gland is a specialized sebaceous gland located around the external ear canal. Zymbal gland tumors present as large, ulcerated swellings or masses within, or ventral to, the ear canal. Squamous cell carcinoma is the most common histologic diagnosis,[23] and although these masses are locally aggressive, they metastasize late to the lymph nodes and lungs. Surgical removal can be curative if adequate surgical margins can be obtained; however, this can be difficult with large masses and usually requires a total ear canal ablation followed by reconstructive surgery.

TAIL AMPUTATION

Degloving injury of the tail is common in gerbils, degus, and chinchillas because the skin on the tail is more loosely attached than in other rodents. The exposed, skinless tail will eventually desiccate and slough off. However, it may be painful or denervated, causing it to be chewed by the patient. Local infection is a subsequent risk. For these reasons, amputation of the degloved portion is recommended.

Inject bupivacaine or lidocaine proximal to the site to block sensation to the tail stump. Place the animal in ventral recumbency and suspend the tail with tape while the site is prepared for aseptic surgery. Place a tourniquet at the base of the tail to

control hemorrhage. Incise the healthy skin with a dorsal and ventral V-shaped incision, 1 to 2 mm proximal to the edge of the degloving, to create fresh skin edges for suturing. Retract the skin proximally as far as possible and disarticulate the tail between the two most cranial coccygeal vertebrae that are exposed. This will allow adequate soft tissue coverage over the vertebral bone. Bleeding from the coccygeal vessels is easy to control with cautery or a ligature. Close the subcutis with 5-0 or 6-0 absorbable suture over the exposed ends of the vertebrae and close the skin with an intradermal suture or with tissue adhesive. Self-trauma to the amputation site is uncommon if gentle tissue handling is used. However, a temporary bandage is recommended to protect the area for 5 to 7 days after surgery.

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Orthopedics in Small Mammals

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FUNDAMENTALS OF FRACTURE REPAIR

Initial Fracture Management

With the exception of ferrets, the small mammal species commonly kept as companions are prey species. This means that they react to stress and pain differently than do dogs and cats. It is important to assess these animals for indicators of shock (see Chapter 38) and neurologic function and to treat them for pain and stress with antianxiolytics (e.g., midazolam), as well as opioids (e.g., hydromorphone, butorphanol, or buprenorphine). These treatments may make it possible to perform a thorough physical examination, as well as to provide additional supportive care (e.g., catheter placement, bandaging).

When handling all open fractures, wear sterile gloves and use aseptic technique, even if the wounds are grossly contaminated. Clip the area around the wound carefully to avoid tearing the delicate skin. A surgical clipper is the best tool for removing fur. Be patient and take care not to further complicate the wound. Carefully debride the wound and lavage the area copiously with warm sterile saline solution. We recommend the use of a 35- or 60-mL syringe with an 18-gauge indwelling catheter attached to a three-way stop-cock and saline drip set for lavage and debridement, because this combination provides a pressure of 7 to 8 psi to remove debris without damaging tissues.[12,65] However, this may not be appropriate for very small patients (<200 g); for these patients, gentle lavage with warm saline solution may be indicated. Take care not to chill the animal because small patients lose body heat very quickly. Remove underpads as they become saturated and provide warmth in the form of recirculating water blankets or gel packs. After lavage and debridement, appropriate wound care for the condition of the wound needs to be instituted.[22]

Ideally, take swab samples from the fracture site for aerobic and anaerobic bacterial cultures and then start broad-spectrum antibiotic therapy. Parenteral formulations are preferred if it is unknown how well the gastrointestinal tract is functioning.

External coaptation in the form of temporary splints or padded bandages may be indicated for some fractures. Manufactured veterinary splints are often too large for use with small mammals; therefore, use cuttable, moldable splints or bandages for temporary immobilization (see below).



Fig. 34.1 Splinting of a fractured tibia/fibula in a chinchilla. (A) Tape stirrups placed on the fractured limb. (B) Padding complete. (C) Completed splint.

Fracture Fixation Methods

The approach to fracture fixation in small mammals requires a basic understanding of the different types of bone healing (direct and indirect). Additionally, the surgeon has to determine whether a biological approach versus an open anatomic approach is best for each fracture. How this is applied to an individual fracture and patient is determined by many factors; generally, a biologic approach is used in high-energy fractures that cannot be reconstructed, and anatomic reconstruction is used in low-energy, simple fractures. Other considerations are age of the animal (which affects how rapidly bone heals and the activity level of the patient), whether the fracture is open or closed (open fractures have loss of blood supply to bone), if the patient has other orthopedic trauma (multiple trauma cases need rigid fixation), ease of managing certain types of fixation, and finances of the owner.

Rabbits have a lower skeletal mass (8%) than do cats (13%),[13] yet rabbits have a haversian bone structure like that of dogs and cats.[43] Therefore, although the fracture healing process is similar, cortical bone is thinner in rabbits than in dogs or cats. Small rodents (mice and rats) have a primitive bone system, and therefore bone healing is somewhat different than in rabbits.[43] Because guinea pigs, ferrets, chinchillas, and other rodent species discussed in this book are not used as animal models of bone healing, there is little to no information on the degree of haversian system development in these species.

Many of the surgical implants that veterinarians are accustomed to using are too large for these small species. Even the smallest bone plates/screws or positive-profile pins available can be too large. Although several companies make bone plates/screws for animals as small as 1.5 mm, this diameter screw is often greater than 40% of the diameter of the bone and therefore too large for use.[30] The recommendation never to use a screw larger than 33% to 40% of the diameter of the bone is extrapolated from studies in sheep.[16] Rabbit bone is very brittle.[4,37] One reason for fissures and failure of bone plating in rabbits is because the guideline of implant diameter in relationship to bone diameter is incorrect for rabbits, as published in a recent study.[37] Pins used for external skeletal fixations have been reported not to exceed 25% of the bone diameter. If placing pins behaves the same as holes made from drill bits, then the pin diameter to bone diameter should not exceed 15% in rabbits.[37] The positive-profile pins that are used with external skeletal clamp systems are often too large for use in small mammals.[53] Available implants will be discussed under the individual headings.

Regardless of what fixation method is used, high quality radiographs are essential to evaluate conditions associated with trauma. All fractures require two orthogonal views of the joint above and below the trauma site, both before stabilizing the fracture and after the fixation is applied. Additionally, obtain two-view radiographs of the whole body to determine whether other injuries are present that were not observed on physical examination.

External Coaptation

External coaptation in small mammals can be used effectively as a definitive orthopedic treatment for closed fractures. External coaptation methods work best for simple fractures affected by bending and rotational forces because they often interdigitate with manipulation and remain reduced. Fractures affected by compressive or shear force, such as short oblique fractures, are poorly immobilized with external coaptation.[14]

Animals will need to be anesthetized or heavily sedated to allow for proper alignment and to prevent further injury. While trying to reduce a fracture in these small animals, take care not to damage soft tissues and the blood supply. External coaptation does not achieve rigid fixation; therefore, maintaining the blood supply is paramount to ensure healing. Achieving good alignment of the joints and at least 50% cortical contact visible from two radiographic views is important for a good result. Apply standard splinting principles: maintain the affected limb in normal position, immobilize and align the joint above and below the fracture, and use a bandage and splint that can maintain adequate reduction until bony union (Fig. 34.1). At each splint change, obtain a radiograph of the limb after placing the splint to ensure adequate reduction. Because the fracture develops a soft callus with inherent stability, a radiograph of the limb will not need to be obtained after each change.

Standard materials used for splints and casts in dogs and cats can be applied in managing fractures of rabbits, ferrets, and other small mammals. Several products work well for splinting small mammals, such as Orthoplast II (AliMed, Dedham, MA) and Vet-Lite (Runlite SA, Micheroux, Belgium;

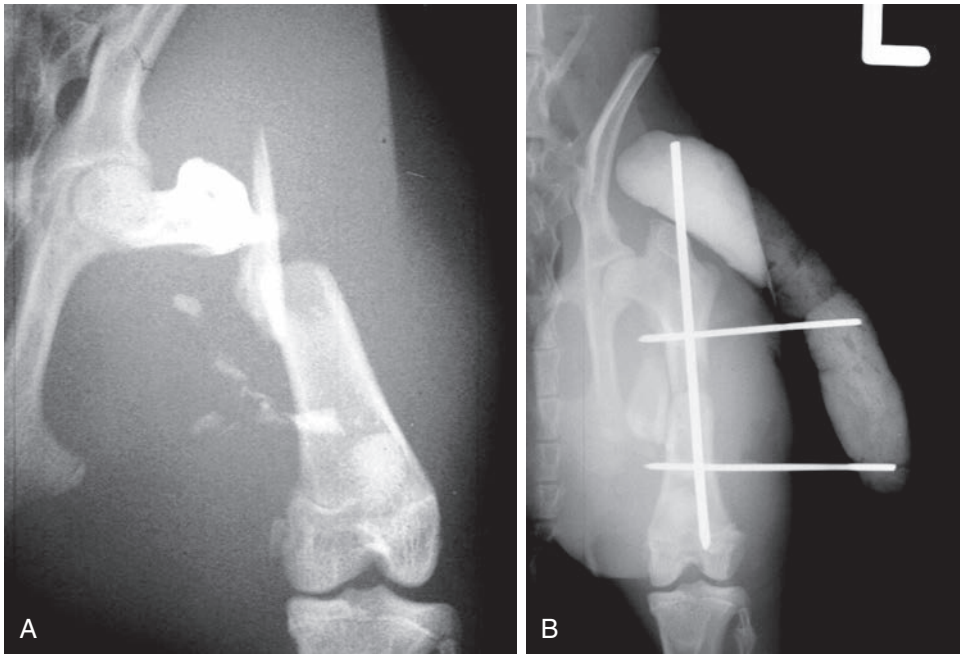


Fig. 34.2 Comminuted mid-diaphyseal femur fracture in a rabbit. (A) Preoperative. (B) Postoperative application of an intramedullary pin and external skeletal fixator.

http://www.runlite.com/vet-lite/). These are materials that are very lightweight, thin, easy to use, and biomechanically strong. They are malleable when heated in boiling water and conform to any shape when molded and allowed to cool. These products work best when used as a half cast with a light modified Robert Jones bandage, avoiding excessive pressure on the limb. Although these materials cost more than routine casting materials, the final cost is reasonable because only a small piece of material is used. Vet-Lite can be layered so that splint thickness and stiffness can be increased if desired. These products are very resistant to chewing by the animal and will not cause oral trauma or break apart and cause gastrointestinal obstruction. Encircling fiberglass casts are difficult to place without causing pressure sores and irritation but can be used with care. Fiberglass casting material can be used in strips to make a splint or bivalve, but the plastic materials, like Orthoplast II, are easier to use and care for. Alternatively, a 5- to 30-mL syringe case can also act as a splint in some cases in these very small animals when cut in half longitudinally, molded with a lighter as needed, and placed appropriately as indicated above.

Monitor animals with splints and casts weekly to prevent complications. Common complications include chewing at the splint, soiling, which leads to the formation of pressure sores or local skin infections, and swelling, which results from excessive activity or from the splint being too tight. Joint laxity and stiffness from the coaptation are also seen.[61]

Intramedullary Pinning

Intramedullary (IM) pinning can be an effective method of internal fixation for small mammals. The small diameter K-wires (pin diameters of 0.9–1.6 mm) will fit many of these species. Ideally, the IM pin should fill about 70% of the diameter of the medullary cavity at the isthmus of the bone. In one study in rabbits, results showed a pin diameter of 75% of the medullary cavity caused iatrogenic fractures when placed; therefore a 50% pin diameter was recommended.[4] Intramedullary pins primarily resist bending forces, and the recommended pin diameter should provide sufficient stiffness and strength for the fracture.[53,54] Because intramedullary pins do not counteract other forces on fractures, such as rotation, tension, and compression, many of the diaphyseal fractures in small mammals will need additional support. External skeletal fixators, separately or in a tie-in configuration, or external coaptation may be combined with IM pins (Fig. 34.2). Because these are small bones, combining apparatuses may not work as well in small mammals as they do in larger domestic species. Therefore choose an intramedullary pin as the fixation method when bending is the major force acting on the bone, for example, in spiral or long oblique fractures. Cerclage wires can be used for spiral and long oblique fractures to help counteract shear forces.

One or more K-wires can be used alone for fractures at the physis or metaphysis. If the fracture fragment has tension forces on it from ligaments or tendons, then wire used as a tension band has to be added. The technique for pins and tension band wires requires two pins, yet only one may fit. However, many of these small mammals will do well with only one pin despite the fact that rotational forces may not be counteracted.

Biodegradable implants are now available that provide adequate mechanical properties yet do not need to be removed and may stress-shield bone less than stainless steel. After implantation, biodegradable intramedullary pins are designed to dissolve into water and carbon dioxide like polylactides after a period of time.[2,5,45] These would be excellent features for an implant in small mammals. Some research on these products has been done in a rabbit osteotomy model.[56] Although results showed adequate stiffness for healing in this model, a clinical

fracture in small mammals has both biologic and biomechanical differences that may affect the outcome. Whether these implants would be stiff enough for clinical use in small mammals is unknown. Interlocking nails currently are not made small enough for small mammals and are not discussed in this chapter.

External Skeletal Fixation

External skeletal fixation is probably the most common method of repairing fractures in small mammals. External fixators provide relatively rigid stability, can be adapted for use in these small species, and cause minimal soft tissue damage.

Basic principles for applying external fixators are similar in all species. The pins should be inserted with low rotational speed (150–300 rpm). Manual insertion causes wobble and leads to premature loosening of the pins. High-speed drilling can cause bone necrosis, which also leads to the premature loosening of pins.[17,18] Smooth pins have poor holding power and tend to loosen prematurely. Smooth pins may be sufficient for these small mammals and, if used, they should be inserted at an angle and do not need to be predrilled. Negative-profile threaded pins tend to break at the thread–non-thread interface and are rarely used now that positive-profile pins are available in small sizes.[35] Predrilling with a drill bit just slightly smaller than the thread pin diameter is the correct method for inserting threaded (positive-profile) pins.[35] Imex (IMEX Veterinary Inc., Longview, TX) produces a mini-clamp-and-bar system that can hold positive-profile K wires that are as small as 0.035 inch (0.9 mm). Many small mammals are too tiny for the connecting bars that are ⅛ inch (3.2 mm). Another option is a smaller acrylic or polymethylmethacralate connecting bar that can be used with the Imex miniature Interface pins (IMEX Veterinary, Inc). The miniature Imex pins are designed as positive-profile pins with a central area that is roughened only to allow acrylic bonding to it. The roughened area is not designed for placement in the bone. Last, the FESSA (Fixateur Externe du Service de Santé des Armées) (Jorgensen Labs Loveland, CO) is a lightweight, reusable connecting bar developed by the French Armed Forces for the use of repairing fractures of the hands and feet of people.[39] It connects by tightening screws that hold the fixation pins. Because of its light weight and versatility, the FESSA may be an optimal option for use in small exotic mammals (Fig. 34.3).

With the design of external fixation clamps that are biomechanically better and the use of positive-profile pins, Type II (bilateral-uniplanar) and Type III frames (bilateral-biplanar) are almost obsolete. In large species, frames other than a Type Ia (unilateral-uniplanar) or Ib (unilateral-biplanar) are sometimes indicated, but this is rare in small mammals. The use of an IM-pin tie-in frame is useful, especially when the fracture forces are large and repair with an external skeletal fixator (ESF) alone may not counteract the forces successfully. When an IM pin is used with an ESF, it only needs to be 30% to 40% of the bone diameter. This leaves room to place the transfixation pins past the IM pin when both are used. This is a common technique used now for small mammals.

Before repairing a fracture with an external fixator, decide whether a limited open approach or closed placement of the pins is best. In species with limited soft tissue covering the bone, it is advantageous not to compromise the tissues by opening the fracture. Therefore, in simple fractures, place the external fixator with a closed technique. With highly comminuted or open fractures that need debridement, use a limited open technique to reduce the fracture and place the pins.



Fig. 34.3 Closed, comminuted, proximal third diaphyseal complete left tibia and fibula fracture with proximal and medial displacement and fibrous callus in a rabbit. (A) Preoperative view. (B) healed postoperative view at 14 weeks after application of an intramedullary (IM) pin and external skeletal fixator (ESF) stabilized with a FESSA connecting bar.

The mechanical studies on pin placements and configurations of ESF for dogs may not apply to small mammals.[43] In these small species, we rarely use more than two to three pins per segment if no IM pin is used, and when a "tie-in" (ESF IM pin) is used, one pin per segment may be sufficient for stability. Results of a recent study in the rabbit femur indicate that the transfixation pin diameter ideally should not exceed 15% of the bone diameter. In other small mammals, a guideline of 25% of the bone diameter is recommended. These recommendations apply to the femur and may not be the same in other long bone fractures.[37] In a retrospective study on the outcome of limb fractures in 139 rabbits,[58] both femoral and humeral fractures had a high incidence of complications, even with ESF fixations. Therefore the size of the transfixation pins in relationship to the size of the bone needs to be studied and potentially applied differently in the various long bones. The position of the connecting bar should be as close to the skin as possible without interfering with the skin and patient movement. Placing the bar too far away from the skin decreases the stiffness and strength of the external fixator. Remember to allow for swelling when placing the connecting bars. Spread the pins evenly across the fracture segment to achieve maximum strength. Also, place the pins through a separate stab skin incision and not through the fracture opening or original incision.[6,17,35]

Bone healing in rabbits with fractures stabilized by external skeletal fixation has been well studied as a research model. The current recommendation for external skeletal fixation in dogs and other research models is to stage the removal of the apparatus so that bone is allowed to begin to load bear at an early stage of fixation. This process has been termed *dynamization*, or *staged disassembly*.[35] In a study of rabbits with tibial osteotomies, the ideal time to remove external skeletal fixators was 6 weeks.[60] The strength and stiffness of the bone were greater if the fixator was removed at 6 weeks than if it was left in place for 12 weeks.[60] Clinically, many factors affect optimal removal time of a fixator, such as the age of the animal, the type of fracture, and the degree of vascular structure disruption. Therefore the key is to examine these patients every 2 to 3 weeks after surgery and to stage removal when there are indications that the fracture has regained normal stiffness, even though strength may not be normal. Experimentally, completely removing the fixator at 4 weeks causes some loss of reduction and is probably not advisable, even in perfectly reduced fractures.[60] When only an ESF is used, the loose pins should be removed first as long as they are not critical for stability. If an IM pin-ESF tie-in is used, the ESF pins should be checked first; if stable, it is ideal to cut the IM pin at the level where it meets the connecting bar for the first step of dynamization, but place tape to prevent the pin from migrating. Then, the second step of dynamization would be to remove the IM pin approximately one week later. If instead the transfixation pins are loose but the IM pin is not loose and the fracture is stable, then the IM pin should be left in place and the pins removed for dynamization.

Bone Plating

The use of a bone plate is appropriate for fracture repair in a ferret. Although a bone plate can be used in most ferret long bones, specifically we like to use bone plates for fractures of the humerus or femur because these can be difficult to manage with an external fixator. The soft tissue coverage over the femur and the humerus is considerable, and external skeletal fixation can be uncomfortable when used in this location. If plating is chosen, the implants commonly used are 1.5-mm and 2.0-mm bone plates. Several companies make a variety of standard and cut-to-length plates that can be used. The cut-to-length plates offer the surgeon flexibility in choosing the appropriate length, and the plates can be stacked for added stiffness. The principles of applying bone plates are covered in other texts and beyond the scope of this chapter.[40,44]

Bone plating in rabbits presents some specific problems, and we no longer recommend this technique. Clinically, the bones of rabbits have extremely thin cortices and the bone is very brittle, making screw placement difficult without stripping the cortex or fissuring the bone. We have experienced complete collapse of the bone while trying to place a screw. Results of a recent large retrospective study of long bone fractures indicated that 27% of femur fractures repaired with bone plates were nonunions. The methods did not describe the type of bone plates placed or show the type of fractures in which bone plates were used.[58] In one study comparing 2.0-mm bone plates and IM pin-ESF tie-in constructs in cadaver rabbit femurs, the authors had difficulty placing the bone screws after drilling and tapping the holes appropriately. The bones often fractured when placing the screws, demonstrating the extreme brittleness of rabbit bone and the difficulty in using bone plates with screws for fracture fixations.[4] Locking compression plates (LCP) (Synthes Vet) were developed and are successful in poor-quality bone in people and dogs, but this has not been the case in rabbits. The stability of the LCP is from the screw locking into the plate instead of the screw compressing the plate to the bone. Therefore LCPs can be placed minimally invasively without excessive contouring over the periosteum, so that rigid fixation is combined with preservation of blood supply to the bone. Locking screws have excellent holding power even when placed unicortically or in osteoporotic bone.[29,30,40,59] We have attempted to use the 1.5-mm LCP in rabbit long bone fractures with and without an IM pin when bridging fixation was indicated. Although placing the plates was successful, in each case the rabbit suffered a complex fracture of the bone that was plated 1 to 2 weeks later. Locking plates and screws function together and do not toggle out of the bone. In the described rabbits, when the locked constructs failed, large bone defects were left, similar to what has been observed in some biomechanical studies of osteoporotic bone in people.[23,68] Additional studies are being conducted to further understand the failure of using bone plates in rabbit bone.

Like biodegradable pins, biodegradable plates and screws were evaluated in the 1980s in rabbit osteotomy models; however, the perfect balance of a biologically sparing and mechanically stiff implant does not yet exist.[45] Biodegradable implants are used clinically only on non-weightbearing bones.[56,57] It is unknown whether these implants will be useful in small mammals.

FRACTURES

Generally, because the anatomy of small mammals resembles that of dogs and cats, small animal orthopedic surgery texts may

be used as guides for surgical approaches, as well as for additional information on fixation techniques for fracture types not discussed here. Important differences are discussed below where relevant and anatomic texts are available for some species.[10,28,48]

Thoracic Limb

Scapula

Scapular fractures are uncommon but can occur, often secondary to significant trauma involving the chest wall. Concurrent fractured ribs or pulmonary complications are common. Treatment recommendations will vary by the fracture location (body and spine, acromion, neck, glenoid or supraglenoid tuberosity). Fractures not involving the articular surface and that are minimally displaced heal acceptably with exercise restriction. Non-weightbearing slings such as the Velpeau may not be tolerated by all patients. Fractures involving the scapular neck or articular surface will lead to osteoarthrosis if not properly aligned, yet clinically small mammals can function well even when articular fractures of the scapular are managed conservatively.

Anatomic considerations. In rabbits, a prominent suprahamate process is present on the caudal aspect of the acromion in addition to the hamate process. The axillary artery should be avoided medially, as well as the subscapular, suprascapular, ulnar, and radial nerves.

Types of fixation. Fixation methods are K-wires in a cross-pin fashion, or tension banding for repair of articular fractures. Rabbits can tolerate a Velpeau sling.

Humerus

Fractures of the humerus most commonly occur in the diaphysis in dogs and cats,[62] and this is consistent with the fractures seen in rabbits by the authors. These fractures result in a non-weightbearing lameness with the limb dropped at the elbow. Temporary or permanent radial nerve damage, in our experience, is uncommon in these species. If there is persistent loss of withdrawal or lack of pain sensation in the limb, amputation is recommended. External coaptation is not recommended because it is difficult to immobilize the scapulohumeral joint.

Anatomic considerations. The brachial artery and vein and the median, musculocutaneous, and ulnar nerves are located medially. The radial nerve runs laterally along the distal third of the humerus and lies superficial to the brachialis muscle and underneath the lateral head of the triceps muscle.

Types of fixation. Acceptable fixation methods are bone plating on the lateral, cranial, or medial surface for ferrets, and intramedullary pins with external fixators (generally Type Ia) on fixators on the lateral aspect of the limb for rabbits. Distal humeral articular fractures should ideally be repaired. Either a bone screw in lag fashion or a cortex screw with instrument compression of the condyle can be used. In very small patients, K-wires may be sufficient to hold the condyle reduced. We have seen rabbits that are able to function even when distal humeral articular fractures are left to heal without stabilization, despite the poor range of motion of the elbow joint. However, this is not recommended because it can lead to chronic pain and lameness.

Radius and Ulna

Fractures of the radius and ulna are common and usually occur together. These fractures are more likely to be open because the soft tissue coverage in this area is poor. This should be considered in the choice for fixation. Fractures in young animals that affect the growth of either the radius or ulna can cause angular limb deformities. If they occur, early surgical intervention to prevent asynchronous growth is indicated.

Anatomic considerations. The median, ulnar, and radial arteries are present on the caudal aspect of the limb, as well as the ulnar nerve.

Types of fixation. External coaptation can be used for minimally displaced fractures or those with either the radius or ulna intact (Fig. 34.4). Extending the splint from the distal limb to the mid-humerus is critically important to provide appropriate support. Because an IM pin can compromise either the proximal or distal joint during placement, an IM pin can be used for ulnar fractures but is never indicated for radial fractures. External skeletal fixators of Types Ia or II can be used; Type Ia is usually sufficient and is placed on the medial or lateral surface depending on where the fracture is located.

Metacarpal Bones

These fractures are uncommonly seen in small mammals but may be managed with external coaptation. Although malunion is common, it is rarely clinically significant. In larger rabbits, small IM pins can be placed to align the metacarpal bones. An external coaptation splint is still necessary. To date, there are no studies that show that internal fixation of the metacarpal bones has significantly better results than using external coaptation alone.[31]

Pelvic Limb

Pelvis

Pelvic fractures (sacroiliac, ilial wing, ilial body, acetabular, ischial, pubis, or pelvic symphysis) usually involve multiple bones because of the box configuration of the pelvis. The animal should be carefully evaluated for spinal trauma, nerve damage affecting the pelvic limbs, as well as damage to the urinary tract because of the significant trauma associated with these injuries. Complications may involve altered urination or defecation if caudal nerve roots are affected.

Always consider surgical fixation for animals with a severely compromised pelvic canal, acetabular fractures, or ilial fractures that compromise the sciatic nerve. Internal fixation of a pelvic fracture has been described in a ferret.[47] Conservative management is indicated for minimally displaced ilial, ischial, or pubic fractures or sacroiliac luxations. Complications of malunion may include colonic stricture if the pelvic canal is compromised. Healing time for animals managed conservatively is similar to that for other mammals, and significant healing should occur by 6 to 8 weeks. Monitor rabbits, guinea pigs, and chinchillas closely for signs of gastrointestinal stasis if exercise is restricted for long periods.

Anatomic considerations. The surgical approach to the hip depends largely on the bones involved and the surgical plan. Take care to prevent damage to the ventral nerve roots,

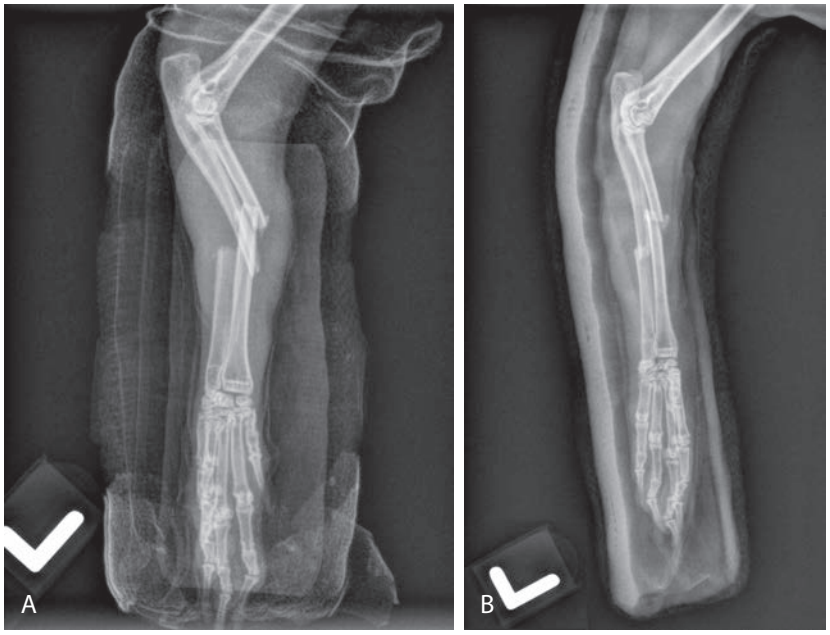


Fig. 34.4 Mid-diaphyseal radius/ulna fracture in a rabbit. (A) External coaptation with poor alignment of the fracture ends. Note that the end of the temporary splint is distal to the proximal aspect of the ulna. (B) The fracture was realigned with the animal under heavy sedation. Note the improved alignment of the fracture ends and the splint extends from the toes to the midhumerus. The splint is slightly long and was trimmed to allow the toes to be visualized.

the sciatic nerve, and the internal iliac artery and its branches during repair of the pelvis.

Types of fixation. Bone plates can be used for larger rabbits and ferrets. Other methods are interfragmentary wiring and pin-and-wire techniques. The type of fixation required will vary greatly by the type of fracture. Consult an orthopedic text for more detailed repair descriptions.

Femur

Femoral fractures are common and often significantly displaced because of the strong musculature in this area. Because Spica-type splints are not tolerated, external coaptation is not acceptable in these animals. Additionally, significant malunion will occur with limb angulation or shortening that limits ambulation. However, some fractures will heal with prolonged strict cage rest (Fig. 34.5). With these fractures, evaluate the sciatic and femoral nerves by testing deep pain perception in the lateral and medial aspects of the digits, respectively.

Anatomic considerations. The lateral approach to the femur is most common for diaphyseal fractures. Use extreme care to avoid the sciatic nerve, which is located caudal to the femoral diaphysis and deep to the biceps femoris muscle. Additionally, the popliteal and caudal femoral arteries are present caudal to the stifle.

Types of fixation. For fixation, IM pins can be placed either normograde or retrograde. Normograde insertion at the trochanteric fossa allows more lateral pin placement and easier avoidance of the sciatic nerve. Type Ia external fixators are generally placed on the lateral aspect of the limb. These may be placed alone or in combination with an IM pin (Fig. 34.2) and can be tied in. Bone plates may be used as described above for ferrets.

Tibia and Fibula

Tibial fractures are common in small mammals, particularly in guinea pigs and chinchillas. Depending on the location and degree of displacement, these may be amenable to external coaptation (Fig. 34.1). The area of the proximal tibia in small mammals, particularly rodents, is characterized by an abrupt change in the diameter of the limb distal to the stifle. This makes it difficult to properly apply splints to the lower limb. Additional padding is needed for the bandage to be cylindrical. If the splint is not placed far enough proximally (at least to the distal $\frac{1}{3}$ of the femur), the splint may slip distally and act as a fulcrum at the fracture site. A lateral-cranial or a combination of caudolateral splint may be applied.

Anatomic considerations. Avoid the saphenous artery, vein, and nerve on the medial aspect.

Types of fixation. For fixation, IM pins can be inserted normograde from the cranial aspect of the tibia, on the tibial crest. A medial surgical approach is used if the fracture site needs be opened. Type Ia external fixators may be applied lateral or medial and may be used in conjunction with an IM pin. The advantage of applying the ESF on the lateral surface is to prevent the ESF from interfering with the body wall. The disadvantage is the large musculature laterally and the fibula. Generally, Type II fixators are not required for stabilization. Bone plates on the medial surface work well in ferrets (Fig. 34.6). Bone plates in rabbits are not recommended. In rodents, bone plates are difficult to use because of the thin nature of the bone as well as the lack of good soft tissue coverage.

Metatarsal Bones

These are relatively uncommon fractures in small mammals and may be treated as described above for metacarpal fractures.

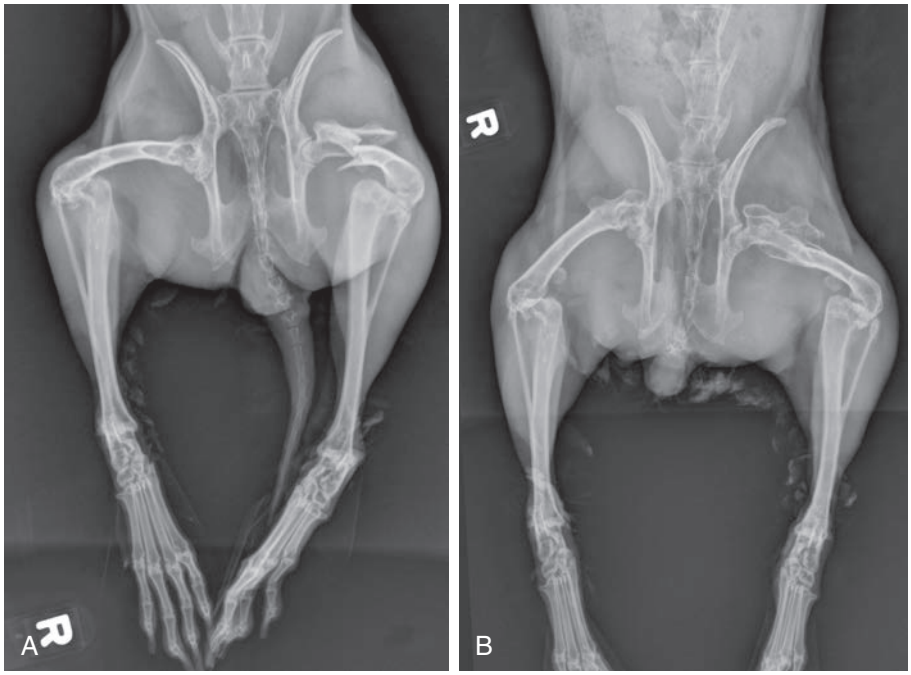


Fig. 34.5 (A) Radiographs of a middiaphyseal femur fracture in a rabbit. Note the congenital malformation of the stifle joints bilaterally. (B) Repeat radiographs 6 months after strict cage rest. A callous is visible at the fracture site and there is remodeling of the fracture ends.

Surgical repair of metatarsal fractures have been reported in the rabbit[33] and the chinchilla.[15]

Vertebrae

Spinal fractures can occur from trauma in any small mammal. Falls, cage trauma, or dog bites are common causes in companion small mammals. In rabbits, improper handling can be another cause of vertebral fractures or luxations (see Chapter 12).[47]

Even though surgical interventions to reduce and stabilize vertebral fractures in small mammals that have some intact neurologic function is feasible, this is more difficult in rabbits than in dogs or cats because of the relative lack of bone strength.[38] Because of the size of small mammals, use of the small positive-profile K-wires and an acrylic connecting bar either internally or externally is suggested. Conservative treatment of vertebral fractures is recommended in minimally displaced and stable fractures.

Skull

Very little information has been published describing treatment of skull fractures in small mammals. These generally occur secondary to severe trauma, and the animal should be carefully assessed for other lesions. A perfectly positioned skull radiographic series can be done but may miss some hard-to-see fractures. Computed tomography or cone beam computed tomography is recommended to fully assess the injuries (see Chapter 35). For animals such as guinea pigs, chinchillas, and rabbits with aradicular hypsodont dentition (long crown without closed root) with continuously erupting teeth, the long-term complications of malocclusion secondary to maxillar/mandibular skull trauma should be clearly explained to the owner. These animals may require dental occlusal adjustments (under anesthesia) every 4 to 12 weeks for life. For rats and mice, this applies to the incisors only. Fractures that do not affect occlusion or significantly reduce the opening of the nasal passage may heal well with medical management. Animals that are reluctant to eat will require placement of an esophageal feeding tube. Nasogastric tubes are inappropriate for long-term management of small hindgut fermenters because providing the fiber particle size necessary for normal digestion is difficult and the tubes are not well tolerated. Esophageal feeding tubes are placed as for dogs and cats.

Types of fixation. Many of the therapies used in dogs and cats for skull fractures apply to small mammals. Caudal mandibular fractures are not amenable to stabilization with implants because of how thin the bone is. Because the masseter muscle supports these fractures laterally and pterygoid muscle medially, medical management of unilateral fractures is often enough. Mandibular symphyseal separation can be managed with wire fixation or gluing a substantial portion of the incisors.[34]

Postoperative Management

Postoperative management of small mammals involves pain management, physical therapy, good husbandry, and frequent monitoring and maintenance of the fixation apparatus. Animals with closed fractures only need perioperative antibiotics (a dose given intravenously within 1 to 2 hours before and every 2 hours during surgery), but open, contaminated fractures may require extended antibiotic therapy. Ideally, choose the antibiotic according to the sensitivity pattern of a bacterial culture taken initially.

Some techniques used in managing open fractures in dogs and cats are not feasible in small mammals. Placing drainage systems or treating open wounds daily with sterile flushes and



Fig. 34.6 Short oblique fracture of the mid tibial/fibular diaphysis with medial, proximal, and caudal displacement in a ferret. (A) Preoperative view; (B) after application of an eight-hole, 1.5-mm locking plate with five bicortical locking screws.

bandages is extremely difficult. Animals chew excessively at bandages or reach the wound unless a hard splint made of one of the casting materials discussed above has been placed on the limb. In some species, daily flushes can only be managed with heavy sedation or anesthesia. This is expensive and stressful, especially for rodent species. Therefore wound management should be definitive at the time of surgery, if at all possible.

Whenever a splint is used, review bandage care with the owner. Have the owner check the toes for swelling or discharge. These species often chew at splints even if they appear comfortable. Extreme discomfort in these animals often manifests as quietness and anorexia. Recheck the splint every week, with the first recheck scheduled within a few days of splint placement.

For fractures repaired with one of the above fixation methods, evaluate the fracture radiographically in 3 to 6 weeks. In these species, this usually requires heavy sedation or anesthesia. Because radiographic findings often lag behind clinical healing, good palpation of the fracture is also important. Depending on the type of fixation, changes can be made in the apparatus as healing becomes evident on radiographs.

Complications

The ultimate goal in fracture repair is bony union. Unfortunately, this does not always occur despite our use of sophisticated techniques, resulting in a delayed union, nonunion, or malunion. Please see orthopedic textbooks for specifics of each condition.[41] Because of their small size, light body weight, and locomotive stance, these animals seem to tolerate deformities with minimal clinical significance.

Posttraumatic osteomyelitis is another potential complication of fractures in rabbits, ferrets, and other small mammals. Wound contamination and bone avascularity are risk factors for posttraumatic or postoperative infection. An infected wound needs more than 10^5 organisms per gram of tissue to induce posttraumatic osteomyelitis.[7,67] Therefore, good surgical debridement and copious lavage are very important in managing open fractures. Adhering to strict sterile surgical technique, careful wound handling, hemostasis, and anatomic closure helps prevent posttraumatic osteomyelitis.[7,67]

Radiographically, rabbits with posttraumatic osteomyelitis show periosteal reactions and osteolysis.[67] Rabbits develop caseous, nondraining abscesses; thus typical drainage techniques are not useful.[44] Treatment of osteomyelitis in rabbits must be aggressive. Collect samples for aerobic and anaerobic cultures, debride the wound, and administer an appropriate antibiotic. Additionally, antibiotic-impregnated beads are recommended to avoid antibiotic inactivation by the loss of blood supply to the infected, traumatized area. Many in vitro studies show varied results depending on the antibiotic used, the form used (powder vs liquid), the antibiotic concentration, the carrier medium (polymethylmethacrylate, hydroxyapatite cement, calcium sulfate, and biodegradable polymers), and the carrier medium surface area.[34,52,65,66] The use of multiple antibiotics within a single bead has been shown to significantly increase the rate of elution.[46,49] Local tissue conditions, including seroma formation, fibrous tissue, and blood supply, also affect elution.[7–9] Because antibiotic beads may continue to elute over an extended period, leaving them permanently at the infected site may be advantageous.[20,26,52] However, nonabsorbable beads potentially can act as foreign bodies and harbor bacteria once the antibiotic concentration decreases.[8] Calcium sulfate beads are resorbed optimally within 4 to 8 weeks (Kerrier.com). When using impregnated beads, use an appropriate antibiotic and dose. Higher doses elute more antibiotic[3,20,49,65]; however, systemic levels of drugs are often nondetectable or are only present initially.[1,9] Use caution if beads contain high levels of antibiotics known to elicit enteritis in rabbits and other hind-gut fermenters.[1,9,44]

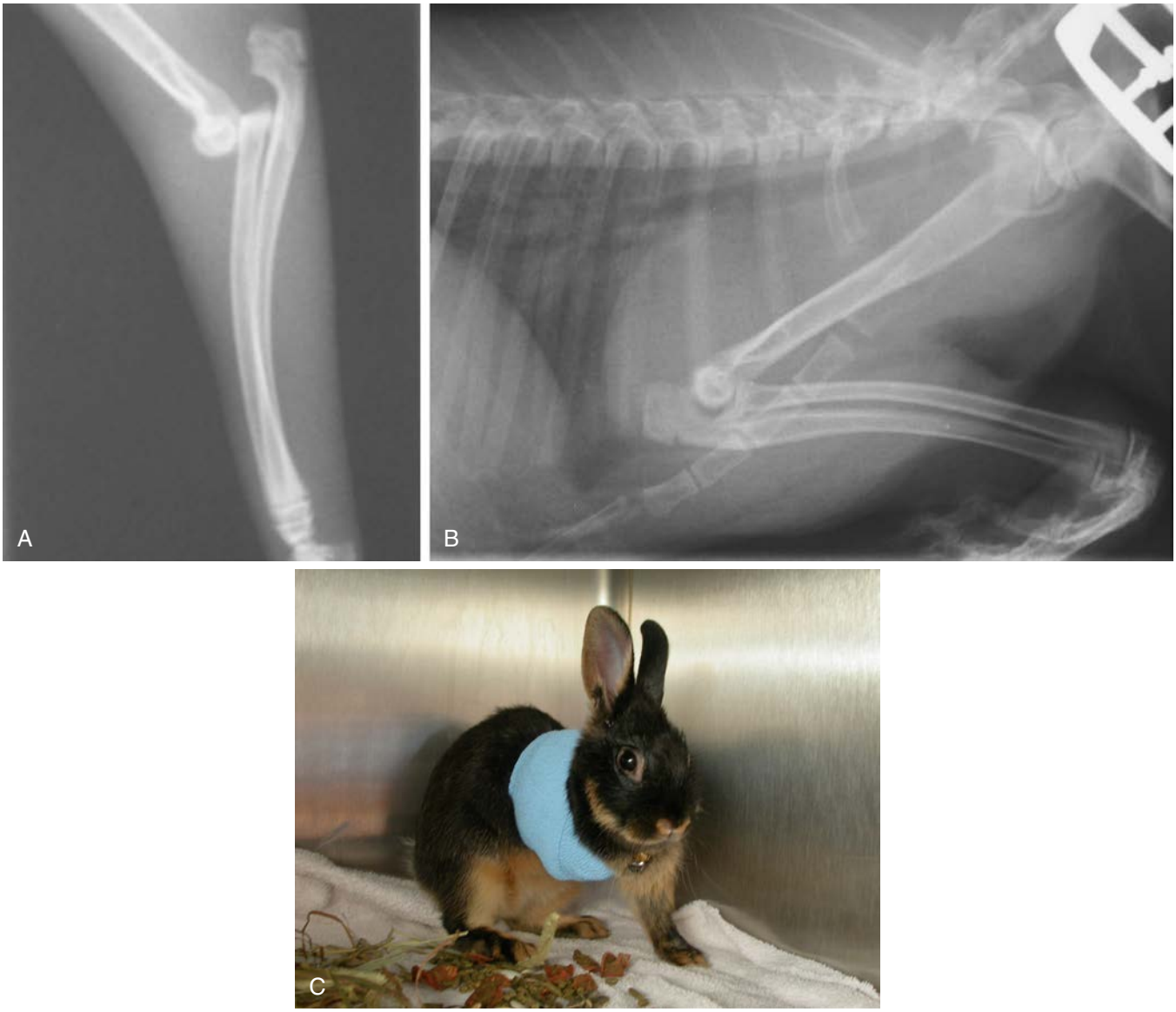


Fig. 34.7 (A) Caudal proximal luxation of the elbow in a rabbit, (B) after closed reduction under general anesthesia and application of a Velpeau sling to maintain the joint in flexion, (C) rabbit with applied Velpeau sling.

A similar type of abscess can develop in small rodents, but the incidence of posttraumatic osteomyelitis appears to be low. Ferrets with posttraumatic osteomyelitis have manifestations similar to those of dogs and cats. Therefore treatment and the use of drainage systems can be similar. In severe cases, antibiotic-impregnated beads can be used as well.

When treatment for posttraumatic osteomyelitis is unsuccessful, which is common in rabbits, amputation of the limb is the only option. This is a salvage procedure that is reserved for only those animals for which prognosis for successful treatment is very poor.

LUXATIONS

Thoracic Limb

Scapulohumeral Joint

Shoulder luxations are rare and can be managed with a transarticular pin technique.

Elbow Joint

Elbow luxations occur occasionally in ferrets[51] and rabbits.[63] These cases present with a non-weightbearing lameness and a very painful, swollen elbow joint. Treatment for elbow luxation involves reduction and stabilization of the joint. In some cases, closed reduction can be performed under deep sedation or general anesthesia, followed by external coaptation for 10 to 14 days. Rabbits require a bandage with the elbow in flexion in a Velpeau sling (Fig. 34.7),[63] whereas ferrets should be position with the elbow in extension in Spica splint or cast that prevents elbow flexion.[51] Many elbow luxations need internal fixation to heal. For internal fixation, place a transarticular pin through the joint and then place a light Orthoplast II or Vet-Lite splint. The transarticular pin keeps the joint reduced while the splint prevents full weight-bearing by the animal (Fig. 34.8). The pin must be removed in approximately 3 weeks. The splint is usually needed for support for another 2 to 3 weeks after pin removal. Elbow luxation repair is usually successful with this technique.

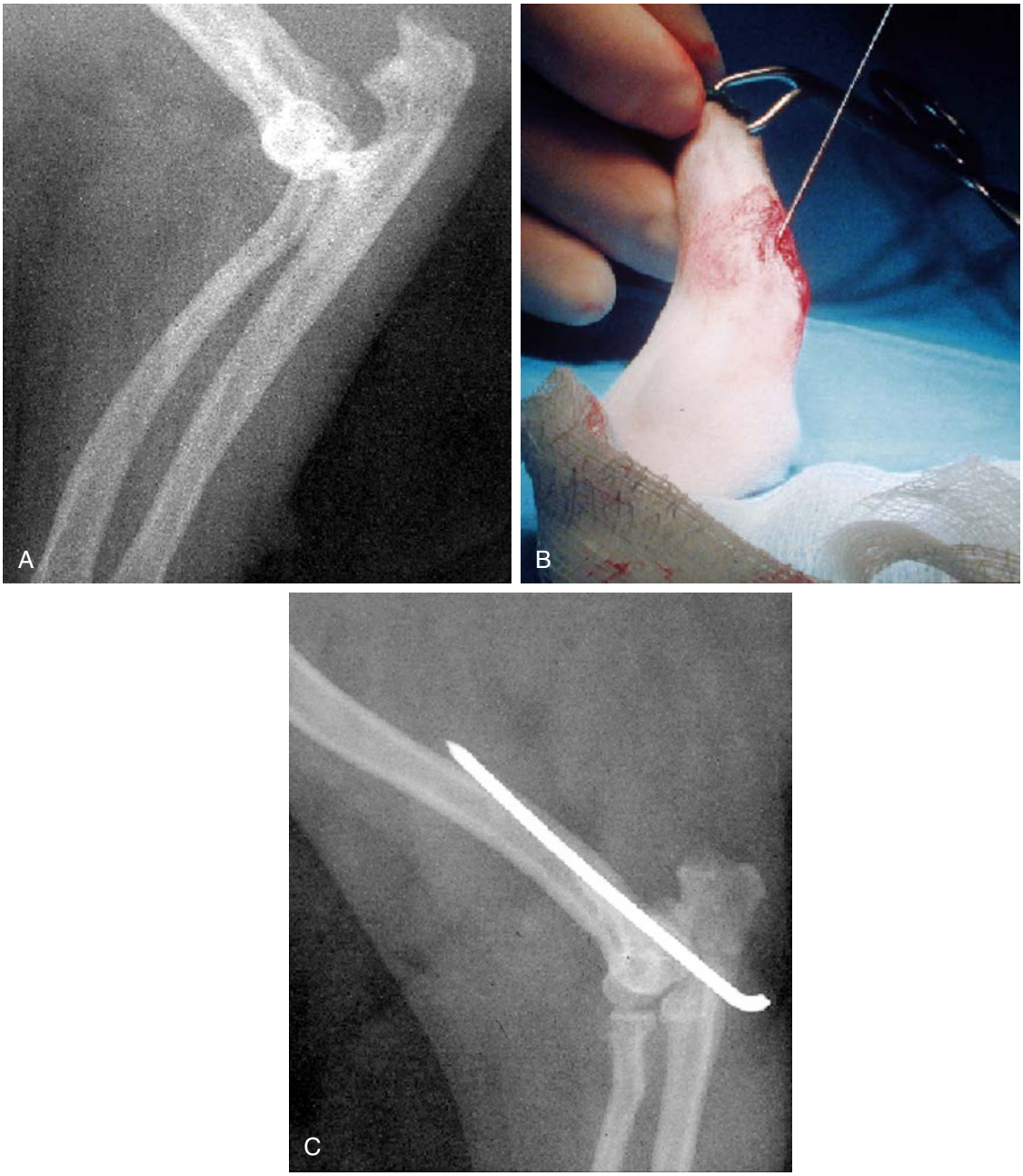


Fig. 34.8 (A) Caudal proximal luxation of the elbow in a ferret. (B) Insertion of a transarticular pin. (C) After insertion of the transarticular pin.

Potential complications of this technique is fracture of the olecranon or fracture of the pin at the interface between the ulna and humerus.[24] Another option is to use a transarticular ESF with positive-profile pins and acrylic connecting bar extending from the humerus to the distal radius. We prefer the transarticular pin technique because it has less chance for iatrogenic fracture of the bones than the transarticular ESF technique. Other techniques described in rabbits include closure of the torn ligaments and muscle mass around the dislocated elbow[24] and replacement of the humeroulnar collateral ligament as described in rabbit cadavers.[63] Because of the size of the collateral ligaments and the thinness of the joint capsule, primary repairs of these structures alone rarely keep the elbow reduced.

Carpal Joint

Luxations of the carpus are an uncommon injury. Primary repairs of the ligaments have the same difficulty as seen in repair of the elbow. External coaptation allowing ankylosis of the joints can be successful. Small K-wires can be used for ankylosis in conjunction with splints. See orthopedic texts for arthrodesis techniques.

Interphalangeal Joint

Phalangeal luxation is an underdiagnosed presentation, and often subclinical. Closed reduction can be attempted. If the luxation recurs or causes pain, amputation can be considered.

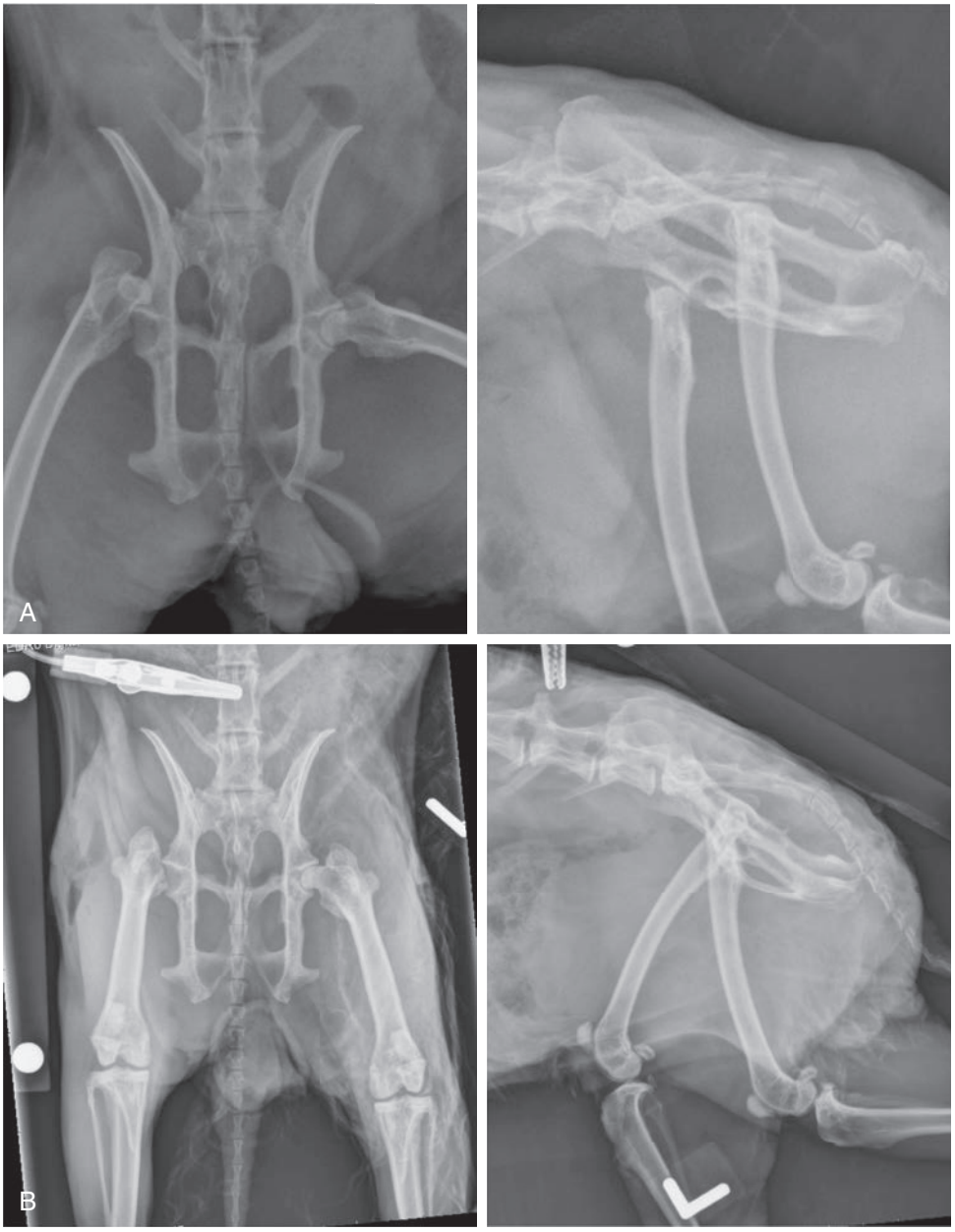


Fig. 34.9 Ventrodorsal and laterolateal radiographic view of a rabbit with craniodorsal coxofemoral luxation (A) before and (B) after surgical excision of the head and neck of the femur.

Pelvic Limb

Coxofemoral Joint

Coxofemoral luxations are also rare and can sometimes be reduced in a closed fashion under deep sedation or general anesthesia. The technique for reduction of the coxofemoral luxation, both craniodorsal and cranioventral, has been described in rabbits.[24] Strict cage rest is required for at least one to two weeks.[24] If closed reduction fails, surgical treatment is indicated. Many techniques successful in keeping the femoral head reduced in larger domestic mammals require implants that are too large for this species.[27] Femoral neck and head ostectomy has been described in detail in rabbits[11] (Fig. 34.9). Other surgical techniques described in rabbits include the placement of a permanent suture through two holes drilled into the greater trochanter and anchored to the origin of the head of the quadriceps just proximal to the joint, mimicking the iliofemoral ligament,[24] and the use of a toggle-pin fixation.[36] Results of a recent retrospective study evaluating nine cases of coxofemoral joint luxation in rabbits concluded that if closed reduction fails, treatment with open reduction and iliofemoral suture may be more appropriate than femoral head and neck osteotomy if the integrity of the hip joint allows it.[21] Postoperative care should include surgical site management, adequate pain management, and initial cage rest followed by physical therapy.

Stifle

Patellar luxation has been reported in rabbits[50] but remains an uncommon presentation. In one report, a trochlear wedge recession sulcoplasty was performed and resulted in temporarily alleviating the lameness for 6 months after surgery.[50]

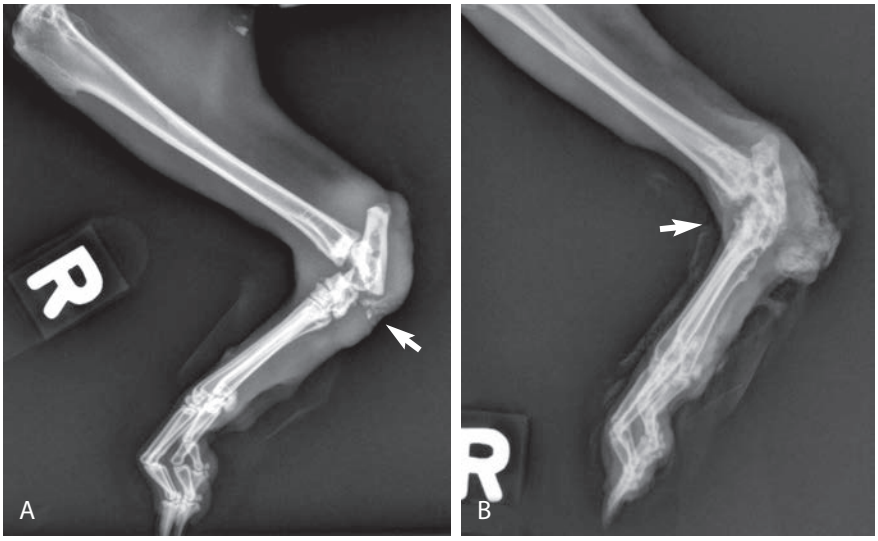


Fig. 34.10 (A) Lateral radiograph of an intertarsal luxation *(arrow)* in a rabbit. (B) Repeat lateral radiograph after 8 weeks of external coaptation. Note the extensive periarticular bony proliferation *(arrow)*.

The reason for ultimate failure of the technique in this case is not known, but it may be related to the concurrent joint effusions.

Tarsal joint. Tarsal luxation is a commonly seen injury in rabbits and often presents as a severely deranged joint. Primary repair of the ligaments have the same difficulty as described in the elbow and carpal joints. A surgical technique has been described in a rabbit in which transosseous tunnels are created where the medial long collateral ligament originates (medial malleolus) and inserts (talus).[55] A nylon suture is passed through the tunnels in a figure-of-eight pattern to replace the function of the damaged ligament. External coaptation during surgical healing was provided by using a Robert-Jones bandage, replaced by a fiberglass cast after 3 weeks. Also, external coaptation allowing ankylosis of the joints can be successful (Fig. 34.10). The patient will develop significant degenerative joint disease, yet clinically most small mammals do well. Deranged tarsal joints can be ankylosed with external fixation with transverse pins in the proximal tibia and distal row of tarsal bones and bolting them into a triangular transarticluar fixator. The external fixator is placed with the limb in a normal standing position for 2 to 6 weeks.[24] Small K-wires can be used for arthrodesis in conjunction with splints. See orthopedic texts for arthrodesis techniques.

CRUCIATE LIGAMENT RUPTURE

Rupture of the cranial cruciate ligament appears to be a common presentation in rabbits and can be unilateral or bilateral.[24] The rabbits present with acute-onset hindlimb lameness. Physical examination reveals a positive cranial drawer sign, and radiographic findings are variable depending on the chronicity. Extracapsular techniques of surgical stabilization have been reported in detail in rabbits,[24,63] similar to those in dogs and cats. Numerous experimental surgical techniques for repair of cruciate ligaments have also been reported in rabbits, as a research model, with variable success.

SEPTIC ARTHRITIS

Septic arthritis is a joint infection caused by bacterial organisms. It can be the result of hematogenous spread from another organ, but more often it is caused by direct bacterial inoculation of joints from pododermatitis or penetrating trauma.[24] Common organisms include *Pasteurella multocida* and *Staphylococcus* species in rabbits, but perform culture and susceptibility testing if considering treatment.[24] Animals are presented with lameness, swollen joints, and reduced range of motion. Radiographic findings range from joint effusion and soft tissue swelling to bone lysis, periosteal new bone formation, joint surface irregularities, and joint subluxation. The treatment includes antimicrobials based on culture and susceptibility, analgesics, and surgical lavage of the joint under general anesthesia with the goal to remove the purulent material. The caseous nature of the rabbit pus makes this procedure difficult. The prognosis depends on the severity and chronicity of the disease. Salvage procedure for chronically painful joints includes arthrodesis or amputation.

AMPUTATIONS

Amputation is indicated in small mammals when orthopedic trauma is so severe that it is unmanageable. These cases include open, infected fractures with exposed bone and compromised vasculature; fractures affecting a joint that cannot be properly aligned; or a limb with fractures involving multiple bones with a high risk of implant failure or future complications (i.e., severe degenerative joint disease, limb deformity). Limbs with pathologic fractures should be amputated as for dogs and cats. Financial constraints of an owner may also dictate the need for amputation.

Fortunately, most small mammals seen in practice will tolerate amputations. In a retrospective study, rabbits tolerated limb amputation well, and most owners were satisfied, but obese rabbits, large rabbits, and those with concurrent musculoskeletal disease, neurologic disease, or pododermatitis developed life-threatening morbidity, and some had to be euthanized.[42]

The level of amputation depends on the lesion site. Covering the amputation site with sufficient soft tissue to prevent trauma to the limb and self-mutilation is very important. After surgery, provide extra cage padding and monitor the animal for foot lesions caused by uneven weightbearing. Because postoperative pain may induce mutilation of the amputation site, consider analgesia when planning these procedures. Use epidural analgesia and local nerve blocks, either preemptively or during surgery, where indicated (see Chapter 37).

Thoracic Limb

Removing the scapula is easier and more cosmetic than amputating at the scapular-humeral joint. Some surgeons prefer to leave the scapula because it serves as a protective barrier to the chest wall. The surgical approach to the scapula in most small mammals is similar to that in dogs and cats; however, rabbits have a prominent suprahamate process on the caudal border of the scapula. The scapula can be abducted from the body after transecting the omotransversarius, the rhomboideus, the thoracic part of the trapezius muscles, and the insertions of the latissimus dorsi, teres major, and cutaneous trunci muscles. This allows for easier isolation and transection of the thoracodorsal nerve, the axillary and the external thoracic arteries, and the brachial and axillary veins. Additionally, transect the median, ulnar, radial, axillary, subscapular and suprascapular nerves. The scapula may then be removed, and closure is routine.

Pelvic Limb

The pelvic limb can be amputated at the mid-femur, which will provide a supportive stump to help with weightbearing when the animal sits. However, the limb can be amputated at the coxofemoral joint for infected fractures involving the proximal femur. The techniques for pelvic limb amputation have been described in ferrets,[19] rabbits,[25] and chinchillas[32] and are similar as those used for dogs and cats. When performing coxofemoral amputation in intact males, consider doing castration at the same time to prevent trauma to the scrotum and testes since this area will be more exposed. The bone has a tendency to shatter, so use caution when the bone is cut. Also, transect the femur proximal to the site where the muscle is transected to allow for sufficient coverage of the remaining femur.

ACKNOWLEDGMENTS

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35

Exotic Mammal Diagnostic and Surgical Endoscopy

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Pet rabbits *(Oryctolagus cuniculus)*, ferrets *(Mustela putorius furo),* and rodents (order Rodentia) represent the third-largest group of companion mammals (behind dogs and cats) in the United States.[1] This group represents an expanding component of small-animal practice, with many clients expecting the same level of medicine for these animals as for more traditional pets. The advent of the certifying college examinations in zoological companion species (American College of Zoological Medicine) and exotic companion mammals (European College of Zoological Medicine), as well as various practitioner boards and certification systems (e.g., American Board of Veterinary Practitioners, Royal College of Veterinary Surgeons) has further galvanized the need for veterinarians to provide the high-quality care being demanded for these species. Most rabbits, ferrets, and rodents presented to practitioners weigh less than 2 kg, and, given their small size, are ideal candidates for minimally invasive diagnostic and surgical endoscopic techniques. Indeed, in some situations, the development of endoscopy has enabled many procedures to be performed for the first time or with significantly reduced morbidity and mortality rates compared with traditional surgery. Considerable advances in exotic animal endoscopy have been made over the past 5 years, and further development and refinement seem assured.[6]

PATIENT SELECTION

Unlike ferrets, which are carnivores, rabbits and rodents are prey animals; as such, they generally mask symptoms until disease is advanced. Consequently, many rabbits and rodents may require nursing support (particularly analgesia, fluid therapy, and nutrition) before anesthesia and endoscopy.

The most common endoscopic procedures performed in rabbits and rodents are stomatoscopy, rhinoscopy, otoscopy, cystoscopy, laparoscopy, and endotracheal intubation. In ferrets, laparoscopy and gastroscopy are most common. In addition to anesthetic contraindications, obesity can hamper laparoscopy; in most cases, however, it is small patient size that presents the greatest challenge to the exotic mammal endoscopist.

PATIENT EVALUATION

Detailed husbandry and medical anamneses are essential, because many ailments are associated with poor management. Ideally, hematologic testing, plasma biochemical analysis, and urinalysis should precede anesthesia; in many cases, however, short-term anesthesia may be required to collect such samples, whereas in small rodents, the required volume may prove difficult to obtain. In addition, regional diagnostic imaging is advised before endoscopy.

ANESTHESIA

The diversity within the exotic mammal group necessitates generalities rather than specifics, and reference should be made to the extensive literature on rabbit, ferret, and rodent anesthesia (see Chapter 37). Anesthesia is required for safe and effective endoscopy in exotic mammals. Intubation and ventilation are essential for laparoscopy, thoracoscopy, and procedures requiring neuromuscular blockade (e.g., rhinoscopy).

TABLE 35.1 Endoscopic Instrumentation for Ferrets, Rabbits, and Rodents

Equipment Description	Primary Indications
Visualization & Documentation	
• Endovideo camera and monitor • Xenon light source and light guide cable • Digital capture device (e.g., TELEPAK VET X LED)	• Required for all endoscopy procedures
Endoscopes	
• 1-mm × 20-cm semirigid miniscope, 0°	• Stomatoscopy, otoscopy, rhinoscopy in animals weighing <500 g • Endotracheal intubation in animals weighing <1 kg
• 1.9-mm × 18.5-cm telescope, 30° oblique, with integrated 3.3-mm operating sheath	• Stomatoscopy, otoscopy, rhinoscopy in animals weighing 500 g-10 kg • Endotracheal intubation in animals weighing 1-8 kg • Laparoscopy in animals weighing <1 kg
• 2.7-mm × 18-cm telescope, 30° oblique 4.8-mm operating sheath	• Stomatoscopy, otoscopy, rhinoscopy in animals weighing 500 g-10 kg • Endotracheal intubation in animals weighing 1-8 kg
• 3-mm × 14-cm telescope, 0°	• Laparoscopy and thoracoscopy in animals weighing 1-8 kg
• 5-mm × 8.5-cm otoendoscope, 0°, with integrated operating sheath	• Stomatoscopy and otoscopy in animals weighing 3-40 kg
Flexible Instruments for Use with Operating Sheaths	
• 1-mm biopsy forceps • 1-mm grasping forceps	• For use with 1.9-mm telescope and integrated sheath
• 1.7-mm × 34-cm biopsy forceps • 1.7-mm × 34-cm single-action scissors • 1.7-mm remote injection needle • 1.7-mm × 34-cm grasping/retrieval forceps • 1.7-mm × 60-cm wire basket retrieval • 1.7-mm needle end radiosurgery electrode	• For use with 2.7-mm telescope and 4.8-mm operating sheath, and 5-mm otoendoscope
Insufflation	
• CO_2 insufflator with silicone tubing • Sterile saline suspended above endoscopy table with intravenous drip line to a port on the operating sheath	• Used for insufflation during laparoscopy • Used for sterile saline infusion for otoscopy, rhinoscopy, cystoscopy, vaginoscopy, and colonoscopy
Rigid Instruments and Cannulas for Multiple-entry Laparoscopy and Thoracoscopy	
• 2.5-mm graphite and plastic cannula • 2-mm Reddick-Olsen dissecting forceps, plastic handle without racket • 2-mm Metzenbaum scissors, plastic handle without racket • 2-mm Babcock forceps, plastic handle with racket	• Used with the 1.9-mm telescope for laparoscopy and thoracoscopy in animals weighing <1 kg
• 3.9-mm graphite and plastic cannula (accommodates 2.7-mm telescope and 3.5-mm protection sheath) • 3.5-mm graphite and plastic cannula (accommodates 3-mm instruments) • 3-mm fenestrated grasping forceps • 3-mm Reddick-Olsen dissecting and grasping forceps • 3-mm short curved Kelly dissecting and grasping forceps • 3-mm atraumatic dissecting and grasping forceps • 3-mm Babcock forceps • 3-mm Blakesley dissecting and biopsy forceps • 3-mm scissors with serrated curved double action jaws • 3-mm micro-hook scissors, single action jaws • 3-mm Mahnes bipolar coagulation forceps • 3-mm irrigation and suction cannula • 3-mm palpation probe with centimeter markings • 3-mm distendable palpation probe • 3-mm ultramicro needle holder • 3-mm knot-tier for extracorporeal suturing • 2 plastic handles without rackets • 1 plastic handle with Mahnes-style racket • 1 plastic handle with hemostat-style racket	• Used with the 2.7-mm telescope for laparoscopy and thoracoscopy in animals weighing 1-8 kg
Radiosurgery Equipment	
• 3.8- or 4.0-MHz dual radiofrequency unit with foot pedal • Monopolar lead to connect to plastic instrument handles • Bipolar lead to connect to 3-mm Mahnes bipolar coagulation forceps	• Enables endoscopic instruments to be used as monopolar devices and facilitates bipolar coagulation

During rhinoscopy of rabbits and larger rodents, intranasal administration of lidocaine and short-term neuromuscular blockade using atracurium further enhance immobilization; otherwise, a much deeper plane of general anesthesia would be required.

INSTRUMENTATION

Given the variation in patient size and the nature of the procedures that may be performed, a variety of different scopes and instruments may be used (Table 35.1). For most practices, the 2.7-mm system offers the greatest versatility, which can be built on as individual practice caseload dictates. This system offers several advantages, including being applicable to single-entry procedures, as well as having ports for air or saline solution infusion and an operating channel for the introduction of 5-Fr instruments (Fig. 35.1). In addition, the 1.9-mm telescope with an integrated sheath and the 1-mm semirigid miniscope are extremely useful for smaller mammals (Fig. 35.2). For multiple-entry endoscopy, the recent application of human pediatric 2- and 3-mm instruments to exotic animal endoscopy has enabled laparoscopy and thoracoscopy to become a reality, and a dedicated 3-mm laparoscope is also available (Figs. 35.3 and 35.4).

Flexible bronchoscopes and gastroscopes are indicated for bronchoscopy and ferret gastroscopy, respectively. Gastroscopes provide a four-way tip deflection, an instrument channel, and air insufflation and have suction and fluid irrigation capabilities. The smaller bronchoscopes provide a one- or two-way deflection tip and an instrument channel.

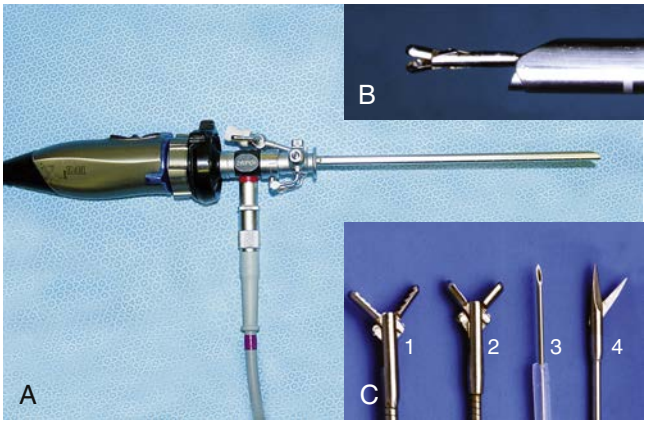


Fig. 35.1 The 2.7-mm telescope system. (A) 2.7-mm telescope housed within a 4.8-mm operating sheath, connected to a light cable and an endovideo camera. (B) 1.7-mm biopsy forceps inserted down the instrument channel and emerging directly in front of the telescope. (C) A variety of 1.7-mm instruments can be used through the operating channel, including retrieval forceps *(1),* biopsy forceps *(2),* remote injection/aspiration needle *(3),* and single-action scissors *(4).* (Courtesy Dr. Stephen J. Divers.)

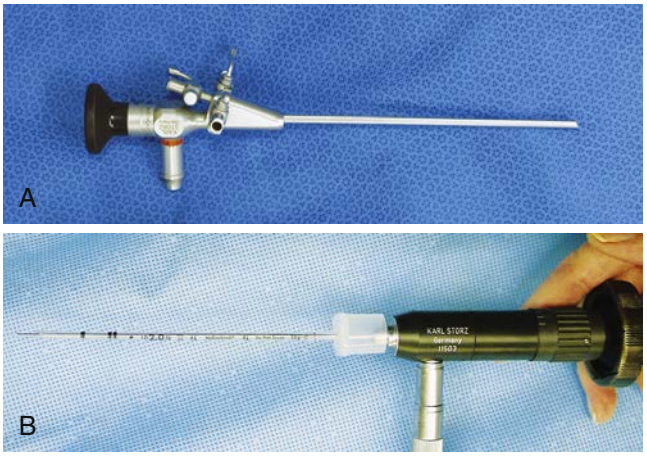


Fig. 35.2 (A) 1.9-mm telescope with integrated operating sheath. (B) 1-mm semirigid miniscope with a 2-mm endotracheal tube placed over the scope in preparation for exotic mammal intubation. (Courtesy Dr. Stephen J. Divers.)

PROCEDURES

In general, the approach to exotic mammal endoscopy is similar to that in dogs and cats, and much can be learned and applied from the domestic animal and human literature.[14] However, in addition to the anatomic peculiarities of these creatures, the exotic mammal endoscopist must be more precise, given the confines within which it is often necessary to work. It is therefore particularly important to use the fingers and thumb of the inferior hand to support the tip of the telescope to ensure accurate control at all times.

Otoscopy

With the anesthetized animal in sternal or lateral recumbency, the ear canals can be evaluated in detail. In cases of severe disease, gently remove superficial exudates and debris before infusing sterile saline solution and working within a fluid environment. Abnormalities can be sampled for histopathology and microbiology by using the biopsy forceps; this technique tends to provide more precise results than introducing a culturette down the ear canal. Depending on the size of the animal, diameter of the scope, and nature of the aural disease, it is often possible to examine the ear canals down to the tympanum (Fig. 35.5). It is especially important to examine the tympanum

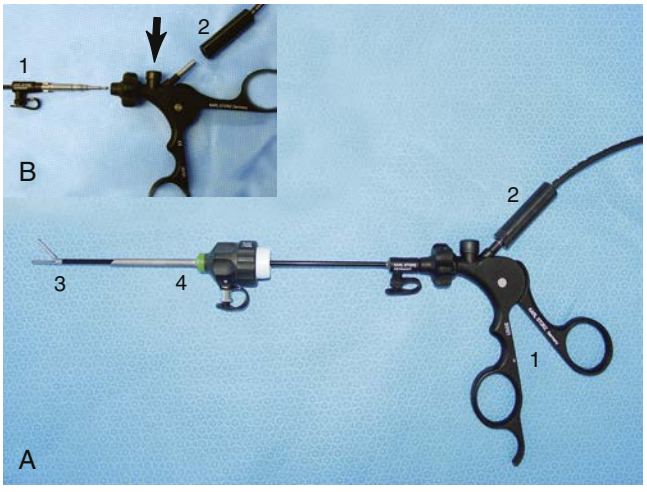


Fig. 35.3 Multiple-entry 3-mm endoscopy system. (A) Plastic, nonracket handle *(1)* attached to radiosurgery *(2),* and a 3-mm instrument *(3),* which is inserted through a 3.5-mm cannula *(4).* (B) Instruments *(1)* are interchangeable by pressing the button *(arrow).* In addition, the radiosurgery connector *(2)* on the handle enables the instrument to be used as a monopolar device. (Courtesy Dr. Stephen J. Divers.)

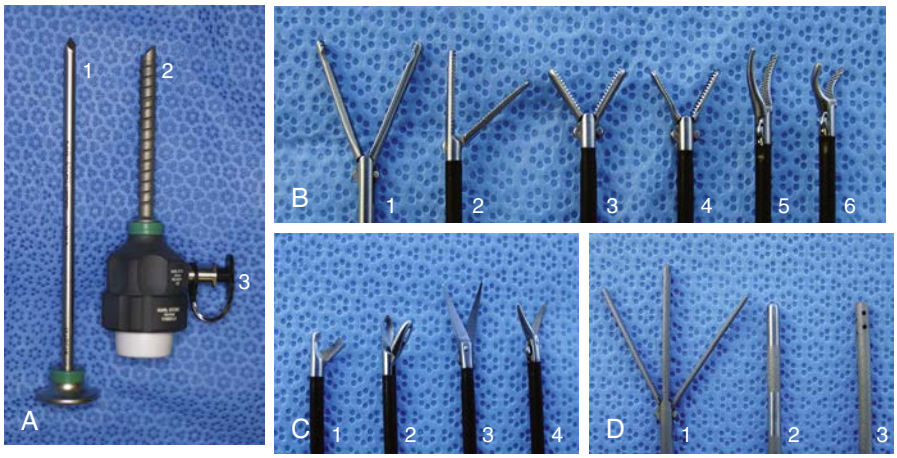


Fig. 35.4 Multiple-entry 3-mm endoscopy system. (A) Trocar *(1)* and 3.5-mm plastic/graphite cannula *(2)* with side insufflation port *(3)*. (B) Forceps: Babcock forceps *(1)*, atraumatic dissecting and grasping forceps with single-action jaws *(2)*, Reddick-Olsen dissecting forceps *(3)*, fenestrated grasping forceps *(4)*, long curved Kelly dissecting and grasping forceps *(5)*, short curved Kelly dissecting and grasping forceps *(6)*. (C) Scissors and biopsy instruments: micro-hook scissors with single-action jaws *(1)*, Blakesley dissecting and biopsy forceps *(2)*, scissors with long, sharp, curved double-action jaws *(3)*, scissors with serrated curved double-action jaws *(4)*. (D) Probes: distendable palpation probe *(1)*, palpation probe with centimeter markings *(2)*, irrigation and suction cannula *(3)*. (Courtesy Dr. Stephen J. Divers.)

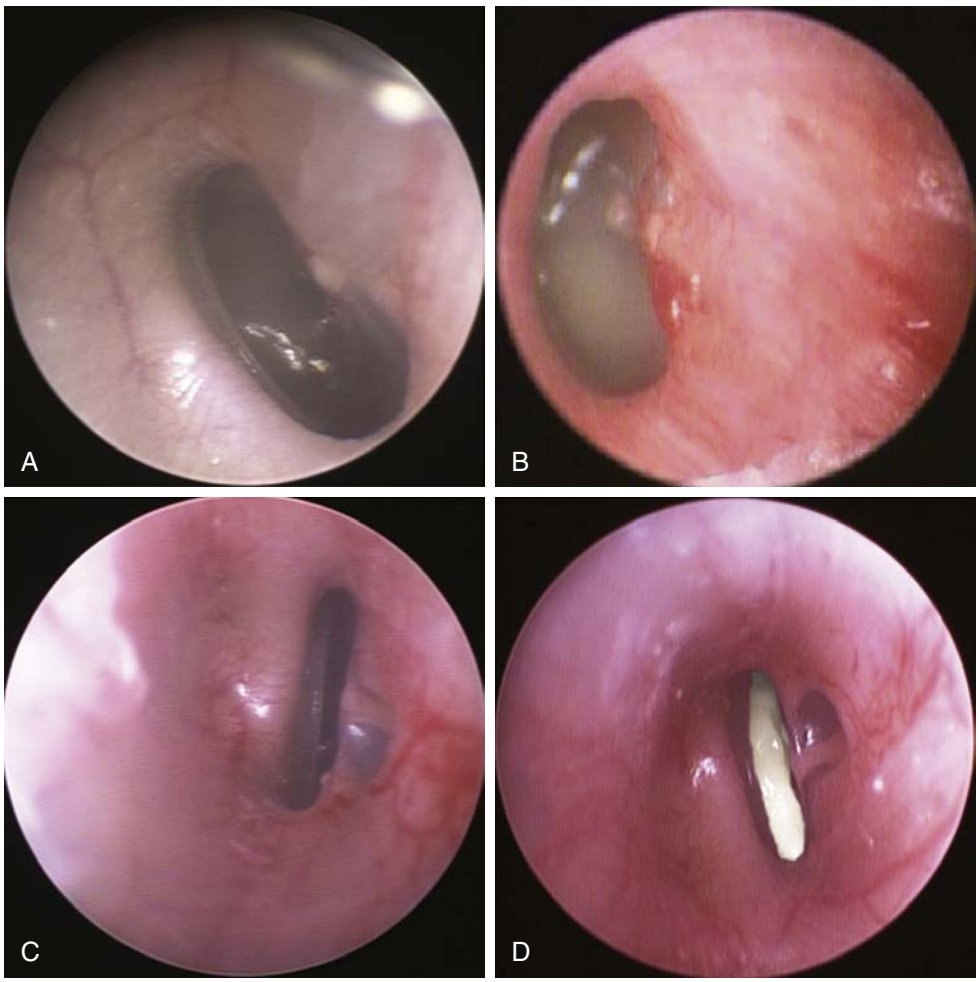


Fig. 35.5 Rabbit otoscopy. (A) Normal horizontal canal and tympanum. (B) Inflamed horizontal canal with caseous debris visible behind an intact tympanum. (C) Ruptured tympanum without evidence of inflammation or infection. (D) Otitis media with ruptured tympanum and caseous debris. (Courtesy Dr. Stephen J. Divers.)

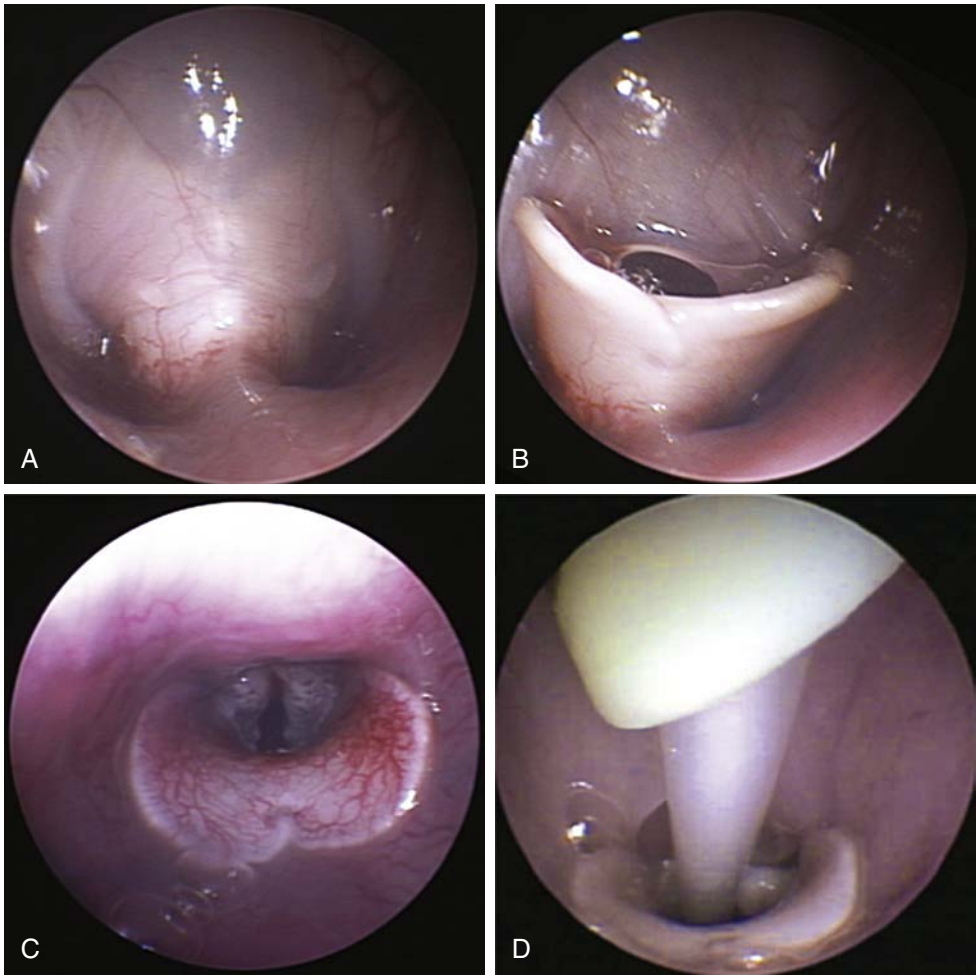


Fig. 35.6 Rabbit intubation. (A) Normal resting position of the epiglottis engaged over the caudal edge of the soft palate in an obligate nasal-breathing rabbit. (B) After induction and with the head and neck extended, the endoscope is used to displace the soft palate dorsad to free the epiglottis. (C) With the epiglottis now lying ventrad in the oropharynx, the glottis can be clearly seen. (D) After the application of local anesthetic, the endotracheal tube and stylet are inserted into the trachea. (Courtesy Dr. Stephen J. Divers.)

in rabbits and rodents because head tilt due to otitis media or interna is common. In ferrets, ear mites and aural neoplasia appear to be more common than bacterial infection.

Stomatoscopy

Position the anesthetized animal in sternal recumbency with the head supported and mouth held open by using a rodent/rabbit table retractor restrainer (Sontec Instruments Inc., Centennial, CO) and cheek spreaders (Sontec Instruments Inc.). Stomatoscopy for evaluation of dental disease is discussed in Chapter 36. Although less common, nondental diseases of the oral cavity include neoplastic masses, abscesses, and foreign bodies. Biopsy specimens of soft tissue masses may be obtained by using the 5-Fr biopsy forceps, whereas foreign bodies may be removed with retrieval forceps.

Endotracheal Intubation

Intubation is more difficult in rodents and rabbits than in dogs, cats, and ferrets, and the endoscope can serve as a useful aid for intubation before a prolonged diagnostic or surgical procedure. The endoscope can be used as a laryngoscope to provide visibility of the glottis to aid direct intubation. We favor inserting the endoscope into the endotracheal tube, passing the endoscope through the glottis, and then advancing the tube off the endoscope and into the trachea (Fig. 35.6). Alternatively, an otoscope can be used for visibility of the glottal opening, with the endotracheal tube passed alongside it into the glottis.

Tracheobronchoscopy

Small flexible bronchoscopes can be used to examine the trachea and bronchi of larger rodents, rabbits, and ferrets. Endoscopic evaluation of bronchial morphology by using a flexible bronchoscope in rabbits has been described.[9] Small telescopes can also be used to gain access to the level of the tracheal bifurcation and beyond (Fig. 35.7). It is vital that, on entering the glottis, the head and neck be kept straight and extended to avoid mucosal damage as the telescope is advanced. Unless oxygenation can be maintained, tracheobronchoscopy evaluations must necessarily be brief.

Rhinoscopy

With the animal intubated and in sternal recumbency in a 10- to 20-degree head-down position, pack the oropharynx with

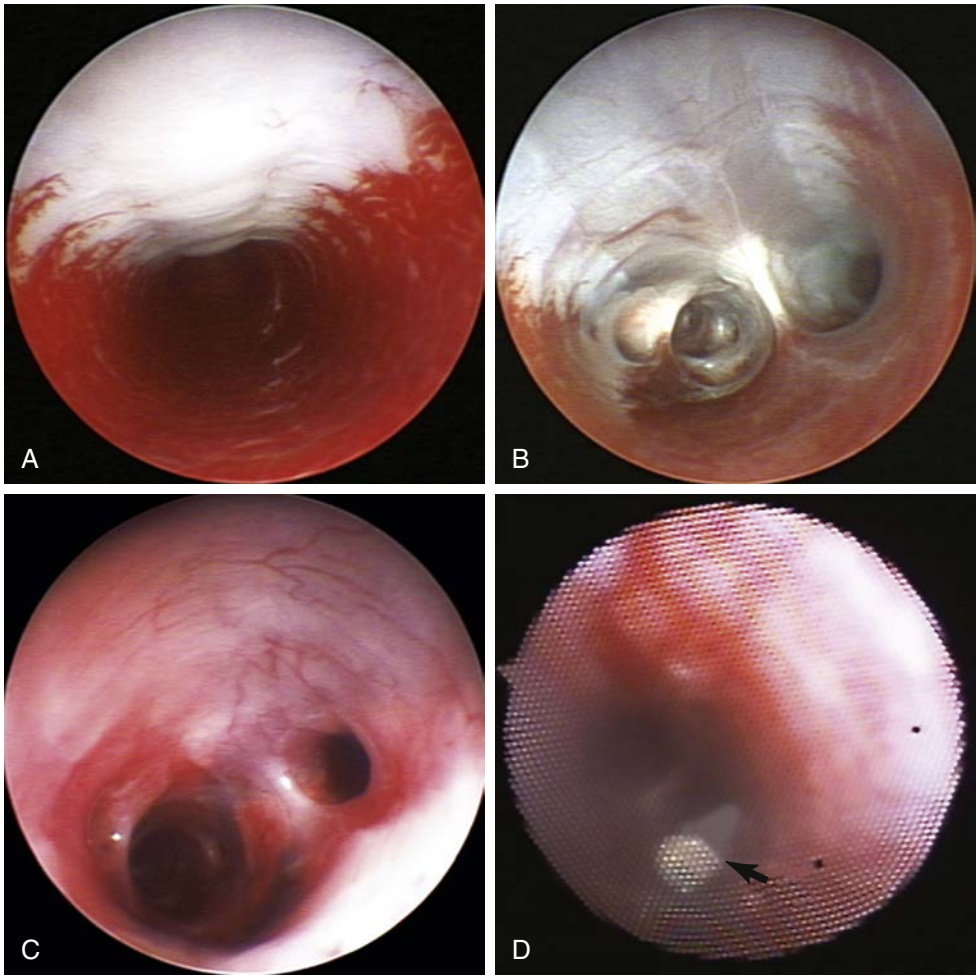


Fig. 35.7 Rabbit tracheobronchoscopy. Telescopic views of the normal anterior trachea (A), bifurcation (B), bronchus, and secondary bronchi (C). (D) Flexible endoscopic view of the bifurcation with a foreign body lodged in a primary bronchus *(arrow)*. (Courtesy Dr. Stephen J. Divers.)

moistened gauze. Flush the nasal cavities with warm sterile saline solution to remove any debris and excess mucus (Fig. 35.8A). Place towels under the animal's head to help prevent flooding of the table and floor. Use the 2.7-mm telescope for animals weighing more than 2 kg (Fig. 35.8B); for smaller animals, the 1.9-mm sheathed telescope is preferred. The use of a sheath enables intraoperative flushing to maintain visualization; however, in small animals, the naked telescope can be used with care, along with intermittent syringe flushing through the nostrils. The ventral and middle nasal meati can be exploited to examine the ventral and middle conchae. In larger animals, the endoturbinates and opening to the nasopharynx can also be seen. Take care to avoid damaging the delicate nasal turbinates, which are prone to hemorrhage. Keep the telescope as medial as possible and always keep it within the meati (Fig. 35.9). Even so, hemorrhage can rarely be completely avoided. Exudates, abscesses, masses, and foreign bodies can be appreciated and biopsied or removed (Fig. 35.10).

The recent advent of 2- and 3-mm rigid instruments also permits biopsy and debridement within the nasal or paranasal sinuses via limited surgical access. There are occasions when dental disease requires an extraoral approach, either alone or in conjunction with intraoral surgery, and the telescope can serve as a useful surgical aid. Extension of hypsodont roots into the nasal cavity may warrant rhinoscopy via the nostrils, as detailed above, or surgical rhinotomy. Dental abscesses affecting the maxilla may enter the paranasal sinuses; in such a case, the telescope can provide evaluation via a small (4- to 5-mm) osteotomy. Even when extensive surgical osteotomy or rhinotomy is performed, surgical access is often very limited in small herbivores. However, the telescope enables detailed evaluation, including areas cranial and caudal to the surgical site (Fig. 35.11).

Vaginoscopy/Urethroscopy/Cystoscopy

Hematuria is not uncommon in rabbits and rodents; it can be related to diseases affecting the urinary or reproductive systems. With the animal in dorsal recumbency and the perineum close to the table edge, insert a small 30° sheathed telescope through the vulva and into the vagina. Using a sterile saline infusion, it is possible to evaluate the vagina, urethra, bladder, and surface of the cervices (Fig. 35.12). A case report described the use of rigid endoscopy for evaluation of vaginal hemorrhage in a rat.[7] In female guinea pigs, transurethral cystoscopy allows endoscopic removal of uroliths (Fig. 35.13).[11,15]

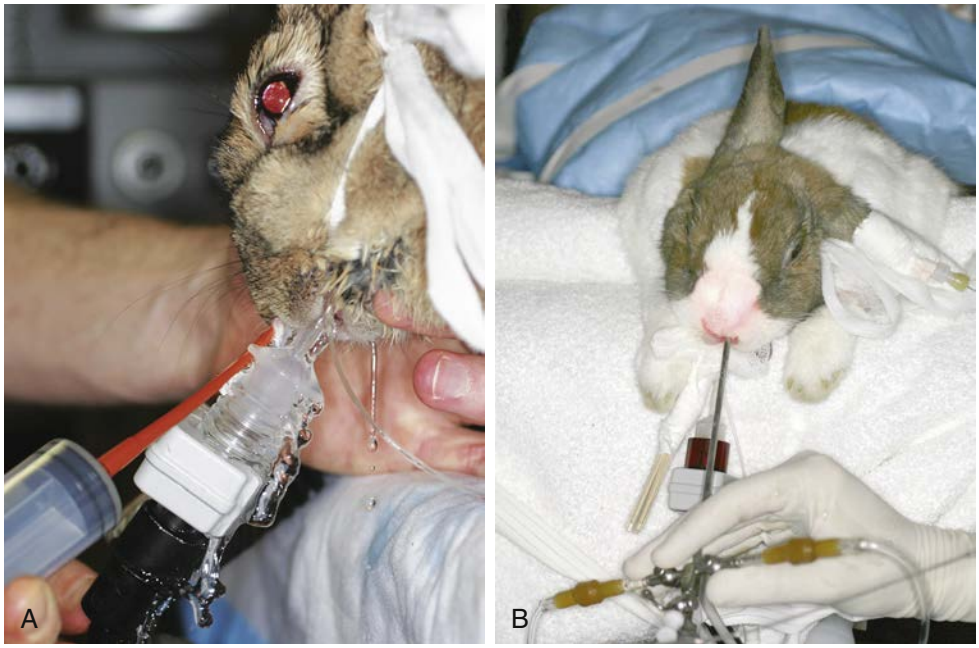


Fig. 35.8 Rabbit rhinoscopy. (A) Flushing the nasal cavities using warm sterile saline solution delivered via a 60-mL syringe and cut-down 8-Fr red rubber catheter. Packing the oral cavity with gauze and use of a cuffed endotracheal tube are essential. (B) Performing rhinoscopy using a 2.7-mm telescope and 4.8-mm operating sheath. A bag of sterile saline solution suspended above the table is connected to one of the sheath ports by an intravenous administration set, facilitating intraoperative flushing. A second administration set is connected to the second sheath port, providing egress to a collection bucket under the table. (Courtesy Dr. Stephen J. Divers.)

Gastroscopy/Colonoscopy

Gastrointestinal diseases such as gastritis, gastric ulceration, neoplasia, and foreign bodies are especially common in ferrets. Ferrets and other small mammals weighing more than 1 kg can often accommodate the smaller flexible gastroscopes, while the stomach can often be reached using telescopes in animals weighing less than 1 kg (Fig. 35.14). The ability to confirm the presence of gastric disease and collect mucosal biopsy specimens for culture and histolopathologic examination should be considered routine when investigating gastric diseases in ferrets (Fig. 35.15A–B). The utility of gastroscopy and gastric and proximal duodenal biopsy was recently evaluated in ferrets.[4,10] Unfortunately, the stomachs of small herbivores are never empty, which can make endoscopic evaluation nearly impossible.

Rodent colonoscopy recently became important because researchers were looking for a means of following the progression of human colon cancer in a rodent model. The 1.9-mm sheathed telescope has been used to examine the rectum and descending colon of mice weighing as little as 20 g. The ability to infuse methylene blue and other chemical markers via the operating sheath has further improved the ability to identify colonic cells undergoing early neoplastic transformation through the use of so-called chromoendoscopy (Fig. 35.15C–D).[2] The same system and technique can be used in companion rodents, with the animal in sternal or lateral recumbency and the perineum close to the table edge.

Laparoscopy

For a detailed discussion of methodology, the reader is referred to the dedicated laparoscopy literature, because only small mammal specifics are highlighted here.[14] Laparoscopy has been shown to offer significant advantages over traditional surgical options, both in human and veterinary medicine. In particular, laparoscopy is, with practice, faster and less traumatic, resulting in less postoperative pain and a faster return to normal function.[12] Studies in rabbits have demonstrated a reduced incidence of adhesion formation with laparoscopy compared with laparotomy, and, in conjunction with current recommendations in canine sterilization, laparoscopic ovariectomy of young rabbits < 9 months should be considered the method of choice.[3,8]

Until the advent of 2- and 3-mm human pediatric equipment, laparoscopy was limited to a single-entry system using the sheathed telescope. However, multiple-entry techniques are now possible and practical for animals weighing more than 500 g to 1 kg. Indeed, laparoscopic ovariectomy is now the authors' sterilization method of choice for female rodents and rabbits because it involves less tissue manipulation and results in less postoperative discomfort and a faster return to normal feeding and behavior.[5]

Single-entry laparoscopy has been used most extensively to collect visceral biopsy samples from rodents and rabbits. In general, make a 3- to 4-mm surgical approach through the umbilicus or at some other convenient point along the linea alba (Fig. 35.16A). After inserting the sheathed telescope, consider placing a mattress suture to create an airtight seal; however, this is seldom necessary if the incision through the linea alba is small. For larger rabbits and rodents, CO_2 insufflation is required; for small rodents, however, it is often possible to simply attach a syringe containing air to one of the sheath ports and manually inject air into the abdomen. Risks associated with air embolism

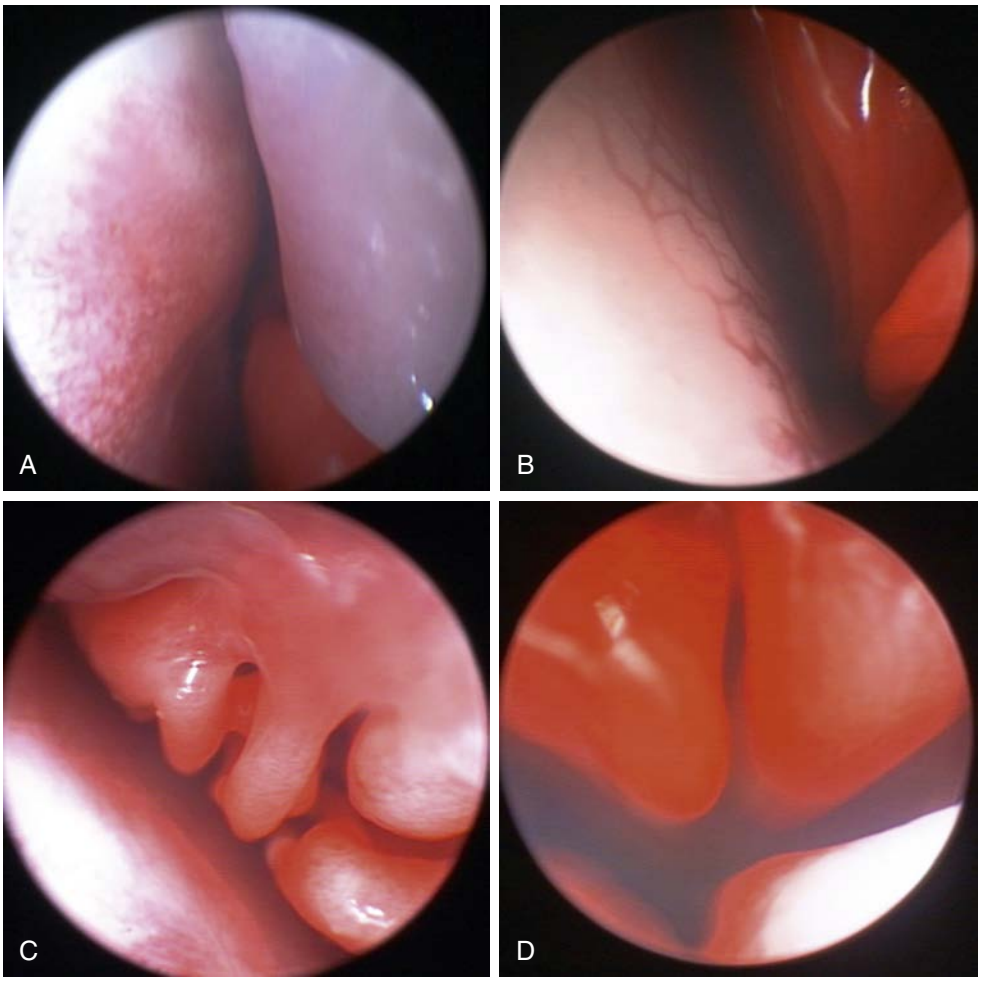


Fig. 35.9 Rabbit rhinoscopy in a normal rabbit. (A) Immediately after entrance through the left nostril, the alar fold is seen on the right, and the nasal septum is on the left. (B) As the scope is advanced caudally, nasal turbinates start to appear. (C) Normal nasal turbinates viewed from within the ventral nasal meatus. (D) As the scope is advanced further caudally, the nasopharyngeal opening is seen. The nasal septum is no longer present. (Courtesy Dr. Stephen J. Divers.)

have not been observed in rodents but should be considered. Single-entry techniques are simple and easy to perform, but the variety of instruments is limited; therefore tissue manipulation and endosurgery are rudimentary. Nevertheless, visceral evaluation and biopsy are practical even in small rodents (Fig. 35.16B–D).

For larger animals, multiple-entry techniques using 2- and 3-mm human pediatric instruments are preferred and provide greater opportunities for endosurgery. There is a wider selection of equipment for 3-mm instruments; these are used with click-line interchangeable handles and connected to a radiosurgery unit for hemostasis. Access to the abdomen is achieved using lightweight 3.5-mm (for instruments) and 3.9-mm (sheathed telescope) threaded graphite cannulas. Cannula placement is determined by the organ of interest, the preference of the surgeon, and the anatomy of the animal in question. A dedicated endoflator for CO_2 insufflation is essential for multiple-entry techniques. Some prefer the use of a Veress needle (i.e., a needle with a spring-loaded obturator used to access the peritoneal cavity before insufflation of the abdomen); however, others, concerned over the risk of damage to internal viscera (especially the voluminous gastrointestinal tract of small herbivores), prefer to place the initial cannula or telescope surgically using the Hasson technique (Fig. 35.17). The ability to rotate the animal from dorsal to lateral positions can greatly assist with access to ovaries, kidneys, and other dorsolateral structures. Joystick-controlled tilting endoscopy tables are commercially available and work well for small mammals.

For procedures involving dorsolateral structures (e.g., ovariectomy; Fig. 35.18), insert the telescope through or just caudal to the umbilicus with two additional cannulas placed 2 to 3 cm cranial and caudal to the telescope along the linea alba. In this way the instruments can be directed to one side. When required to examine the other side, the surgeon simply moves around the table. It is often helpful to have a second slave monitor located on the other side of the operating table rather than moving the entire endoscopy tower.

For access to the liver, gastrointestinal tract, spleen, pancreas, and bladder, again pass the telescope through the linea alba or umbilicus; however, insert the instruments transversely across the abdomen rather than longitudinally. In this manner, the telescope and instruments can be advanced into the cranial

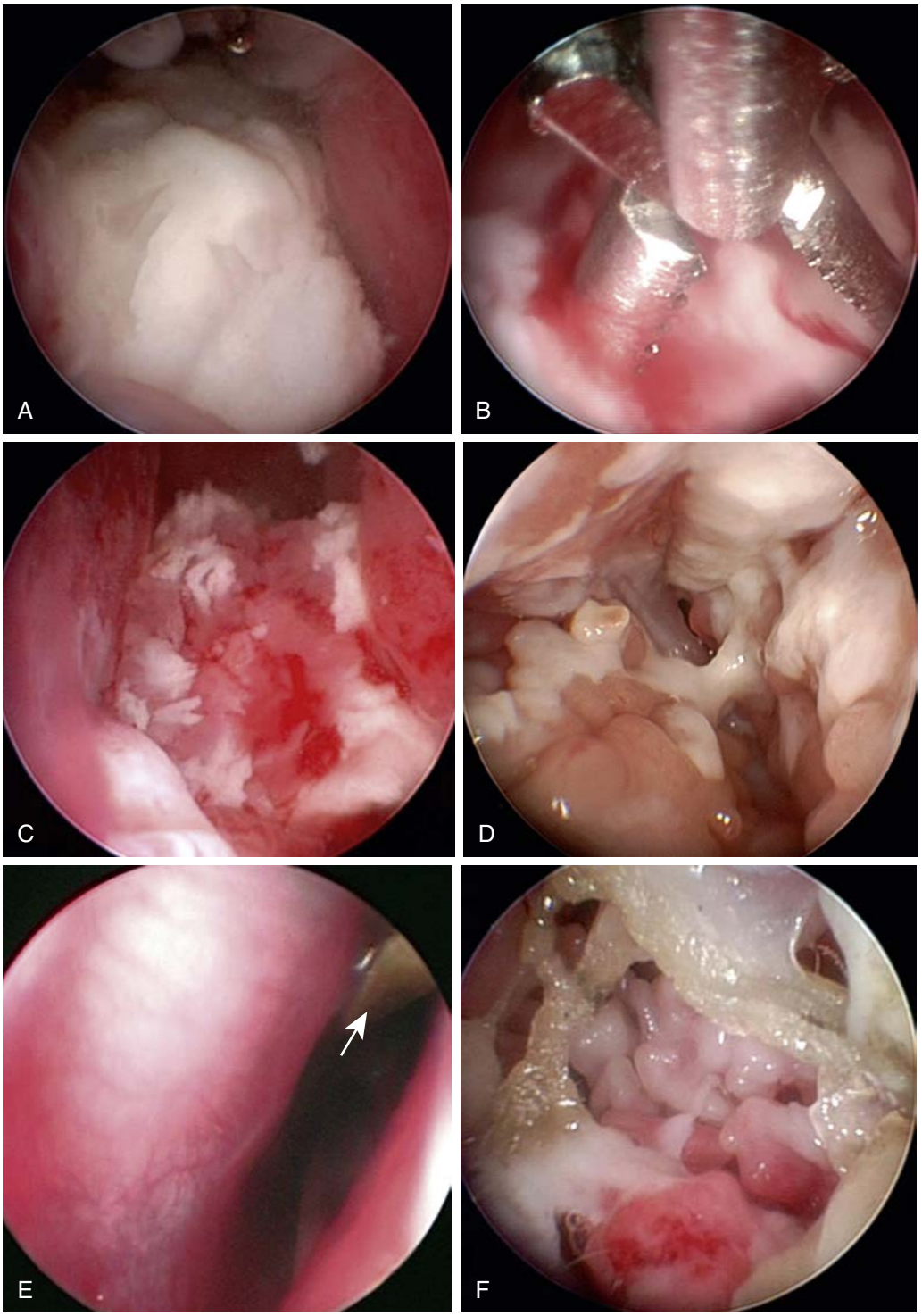


Fig. 35.10 Rabbit rhinoscopy. (A) Abscess in the caudal aspect of the ventral nasal meatus in a rabbit unsuccessfully treated for chronic rhinitis. (B) Endoscopic abscess debridement using grasping forceps. (C) Same abscess following endoscopic debridement. Abscessation was resolved with the help of post-operative antimicrobials based on biopsy culture and sensitivity testing. (D) Granulomatous rhinitis with destruction of the nasal septum due to *Mycobacterium* species. (E) Hay foreign body *(arrow)* within the cranial aspect of the ventral nasal meatus, immediately caudal to the alar fold. (F) Ventral conchal atrophy and chronic rhinitis. (Courtesy Dr. Stephen J. Divers.)

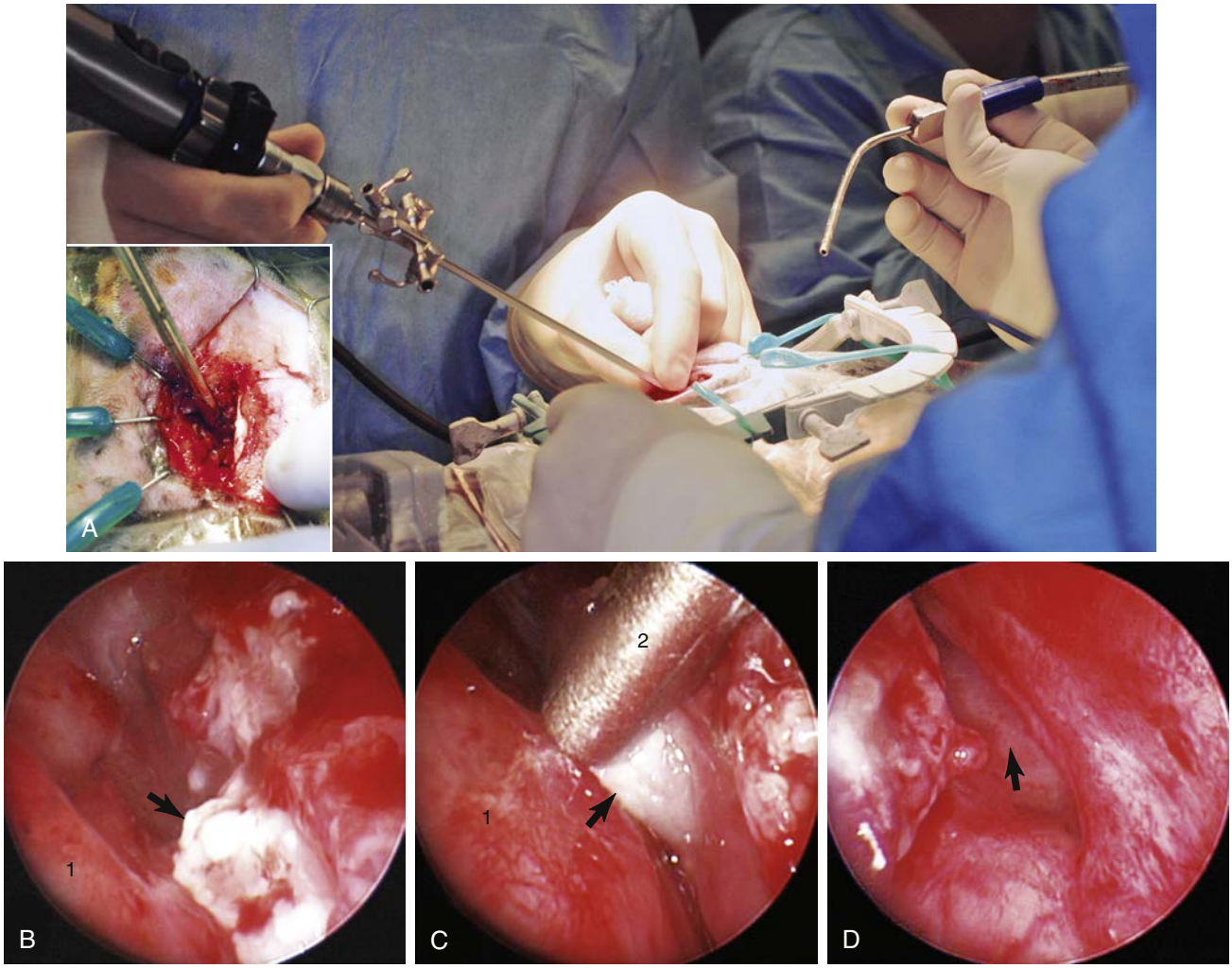


Fig. 35.11 Surgical rhinotomy and rhinoscopy in a rabbit. (A) Intraoperative view illustrating the use of the telescope to examine the nasal cavity after rhinotomy. (Insert) Closeup of the introduction of the telescope through the rhinotomy. (B) Endoscopic view of caseous exudate *(arrow)* within the ventral nasal meatus after the removal of chronically infected turbinates. The nasal septum *(1)* is labeled for orientation. (C) Exposure of an overgrown maxillary tooth *(arrow)* that has extended into the nasal cavity and caused the infection. The nasal septum *(1)* is labeled for orientation, and the suction probe *(2)* is also visible. (D) Intraoperative view after tooth extraction and flushing of the site, revealing a now-clear and unhindered ventral nasal meatus leading to the nasopharynx *(arrow)*. (Courtesy Dr. Stephen J. Divers.)

abdomen for access to the liver, stomach and intestinal tract, spleen, and pancreas or advanced caudally toward the large intestine and bladder (Fig. 35.19). Single- and double-entry laparoscopy was recently described in rabbits for collecting liver biopsy specimens.[13] Aspirating all abdominal gas after surgery is important because the presence of residual gas is a source of postoperative discomfort. Close cannula holes by placing a single suture.

Thoracoscopy

Thoracoscopy remains in its infancy, and few clinical applications have been realized in rabbits, rodents, and ferrets. Given the recent advances in human pediatric equipment, the surgeon's ability is probably the major limiting factor, although the relatively small thoraces of rodents and rabbits will always present greater challenges. To date, a handful of thoracoscopic procedures have been performed in small mammals. All cases involved evaluation and biopsy of an intrathoracic mass where less-invasive, ultrasound-guided, fine-needle aspirate had proven inconclusive on cytologic examination. In all cases, a single-entry system was used, with targeted telescope entry based on preoperative imaging. In general, the paraxiphoid approach is easier in most rabbits and rodents weighing less than 2 kg, whereas an intercostal approach is preferred for ferrets and larger rabbits and rodents. Again, close the ports using single sutures. Although placing a chest drain is not always necessary if all air has been aspirated from the thoracic cavity, it should be considered in cases of poor oxygen status and abnormal blood gas values. When chest tubes are used, intermittent negative pressure is applied, and the tubes are removed once they are nonproductive for more than 30 minutes.

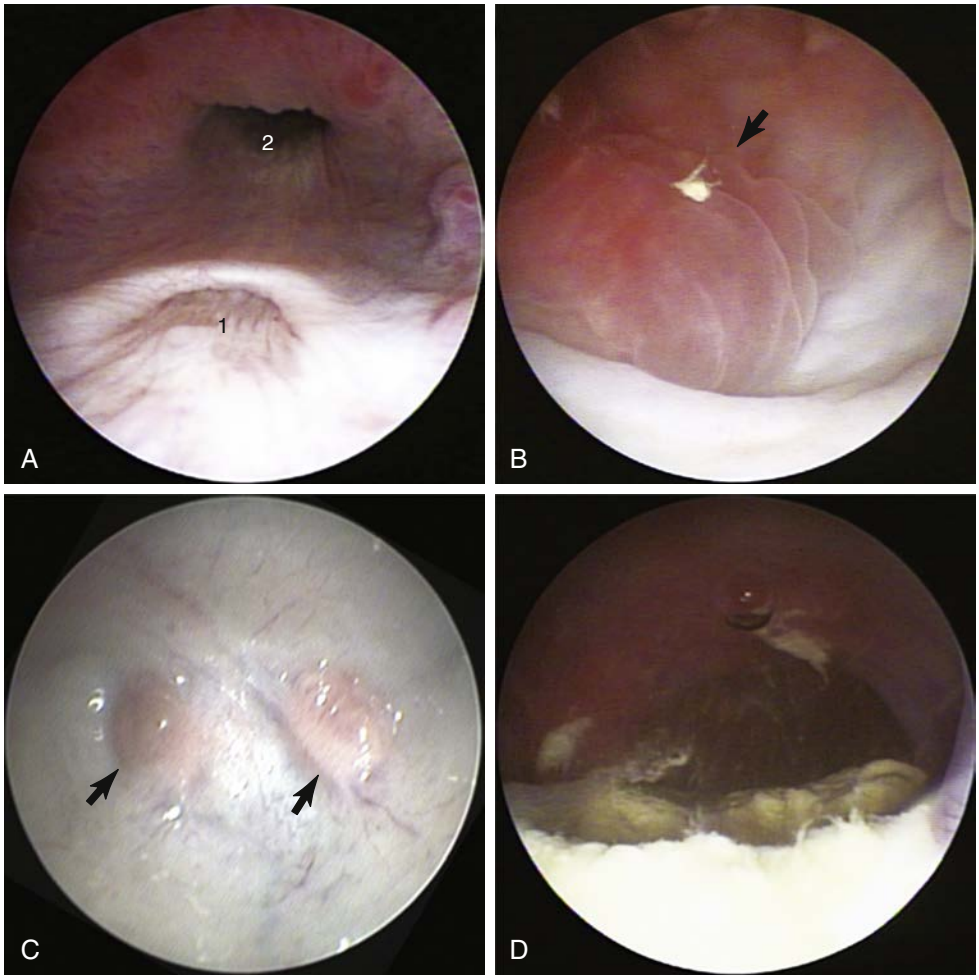


Fig. 35.12 Rabbit urogenital endoscopy. (A) View within the anterior vagina demonstrating the urethra *(1)* and caudal vaginal vault *(2)*. (B) Urethral carcinoma *(arrow)* seen within the anterior vagina. (C) Cervices *(arrows)* seen from within the caudal vagina. (D) Urinary sand seen within a saline solution–infused bladder. (Courtesy Dr. Stephen J. Divers.)

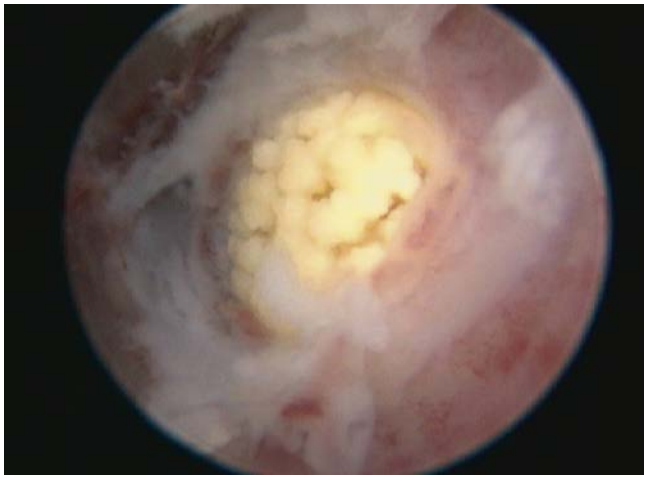


Fig. 35.13 Guinea pig cystoscopy. View of the bladder with a urolith embedded in the bladder wall using a 1.9-mm integrated telescope. Note the inflamed bladder mucosa. (Courtesy Dr. Stephen J. Divers.)

COMPLICATIONS

The major complications encountered with diagnostic and surgical endoscopy are typically associated with anesthesia and related to issues of debilitation, poor ventilation, lack of vascular access, and hypothermia. The importance of a thorough preoperative evaluation, endotracheal intubation, intravenous or intraosseous catheterization, and warm air/water blankets cannot be overemphasized. Hemorrhage after rhinoscopy or tissue biopsy is common but seldom severe, although it is wise to have hemostatic agents available. Most endoscopy issues are related to operator error, which may sometimes occur until experience and ability have been gained. To facilitate the endoscopy caseload without compromising clients or patients, the surgeon should retain the option to convert to a traditional surgical approach if required.

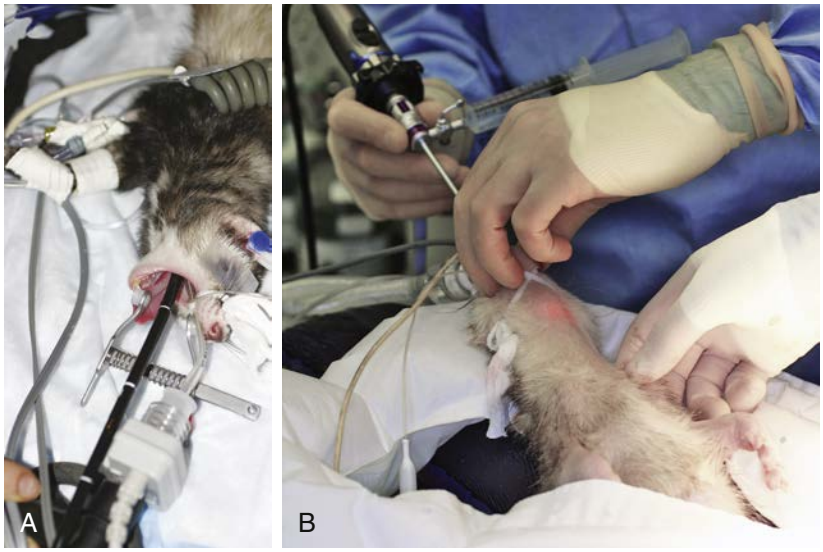


Fig. 35.14 Ferret gastrointestinal endoscopy. (A) Flexible gastroscopy using a 8.6-mm gastroscope. Such endoscopes provide greater flexibility but are limited to mammals weighing more than 1–2 kg. (B) Esophagostomy and gastroscopy being performed with a 2.7-mm telescope and sheath with sterile infusion provided by the attached syringe. Such techniques can be used in mammals weighing less than 1 kg. (Courtesy Dr. Stephen J. Divers.)

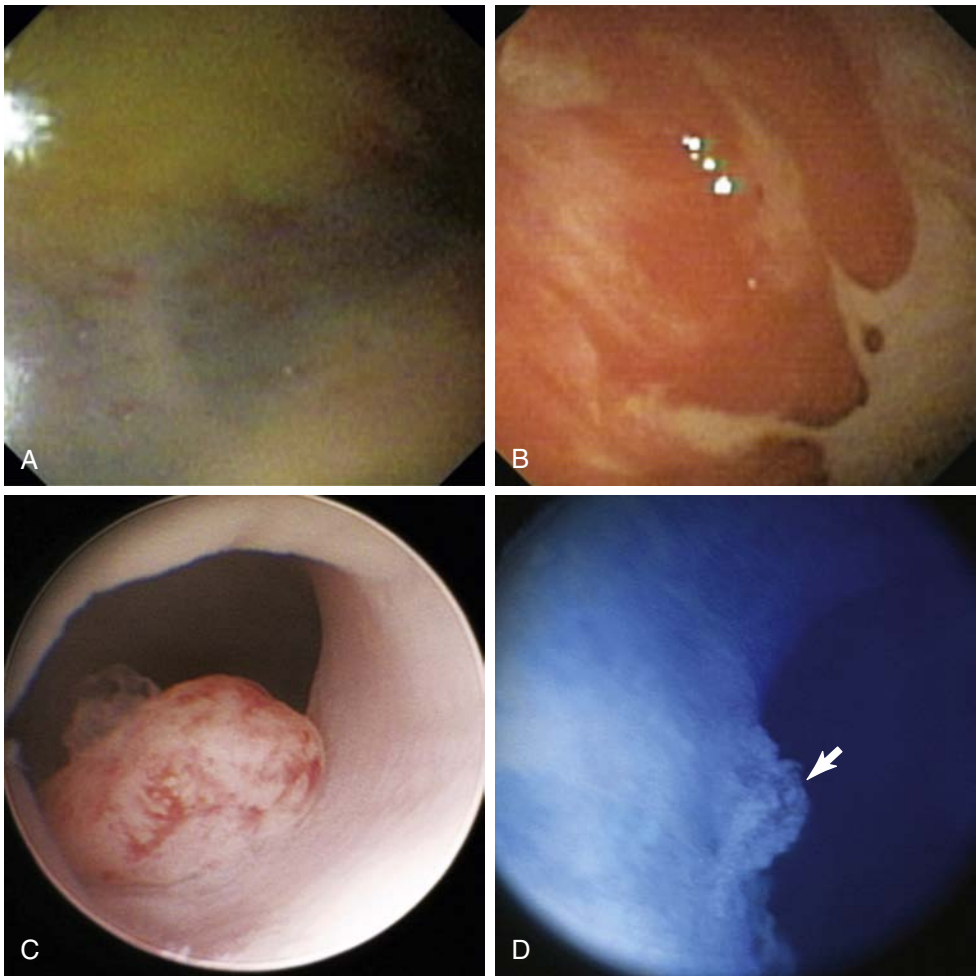


Fig. 35.15 Gastrointestinal endoscopy in ferrets and rodents. Flexible endoscopic views of the normal gastric mucosa (A) and gastric ulceration due to *Helicobacter mustelae* (B) in ferrets. (C) Telescopic view of a carcinoma protruding into the lumen of the descending colon in a mouse. (D) Early neoplastic transformation in the colon *(arrow)* can be detected more easily using methylene blue dye. (Courtesy Dr. Stephen J. Divers.)

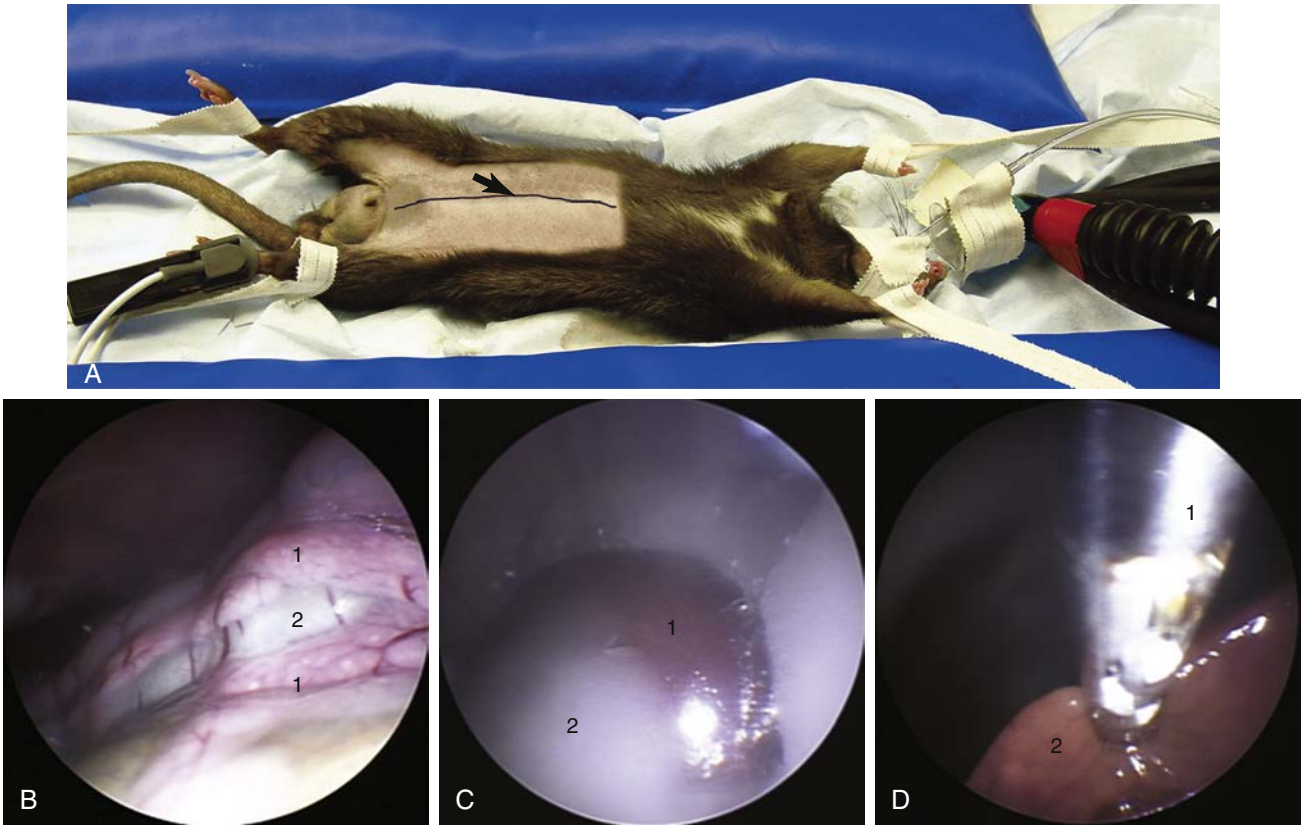


Fig. 35.16 Single-entry rodent laparoscopy. (A) Rat intubated, positioned in dorsal recumbency, and prepared for laparoscopy. The linea alba is indicated, and the preferred insertion point is the umbilicus *(arrow)*. (B) View of the right cranial quadrant illustrates the pancreas *(1)* and duodenum *(2)* of a guinea pig. (C) Normal rabbit kidney *(1)* partially obscured by retroperitoneal fat *(2)*. Obesity is commonly encountered, complicating laparoscopy. (D) Biopsy forceps *(1)* harvesting a liver sample *(2)* from a rat. (Courtesy Dr. Stephen J. Divers.)

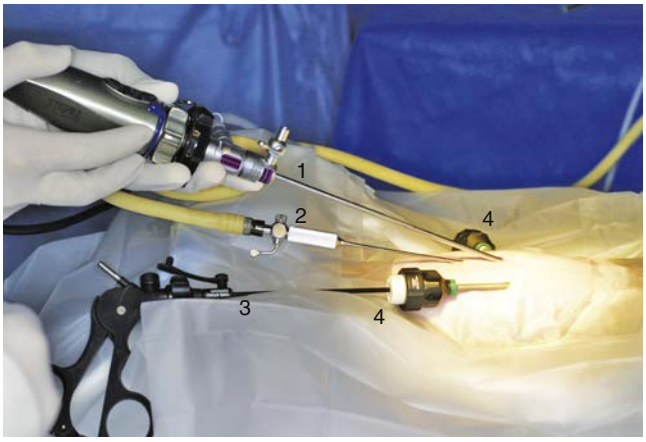


Fig. 35.17 Multiple-entry laparoscopy in a ferret. The telescope *(1)* has been inserted through the umbilicus, cranial to the Veress needle *(2)* and CO_2 insufflation line. A 3-mm instrument *(3)* has been inserted through one of two 3.5-mm cannulas *(4)*. (Courtesy Dr. Stephen J. Divers.)

POSTOPERATIVE CARE

The immediate postoperative period after extubation is usually the most critical; therefore maintain oxygen and thermal support until the animal is fully conscious and ambulatory. Administer analgesics as indicated for the more-invasive procedures, such as laparoscopic surgery, or where extensive debridement and tissue trauma have occurred. Rabbits and rodents are expected to resume feeding within 2 hours; otherwise, assisted feeding is initiated and fluid therapy continued. In addition, auscultation of the gastrointestinal tract is routine.

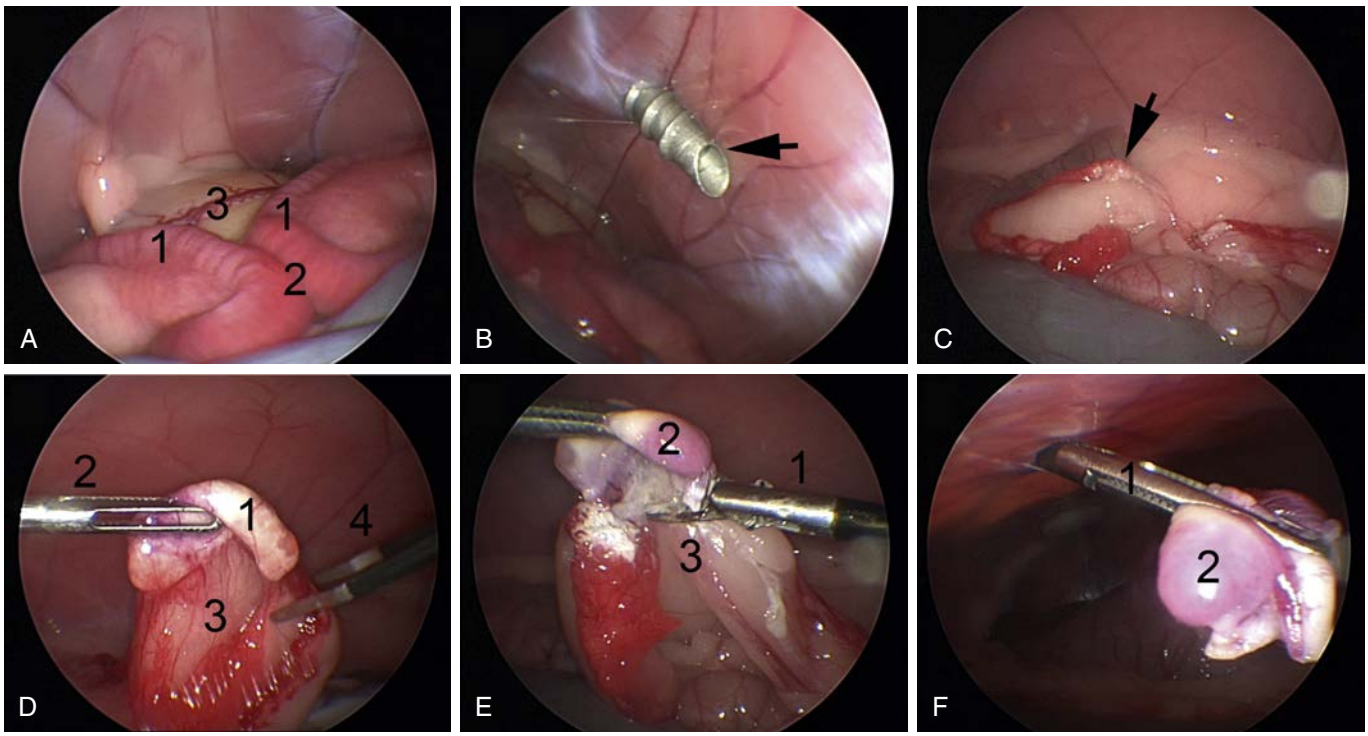


Fig. 35.18 Endoscopic oophorectomy in a rabbit. (A) Initial view of the caudal abdomen revealing normal uteri (1), vagina (2), and bladder (3). (B) Placement of a 3.5-mm graphite/plastic endotip (threaded) cannula (arrow) under endoscopic direction. (C) View of the right ovary (arrow) at 30° lateral tilt. (D) View of the ovary (1) elevated using grasping forceps (2) to reveal the vasculature within the mesovarium (3). The bipolar forceps (4) are advanced to coagulate the vessels before transection in this large rabbit. (E) Monopolar scissors (1) being used to coagulate and cut to dissect the ovary (2) free from the mesovarium (3). (F) The cannula has been slid up the shaft of the grasping forceps (1) and is no longer visible. The forceps and ovary (2) are gently withdrawn through the hole in the body wall. (Courtesy Dr. Stephen J. Divers.)

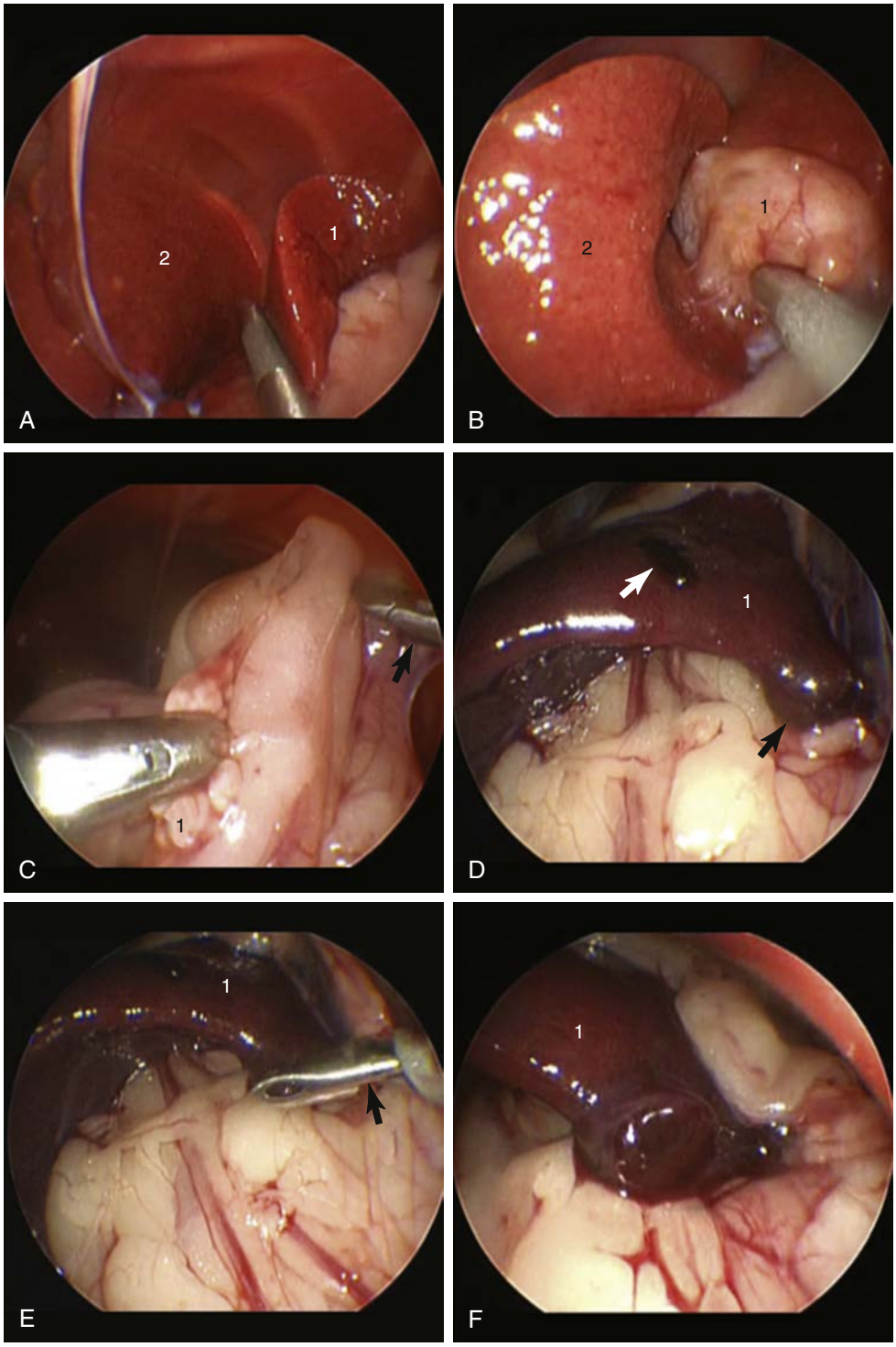


Fig. 35.19 Multiple-entry ferret laparoscopy. (A) Using a palpation probe to examine between the left lateral *(1)* and left medial *(2)* lobes of the liver. (B) Identification of an abnormally thickened gall bladder *(1)* between the quadrate and right medial liver lobes *(2)*. (C) Endoscopic biopsy of the pancreas *(1)* with 3-mm biopsy forceps that confirmed the presence of an insulinoma. Note the use of 3-mm atraumatic tissue forceps *(arrow)* to retract the mesentery. (D) View of the spleen *(1)* demonstrates a nodular abnormality *(black arrow)* and the previous site of attempted ultrasound-guided fine-needle aspiration *(white arrow)*. (E) Biopsy of the spleen *(1)* with 3-mm biopsy forceps *(arrow)*. (F) Postbiopsy view of the spleen *(1)*. Note the absence of severe hemorrhage. (Courtesy Dr. Stephen J. Divers.)

OUTCOME

Return to normal behavior and weight gain are often the most useful indicators of improvement. Clinicopathologic results can be useful if abnormalities are detected before surgery. Use serial endoscopic evaluations of the ears, nose, and mouth to monitor patients with otitis, rhinitis, and oral disease, respectively.

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Small Mammal Dentistry

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Dental disease is common in many species of exotic companion mammals, in particular those with continually growing (elodont) dentition. An incomplete understanding of the cause and pathophysiology presents considerable challenges in terms of prevention and treatment. Dental disease is a syndrome (i.e., a complex of clinical signs) with associated primary and secondary diseases and/or complications. This understanding helps guide the clinical approach.

DENTAL EQUIPMENT

Dental equipment for exotic companion mammals includes instruments for diagnosis and for treatment.[6,12,15] Although a cursory examination can be performed in most conscious animals, this is increasingly complicated in rabbits and rodents, especially smaller patients. Otoscopes with various sized cones, laryngoscopes, nasal speculums, and vaginoscopes have been used for examination and with practice may reveal abnormalities. Subtle lesions are easily missed; therefore a thorough oral examination should be performed in the deeply sedated or anesthetized animal.[6,12,35]

The small long, narrow oral cavity of rabbits and herbivorous rodent species is best viewed in the anesthetized patient with specialized mouth gags (Fig. 36.1) and cheek dilators. Various sizes and shapes of cheek dilators are available, including longer blades for rabbits, and modified "open blade" style, more appropriate for very small rabbits or rodents. A guinea pig cheek dilator is particularly useful for the double-folded cheek opening in this species, as well as in chinchillas and smaller rodents. Mouth gags are positioned on the clinical crowns of incisor teeth, but use these with extreme care to prevent excessive stretching of the masticatory muscles and the ligaments of the temporomandibular joint. The "table-top" mouth gag is a platform-style positioner that allows a hands-free approach (Fig. 36.2). A light source (e.g., head light) and magnifying loupes (Fig. 36.3A) or the use of a rigid endoscope or otoscope (Fig. 36.3B) are strongly recommended because these provide focal illumination and magnification.

Other dental diagnostic instruments used in small mammals and applicable for exotic species are the periodontal probe, dental explorer, and a dental spatula. Instruments and equipment



Fig. 36.1 Dental equipment. (A) Standard hand-held mouth gag for rabbits and larger rodents. (B) Cheek dilator with long blades suitable for rabbits. (C) Cheek dilator suitable for chinchillas, guinea pigs, and rats. (Photos courtesy C. Mans, DVM.)

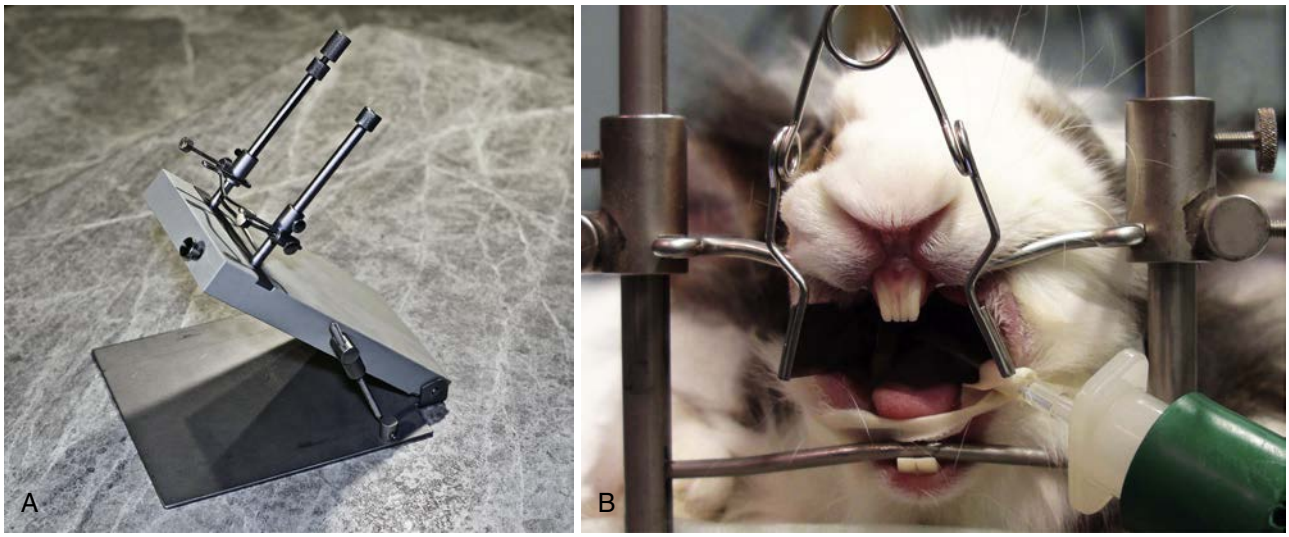


Fig. 36.2 (A) Tabletop mouth gag for rabbits and rodents. (B) Close-up view of a rabbit positioned on the restrainer with the cheek dilator. (Used with permission from Angela Lennox, DVM (A) and Vittorio Capello, DVM (B).)

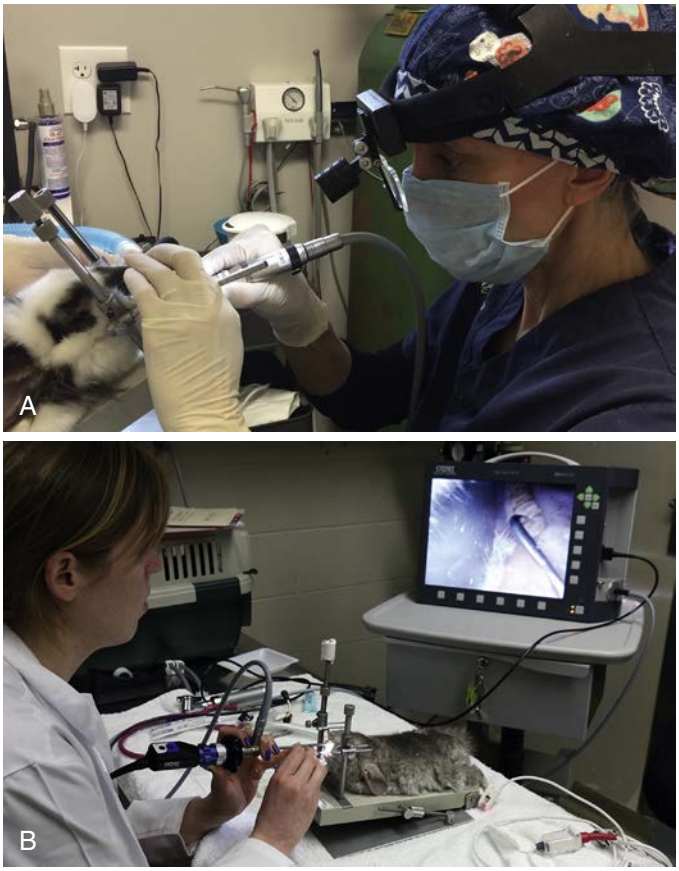


Fig. 36.3 (A) Rabbit undergoing an intraoral dental procedure; note the loupes that provide both magnification and a focal light source, the use of the dental spatula, and the straight high-speed handpiece. (Used with permission from Angela Lennox, DVM.) (B) Use of a rigid endoscope, camera, and monitor to perform an endoscopy-guided intraoral examination (stomatoscopy) in an anesthetized chinchilla. (Courtesy Christoph Mans, DVM)

designed for treatment of dental disease in traditional pet species can be used for exotic carnivores. A specially designed mouth gag for ferrets can be used for other similarly sized carnivore patients as well (Fig. 36.4).

A variable-speed dental unit is ideal for dental treatment in small mammals. A straight dental handpiece is used to reduce the coronal length and restore the normal shape of elodont teeth in rabbits and herbivorous rodent species. Many different types, shapes, and sizes of burrs are available; diamond burrs are especially recommended. Diamond rasps and cutters for rabbit cheek teeth are available, but their use carries risk of fracture of cheek teeth and damage to adjacent soft tissues. Treatment of dental-related abscesses and osteomyelitis requires a basic surgical set of small instruments with the addition of small bone curettes and burrs to debride necrotic bone or to perform selected osteotomy/ostectomy procedures. Transparent or adhesive surgical drapes and small, delicate retractors may be useful as well.

Instruments for tooth extraction in rabbits include specially designed luxators for incisor and molariform teeth (Fig. 36.5).[12,15,35] For rodents, appropriately contoured needles or specifically designed curved luxators are used for extracting incisors and are shaped to match the size and curvature of the tooth.[12,46] However, contoured needles may be used also



Fig. 36.4 Use of a mouth gag in an anesthetized ferret. (Used with permission from Vittorio Capello, DVM.)



Fig. 36.5 Dental luxators. (A) Rabbit incisor luxator. The ends are curved to match the curvature of the upper and lower incisors. (B) Rabbit molar luxator. The sharp end is used to break down the periodontal ligaments. (Courtesy Christoph C. Mans, DVM.)

for rabbits.[12,15] Standard needle holders are frequently used to extract the primary incisor teeth, and curved extraction forceps are available for cheek teeth. Smaller forceps, needle holders, or curved hemostats aid extraction of secondary incisor teeth.

THE DENTAL EXAMINATION

Dental disease is a syndrome and can produce a wide range of clinical signs and symptoms.[6,59] These may be related specifically to the primary dental problem (reduced food intake, anorexia, dysphagia, changes in fecal quantity and size, weight loss) or to complications associated with dental disease (excessive grooming, excessive salivation and drooling, facial swellings, epiphora, exophthalmos, nasal discharge, dyspnea). Other signs indicate diseases or conditions secondary to dental disease (poor general condition, gastrointestinal problems, poor coat, skin diseases, ocular diseases, and death).[6,15,43]

Before performing a physical examination, collect a thorough history and review the diet and feeding habits of the animal with

the owner. Considering the capability of prey species to mask or hide signs of disease, the absence of a clear clinical history does not rule out the possibility of dental disease. Reduced food intake and abnormal feces in rabbits and rodents are common early signs frequently missed by owners, especially when pets are kept in pairs or groups. A thick hair coat can hide evident signs like weight loss or the presence of facial swellings.[6,18]

Examination should include palpating the external maxillary and mandibular profiles (including the ventral aspect of the mandible and the temporomandibular joints) to detect bony irregularities or swelling. In patients with elodont cheek teeth, bony deformities often indicate apical elongation of cheek teeth, periapical deformities, or osteomyelitis. Bony changes are less common in guinea pigs. Inspect the incisors from both the rostral and lateral aspects. Evaluate the lateral mobility of the mandible to indirectly assess the cheek teeth.

In conscious rabbits and some large rodents, the oral cavity can be inspected with an otoscope or similar instrument. However, dental lesions easily can be missed using this technique. When dental disease is a presumptive or a differential diagnosis, always sedate or anesthetize the patient for a complete the oral examination. Include examination of the eyes and periocular structures in the dental examination of the conscious patient. If indicated, evaluate patency of the nasolacrimal duct in rabbits by flushing with saline solution or with fluorescein dye (see Chapter 40).

Safe restraint and effective oral examination are much more difficult in small rodents and other patients such as sugar gliders, and evaluation is limited to the incisors. For complete inspection and proper diagnosis of dental disease in these patients, general anesthesia is necessary.

Ferrets may be presented for chewing problems, but apart from advanced dental disease, they rarely show clear clinical signs. For this reason, routinely perform a thorough dental examination on ferrets brought in for physical examination.[36] Pay special attention to the most caudal teeth, which may be covered by the commissure of the lips.

DIAGNOSTIC IMAGING

All patients with suspected or evident dental disease benefit from diagnostic imaging, which is critical to evaluate the reserve crowns and apices of elodont teeth, of roots in case of anelodont teeth, and of surrounding bony structures. Deep sedation or general anesthesia is necessary for optimal positioning. Although some patients are routinely intubated for anesthetic procedures, the endotracheal tube may interfere with the radiographic image or may hamper selected intraoral procedures.

Radiography

Good-quality skull radiographs can be obtained with the use of standard radiographic equipment (see Chapter 38). Multiple views are necessary to fully evaluate the dental and bony anatomy[6,8,55]; do not base a diagnosis or prognosis on any single radiographic image.

Intraoral radiographic techniques are reported in rabbits and selected rodent species and are helpful during some dental procedures.[2,10] While useful, intraoral films should be coupled with either standard radiographic views of the entire skull or computed tomography (CT) (see below) to detect related complications such osteomyelitis of the mandible and empyema of the preformed cavities of the skull (nasal cavities, tympanic bullae).[10]

For extraoral radiography in rabbits and larger rodents, include at least five standard projections in the radiographic series: laterolateral (LL), left-to-right and right-to-left lateroblique (LO), dorsoventral (DV), ventrodorsal (VD), and rostrocaudal. Additional views such as LO with a different degree of obliquity, slight LO in the rostrocaudal direction rather than the standard dorsoventral, slight obliques from the VD position, VD with the mandible shifted laterally, and intraoral (IO) projections may be useful or required for the radiographic study of a specific patient.[8,10] The lateral view is useful to evaluate the occlusion of the maxillary and mandibular incisors, the occlusal plane of the cheek teeth, and the overgrowth of clinical crowns (Fig. 36.6). The normal appearance of the occlusal plane of the cheek teeth is a zigzag line. An ideal oblique projection has minimal (15°–20°) rotation, and the contralateral oblique view should always be obtained for comparison. Each projection is especially useful to evaluate reserve crowns and apices of mandibular cheek teeth on one side of the head and the same dental structures of maxillary cheek teeth on the other. The ventrodorsal or dorsoventral view is useful to evaluate overgrowth of cheek teeth and deformities of the mandible. Superimposition of mandibular and maxillary structures impairs evaluation; shifting the tip of the mandible laterally permits visibility of an entire group of maxillary cheek teeth. Ideal positioning in the rostrocaudal projection allows evaluation of the occlusal plane of the cheek teeth and the temporomandibular joints. Excellent symmetrical positioning is mandatory for both the ventrodorsal and the rostrocaudal projections.

In guinea pigs, the normal slant of the cheek teeth occlusal plane (see "Anatomy" below) does not allow visualization of the occlusal plane on the lateral projection; the rostrocaudal projection is the only one allowing proper evaluation of the occlusal plane.

In ferrets, radiographs of the skull and teeth are very important when the oral examination suggests the possible presence of retained roots, periodontal infection or abscess, or osteomyelitis. Open-mouth projections and intraoral projections using small films can be added to standard projections.[8]

Computed Tomography

Computed tomography is superior to skull radiography in most cases and is particularly useful for evaluating complications of dental disease such as facial abscesses and osteomyelitis, as well as concurrent rhinosinusitis and otitis media. Although radiographs may provide higher resolution, CT allows visibility of important details impossible to see radiographically due to superimposition of different anatomic structures on a single plane. Also, CT provides detailed diagnostic information that may be critical for proper prognosis and surgical planning of difficult dental cases.[5,10,19] In particular, three-dimensional volume and surface renderings of the skull can provide excellent information for the diagnosis of dental disease or dental-related problems, such as abnormalities of the temporomandibular

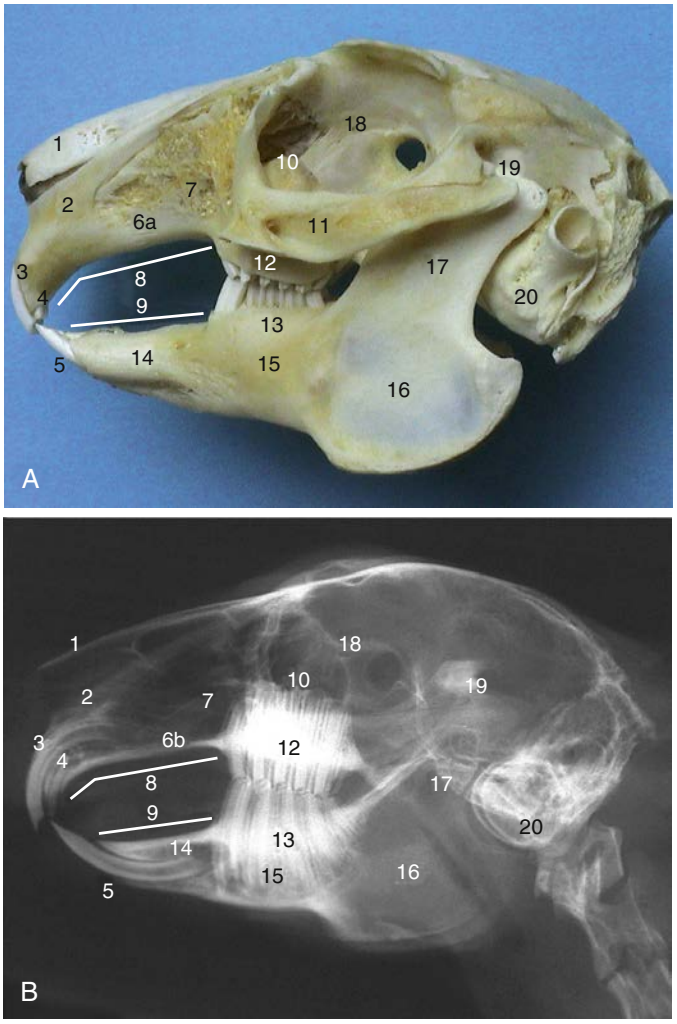


Fig. 36.6 Gross (A) and radiographic (B) anatomy of the skull and teeth the domestic rabbit. Lateral view. *1,* Nasal bone. *2,* Incisive bone. *3,* First maxillary incisor tooth. *4,* Second maxillary incisor tooth. *5,* Mandibular incisor tooth. *6a,* Maxillary bone. *6b,* Palatine process of the maxillary bone. *7,* Perforated surface of the maxillary bone. *8,* Maxillary diastema. *9,* Mandibular diastema. *10,* Alveolar bulla. *11,* Zygomatic arch. *12,* Maxillary cheek teeth. *13,* Mandibular cheek teeth. *14,* Incisive part of the mandible. *15,* Body of the mandible. *16,* Masseteric fossa. *17,* Coronoid process of the mandible. *18,* Orbital fossa. *19,* Temporomandibular joint. *20,* Tympanic bulla. (Modified from Capello V, Gracis M: *Rabbit and Rodent Dentistry Handbook*. Zoological Education Network (2005). Hoboken, NJ: Wiley-Blackwell Publishing (2007), with permission.)

joints in guinea pigs. Micro-CT has recently emerged in private practice for small exotic mammals. Originally designed for laboratory animal imaging,[38] micro-CT may represent a new modality for diagnosis of dental disease in rabbits and rodents.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) represents the diagnostic imaging procedure of choice for soft tissues. It is most commonly used for the central nervous system, but other soft tissues can be visualized in detail. For soft tissues, MRI has superior quality to CT, even exceeding CT with contrast. Different types of sequences (images) are produced and visualized in one of the three standard views (transverse or axial, dorsal or coronal, lateral or sagittal).[24] Thick pus and the capsule, typical of rabbit and rodent odontogenic abscesses, have a signal intensity similar to other soft tissues. However, fluid pus can be displayed as well. For this reason, MRI of the head for indications other than investigation of the central nervous system represents an interesting and very useful application in pet rabbits and rodents to diagnose the presence and the extent of abscesses.[10,24]

Oral Endoscopy

Oral endoscopy allows for a thorough inspection of the oral cavity and greatly facilitates detection of subtle lesion as it provides magnified perspective of dental structures. Instruments and techniques for oral endoscopy have been reported[20] (see Chapter 35), and normal and pathologic endoscopic patterns have been described. Although endoscopy is very useful in rabbits, it is an integral part of the intraoral examination in rodent species (Fig. 36.4B).[10,12]

OTHER DIAGNOSTIC TESTING

Aerobic and anaerobic bacterial culture and sensitivity testing is important for proper treatment of periapical infections and abscesses and should be performed in addition to cytologic examination. In rabbits, aerobic gram-positive and anaerobic gram-negative pathogenic bacteria have been identified as causative agents, including *Pseudomonas, Pasteurella*, *Staphylococcus*, *Streptococcus, Prevotella*, *Fusobacterium*, *Peptostreptococcus, Bacteroides*, and *Actinomyces* species.[23,49,57,58] Histopathology can be useful in select cases, particularly when bone neoplasia is suspected.

NOMENCLATURE SYSTEMS

Accurate numbering of teeth for recording can been accomplished in many ways: anatomic description, actual numbering, practical numbering (molariform), and the modified Triadan system.[21,22] The Triadan system is preferred by some specialists and has the advantage of being completely numerical and consistent across any mammal species. The system is based on the permanent dentition of the pig and includes 44 teeth, 11 per quadrant. Each of the four quadrants is numbered: 1 (right maxillary), 2 (left maxillary), 3 (left mandibular), and 4 (right mandibular) (Fig. 36.7). The quadrant represents the first digit of each number. The teeth are then numbered from the rostral midline (the mesial aspect of the quadrant) to distal. Therefore the incisors are 01, 02, and 03. Canine teeth in all quadrants end with 04. The four premolars are numbered 05 to 08 and the three molars 09 to 11. For example, the ferret's left mandibular quadrant has three incisors (301, 302, 303), one canine tooth (304), 305 is missing, followed by three premolars (306, 307, 308), and two molars (309, 310; tooth 311 is missing in the ferret). The Triadan numbering for teeth on the left maxillary quadrant for cavy-like rodents such as the guinea pig, chinchilla, or degu is incisor (201), followed by a long diastema missing 202–207, and with one premolar tooth and three molar teeth numbered 208, 209, 210, and 211 (Fig. 36.8). When referring to deciduous teeth, the number 4 is added to each quadrant number, and quadrant numbers become 5, 6, 7, and 8.

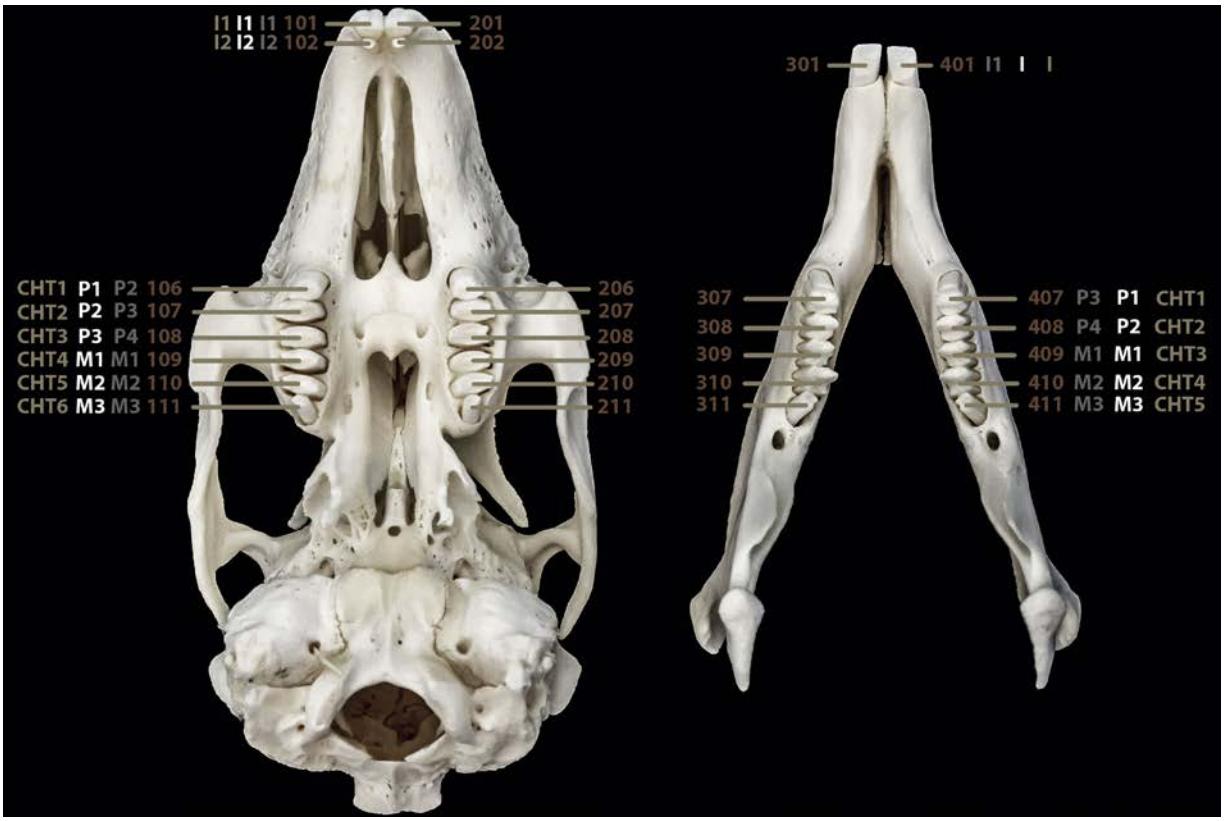


Fig. 36.7 Dentition of the rabbit, displaying various numbering methods of teeth. *I,* incisor; *C,* canine; *CHT,* cheek tooth; *P,* premolar; *M,* molar; *CHT,* cheek teeth. (Used with permission from Angela Lennox, DVM.)

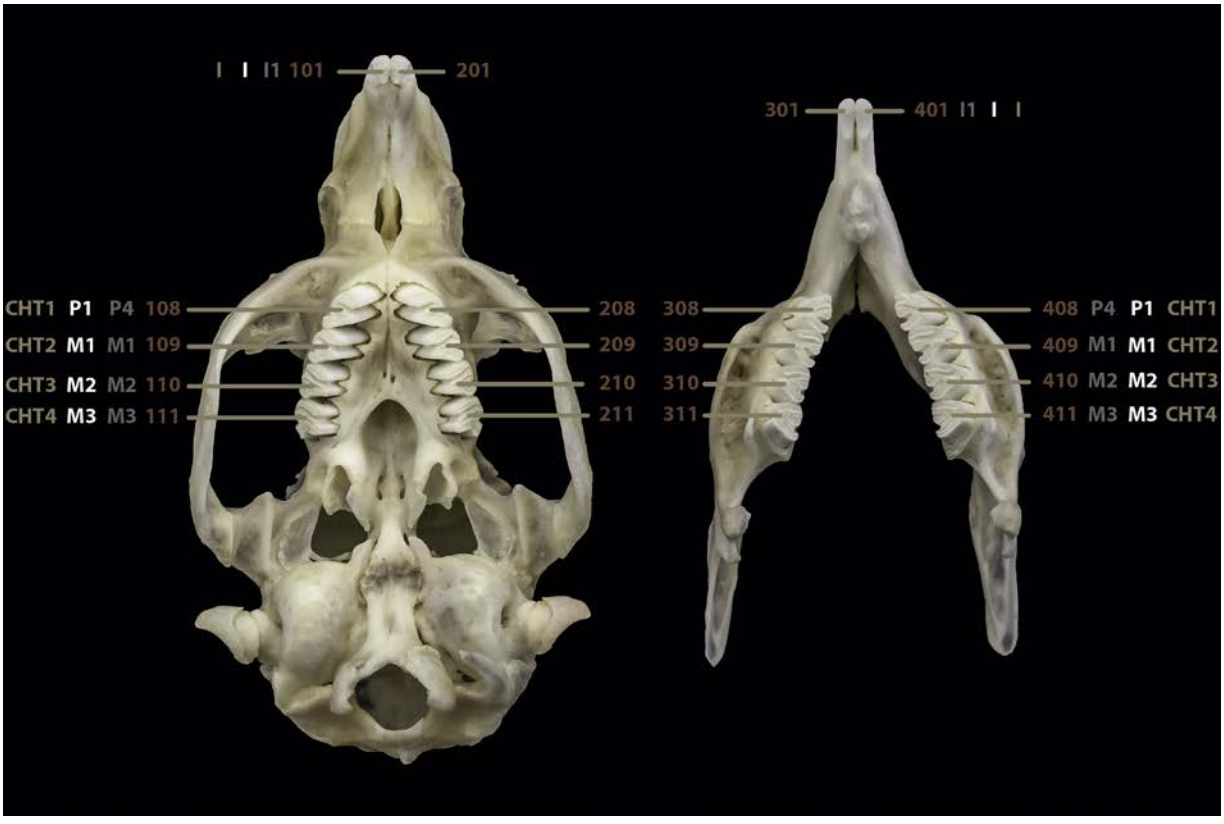


Fig. 36.8 Dentition of the guinea pig, displaying various numbering methods of teeth. *I,* incisor; *C,* canine; *CHK,* cheek tooth; *P,* premolar; *M,* molar; *CHT,* cheek teeth. (Used with permission from Angela Lennox, DVM.)

Three other nomenclature systems do not include identification of the specific quadrant.[21] Two of them differentiate between premolars (P or PM) and molars (M) (Fig. 36.7). Veterinary dentists prefer to include teeth that have been lost during development. With this method, the most caudal premolar is always numbered P4. Maxillary premolars of the rabbit are therefore labeled as P2, P3, P4, while the mandibular premolars are labeled as P3 and P4. A similar but alternative system, used most commonly by general and exotic animal practitioners, numbers the existing teeth beginning from the rostral (mesial) end of the quadrant. Maxillary premolars of the rabbit are labeled as P1, P2, P3, while the mandibular premolars are labeled as P1 and P2. A fourth method does not differentiate between premolars and molars in species with elodont teeth (such as the rabbit and cavy-like rodents) because those teeth are not anatomically different. This method may also be applied to rodent species with anelodont premolar and molar teeth because they have a diastema separating the two functional units of incisor and cheek teeth. This method is most commonly used by exotic animal practitioners and names them *molariform* or *cheek teeth* (CHT), numbering maxillary cheek teeth CHT1 through CHT6 in the rabbit (CHT1-CHT4 in elodont rodents) from the mesial to the distal end of the quadrant, and mandibular cheek teeth from CHT1 through CHT5 in the rabbit (CHT1-CHT4 in elodont rodents).

RABBITS

Anatomy and Physiology of the Skull and Teeth

Rabbits are highly specialized herbivorous mammals, and the anatomy and physiology of the skull and teeth accommodate their unique diet.[6,17] Skull morphology is typical of true herbivores, similar to larger species like horses, cattle, sheep, and goats (Figs. 36.6 and 36.7). The oral cavity is long and narrow, with a narrow opening. The temporomandibular joint is dorsal to the dental occlusal plane. Rabbits are anisognathic, with the mandible narrower than the maxilla. The incisors of lagomorphs are similar anatomically and partially functional to those of rodents. For this reason, the order Lagomorpha was previously classified as a rodent suborder (Rodentia). However, lagomorphs differ from rodents because they have two pairs of maxillary incisors (duplicidentata), while rodents have only one pair (simplicidentata).[6,21] Also, lagomorphs are diphyodont, with two sets of teeth (deciduous and permanent), whereas rodent species are monophyodont.[6,17,21] However, this physiologic trait does not have practical relevance because the first set is shed before or immediately after birth. The labial maxillary incisors (also called "first," or "primary") are larger than the palatal incisors (also called "second," "secondary," or "peg"). The mandibular and the maxillary first incisors are typically chisel-shaped. Rabbits lack canine teeth; incisors are separated from premolar and molar teeth by an edentulous gap (diastema) (Figs. 36.6, 36.7). The diastema allows the lips to fold inward (*inflexa pellita*).[21] This effectively forms an antechamber in the rostral part of the mouth. A median cleft of the dorsal lip (harelip) allows easy exposure of the incisors rostrally and is seen in lagomorphs and rodents.[21]

Premolar and molar teeth are anatomically similar and are often simply called "cheek teeth." They are set closely together, without any significant interproximal space in between. Because maxillary and mandibular cheek teeth differ in number, each mandibular tooth occludes with two maxillary cheek teeth, with the exception of the smaller first and sixth maxillary cheek teeth. The occlusal surface is not an even plane. Transverse ridges form a zigzag occlusal surface that can be seen from the lateral view both on the skull and on radiographs (Fig. 36.6).

All rabbit teeth are hypsodont (long-crowned) and elodont (continuously growing and erupting) teeth. They are defined as aradicular teeth because they do not develop anatomic roots. The anatomic parts of rabbit elodont teeth are the portion above the gingival margin (clinical crown), the portion below the gingival margin and inside the alveolus (reserve crown), and the open root (apex).[6]

The diastema separates the dental quadrant into two functional units: the incisors and the cheek teeth. The function of the incisors of lagomorphs is to cut grass and other plants. Food is then chewed with the rough occlusal surface of the cheek teeth. Mandibular movements occur in three directions. Rostrocaudal movements are limited in lagomorphs[6,21,60]; dorsoventral chewing movements similar to those of carnivores are very limited as well. Anisognathism explains the importance of laterolateral movements of the mandible. Because the mandibles are anatomically narrower than the maxillae, the mandibular cheek teeth rest with their buccal edges occluding with the palatal edges of the maxillary cheek teeth. Occlusal surfaces of cheek teeth come into full contact alternatively during chewing. Transverse ridges on the occlusal surface interlock with the opposite teeth during chewing, providing an efficient rough surface for grinding and crushing fiber. [21,54]

During normal chewing of fibrous foods, the clinical crowns of elodont teeth are constantly worn and continuously replaced by the reserve crown. The lateral movements allow wearing of the occlusal plane of the incisors.

Pathophysiology of Dental Disease

Any process interfering with normal tooth growth or wear will result in some degree of dental disease. Trauma is well described and understood as a primary cause for dental disease. Three different nontraumatic primary causes have been reported and proposed in the rabbit: congenital and developmental abnormalities, abnormal wear related to inappropriate diet (diets low in rough fiber and silicates), and metabolic bone disease. Congenital jaw mismatch may be caused by prognathism of the mandible or brachygnathism of the maxilla.[6,18,21] This anatomic condition is common in purebred dwarf rabbits weighing less than 1 kg and in lop rabbits (Fig. 36.9).

Inability to wear normally from any cause can potentially produce a cascade of abnormal changes. Elongation of cheek teeth produces bending that often follows a typical pattern: the mandibular cheek teeth typically bend medially (showing lateral convexity), while maxillary cheek teeth begin to bend laterally, with medial convexity.[6] This further reduces the occlusal wear of cheek teeth arcades because lateral chewing movements are not adequate to wear all occlusal surfaces evenly. When occlusal planes



Fig. 36.9 Congenital incisor malocclusion in an 8-month-old rabbit. The maxillary incisors were fractured at the time of presentation. (Used with permission from Angela Lennox, DVM.)

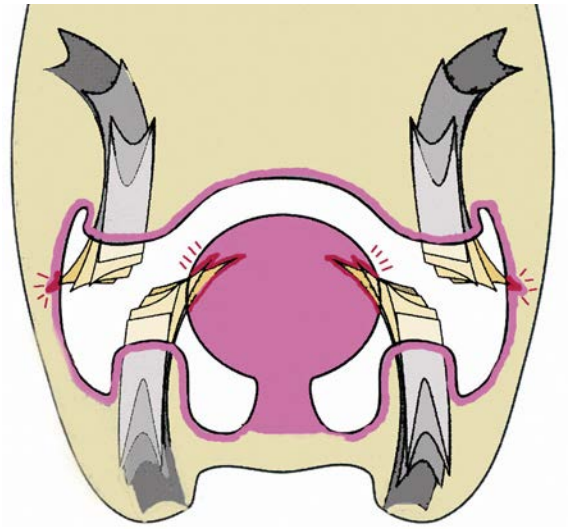


Fig. 36.10 Pathophysiological pattern of acquired dental disease as a result of insufficient wear. (Modified from Crossley DA: Oral biology and disorders of Lagomorphs. *Vet Clin No Am Exot Anim Pract* 2003;6:629–659.)

malocclude, the rabbit may reject hay, looking for food easier to crush (if available) and thus further reducing the amount of fiber and the lateral chewing movements. The occlusal planes do not wear on the lateral (buccal) margin of the maxillary cheek teeth and on the medial (lingual) margin of the mandibular cheek teeth, causing spikes and spurs to form (Fig. 36.10). These can be very sharp, creating discomfort and leading the rabbit to further reduce the degree of lateral chewing movement. Injuries and ulcerations of the tongue (from the mandibular cheek teeth) and the buccal mucosal surface (from the maxillary cheek teeth) are often severe and represent secondary complications. Elongation of reserve crowns leads to apical deformity and stretching and perforation of the cortical bone. Vascular support to the apex is reduced or impeded and diseased teeth partially lose their capability to grow, becoming more fragile and prone to fractures. Increased interproximal space and widened periodontal space, caused by bending of the cheek teeth, lead to food impaction and increase the risk of periapical infection. Perforation of the cortical bone and periapical infection lead to the most common complication of acquired dental disease: infection of soft tissues and odontogenic abscesses.

Excessively elongated cheek teeth, particularly the mandibular first premolars, may also lead to functional prognathism of the mandible.[6,18] Once the crowns have elongated, the jaw is held wider than normal and the mandible slides rostrally into a functional prognathic position, leading to malocclusion of incisors. This condition is often incorrectly diagnosed as congenital, even in aging rabbits.

Metabolic bone disease as a cause of acquired dental disease has been extensively studied and reported.[27,28,33] In one study in pet rabbits, parathyroid hormone concentrations were abnormally high and calcium concentrations were low, suggesting metabolic bone disease as a predisposing condition for acquired dental disease.[27] Most affected rabbits demonstrated demineralized skull bones and radiographic findings consistent with osteodystrophic disease of both the teeth and the skull bones. Demineralization of the bone matrix and weakness of the alveolar bone lead to loosening of the teeth, bending and rotation of the cheek teeth within the alveolus, and widened interproximal spaces. These changes lead to improper occlusion of cheek teeth and resulting abnormal wear of the clinical crowns. The ventral cortical bone becomes deformed, and the periostium of the mandible and the maxilla eventually becomes perforated, leading to secondary complications such as abscesses.

Specific findings in particular patients seem to defy current pathophysiologic theories, including rabbits with catastrophic dental disease of a single quadrant, rabbits on obviously deficient diets with near-normal dentition and vice versa, and similar patterns of dental disease in related siblings. For this reason, multiple factors, including genetic, may be involved in the expression of dental disease.[33]

Dental Disease

Although dental disease affecting the cheek teeth is more prevalent, disease affecting the incisors is more apparent to the owners. In the most common pattern of malocclusion, the mandibular incisors tend to elongate labially, while the maxillary incisors tend to elongate palatally.[6] For this reason, overgrown mandibular incisors usually do not produce secondary lesions because they are anterior to the upper lip and nose, whereas overgrown maxillary incisors curve dorsally and may damage the lips or the palate. Very elongated incisors may fracture. With end-stage dental disease, growth may be slowed or arrested. Dental disease of the incisors also affects the reserve crown. Abnormal elongation and apical deformity can lead to partial or complete obstruction of the nasolacrimal duct. Epiphora, dacryocystitis, subsequent ocular lesions, or facial dermatitis are common possible sequelae (see Chapter 40).[6]

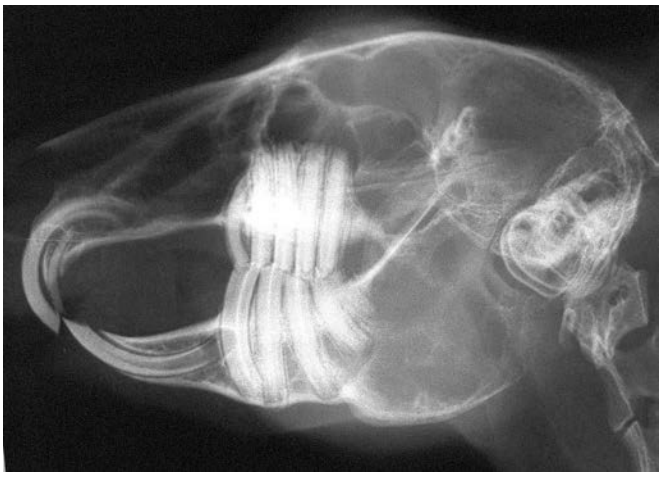


Fig. 36.11 Early stage of acquired dental disease of cheek teeth in a rabbit. Radiographic signs are elongated clinical and reserve crowns, widened interproximal spaces of cheek teeth, abnormal curvature of first premolars, and deformity of the ventral mandibular profile caused by apical overgrowth. Malocclusion of incisor teeth and clinical signs are usually not present at this stage. (Reprinted from: Capello V, Gracis M: *Rabbit and Rodent Dentistry Handbook*. Zoological Education Network (2005), Hoboken, NJ: Wiley-Blackwell Publishing (2007), with permission.)

Rabbits with acquired dental disease of the cheek teeth may present at different stages, but clinical signs may not be consistent with the degree of disease. The earliest stage is tooth elongation. Radiographically the normal occlusal plane and its zigzag pattern are lost; the first premolars are curved, interproximal spaces widen, and the ventral profile of the mandibular cortical bone deforms slightly due to increased pressure (Fig. 36.11). Clinical signs are usually not present at this stage, but the rabbit may be selective at feeding, reluctant to eat hay or other hard food; this may be inferred from a detailed history. In later stages, dental abnormalities become more severe. Clinical crown elongation and the abnormal occlusal plane appear as "wave mouth" or "step mouth" on oral examination (Fig. 36.12).[6] Sharp spurs may develop on the cheek teeth, leading to lesions of the tongue or the buccal mucosa (Fig. 36.12C). Excessive coronal elongation of cheek teeth may result in fractures, especially longitudinal fractures of mandibular premolars. End-stage dental disease of the cheek teeth is frequently associated with resorption of bony and dental tissue.

Common complications of acquired dental disease are periapical infections, osteomyelitis, and facial abscesses. The latter appear as large masses usually located at the ventrolateral aspect of the mandible or the lateral aspect of the maxilla (Fig. 36.13) or lead to unilateral exophthalmos in cases of retrobulbar abscesses. Early small abscesses are usually missed by the owners because of their location and the presence of fur, especially in long-haired rabbits.

The prognosis of dental disease is based on the severity by the time of diagnosis and on an accurate diagnosis, which results from a thorough workup. In these cases, discuss every clinical and practical aspect of treatment and management with owners, including severity of disease, general patient condition, continued required care and subsequent dental procedures, compliance, and expected costs. Many rabbits can have a good quality of life for years, even with severe to end-stage dental disease, if appropriately managed.

Treatment of Dental Disease

The general guidelines of intraoral dental procedures consist of reducing abnormal tooth length, restoring the occlusal plane to as near normal as possible, and extracting severely diseased teeth. Complications and secondary diseases such as periapical infections, osteomyelitis, and abscesses are treated with combined intraoral dental procedures, extraoral surgery, and systemic antimicrobial therapy.

Anesthesia of small mammals is discussed in Chapter 37. Local anesthesia is an important adjunct for extraction of both incisor and cheek teeth.[44] Dental blocks have been used anecdotally in rabbits and other rodents and are based on techniques and landmarks used in dogs and cats.

Medical Treatment

Medical therapy alone is not sufficient for the treatment of dental disease. However, it is often important for temporary palliative or supportive treatment before and in addition to surgical procedures.[6,12] The aim of medical therapy is to address several concerns such as antibiotic, analgesic, and supportive treatment. In choosing an antibiotic, base the selection on results of both aerobic and anaerobic culture and sensitivity testing when possible, and consider any species-specific contraindications, such as oral administration of penicillins in rabbits and herbivorous rodents.[59] Oral metronidazole and azithromycin and subcutaneously administered penicillin G procaine/benzathine and long-acting ceftiofur are routinely used against anaerobic bacteria involved in periodontal infections. Analgesia is critical to prevent pain-related anorexia. Supportive treatment includes rehydration, if indicated, and syringe feedings.

Dental Procedures

Treatment of disease of the incisors includes coronal reduction and extraction.[12,18,26] Coronal reduction is limited to cases in which the malocclusion is minimal and has been diagnosed early, and proper occlusion of both incisor and cheek teeth can be restored. Reducing and reshaping of the incisors must be performed on anesthetized animals with low- or high-speed dental equipment and appropriate diamond cutting discs or burrs.[15] Do not use trimmers, clippers, or similar instruments to cut elongated or abnormal incisors. These instruments do not allow the restoration of a normal incisal edge, and they frequently lead to complications such as fractures, damage of the apical germinative tissue, pulp exposure, and endodontic or periodontal infections.[6]

Extraction is the only curative and completely effective treatment for severe malocclusion and acquired dental disease of incisor teeth (Figs. 36.14 and 36.15). Rabbits adapt easily to lack of incisors and are able to eat normally by using their lips and tongue to prehend food.

The technique for extraction of incisors is described in Box 36.1 and shown in Fig. 36.15. Extracting the entire set of six incisors in rabbits is usually necessary. In selected cases of fracture or infection of a single incisor tooth in the absence of overall

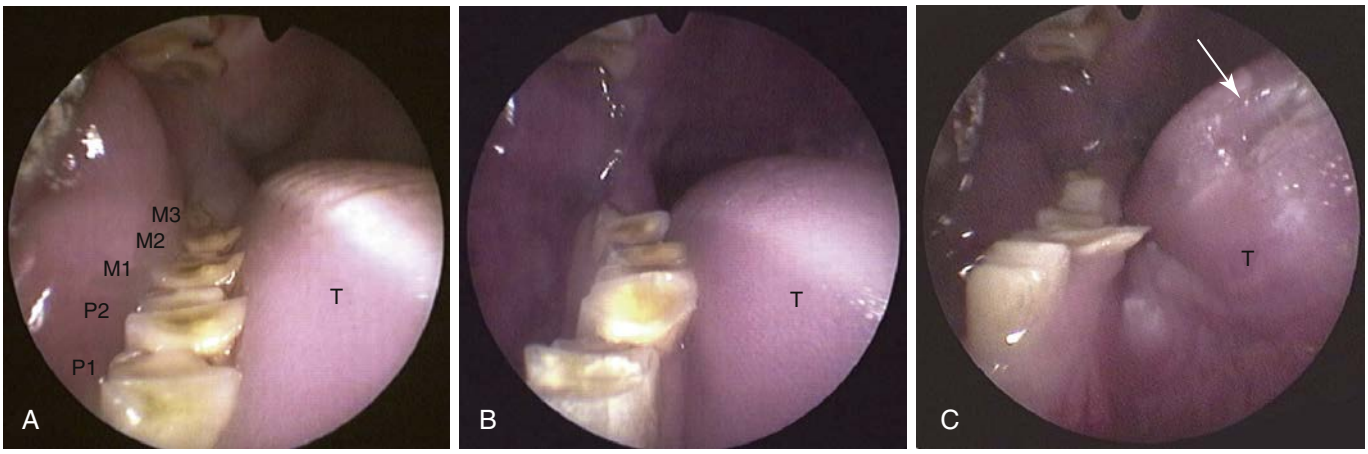


Fig. 36.12 Oral endoscopy in rabbits. (A) Normal appearance of cheek teeth, right mandibular quadrant. Note that the lingual points are normal in rabbits. (B) Malocclusion of the right mandibular quadrant. Abnormal elongation (or shortening) of clinical crowns, uneven occlusal plane (referred to as "step mouth"), and initial lingual bending of the teeth. Clinical signs are usually absent at this stage. (C) Sharp lingual spike of the second molar tooth caused by improper wearing, and related lesion of the lingual mucosa *(arrow). P,* premolar; *M,* molar; *T,* tongue. (Reprinted from: Capello V, Gracis M: *Rabbit and Rodent Dentistry Handbook*. Zoological Education Network (2005). Hoboken, NJ: Wiley-Blackwell Publishing (2007), with permission. B and C used by permission from Vittorio Capello, DVM.)



Fig. 36.13 Surgical treatment of periapical infection of a mandibular cheek tooth in a rabbit. (A) Mandibular abscess, after shaving. (B) Exposure of the abscess. After complete exposure, the junction between the capsule and mandibular bone is incised with blunt scissors. (C) Appearance of the osteomyelitic lesion after the abscess was excised and the adjacent soft tissues were debrided. The diseased fragment of the involved tooth is extracted by the extraoral approach. (D) Marsupialization of the surgical site. (E and F) Follow-up 10 days and 20 days after surgical treatment. (Used with permission from Vittorio Capello, DVM.)

malocclusion, extracting that incisor tooth may be indicated. The remaining incisor may be able to maintain a normal occlusal plane of the opposing teeth due to lateral chewing movements.[12]

Postoperative skull radiographs help in detecting possible remaining tooth fragments. Partially removing a tooth or failing to destroy pulp tissues can result in partial or complete regrowth, which can be addressed at a later time.

Dental procedures of cheek teeth in rabbits include reducing clinical crowns and extracting severely diseased teeth.[12,26] Coronal reduction should be aimed at restoring the normal height and angle of the occlusal plane as near to normal as possible. Although it is impossible to restore the normal zigzag-shaped occlusal plane or reverse abnormal changes affecting the reserve crowns and the apices of cheek teeth, this procedure

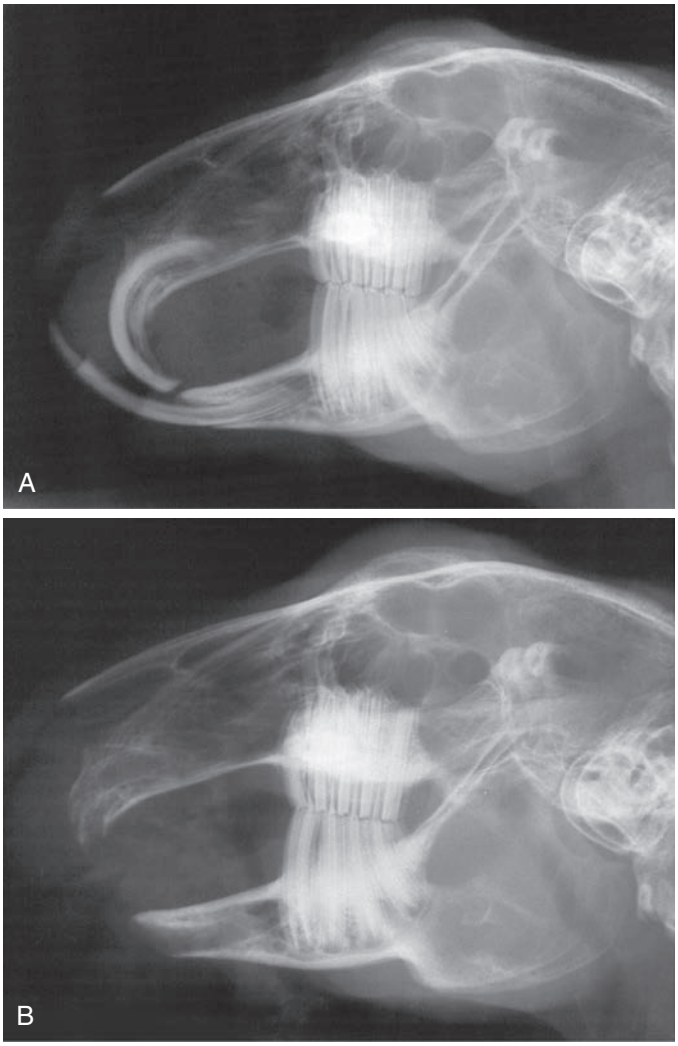


Fig. 36.14 (A) Coronal elongation and malocclusion of the incisor teeth due to congenital brachygnathism of the maxilla in a rabbit. The maxillary diastema is shorter than normal, and its length is similar to that of the mandibular diastema. Cheek teeth are normal, including the zigzag line at the occlusal plane. (B) Postoperative radiograph after extraction of incisor teeth. (Used with permission from Vittorio Capello, DVM.)

is clinically useful for many reasons. Sharp spurs are burred, allowing mucosal lesions to heal and reducing discomfort. Clinical crowns are shortened, reducing pressure and allowing easier lateral movements during chewing. Diminished pressure counteracts some of the pathophysiologic steps described above, like bending of the teeth, apical deformity, and cortical bone deformity. Therefore reducing crown length is especially useful in the early stages of acquired dental disease, and in rabbits with concurrent metabolic bone disease, when the surrounding bone is weaker than normal. In many cases, overgrowth of gingival tissue may mask elongated crowns, making accurate analysis of preoperative radiographs very important. Postoperative radiographs are also recommended to determine whether crowns have been reduced adequately and the occlusal plane is restored.

A straight, low-speed dental handpiece should be used in rabbits. Protect soft tissues with a flat or concave dental spatula and remove accumulated tooth dust with moistened cotton swabs. Another option is a burr protector that fits over the end of the burr tip to protect soft tissues from damage during drilling (Fig. 36.16). Prevent thermal damage to teeth by avoiding prolonged contact with the drill in one location.

The most common indication for extraction is to remove cheek teeth that are mobile due to fracture or periapical infection.[12,19,40] Markedly deformed teeth that are not easily corrected by burring or that require frequent re-treatment may be considered for extraction as well. Limit extractions to as few teeth as possible to allow proper crushing of food. Although rabbits adapt surprisingly well to progressive dental disease and chronic lack of cheek teeth, we have noted that multiple extractions from a single quadrant can be associated with discomfort and slower postsurgical recovery. After extraction, opposing cheek teeth may or may not require burring, depending on the stage of dental disease and their ability to grow. Interestingly enough, as dental disease progresses, opposing cheek teeth may slow or cease to grow in some cases.

Extracting cheek teeth can be challenging, depending on the position and condition of the affected teeth. Even with proper luxation, and the use of suitable extraction forceps, teeth are easily fractured during extraction. Complete intraoral extraction is also extremely difficult when fracture of the reserve crown, severe apical deformity, retained apices, and dental ankylosis are present. In these cases, combined intraoral and extraoral extraction of fragments is necessary. When periapical infection is not present, the socket is protected after extraction to prevent food impaction and infection. When feasible, the gingiva may be sutured over the socket; if this is not possible, the socket can be filled with doxycycline hyclate gel (Doxirobe gel; Pfizer Animal Health, Kalamazoo, MI). In case of periapical infection, osteomyelitis, and concurrent abscess, the socket may be filled with Doxirobe gel or left open and treated after surgery as described below.

Treatment of Periapical Infections and Abscesses

The aim of most treatment protocols, except wound-packing as described below, is to remove the entire abscess including the capsule, extract the tooth fragment(s) involved, and debride the osteomyelitic bone.[14,25,59] Different surgical options have been reported beyond the simple (and usually ineffective) incision of the abscess and flushing of the purulent material. Excision of the entire abscess, followed by either primary closure alone or after packing the surgical site with antibiotic-impregnated polymethylmethacrylate (AIPMMA) beads, or marsupialization and packing of the surgical site with antibiotic cream, honey or sugar solution, or bioactive ceramics have been reported.[25] Calcium sulfate beads (Kerrier, Palm Beach Gardens, FL; www.kerrier.com) have recently become available to use in place of AIPMMA beads. Advantages of calcium sulfate beads are that they are fully resorbable, do not have to be removed, and have predictable elution properties. Although AIPMMA beads can remain in place, they are nonresorbable and in some cases act as an infection nidus and require removal.

A technique in which the capsule is not removed has been reported in rabbits with dental abscesses.[57] The procedure involves lancing the abscess, minimally debriding and cleaning the abscess cavity, and packing the cavity with strips of

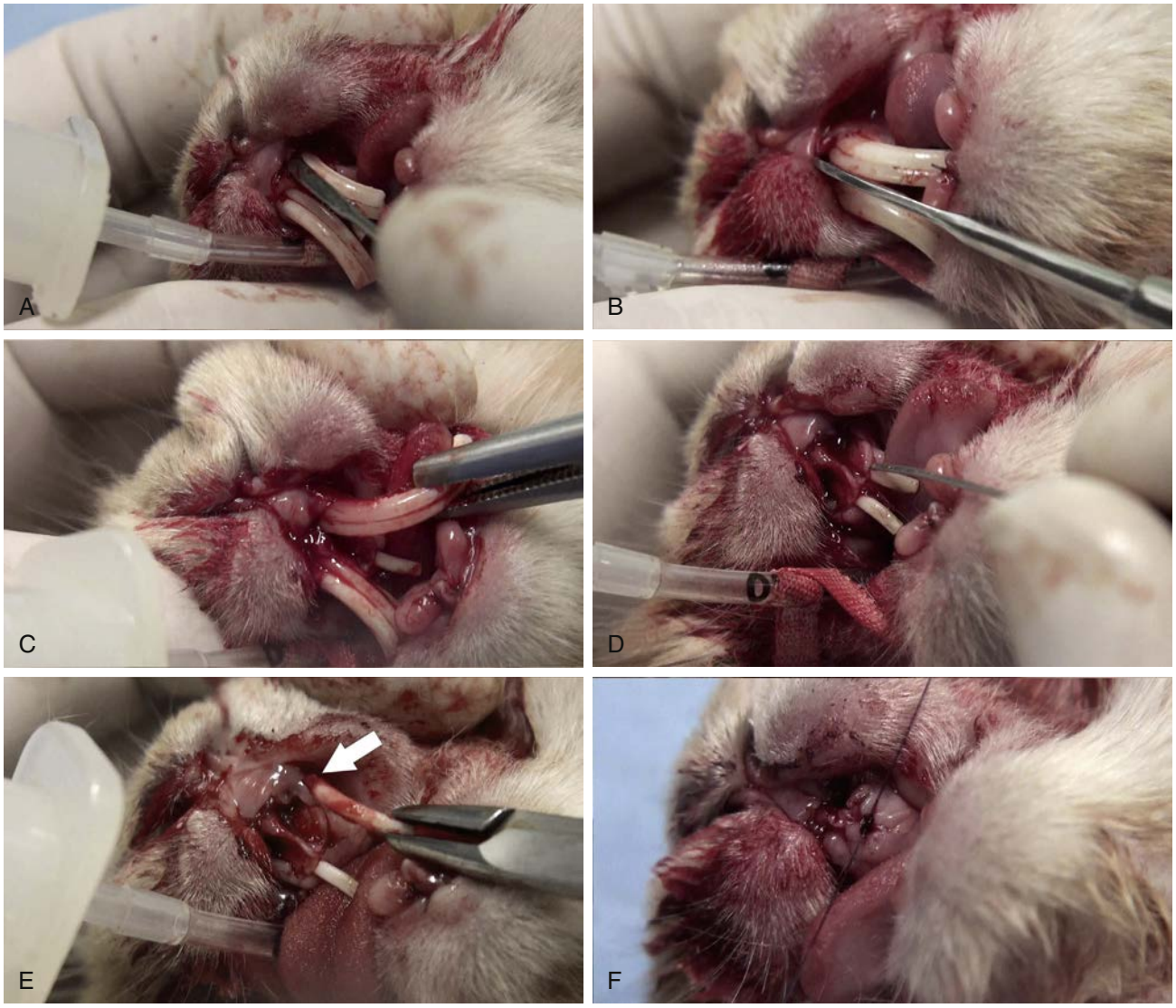


Fig. 36.15 Extraction of maxillary incisor teeth in a rabbit. (A) A flattened and curved contoured 18-gauge needle is used to break down the periodontal ligament on the labial aspect of the primary incisor tooth. (B) The maxillary edge of the Crossley's luxator is inserted in the periodontal space on the mesial aspect of the tooth. (C) When the tooth is mobile, the clinical crown is grasped with suitable extraction forceps (a large hemostat, in this case). The tooth is pulled gently, following the natural curvature of the reserve crown, and applying a slight distal (lateral) rotation during extraction. (D) A flattened and curved contoured 21-gauge needle is used to perform luxation of the rostral aspect of the secondary ("peg") incisor tooth. (E) The peg tooth is extracted using a small needle holder. Note the red germinative tissue at the apex (arrow), demonstrating complete extraction. (F) Purse-string suture of the gingiva using 4-0 absorbable suture material (poliglecaprone, Monocryl). (Used with permission from Vittorio Capello, DVM.)

≈5-mm–diameter sterile gauze impregnated with antibiotics, most commonly ampicillin. Rabbits are concurrently treated with systemic antibiotics, and gauze packings are replaced under general anesthesia every 7 days until resolution of infection. In this retrospective study, 5 ± 2 abscess packings were required to achieve resolution in 13 of 14 abscesses with a follow-up time of 33 ± 24 months.[58] This technique may be an option in rabbits with minimal osteomyelitis; however, efficacy in rabbits with extensive osteomyelitis or bony sequestra is not reported.

Marsupialization of the soft tissues around the area of the affected bone is the recommended treatment by the authors. This is followed by daily postoperative flushing and further gentle debridement of the surgical site, applying antiseptics or other products to promote healing, and constant direct monitoring of healing process (Fig. 36.13).[14] Slow healing by secondary intention is also critical in cases of simultaneous extraction of one or two cheek teeth, where suturing the gingiva may be very difficult or impossible. In these cases, the alveolus may become impacted with food. Marsupializing the tissues may allow flushing of the intraoral fistula through the cutaneous opening until the new bone apposes and the gingiva heals, effectively closing the fistula.

In our experience, marsupialization is well tolerated by rabbits, despite exposure of part of the deep bone.

BOX 36.1 Step-by-Step Procedure for Extracting Incisor Teeth in Rabbits

1. Take diagnostic radiographs in five standard projections, add complementary intraoral views where appropriate, or perform computed tomography scanning before the dental procedures.
2. Place the patient under general anesthesia in dorsal or lateral recumbency.
3. Perform intraoral dental procedures as needed before extracting the incisor teeth.
4. Scrub the gingiva with 0.1% chlorhexidine solution.
5. For optional adjunct analgesia, perform local blocks for the mental nerve and the rostral infraorbital nerve for extraction of mandibular and maxillary incisor teeth, respectively.

Extraction of the Mandibular Incisor Teeth

6. Incise the gingival attachment circumferentially around the whole tooth with the tip of a No. 11 or 15 scalpel blade.
7. Insert a luxator in the periodontal space on the medial side of the tooth until resistance is felt. Hold the luxator in position for a few seconds to stretch and disrupt the periodontal ligament. Gradually move the tip of the luxator toward the apex of the tooth. Use your free hand to hold and stabilize the mandible at all times. Perform the same procedure on the lateral aspect of the tooth.
8. Following the same technique, use a contoured, 18-gauge hypodermic needle to break down the periodontal ligament on the lingual and labial sides of the tooth. The tooth should be loose and very mobile at this point.
9. Grasp the tooth with the extraction forceps as close to the gingival margin as possible and extract it using steady, slowly increasing force, following the curvature of the root. Once loosened, gently intrude the tooth in the socket to destroy the germinal tissues at the bottom of the alveolus. If the periodontal ligament has been completely and correctly severed and the tooth is not severely deformed, it can be extracted without the use of significant force. Bleeding is usually minimal.
10. Once it is extracted, examine the tooth to ensure that the entire tooth and its pulp tissues have been removed.
11. After extraction, insert a needle into the alveolus to curette the alveolar walls and damage any germinal tissue to prevent tooth regrowth.
12. Flush the alveolar cavity with saline solution to remove any debris and dental or bony fragments. If periapical infection is present, use dilute 2% povidone iodine or 0.05% to 0.1% chlorhexidine solution to flush.
13. Close the alveolus by suturing the gingiva with simple interrupted sutures or a purse-string suture pattern using 3-0 or smaller absorbable suture material. The pursue-string suture must have at least four points of fixation before being tightened. Do not suture when infection is present.

Extraction of the Maxillary Incisor Teeth

14. Use a contoured needle to sever the periodontal ligament on the labial and palatal sides of the maxillary incisor teeth, similar to the procedure described for mandibular incisors.
15. Sever the periodontal ligament on the medial and lateral aspects of the teeth with Crossley's luxator. The periodontal ligament is particularly tight on the medial aspect of the tooth.
16. Once it is loose, gently grasp the tooth with suitable extraction forceps or a pair of needle holders. To avoid dental and bony fractures, gently extract the tooth following the natural shape of the tooth, applying slight distal rotation.
17. Completely extract the tooth and examine it for the presence of pulp tissues. Repeat the procedure on the contralateral incisor tooth. Control bleeding with sterile cotton swabs.
18. Use a thin hypodermic needle to loosen the second incisor teeth. When the tooth is completely luxated, extract it with small extraction forceps or thin hemostats, taking care to avoid crushing the tooth.
19. After extraction, curette the alveoli to remove any remaining pulp tissues and rinse with saline solution or 0.1% chlorhexidine solution.
20. To promote gingival healing, close the extraction site with simple interrupted sutures or a purse-string suture pattern with 3-0 or 4-0 absorbable suture material. Do not suture the extraction site when infection is present. In using a purse-string pattern, fix the suture material at a minimum of six points before tightening it.
21. Obtain a lateral view postoperative radiograph to confirm complete extraction of all six incisor teeth.

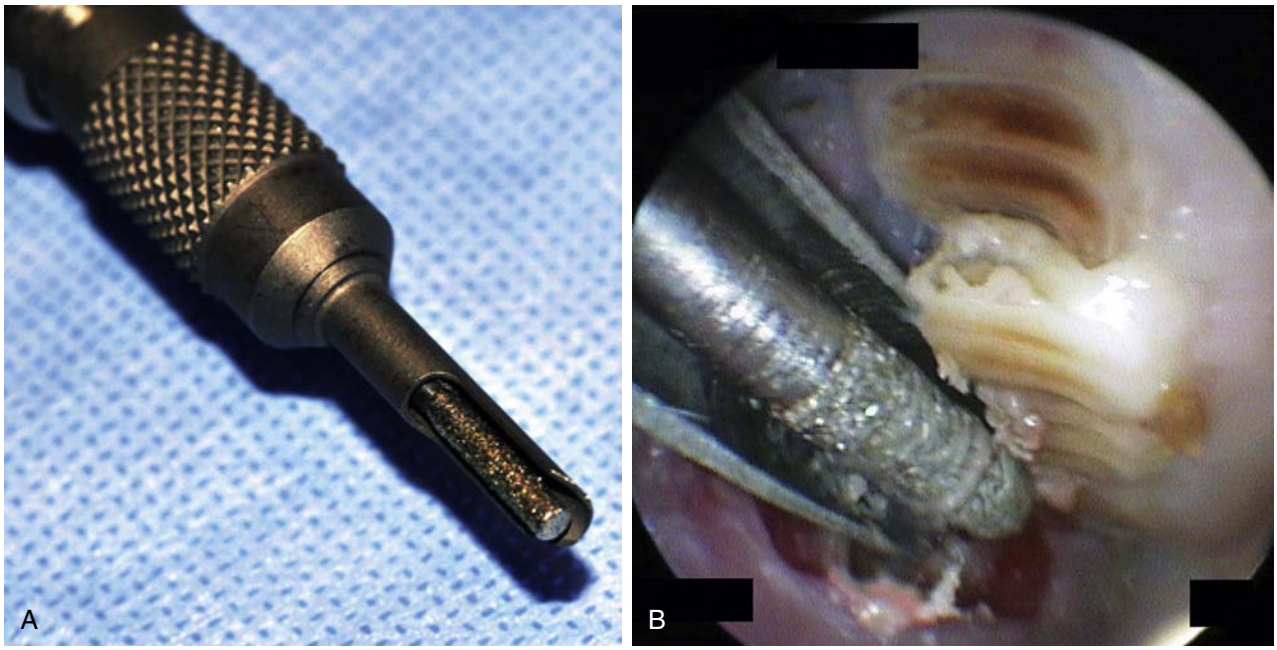


Fig. 36.16 (A) Soft-tissue guard partially covering a diamond burr, attached to a straight dental handpiece. (B) Diamond burr used to adjust the clinical crowns of the cheek teeth in a chinchilla. Note the soft tissue guard covering 180 degrees of the burr tip and thereby protecting the soft tissue from iatrogenic trauma. (Courtesy Christoph Mans, DVM.)

A longer postoperative period, temporarily unattractive cosmetic appearance, and significant owner commitment must be discussed before surgery.

The technique for excising odontogenic abscesses, debriding the osteomyelitic site, and marsupialization of the soft tissues is shown in Fig. 36.13.

Facial Surgery and Surgical Treatment of Specific Conditions

In cases of severe complications of acquired dental disease in rabbits, the severity of the bone infection is not directly related to the severity of the clinical signs. This is why accurate diagnosis and proper prognosis are the keys to successful surgical treatment. Before planning surgical debridement of an abscess and the related osteomyelitic bone, it is essential to determine which tooth or teeth are involved and the extent of the osteomyelitis. Beside conventional radiographs, the use of computed tomography is extremely helpful and in most cases necessary for accurate diagnosis, proper prognosis, and surgical planning.[10] Without advanced diagnostic tests, the surgical approach to the abscess and the underlying affected bone should be considered an exploratory surgery. Purulent material follows the path of least resistance, and it is not uncommon for purulent material to accumulate some distance from the affected tooth or bone.

Periapical infection and osteomyelitis of mandibular CHT 4 and 5 are less common but carry a difficult prognosis because the abscess usually spreads beneath the masseter muscle, making both surgical access and treatment more challenging.[25] Also, debriding infected bone is not feasible because the cranial portion of the masseteric fossa is much thinner than the body of the mandible, carrying much higher risk of iatrogenic fracture.[14]

When treatment of periapical infections and osteomyelitis fails, extensive osteomyelitis of the body of the mandible may be a sequela.[14] Thorough and deep surgical debridement is difficult to perform, and bone healing by secondary intention may be impossible when the entire body of the mandible is affected. In severe cases, unilateral rostral (partial) mandibulectomy may be an option.[54] However, due to the continuously growing teeth, the consequences and complications of this procedure are greater than in carnivores.[1] Reported frequent complications include oral wound dehiscence, oral fistula formation, mandibular shifting resulting in severe cheek teeth and incisor teeth malocclusion, and the inability to return to normal food intake and therefore requiring life-long assisted feeding.[1,54] Therefore this type of procedure in rabbits should be considered only as a salvage procedure for cases in which all other treatment modalities have failed.[1]

In rabbits, the alveolar bulla of the skull includes the reserve crowns and the apices of the four caudal maxillary cheek teeth.[14] Because of the anatomic relationship with the orbital fossa, retrobulbar abscesses are a relatively common sequelae of periapical infection of these teeth.[14,25] The alveolar bulla can fill with food debris, tooth fragments, and pus and the infection can then spread to the retrobulbar space. The typical presentation is unilateral exophthalmos without a history of trauma, possibly complicated by panophthalmitis. A CT of the skull is necessary in cases of retrobulbar abscess to determine which cheek teeth are involved. Advanced cases may necessitate enucleation of the globe. Diagnosis of impaction and periapical infection or abscessation of the alveolar bulla is ideally made before a retrobulbar abscess develops and the eye is compromised. An extraoral lateral surgical approach for abscesses of the two most rostral premolars is feasible because they are located cranial to the zygomatic arch. However, the zygomatic arch prevents a direct approach to the alveolar bulla. Potential choices for access to this space include (1) via the intraoral fistula after extraction of the diseased maxillary cheek tooth or teeth, ± endoscopic guidance, (2) a lateral extraoral approach via partial ostectomy of the zygomatic arch, or (3) a lateral approach dorsal to the lateral margin of the orbital fossa in case of exceptionally large abscesses.[14,47]

Chronic septic pararhinitis and rhinitis secondary to severe or end-stage dental disease can be a result of empyema of the alveolar bulla and/or empyema of the maxillary recess. Long-term medical treatment is usually unrewarding but can provide temporary and palliative improvement. Rhinotomy or pararhinotomy may be required.[13]

Unilateral rostral mandibulectomy has been reported for surgical treatment of bone tumors.[50,54] Oral tumors reported in rabbits include ameloblastoma, complex odontoma, giant cell epulis, cementoma, chondrosarcoma, and osteogenic sarcomas.[50,51,54]

RODENTS

Anatomy and Physiology of the Skull and Teeth

All rodent species have one pair of well-developed maxillary and mandibular incisor teeth, representing the best-known anatomic peculiarity of this taxonomic order. Incisors vary in shape, color, and thickness among species, and only the labial aspect is covered in enamel.[17,45,53] The enamel can be white (e.g., guinea pigs) or yellow-to-orange (e.g., chinchillas, rats). The length of the clinical crown of incisors differs between species. For example, in guinea pigs, the length of the mandibular incisors is normally triple the length of the maxillary incisors. Differences in normal anatomy should be kept in mind to avoid misinterpreting abnormal patterns. In all rodent species, both maxillary and mandibular incisors present a chisel-shaped occlusal surface and are elodont teeth. As in rabbits, all rodents lack canine teeth, and a diastema is present between the incisor and the first premolar (or molar) tooth. Premolar and molar teeth vary among rodent species (Table 36.1).

Within the order Rodentia, suborders based on anatomic and functional differences of the masseter muscles exists and companion exotic mammals can belong to one of the following clinically relevant suborders: Hystricomorpha ("porcupine-like," with the infraorder Caviomorpha "guinea pig-like," which includes all South American hystricognaths), Myomorpha ("mouse-like" or "rat-like"), and Sciuromorpha ("squirrel-like").[45] The suborders have different dental formulas (Table 36.1), but from the standpoint of the dental anatomy and physiology, they can be simply reduced to two groups.[45] The porcupine-like rodent species (e.g. guinea pigs, chinchillas, degus) have complete elodont (continuously growing) dentition. Premolar and molar teeth are anatomically indistinguishable and may be simply called "cheek teeth" (Fig. 36.8).[6,45] Despite differing dental formulas, the dentition is physiologically similar to rabbits. Rat-like and squirrel-like

TABLE 36.1 Dental Formulas of Common Exotic Companion Mammals

	INCISOR TEETH	CANINE TEETH	CHEEK TEETH		
	Maxillary/ Mandibular	Maxillary/ Mandibular	Premolars Maxillary/ Mandibular	Molars Maxillary/ Mandibular	Total No. of Teeth
Rabbit	2 × 2/1 (E/H)	0/0	2 × 3/2 (E/H)	2 × 3/3 (E/H)	28
Guinea pig, chinchilla, degu	2 × 1/1 (E/H)	0/0	2 × 1/1 (E/H)	2 × 3/3 (E/H)	20
Rat, mouse, hamsters, gerbil	2 × 1/1 (E/H)	0/0	0/0	2 × 3/3 (A/B)	16
Prairie dog, squirrels	2 × 1/1 (E/H)	0/0	2 × 1–2/1 (A/B)	2 × 3/3 (A/B)	20–22
Ferret	2 × 3/3 (A/B)	2 × 1/1 (A/B)	2 × 3/3 (A/B)	2 × 1/2 (A/B)	34
Hedgehog	2 × 2/2 (A/B)	2 × 1/1 (A/B)	2 × 3/2 (A/B)	2 × 3/3 (A/B)	34
Sugar glider	2 × 3/2 (A/B)	2 × 1/0 (A/B)	2 × 3/3 (A/B)	2 × 4/4 (A/B)	40

A/B, anelodont/brachyodont; E/H, elodont/hypsodont.

rodent species have elodont incisors but anelodont (rooted, not growing throughout life) cheek teeth. This distinction between species with elodont and anelodont cheek teeth is clinically very important. Malocclusion and acquired dental disease of the cheek teeth is not common in myomorph or sciuromorph species, as it is in rabbits and hystricomorph species, and coronal reduction of cheek teeth should never be performed. A minor distinction between myomorph and sciuromorph species is that the first group lacks premolar teeth.

Rodent species are monophyodont with a single set of teeth.[45] As true herbivores, the occlusal surface of cheek teeth of hystricomorph rodents is rough and uneven owing to enamel crests and dentinal grooves. Unlike those of rabbits, these occlusal surfaces are flat and do not present a zigzag pattern. In guinea pigs, the cheek teeth are curved; the mandibular teeth have a buccal (lateral) convexity while the maxillary teeth have a palatal (medial) convexity.[18,53] This results in a 30-degree oblique occlusal plane that slopes from dorsobuccal to ventrolingual/palatal (Fig. 36.17). The clinical crowns are much shorter than those of rabbits, in particular in chinchillas. Cheek teeth of prairie dogs have multiple roots. Although these animals are herbivorous ground squirrels, their dental structure is similar to that of primates, with cusps and ridges that create a rough occlusal surface.[45]

The temporomandibular joint and masticatory muscles of rodent species (especially those with anelodont cheek teeth) allow much greater rostrocaudal movements than in rabbits.[6,18] As in rabbits, elodont cheek teeth of hystricomorph rodents are worn during normal chewing activity. In some species (e.g., rats and squirrels), the cartilaginous tissue between the mandibular symphysis is not ossified, allowing a certain degree of movement between the mandibles.[34]

Pathophysiology of Dental Disease

As in rabbits, the primary cause of dental disease in hystricomorph rodents is under debate; theories include insufficient wear due to inappropriate diet and underlying metabolic bone disease or other nutritional deficiencies.[31,39,46] Hypovitaminosis C (scurvy) can cause irregular dentin formation. Secondary nutritional hyperparathyroidism with fibrous osteodystrophy has been reported in guinea pigs with dental problems.[38] In degus, feeding a diet high in phosphorus (Ca:P balance 1:1) resulted in dental disease within 6 months.[31] This syndrome does not occur in rodent species with anelodont cheek teeth, such as rats, hamsters, and prairie dogs. However, these patients can develop dental problems of the cheek teeth due to excessive wear, cavities, and decay.[45]

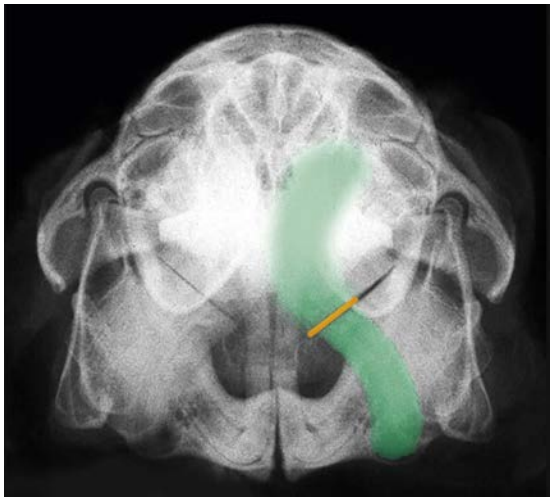


Fig. 36.17 Rostrocaudal projection of the skull of a guinea pig with normal dentition. Green superimposition indicates the shape and size of the left premolars; the orange line indicates the oblique occlusal plane. (Modified from Capello V, Gracis M. *Rabbit and Rodent Dentistry Handbook*. Zoological Education Network (2005). Hoboken, NJ: Wiley-Blackwell Publishing (2007), with permission.)

Primary congenital malocclusion of incisor teeth has been described in some rodents, in particular hamsters.[45] However, this condition may be difficult to distinguish from acquired malocclusion of traumatic origin in adult animals, as often the initial injury is not recognized by most owners. Acquired malocclusion and severe deviation of incisors occur most often after repeated trauma and fractures. Primary incisor malocclusion is rare in guinea pigs; abnormalities are usually a result of dental disease of cheek teeth.[39]

Clinical Presentation by Rodent Species

Guinea pigs with dental disease commonly are presented with reduced food intake, labored chewing, dysphagia, anorexia, and weight loss. Clinical signs tend to be more specific than in

rabbits and chinchillas, because guinea pigs appear less tolerant of dental abnormalities.[9] Because of the peculiar anatomy of their cheek teeth, a slight alteration of the sloped occlusal plane is enough to hamper chewing, and a slight overgrowth of clinical crowns is enough to interfere with movements of the tongue and swallowing.[9] Malocclusion of incisors often presents as excessive elongation or lateral deviation of the clinical crown of mandibular incisors.

Unlike guinea pigs, chinchillas tend to demonstrate clinical signs only when dental disease is advanced.[6,46] The most common presenting signs are reduced activity, food intake, and fecal production. Because dental disease often leads to ptyalism and pawing of the mouth, other presenting signs are wet fur over the mouth, chin, and forelimbs. Weight loss and emaciation are common in chinchillas with dental disease but are frequently missed by the owner because of the heavy fur coat.[9] As in guinea pigs, incisor malocclusion is rarely the only cause of dental disease and is usually associated with acquired dental disease of cheek teeth. Two signs of early dental disease that are often missed during routine physical examination in asymptomatic chinchillas are epiphora and mandibular cortical bone deformities.[9,46] Both are related to elongated reserve crowns and deformed apices of maxillary and mandibular cheek teeth. These abnormalities represent more advanced dental disease, as these changes are permanent and cannot be corrected.

In prairie dogs, dyspnea caused by apical deformities of maxillary incisors (pseudoodontoma) leads to reduced nasal air passage. In this obligate nasal breather, dyspnea is the most common clinical sign of dental disease.[6,45]

Rats, hamsters, and other rat-like species are frequently presented for evident malocclusion of incisors.[6,45] However, dental disease of incisors is usually missed by the owner, and patients are presented for reduced activity and food intake, emaciation, and in some cases ptyalism. Myomorph rodents generally do not display clinical signs related to diseases of the cheek teeth. More common signs include facial swellings related to periapical infection and abscessation, which occasionally affect the ocular and periocular structures.[6,45]

Common Types of Dental Disease

The typical pattern of rabbit incisor malocclusion, where mandibular incisors elongate labially, is not commonly seen in rodents. This may be because of their physiologic ability to compensate for any moderate primary incisor abnormalities through rostrocaudal movements of the jaw, which permit normal wearing of incisors.[9,18] In guinea pigs, the most frequent cause of malocclusion of incisors is elongated clinical crowns (especially mandibular) of cheek teeth.[9,39]

Coronal elongation and malocclusion of the cheek teeth is very common in guinea pigs. Because of the orientation of the cheek teeth in guinea pigs, mandibular clinical crowns always elongate lingually, and maxillary clinical crowns elongate with a buccal direction. Overgrowth of the crown is not as evident, and spur formation is much less common than in rabbits. Mandibular cheek teeth tend to bend over the tongue, and a typical bridge-like malocclusion develops when the first mandibular premolars occlude or even cross each other (Fig. 36.18). The sharp buccal border of the entire maxillary cheek teeth can cause severe discomfort to the mucosa. Even very early malocclusion and subsequent alteration of the sloped occlusal planes are enough to elicit reduced food intake or anorexia.

In chinchillas and degus, elongated crowns of mandibular cheek teeth are not as evident as in guinea pigs. The occlusal planes can develop "step mouth" and "wave mouth" patterns in a rostrocaudal direction. Excessive elongation of the reserve crowns leads to apical deformities of both the maxillary and mandibular cheek teeth (Fig. 36.19). Typical firm swellings can be palpated on the ventrolateral aspect of the mandible. Apical deformities can also result in perforated cortical bone, with resulting exposure of the apices. On oral examination, this marked abnormal curvature appears as widened interproximal spaces on the mandibular quadrants, and

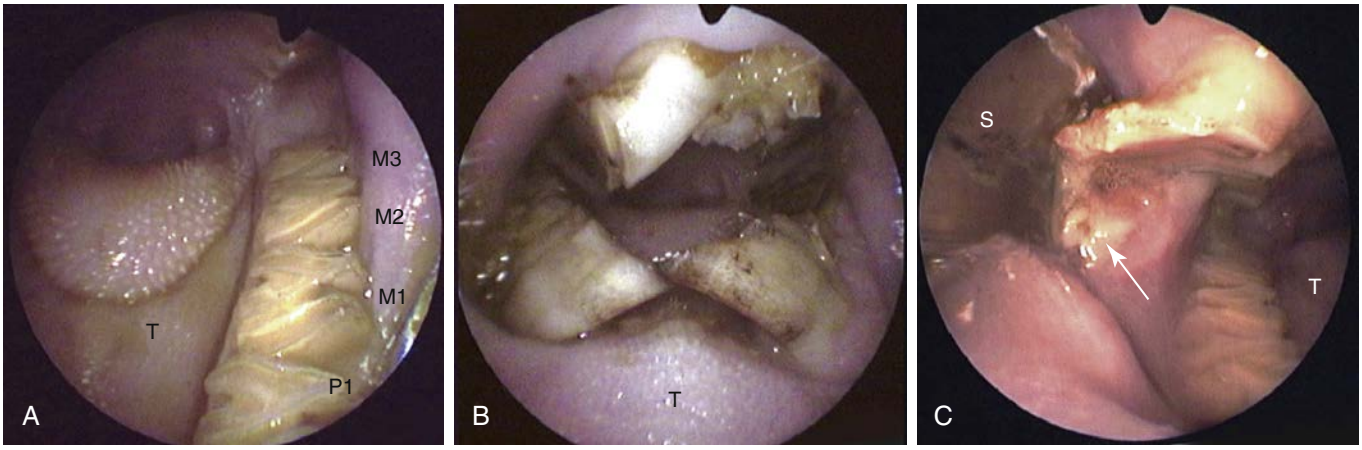


Fig. 36.18 Oral endoscopy in the guinea pig. (A) Normal appearance of cheek teeth, left mandibular quadrant. Note the enamel crests and dentinal grooves. (B) Severe coronal elongation and uneven occlusal plane of cheek teeth. Right and left mandibular premolars cross each other in a "bridge-like" malocclusion over the tongue. (C) Sharp buccal spur of the right maxillary premolar following improper wearing, causing ulceration of the buccal mucosa *(arrow)*. Spurs must be carefully detected during inspection. *P,* premolar; *M,* molar; *T,* tongue; *S,* spatula. (Used with permission from Vittorio Capello, DVM.)

buccal sharp edges on the maxillary cheek teeth. Also, elongated crowns of maxillary cheek teeth are frequently accompanied by increased height of both the alveolar crest and the gingival margin. Caries, resorptive lesions, and fractures may also be present in chinchillas.[16,46] Periodontal disease, after food impaction due to tooth loss and widened interproximal spaces, is also very common in chinchillas, and is much less common in guinea pigs or degus.[46,48]

In myomorph rodents, every pattern of malocclusion of incisors can be seen, from mild to severe. The most common is slightly elongated or fractured mandibular incisors and maxillary incisors curved toward the palate. Secondary lesions of the lips, tongue, and palate can be present, with perforation of the hard palate and resulting oronasal fistulas.[6,45]

Sciuromorph rodents (especially prairie dogs and ground squirrels) often present with fractured incisors. Fractures can occur along the clinical crown, resulting in a visibly shortened tooth, or along the reserve crown beneath the gum line, resulting in a tooth that appears loose because it is attached only to the gingiva.[45]

Elodontomas and pseudoodontomas affect elodont incisor teeth of several rodent species. Dental disease with histologic, clinical, and radiographic elements consistent with elodontomas (formerly odontomas) have been reported in guinea pigs,[7] degus,[32] pet tree squirrels *(Paraxerus cepapi)*,[3] rats,[30] and mice.[29] Dental disease with histologic, clinical, and radiologic elements consistent with pseudo-odontomas has been reported in prairie dogs [4,52] (reported also as elodontomas[56] or complex odontoma[11]). Various theories have been proposed as a cause of odontomas, elodontomas, and pseudo-odontomas in prairie dogs and other squirrels. These include osteopetrosis, repeated trauma or fractures (from chewing on cage bars, falls from a height, or improper trimming of malocclused incisors), nutritional imbalances, and local infection near the apical tissue of incisors. Whether pseudoodontomas represent an early stage potentially progressing to elodontoma or the fact that trauma could potentially result in two different pathologic processes has not been determined.

Treatment of Periapical Infections and Abscesses

Despite similar anatomy and physiology of the teeth and frequent perforation of the cortical bone by elongated apices in chinchillas, guinea pigs and chinchillas are much less prone to periapical infections and osteomyelitis than rabbits. The general treatment guidelines are the same as those described for rabbits.[6,9,39,41] Unlike rabbits, the cheek teeth of guinea pigs always lie beneath the masseter muscle, making both surgical access and marsupialization more challenging. Advanced diagnostic imaging is of paramount importance for planning the surgical approach. Periapical infections subsequent to malocclusion and fractures of incisors are also relatively in frequent.

Prognosis

The prognosis for dental disease in rodent species is usually more guarded than in rabbits; however, because pathologic patterns vary among species, prognosis must be formulated for each individual case.[9] Unless the animal is in poor general condition, prognosis for treatment of dental malocclusion of cheek teeth in guinea pigs is fair to good. Incisor malocclusion is usually addressed as a consequence of elongated cheek teeth, and extraction is rarely needed. Unlike rabbits, guinea pigs may not improve immediately after a dental procedure because of stretching of the masticatory muscles and associated pain and inflammation. Subluxation of the temporomandibular joint may also be present. Guinea pigs that do not begin eating immediately may not wear teeth down to the degree required to prevent repeated overgrowth.[9,39] These patients may require additional dental treatment until the soft tissues heal and the animal is able to eat enough high-fiber food to allow normal wearing.

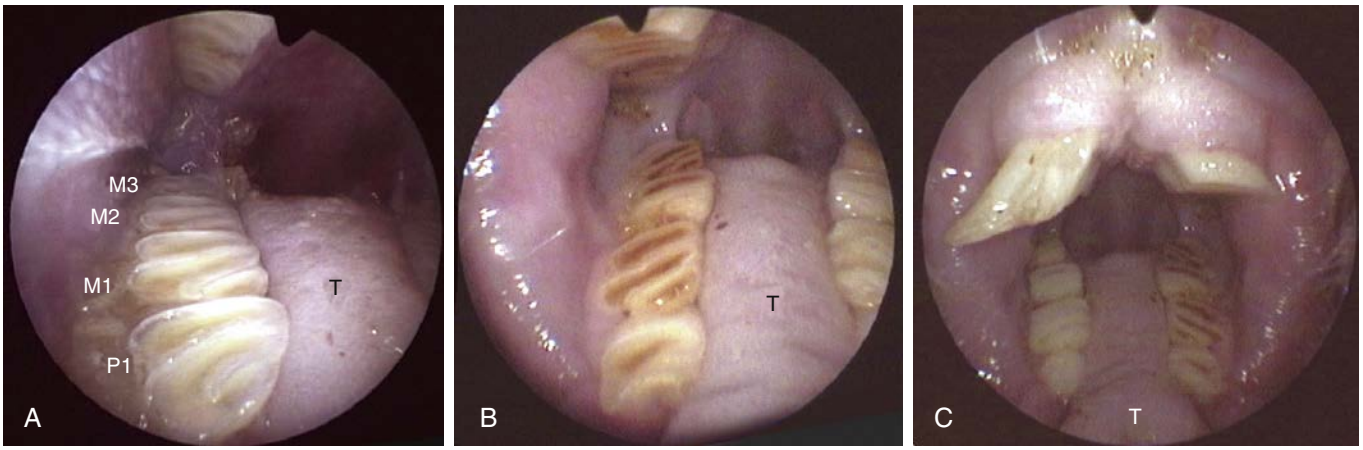


Fig. 36.19 Oral endoscopy in the chinchilla. (A) Normal appearance of cheek teeth, right mandibular quadrant. Note the enamel crests and dentinal grooves. Clinical crowns are much shorter than in rabbits and guinea pigs, and the occlusal plane is not oblique, as in guinea pigs. (B) Acquired dental disease of cheek teeth. Coronal elongation, "wave mouth," widened interproximal spaces, and a laterally deviated occlusal plane are present. (C) Severe coronal elongation and sharp buccal spikes of the right maxillary premolar tooth caused by improper wear. Increase of both the alveolar crest and the gingival margin of the maxillary cheek teeth is common in chinchillas with advanced dental disease. *P,* premolar; *M,* molar; *T,* tongue. (Used with permission from Vittorio Capello, DVM.)

Two authors (A.L., V.C.) have had apparent but subjective success with "physiotherapy," which involves training owners to perform daily passive lateral movements of the mandible and maxilla in guinea pigs to help wear cheek teeth in between dental treatments. The maxilla and mandible are gently grasped, and lateral movements are applied to simulate teeth wear. Not all guinea pigs and owners are able to accomplish this. The neoprene "chin sling" is a device that provides support to help keep the cheek teeth in constant contact, facilitating improved wear. One author (L.L.) finds use of the chin sling effective in increasing the time span between dental treatments.[39]

In chinchillas, prognosis is related to the stage of dental disease when the diagnosis is made, because severe to end-stage dental disease is frequently diagnosed at first presentation. In most cases, repeated dental treatments are only palliative, as restoring dental anatomy to normal is not possible. Periodontal disease is associated with increased discomfort and more guarded prognosis. Conversely, chinchillas tolerate advanced dental disease remarkably well. Incisors can be extracted in chinchillas, but this is rarely indicated.

Prognosis for pseudoodontomas in prairie dogs is related to the stage of disease at the time of diagnosis, whether disease is unilateral or bilateral, the impact on the respiratory tract, overall patient condition, and therapeutic approach. Prognosis for end-stage dental disease of cheek teeth is usually poor.

Dental disease of smaller myomorph or sciuromorph rodents carries a fair prognosis in cases of uncomplicated malocclusion of incisors. Prognosis for diseases related to cheek teeth is guarded to poor because of patient size and the difficulties related to any surgical approach.

FERRETS

Anatomy and Physiology of the Skull and Teeth

Ferrets are strict carnivores. Therefore the morphology of the skull and teeth is similar to that of larger carnivores like cats and structured to accommodate the diet.[37] The oral cavity is short and wide, with a wide opening. Ferrets are anisognathic, with the mandible narrower than the maxilla, allowing shearing of food during chewing. The temporomandibular joint has a transverse articular fossa and a well-developed articular process that prevents dislocation of the mandible if the mouth is opened wide for a strong bite.[37] Ferrets have 28 to 30 deciduous teeth that shed between 7 and 11 weeks of age. The dental formula of the 34 permanent teeth is reported in Table 36.1, and dentition is shown in Fig. 36.20. The mandibular second molar is congenitally missing in some ferrets, which changes the formula to a total of 32 teeth.[37] There may also be supernumerary teeth, most commonly found between the first and second maxillary incisors.[37] Permanent teeth are anelodont (rooted) and brachyodont (short-crowned). Mandibular canine teeth occlude rostrally to maxillary canine teeth. The fourth maxillary premolar is the most developed, has three roots, and is called the *carnassial tooth*. There is a single maxillary molar and two mandibular molars. The first mandibular molar is the most developed and is the mandibular, carnassial tooth (Fig. 36.20).

Dental Disease

The effect of diet on the dentition and dental disease of pet ferrets as compared with wild ferrets and polecats is under investigation and somewhat controversial. Consumption of kibble reduces dental attrition because teeth, in particular carnassial teeth, fracture the dry food. In consuming whole prey, carnassial teeth act like scissors, increasing and prolonging the contact. Those movements likely keep the occlusal plane sharp and prevent the formation of plaque and calculus. However, many other factors beyond the type of food can pose a risk for dental disease, such as dental bacterial flora, pH of saliva, systemic disease, higher inbreeding compared with wild counterparts, differences in skull development, and reduced muscle mass after early spay and neutering.[37]

Calculus is the outcome of mineralized plaque on the tooth surface.[37] The accumulation of plaque depends on the content and consistency of the diet, the presence of food debris, bacterial by-products, and the pH of saliva. The powerful chewing movements typical of carnivores seem to be a predisposing factor because this allows pocketing of food material beneath the gingival sulcus. Plaque and calculus accumulate and extend, creating gingival pockets, gingival retraction, and gingivitis. Later stages of periodontal disease are represented by periodontal infection, involvement and destruction of periodontal ligaments, and root infection. Further complications may include periapical abscesses and osteomyelitis.[37] A grading system for dental disease in ferrets has been reported.[37] Stage 1 is gingivitis, mostly caused by plaque; stage 2 is early periodontitis, usually with gingival swelling, retraction, and pockets, but the teeth are not loose and there are no radiographic abnormalities; stage 3 corresponds to moderate periodontitis, with possible root exposure and food impaction of gingival pockets; and stage 4 is advanced periodontitis with evident gingival and bone recession. At stage 4, teeth may be mobile, with more than 50% loss of attachment; pulp or enamel lesions and complications such as periodontal abscess and osteomyelitis may also be present. Diseased teeth usually appear dark.

Malocclusion of incisor teeth is a common incidental finding and usually appears as the mandibular second incisor teeth positioned caudal to the other incisors.[37] As a ferret ages, the canine teeth extrude, accompanied by gingival recession. The gums may also bulge around the crown. Also, teeth may show wearing of the crowns.[37] Ferrets are frequently presented for fracture of the tips of the canine teeth.[37] Pet ferrets frequently fracture the canine teeth from biting cage bars, playing with toys, or because of falls. Fractures of the tips of the maxillary canine teeth are more common than those of the mandibular teeth. Usually, the pulp is exposed after fracture of the tip, and infection is a common sequela. Teeth may be lost with advanced periodontal or dental disease or from severe trauma. Tooth loss is mostly caused by trauma or dental disease and may involve only the crown, but retained roots can be present. Periapical infections and abscesses represent a complication of either periodontal or endodontal diseases mentioned above. Local osteomyelitis is not an obligate sequela, as in rabbits and other hypsodont species, but may occur.



Fig. 36.20 Dentition of the ferret. This specimen is from an older patient; note abnormalities such as blunting of the maxillary canine teeth and malalignment of mandibular incisor teeth. *I,* incisor; *C,* canine; *P,* premolar; *M,* molar. (Used with permission from Angela Lennox, DVM.)

Treatment and Prevention

For both preventive and therapeutic dental procedures, general anesthesia is necessary. Removal of calculus and polishing are routinely performed with a dental scaler and a low-speed handpiece. Advise the owner to schedule this procedure regularly well before the ferret shows clinical signs of dental disease.[37]

Endodontic procedures like partial pulpectomy and pulp capping in case of pulp exposure of fractured canine teeth may be challenging because of the small size of the teeth.[37] These procedures require a high-speed dentistry unit and restorative materials and are done as in dogs and cats. Refracture may occur because the biting behavior is difficult to control or prevent.[37]

To extract teeth or retained roots, a local block with lidocaine and/or bupivacaine is a useful adjunctive analgesia. Partial gingivectomy and removal of a small section of the alveolar bone may be necessary. An 18- or 20-gauge needle can be used as an elevator. Pack the cavity of an open alveolus with bone matrix material or antibiotic gel, and suture the gingiva to prevent food impaction.

Encourage owners to institute a dental prophylactic program. Routine teeth cleaning and brushing can be performed with cotton swabs and enzymatic toothpaste. Tooth brushing may or may not be feasible depending on the ferret's behavior.

HEDGEHOGS

Hedgehogs were formerly classified within the order Insectivora, but they are not strictly insectivorous. Besides invertebrates, wild hedgehogs eat eggs, fruits, and occasional vertebrate prey, with dentition more similar to that of carnivores and omnivores.[42] All teeth are anelodont brachyodont. The dental formula is reported in Table 36.1 and Fig. 36.21.

Abnormalities in tooth number are frequent in hedgehogs, including supernumerary incisors or the absence of the second pair of mandibular incisors.[42] For this reason, their dental formula has been reported with 2 × 2/2 incisors. The absence of the second maxillary premolar has been reported in African pygmy hedgehogs.[42] The first maxillary incisors are long and widely spaced, projecting slightly forward[42]; for this reason, they are sometimes misinterpreted as canine teeth. Canine teeth are small and similar to the second (or third) pair of incisors and the first premolars. Premolars show prominent cusps, more similar to those of carnivores. The third maxillary premolar has three cusps and shears against the first mandibular molar, resembling the carnassial tooth form of carnivores. The first two maxillary teeth have four cusps, resembling the molars of primates.

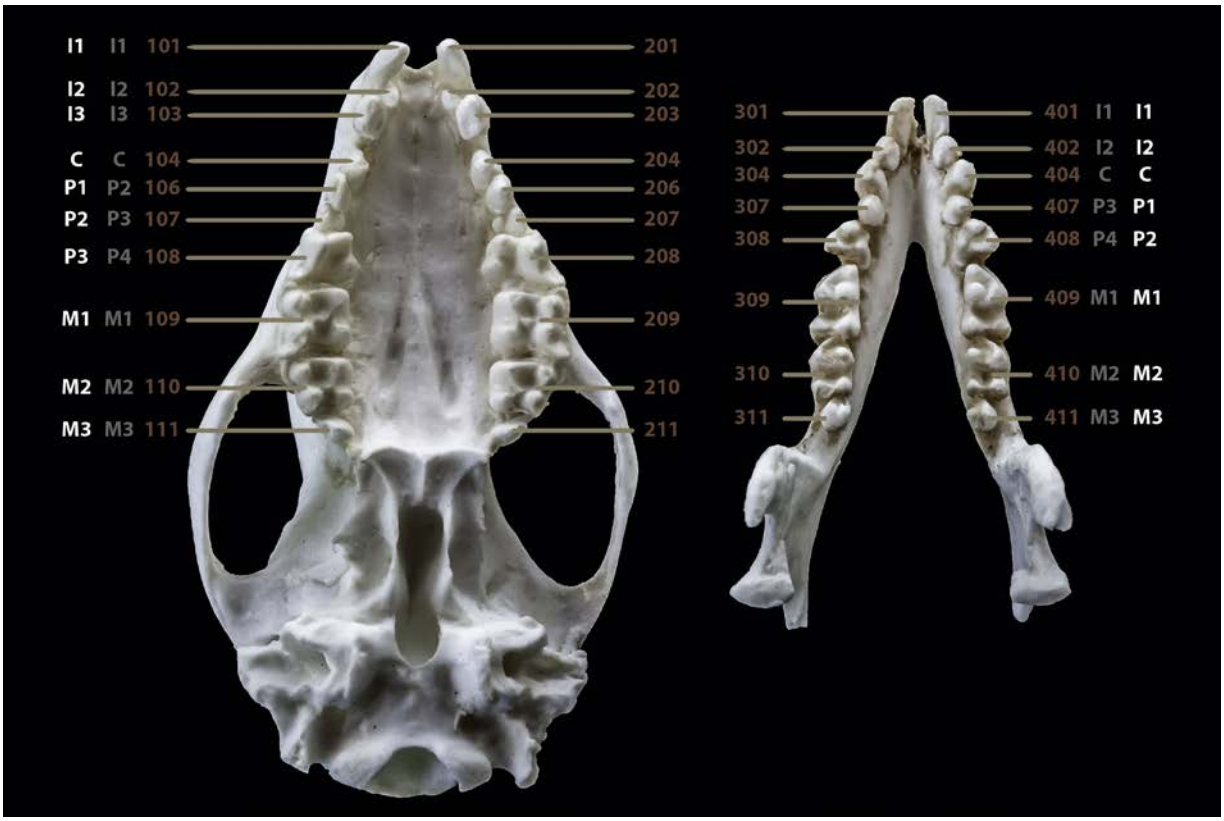


Fig. 36.21 Dentition of the African pygmy hedgehog. *I,* incisor; *C,* canine; *P,* premolar; *M,* molar. (Used with permission from Angela Lennox, DVM.)

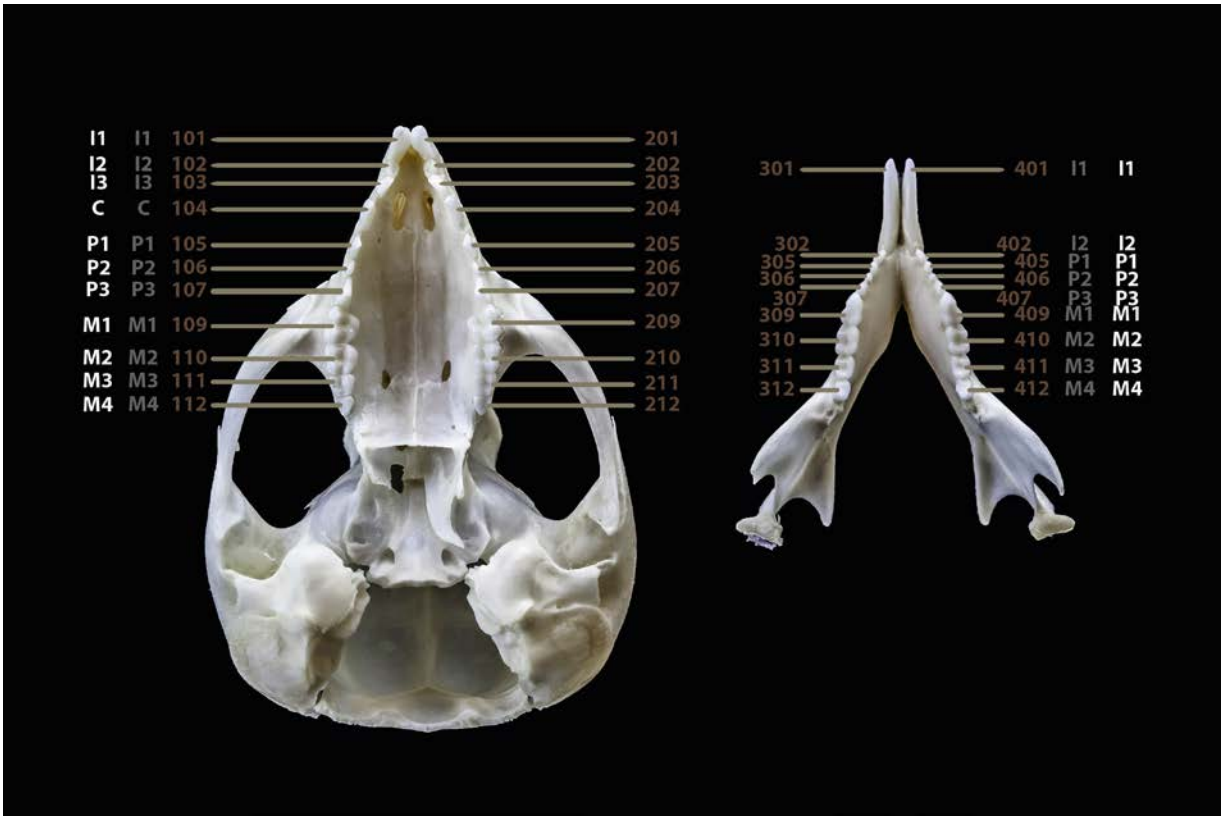


Fig. 36.22 Dentition of the sugar glider. *I,* incisor; *C,* canine; *P,* premolar; *M,* molar. (Used with permission from Angela Lennox, DVM.)

Dental disease similar to that described for ferrets is common in pet hedgehogs. Calculus, gingivitis, gingival recession, periodontitis, tooth fractures, gingival neoplasia, and periodontal abscesses may be present. Clinical signs are ptyalism, pawing at the mouth, decreased food intake, and bad breath. Perform diagnosis and treatment as in other species with anelodont teeth.

SUGAR GLIDERS

Sugar gliders are marsupials; in the wild, their nutrition comprises plant exudates (from eucalyptus and acacia trees) and insects. They are also partially frugivores. Glider teeth are small with the exception of the mandibular first incisors, which are prominent, sharp, and specialized for gouging.[42] While these may resemble the incisors of hamsters, the teeth are not elodont. The dental formula is listed in Table 36.1 and Fig. 36.22. A few sources mention specific dental disorders in sugar gliders including trauma, periodontal disease, and calculus, but there are no published case reports.[42]

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Anesthesia, Analgesia, and Sedation of Small Mammals

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GENERAL PRINCIPLES AND CHALLENGES IN ANESTHETIZING SMALL MAMMALS

Anesthetizing small mammals can be challenging. It is more difficult to obtain preoperative blood work, secure an airway or intravenous access, monitor anesthesia, and prevent hypothermia once the animal is anesthetized. Small mammals have higher metabolic rates and smaller glycogen reserves, predisposing them to hypoglycemia. Metabolism and excretion of parenterally administered drugs are faster; therefore they have shorter durations of action. Small mammals have higher oxygen consumption and may suffer central nervous system injury more rapidly during respiratory arrest. Time becomes critical during anesthesia; complications occur more quickly, and the time for intervention is shorter. Drug doses have often been established in studies of young, healthy laboratory animals, so we must critically evaluate the information before using it in a sick or debilitated companion animal. A large-scale prospective study reported an overall perianesthetic mortality rate in healthy pet rabbits and guinea pigs of approximately 1.4% and 3.8%, respectively, values 5 to 10 times higher than those found in dogs and cats.[11] Other recent studies have reported similar

results.[71,85] There is substantial room to decrease mortality rates during anesthesia in these patients.

PREANESTHETIC CONSIDERATIONS

Patient Evaluation and Preparation

Before any anesthetic event, obtain a complete history and perform a physical examination to assess preexisting clinical problems and record baseline values for comparison. Age should be considered, because the margin of safety is wider in younger animals. Obtain an accurate body weight for fluid and drug dose calculations. Evaluate hydration status, and correct dehydration before anesthesia. Compensatory mechanisms are blunted under anesthesia, exacerbating underlying hypotension and poor peripheral perfusion. For procedures in sick and elderly animals, perform a complete blood count and biochemical profile before anesthesia. Severe anemia should be corrected, because the patient may not be able to compensate for decreased oxygen delivery. The packed cell volume may decrease 3% to 5% during anesthesia because of vascular hemodynamic changes.[83] Monitor glucose concentration and supplement as necessary. The type of surgery to be performed and potential for blood loss should be assessed for fluid plan preparation.

Nutritional Status and Fasting

Prolonged anorexia leads to negative energy balance and hypoglycemia, requiring nutritional support in the perianesthetic period. Fasting induces catabolism, in particular in small patients with high metabolic rates, such as rats or hamsters. Rabbits and rodents do not vomit because of physiologic and anatomic factors, including lack of emetic neurologic pathways, their well-developed lower esophageal sphincter, and limiting ridge of the stomach.[68a] Fasting for more, than 1 hour is unnecessary. Many rodents store food in their oral cavity or are coprophagic; thus, clean the oral cavity before anesthesia by gently syringing water into the mouth to remove this material in tolerant awake patients or swab with wet cotton tips immediately after induction. Elevate the head during anesthesia if there is any concern of aspiration.

In ferrets, hedgehogs, and other small mammals that can vomit, recommended fasting times are 1 to 4 hours, with prudence used to weigh the risks and benefits in the specific patient. In ferrets, fasting exhausts glycogen stores and results in hypoglycemia and may significantly contribute to perianesthetic ileus and potentially exacerbate pancreatic tumors in ferrets. Schedule procedures early in the day to reduce fasting times.

Vascular Access

Vascular access is necessary for fluid administration and to deliver anesthesia and emergency medications. Sites for intravenous catheterization are the cephalic, lateral saphenous, and femoral veins in large mammals and the superficial lateral tail veins in the rat (see Fig. 37.1*A*). Sedation may be necessary for intravenous catheter placement.

Intraosseous (IO) cannulation can be useful in small patients for anesthesia or during cardiovascular collapse (see Fig. 37.1 *B*). Products that can be used as IO cannulas are 18- to 25-gauge, 1- to 1½-in spinal needles or 18- to 25-gauge, 1-in hypodermic needles, depending on the animal's size. The cannula should be long enough to extend through one-third to one-half the length of the medullary cavity. A wire stylet reduces the potential for a bone core. Prepare several hypodermic needles (25- to 18-gauge) with wire stylets (stainless steel suture) and sterilize them for IO catheterization. Common sites for IO cannula placement are the trochanteric fossa of the femur and the tibial crest (see Fig. 37.1 *B*). Placement is similar to that of a normograde intramedullary pin and requires strict aseptic technique during placement and maintenance. Once the cortex is penetrated, the cannula should advance easily, with little resistance. Flush the cannula with heparinized saline solution immediately to prevent clotting. Cover the insertion site with an antibiotic ointment and secure the cannula with tape, suture, and a bandage. An IO cannula can remain patent for 72 hours without flushing but should be flushed with heparinized saline solution twice daily if fluid therapy is not continuous. Complications associated with IO catheterization are penetration of both cortices, failure to properly enter the medullary cavity, and extravasation of fluids with associated pain. An IO catheter is used primarily for short-term vascular volume expansion until an intravenous (IV) catheter site can be obtained. Many animals become uncomfortable on limbs supporting IO catheters, even after short-term placement. An IO catheter is contraindicated in septic patients and those with metabolic bone disease. Osteomyelitis may occur because

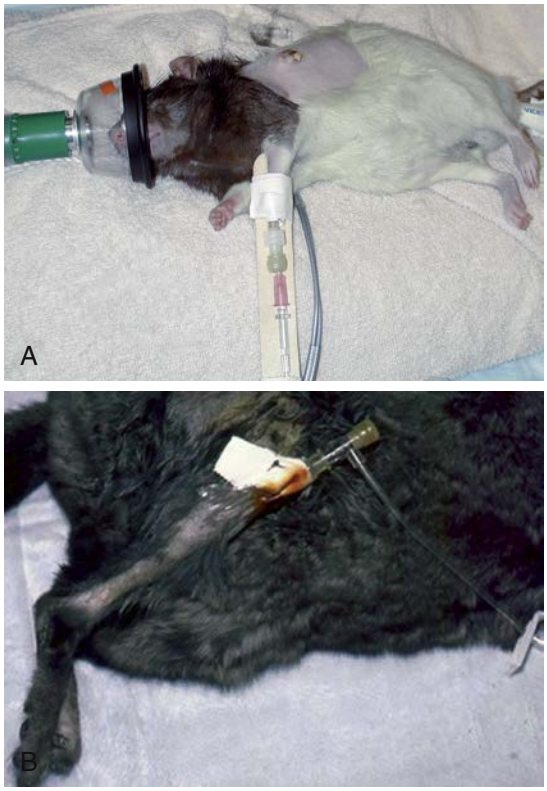


Fig. 37.1 Catheterization of the cephalic vein in a rat (A); the lateral saphenous, jugular, or femoral veins and the superficial lateral tail veins in the rat can also be used for IV catheters. Catheters are taped and bandaged for security; additional stability can be provided with tongue depressors for very small limbs. In animals where IV catheterization is not possible, an intraosseous (IO) catheter can be placed in the tibia (B) or femur for short-term use.

of duration or placement of the IO catheter, and administration of alkaline or hypertonic solutions can contribute to osteomyelitis and cause pain. Dilute these solutions before administration and flush the catheter with heparinized saline solution after any drug injection.

Arterial catheterization to evaluate direct arterial blood pressure, blood gas tension, and pH can be done in many species. The most common sites are the pedal arteries in most species, the central auricular artery in the rabbit, and the ventral tail artery in the rat and ferret. The catheters are usually placed percutaneously, but a cut-down procedure is sometimes used.

Equipment

Equipment may malfunction, and it is important to ensure that any machines used to provide or assist with anesthesia have been carefully examined before starting. The most efficient way of doing this is to have a comprehensive checklist that is used every time an animal is to be anesthetized (e.g., https://ava.eu.com/resources/checklists/).

Breathing Circuits

Nonrebreathing circuits (Ayre's T-piece, Mapleson systems, Magill, Jackson-Rees, Norman elbow, and the Bain circuit) are most commonly used for anesthetizing small mammals because of the low resistance to breathing. The nonrebreathing system depends on high rates of fresh gas flow to remove carbon dioxide (CO_2) and provides rapid changes in inhalant concentration when the vaporizer setting is changed. Circle systems have greater resistance and are heavier and bulkier, which predisposes to accidental extubation and difficulty working around the head.

The flow rate used for a T-piece or Norman elbow should be two to three times the minute ventilation, but in the Bain circuit, a flow rate of 150 to 200 mL/kg per minute appears effective. Removal of waste gases from the circuit occurs during the pause between expiration and inspiration. Thus if the respiratory rate is high (shorter pause and therefore more mixing of inspired and expired gases), a higher flow rate should be used (e.g., if respiratory rate >40 breaths/min, increase the flow rate to 300 mL/kg/min). When a capnograph is used to monitor the animal, rebreathing will be evident as an increase in inspired CO_2, and so the flow rate can be adjusted to reach the point where the inspired CO_2 is less than 5 mmHg.

Ventilators

Ventilators appropriate for small mammals must cope with the range of tidal volumes in the different species. In very small patients, this may be less than 1 mL; but tidal volumes in some giant-breed rabbits might need to be as high as 500 mL. In general, the three things that must be controlled by a ventilator are the tidal volume, the rate at which the tidal volume is delivered, and the number of breaths per minute. The way in which each of these is controlled varies by ventilator.

Preanesthetic Medications

Preanestheic medications are used to provide optimal conditions to place catheters or other access to the circulation, help with handling the animal, and minimize stress and potentially counteract perioperative autonomic stimuli, as well as provide analgesia and reduce the dose of other anesthetic drugs. Combinations of drugs with different effects are most commonly used. For example, an alpha-2 agonist might be used to provide sedation and analgesia, whereas the addition of an opioid improves sedation and analgesia and a benzodiazepine improves muscle relaxation and relieves anxiety. The use of injectable anesthetic combinations recently has increased considerably in small mammals. Drugs that are normally considered to be anesthetics (induction drugs) also can be used at lower doses to facilitate preoperative preparation (e.g., ketamine).

Certain breeds or even strains of small mammals have differing responses to injectable anesthetics.[8] Little work has been published evaluating different injectable combinations for common surgical procedures in pet small mammals of differing age, sex, breed, and health status in the clinical setting, so use caution when extrapolating injectable doses from laboratory animal studies. Using reversible injectables provides better control of anesthetic depth, fewer perianesthetic effects, and shorter recovery times.

Route of Administration

When deciding on a route of administration, the clinician must consider the nature of the drug and the type of animal receiving the drug. In very small patients, it can be difficult to catheterize or even find enough muscle to inject into without causing tissue damage, so other administration routes such as subcutaneous, intranasal, or intraperitoneal injection are used. Although most rabbits have enough muscle for intramuscular (IM) injection, they can react quite violently to such injections, with risk of vertebral fractures if not carefully restrained. Therefore, where appropriate, the subcutaneous (SC) route is a less painful and safer alternative. Drugs with vasconstrictive properties (e.g., alpha-2 agonists) or with very high lipid solubility (e.g., buprenorphine) may not be absorbed well from subcutaneous injection. However, increasing the dose can overcome the diffusion problems, as shown in rabbits with high-dose dexmedetomidine/medetomidine with ketamine and in other species with high doses of buprenorphine.[26,64] Muscle necrosis and cutaneous reactions can occur in any patient administered IM injections, depending on the drug formulation and volume delivered. Supplemental oxygen and assisted ventilation should always be available when injectable anesthetics are used, regardless of their route of administration.

Anticholinergics

Anticholinergics are commonly used to minimize salivary and bronchial secretions and vagally induced bradyarrhythmias. In rabbits, atropine can stop salivary secretion completely, but up to 60% of rabbits have high circulating concentrations of atropinesterases, with a higher prevalence in males.[89] This reduces the efficacy of atropine and prompts the use of much higher atropine dose, with redosing as often as every 10 to 15 minutes during bradycardia.[60] Large doses of parasympatholytics can alter gastrointestinal (GI) motility in hind-gut fermenters; therefore, use the lowest dose necessary. Glycopyrrolate has a

TABLE 37.1 Injectable Preanesthetic, Sedative, and Tranquilizer Drugs (mg/kg) Used in Small Mammals[a]

	Ferret	Rabbit	Guinea Pig	Chinchilla	Rat	Comments
Atropine	0.05 SC, IM, IV	0.2–1.0 SC, IM, IV	0.05 SC, IM, IV	0.05 SC, IM, IV	0.05 SC, IM, IV	Higher doses may be necessary in rabbits
Glycopyrrolate	0.01-0.02 SC, IM, IV	0.01–0.02 SC, IM, IV	0.01–0.02 SC, IM, IV	0.01–0.02 SC, IM, IV	0.02–0.1 SC, IM, IV[36]	
Alfaxalone	—	4-6 IM[70]	5 IM[28] 20 SC[25]	—	—	
Atipamezole	—	—	—	—	—	10 × dose (in mg) of administered dexmedetomidine or 5 × the dose (in mg) of administered medetomine
Dexmedetomidine	0.04–0.1 IM, SC, IV	0.025–0.125 SC, IM, IV	0.05 SC, IM	—	0.015-0.5 SC, IM	Light sedation, rarely used alone
Flumazenil	0.05–0.1 SC, IM, IV	0.05–0.1 SC, IM, IV	0.05–0.1 SC, IM, IV	0.05–0.1 SC, IM, IV[67]	0.1–1.0 SC, IM, IV[36]	Reversal of benzodiazipines
Medetomidine	0.01–0.2 SC, IM[80,89]	0.1–0.25 SC, IM	0.1 SC, IM —	—	0.03–0.1 SC, IM[36]	Light sedation, rarely used alone
Midazolam	0.25–0.5 SC, IM, IV	0.25–2.0 SC, IM, IV	0.5–2.0 SC, IM, IV	1–2 SC, IM, IV	1.0–2.5 SC, IM, IV[36]	Lower doses for premedication

[a]These are suggested doses based on published information and the authors' clinical experience. Species and individual variation in response to a given drug can be uncertain, so adjust the dose depending on the clinical response of the animal. All doses are in milligrams per kilogram unless specified otherwise.

longer duration of activity than atropine (see Table 37.1). In rats, glycopyrrolate increased heart rates for 240 minutes versus 30 minutes with atropine.[95] The same study demonstrated that 0.1 mg/kg glycopyrrolate administered to rabbits increased heart rate for 60 minutes, but atropine doses ≤2 mg/kg did not increase heart rate for any duration.[95] Anticholinergics should be considered for premedication if a vagal response to manipulation is expected (e.g., nasal intubation of rabbits) or if salivation is excessive.

SEDATIVES AND TRANQUILIZERS

Benzodiazepines

Diazepam can be administered orally (PO) or IV, but if IV is used, the patient must be monitored for hypotension caused by the propylene glycol found in many diazepam formulations (see Table 37.1). Because of the solution's high osmolality (>7000 mOsm/kg), IM and SC absorption is erratic and therefore not recommended. Midazolam is a short-acting benzodiazepine that is water-soluble, so it can be given IM and SC (see Table 37.1). Midazolam is used as a sole sedative for minor, nonpainful procedures in rabbits and rodents. Lower doses are most often used for preanesthetic sedation. Flumazenil will reverse benzodiazepines, but because its half-life is shorter than that of midazolam, resedation may occur. Slowly titrate the flumazenil dose, starting with 25% of the calculated dose, to avoid the reversal of the beneficial anxiolysis, sedation, and muscle relaxation. Benzodiazepines coupled with opioid medications provide excellent sedation and preoperative analgesia. In ferrets, midazolam combined with butorphanol results in excellent sedation.

Alpha-2 Agonists

Xylazine, detomidine, medetomidine, and dexmedetomidine are alpha$_2$ adrenergic receptor agonists (see Table 37.1). Their major advantages are that they provide good sedation and muscle relaxation and can be reversed with yohimbine, atipamezole, or tolazoline (see Table 37.1). If these drugs are administered SC, uptake may be slow or erratic because of the local vasoconstriction induced by the drug. These drugs can have significant dose-dependent cardiovascular effects, including vasoconstriction, decreased cardiac output, second-degree heart block, bradyarrhythmias, and increased sensitivity to catecholamine-induced cardiac arrhythmias (xylazine).[67] Because of the many adverse cardiovascular effects reported for this class of drugs, their use is not recommended in small mammal patients with evidence of cardiovascular compromise. Supplemental oxygen, and in some cases assisted ventilation, should always be available when these drugs are being used. Although these drugs can be used alone, they are most commonly combined with other drugs such as ketamine, opioids, and benzodiazepines.

Significant breed and strain differences in response to medetomidine sedation doses have been reported for rabbits and rats.[7,8] In rabbits, ketamine/medetomidine allowed for more rapid intubation, a greater isoflurane-sparing effect, and less esophageal temperature loss than with ketamine/midazolam, but the rabbits thus treated were more prone to laryngospasm.[53] Medetomidine/ketamine provided better quality and duration of surgical anesthesia in healthy rabbits than did medetomidine/midazolam/fentanyl. Arterial pH and partial pressure of oxygen were significantly decreased in both groups, and apnea occurred postintubation with medetomidine/midazolam/fentanyl.[67]

The effects of alpha-2 agonists with ketamine seem to be less uniform in guinea pigs, and they may not become sufficiently anesthetized.[102] Dexmedetomidine-ketamine anesthesia in chinchillas provides a consistent level of light to surgical anesthesia with rapid induction and recovery times. However,

TABLE 37.2 Injectable Anesthetic Drugs and Drug Combinations (mg/kg) Used in Small Mammals[a]

	Ferret	Rabbit	Guinea Pig	Chinchilla	Rat	Comments
Alfaxalone	3–5 IV[49]	2–3 IV [55,70]	—	—	—	
Etomidate	1–2 IV	1–2 IV	—	—	—	Administer 15–20 minutes after benzodiazepine
Ketamine (K)/ dexmedetomidine (D)	—	—	—	5 K / 0.015 D[44]	—	
Ketamine (K)/ medetomidine (M)	4–8 K/0.08-0.1 M IM[36,80]	5–35 K/0.25–0.5 M IM	5–40 K/0.05–0.5 M IM[36]	5 K/0.06 M IM	45–75 K/0.3–0.5 M IM[57,65]	
Ketamine (K)/medetomidine (M)/butorphanol (B)	5 K/0.08 M/ 0.1–0.2 B IM[80]	5-15 K/0.1–0.5 M/ 0.4–0.5 B SC, IM[64]	—	—	—	
Ketamine (K)/ midazolam (Mi)	5 K/0.1–0.3 Mi IM, IV	5 K/0.25–1.0 Mi IM, IV	5 K/0.5 Mi IM, IV	5 K/0.5 Mi IM, IV	—	Induction
Propofol	3–6 IV	3–6 IV	3–6 IV	3–6 IV	3–10 IV	Doses for routine induction, intubation and ventilation necessary
Tiletamine/zolazepam	3–10 SC, IM, IV[80]	5–15 SC, IM, IV[24]	—	—	—	Avoid high doses in rabbits due to potential for renal injury[24]

[a]These are suggested dosages based on published information and the authors' clinical experience. Species and individual variation in response to a drug or combination of drugs can be uncertain, so the dosage should be adjusted depending on the clinical response of the animal. All doses are in milligrams per kilogram unless specified otherwise.

postanesthetic food intake and fecal output are reduced with this protocol compared with isoflurane anesthesia.[27,44,99] Observed changes in echocardiographic parameters with this combination are similar to those previously reported in chinchillas anesthetized with isoflurane.[27]

INDUCTION AND MAINTENANCE OF ANESTHESIA

Preoxygenation should be performed routinely and always when there is potential for hypoxemia. Preoxygenation can produce an oxygen reservoir, with the benefits achieved in ≤1 minute of high inspired oxygen concentration in a healthy patient but in ≥5 minutes in a patient with compromised respiratory function. Preoxygenation can be done with an oxygen cage or an induction chamber in an unrestrained animal or with a face mask in a restrained patient. Levels rise more slowly in an unprimed oxygen cage or induction chamber. The partial pressure of oxygen is expected to decrease rapidly if oxygen delivery is interrupted and the animal begins to breathe room air again. Supply supplemental O_2 throughout the anesthesia, and intubate whenever possible.

Balanced Anesthesia

The concept of "balanced anesthesia" originated to provide the elements of anesthesia (unconsciousness/amnesia, immobility, muscle relaxation, reduced autonomic response to noxious stimuli) by using multiple drugs at lower overall doses to minimize the adverse effects of each drug while still providing appropriate anesthesia and analgesia for the procedure. This approach reduces the magnitude of cardiovascular depression under anesthesia and promotes hemodynamic stability. Even with balanced anesthesia protocols, morbidity and mortality rates increase with increased duration of anesthesia. To minimize anesthesia time, prepare the patient, as well as all drugs and equipment, in advance and provide close patient monitoring so that adjustments in anesthesia are identified and corrected immediately. Morbidity and death also occur during recovery, and animals must be continually monitored until they are fully recovered.

INJECTABLE ANESTHETICS

Ketamine

Ketamine is a noncompetitive *N*-methyl-*D*-aspartate receptor antagonist that can prevent central sensitization, provide analgesia, and cause dissociative anesthesia (see Table 37.2). Ketamine is generally well tolerated in the stable patient, but it has sympathomimetic properties that can cause increases in heart rate, myocardial contractility, and peripheral vascular resistance. It is also a direct negative inotrope; therefore patients that are highly stressed (especially rabbits) may become hypotensive after ketamine injection because they have maximized their sympathetic output, thus "unmasking" the negative inotropic effect of the drug. Patients with hypertrophic cardiomyopathy may be at an increased risk of heart failure because they may not be able to cope with the increased myocardial demand caused by sympathetic stimulation. For these reasons, ketamine is not recommended for patients with hypertrophic cardiomyopathy or renal disease (in those species where the metabolic pathway is unknown) or in severely stressed small mammal patients. Ketamine is normally metabolized to norketamine, which has about 35% of the activity of the parent compound and is renally excreted. In many species this is then metabolized to dehydronorketamine or hydroxynorketamine, which are inactive. In cats, metabolism stops at norketamine, so a cat with renal insufficiency may have a prolonged recovery because of the decreased renal elimination of ketamine and norketamine. In rats, mice, and rabbits, ketamine is metabolized beyond norketamine, so a prolonged recovery is unlikely in these species,

but the metabolism of ketamine has not been documented in other small mammals.[88] Salivation increases and secretions can obstruct the airway. Ketamine has a very short duration of clinical effect in rabbits and varies within strains, partly owing to redistribution and renal elimination.[8] Another disadvantage is the potential for the development of apneustic ventilation, a pattern characterized by a prolonged pause after inspiration. Despite these disadvantages, ketamine combined with one or more drugs is still considered a first-choice injectable anesthetic.

Ketamine is commonly combined with alpha-2 agonists, benzodiazepines, or both as induction agents to improve relaxation and anesthetic depth (see Table 37.2). Ketamine/alpha-2 agonist combinations, particularly at higher doses, produce mild to severe dose-dependent hypotension and bradyarrhythmias; ketamine/benzodiazepine combinations produce less cardiopulmonary depression and analgesia and provide good muscle relaxation.[53] Low-dose IV ketamine/midazolam is used by the authors to induce anesthesia in small mammals. Whereas the addition of tramadol to this combination in rabbits does not provide analgesia, it significantly shortens time to onset of action compared with ketamine and midazolam alone.[94] Opioids added to ketamine combinations further reduce the dose and minimize the adverse effects of each drug. Reversal of other drugs in ketamine combinations allows for its specific undesirable effects to become apparent.

Tiletamine-Zolazepam

Tiletamine-zolazepam at >30 mg/kg can cause nephrotoxicity, related to the tiletamine, in New Zealand white rabbits (see Table 37.2).[24] The advantage of this combination over ketamine is that much smaller volumes of drug are needed, so it is less likely to cause muscle damage if given IM.

Propofol

The need for IV or IO access and ventilatory support has limited the use of propofol. Rapid, excitement-free induction and recovery occur at clinically relevant doses in most mammals (see Table 37.2), but recovery times can be prolonged with prolonged anesthesia times.[87] Anesthesia has been maintained with doses of 24 to 36 mg/kg per hour propofol, but deaths have been reported in rabbits after propofol infusions.[106]

Balanced anesthesia may produce propofol-sparing effects, reducing its respiratory disadvantages. Propofol takes about 2 minutes to reach peak effect. This translates to lower doses being administered slowly for the effect to be estimated before more drug is given. A calculated propofol induction dose can be given in one-quarter increments, each administered over 30 to 60 seconds, to allow more accurate dosing and minimize apnea and hypotension during induction. A combination of propofol and ketamine (ketofol) has been used in an attempt to reduce the cardiopulmonary depression of propofol.[109]

Alfaxalone

Alfaxalone is a steroid anesthetic that is dissolved in a cyclodextrin base. It is licensed for IV administration for induction of anesthesia in dogs, cats, and rabbits, with no adverse effects noted from the base (Alfaxan; Jurox, North Kansas City, MO). The drug has a rapid onset and a short duration of action, with relatively less effect on respiration and circulation than propofol. It is absorbed after IM and SC injection, although it is only likely to be useful as a sedative if used alone by this route because of the large volumes needed to get to an anesthetic plane. If used as an anesthetic, remember that, like propofol, alfaxalone does not provide analgesia. In rabbits it has been used by both the IM and IV routes in combination with other drugs, giving a relatively rapid induction and smooth recovery.[55,70] Doses of 4 mg/kg and 6 mg/kg IM were tolerated well, but one rabbit died after respiratory and then cardiac arrest 10 min after an 8 mg/kg IM dose.[70] Apnea lasted for about three-quarters of a minute after IV administration at any dose, so prexoygenation is advisable. A combination of alfaxalone (6 mg/kg), dexmedetomidine (0.2 mg/kg), and butorphanol (0.3 mg/kg) administered IM to rabbits produced anesthesia lasting about 1 hour with a recovery time of approximately 2.5 hours.[10] In guinea pigs, alfaxalone at 5 mg/kg IM induced sedation within 2.7 ± 0.6 minutes, suitable for diagnostic imaging and other minor noninvasive procedures. Duration of sedation was 29 ± 3 minutes, and no significant effects on cardiorespiratory parameters occured.[28] When alfaxalone was administered at 20 mg/kg SC to guinea pigs, sedation suitable for nonpainful procedures lasted less than 60 minutes.[28] In chinchillas, alfaxalone IM or SC at 5 to 10 mg/kg did not result in satisfactory levels of sedation or anesthesia.[99] Combined with butorphanol (0.5 mg/kg), alfaxalone (5 mg/kg) administered IM resulted in rapid induction of short-term anesthesia of inconsistent depth and length. In addition, a pronounced decrease in food intake and fecal output was associated with this protocol, and therefore its use in chinchillas is not recommended.[99] Alfaxalone alone at 5 to 10 mg/kg IM or in combination with tramadol at 5 mg/kg IM did not produce satisfactory anesthetic results in ferrets; two ferrets treated with alfaxalone alone at 10 mg/kg and 20 mg/kg, respectively, died.[49] But alfaxalone administered at 2.5 mg/kg plus medetomidine at 20 µg/kg provided effective anesthesia in ferrets, but pulse rate progressively decreased during the first 30 minutes before stabilizing.[49] In rats, intraperitoneal (IP) alfaxalone, even up to 45 mg/kg, did not produce anesthesia, and the dose required for males was three times that of females. Alfaxalone at 20 mg/kg (females) and 60 mg/kg (males) combined with fentanyl (0.1 mg/kg) and dexmedetomidine (0.05 mg/kg) provided sufficient anesthesia and analgesia for a surgical procedure.[6]

Etomidate

Etomidate is a potent short-acting hypnotic induction and maintenance agent. It has a rapid onset, a short recovery period, and minimal cardiopulmonary effects.[90] As an IV induction agent, etomidate has minimal depressive effects on the sympathetic nervous system but may stimulate sympathetic outflow at low doses. Etomidate is sold as a hyperosmolar solution with propylene glycol and can cause hemolysis, thrombophlebitis, and pain on injection. An aqueous formulation has been developed, which may be safer than the current commercial product.[90] To reduce the impact of the hyperosmolarity, IV crystalloid fluids are given simultaneously. The larynx is often reactive with this drug, so topical laryngeal lidocaine is helpful. Etomidate inhibits cortisol secretion, so it should not be used in animals with adrenal insufficiency. Cortisol suppression can easily be mitigated by administering a glucocorticoid immediately before or after etomidate.

TABLE 37.3 Injectable Drugs Administered as Intravenous CRIs Used for Perioperative and Postoperative Analgesia in Small Mammals[a]

	Ferret	Rabbit	Guinea Pig	Chinchilla	Rat	Comments
Butorphanol						Less respiratory depression than with fentanyl
Loading dose	0.05–0.2 mg/kg	0.2–0.4 mg/kg	0.2–0.4 mg/kg	0.2–0.4 mg/kg	0.2–0.4 mg/kg	
Perioperative rate	0.1–0.4 mg/kg/h	0.2–0.4 mg/kg/h	0.2–0.4 mg/kg/h	0.2–0.4 mg/kg/h	0.2–0.4 mg/kg/h	
Fentanyl citrate						Apnea common, expect to ventilate patient. Combine with ketamine CRI to reduce overall doses
Loading dose	2–5 μg/kg	5–10 μg/kg	5–10 μg/kg	5–10 μg/kg	5–10 μg/kg	
Perioperative rate	5–10 μg/kg/h	10–40 μg/kg/h	10–30 μg/kg/h	10–30 μg/kg/h	30–60 μg/kg/h	
Postoperative rate	0.5–2 μg/kg/h	1.25–5.0 μg/kg/h	1.25–5.0 μg/kg/h	1.25–5.0 μg/kg/h		
Ketamine						Less respiratory depression than opioids given CRI
Loading dose	2–5 mg/kg	2–5 mg/kg	2–5 mg/kg	2–5 mg/kg		
Perioperative rate	1–2 mg/kg/h	1–2 mg/kg/h	1–2 mg /kg/h	1–2 mg /kg/h		
Postoperative rate	0.25–1 mg/kg/h	0.25–1 mg/kg/h	0.25–1 mg/kg/h	0.25–1 mg/kg/h		
Lidocaine						
Loading dose		2 mg/kg				
Perioperative rate		3–6 mg/kg/h				
Postoperative rate		3–6 mg/kg/h[111,112]				

[a]These are suggested doses based on published information and the authors' clinical experience. If using for postoperative analgesia only, a loading dose should be used. Gradually wean from postoperative CRI over 12–24 hours. Species and individual variation in response to a drug or combination of drugs can be uncertain, so the dosage should be adjusted depending on the clinical response of the animal.
CRI, Constant rate infusion.

Constant-Rate Infusions

Intravenous constant-rate infusions (CRIs) of anesthetic and analgesic drugs for total intraveous anesthesia have been evaluated in small mammal balanced anesthesia/analgesia protocols (see Table 37.3).[62,63,87] Analgesic medications administered IV as a CRI can be titrated to effect, potentially reducing other drug doses within the anesthetic protocol. Disadvantages of CRIs in small mammals are the need for patient IV or IO access and for a syringe pump to accurately deliver low IV/IO doses. Plasma drug concentrations increase slowly when used as a CRI, so a loading dose of the drug is commonly given before initiating the CRI.

Microdose ketamine via CRI can be an effective analgesic. It is very useful in patients that cannot be intubated, as it has a low potential for respiratory depression at these doses. Ketamine administered at 9 mg/kg per hour significantly reduced isoflurane minimum alveolar concentration (MAC) in rabbits.[47] Opioid medications can also be used for CRI. All mu (μ) receptor agonists can cause respiratory depression; thus they should be used only when an airway is secure and ventilation is available. Fentanyl citrate is a μ receptor agonist that is used as a single-agent CRI, and it has been assessed in rats and rabbits. In rabbits, fentanyl IV CRI reduced the MAC of isoflurane by 24% and 42%[9]; the predicted infusion rates needed to achieve these reductions would be 21 and 44.5 μg/kg per hour, respectively. The higher concentration of fentanyl was associated with improvements in blood pressure but no change in cardiac output.[119] We have used fentanyl CRIs in clinical patients with no appreciable effect on gastrointestinal function. Remifentanil is an ultra-short-acting μ agonist opioid, making it very suitable for CRI because it can be used without a loading dose if the infusion is expected to last more than 30 minutes. Sufentanil combined with midazolam as total intravenous anesthesia was similar to sevoflurane anesthesia for ovariohysterectomy in rabbits.[63] Lidocaine administered as a CRI at 50 to 100 μg/kg per minute reduced isoflurane MAC but significantly decreased heart rate and arterial blood pressure, so close monitoring is warranted.[111] Rabbits receiving postoveriohysterectomy lidocaine via CRI had significantly higher gastrointestinal motility, food intake and fecal output, exhibited more normal behaviors, and had lower heart rates than did rabbits receiving buprenorphine.[112]

INHALANT ANESTHESIA

Inhalant anesthetics offer rapid induction and recovery and the ability to rapidly change anesthetic depth; moreover, their use does not require an accurate determination of body weight. Very little is metabolized, reducing the impact on hepatic and renal function, and recovery is independent of either. Small mammals require approximately the same concentration of inhaled anesthetic for an equivalent amount of stimulation as other mammals do. This is embodied in the concept of the MAC at which 50% of the animals do not respond to a supramaximal stimulus. The MAC values for the inhalant anesthetics are fairly consistent across species. However, inhalant anesthetics

can induce cardiovascular and respiratory depression, which may be life-threatening. All inhalants currently in use are potent negative inotropes; therefore a dose-related decrease in cardiac output is expected, which is reflected as a decrease in blood pressure. Thus the primary function of the anesthetist using inhalants is to maintain the lightest plane of anesthesia possible, allowing for minimal cardiopulmonary depression and completion of the procedure. In some cases, these goals may not be achieved by simply reducing the inhalant; balanced anesthetic/analgesic protocols or the addition of volume or positive inotropes may be necessary to offset inhalant-induced hypotension.

Isoflurane, sevoflurane, and desflurane are the currently available inhalants. Their speed of onset and offset is largely determined by their solubility and isoflurane > sevoflurane > desflurane. Despite these physicochemical differences, the clinical separation may be fairly small.[83] All three agents appear to have many of the same dose-dependent cardiovascular effects. Sevoflurane has a less pungent odor than other inhalants and therefore is generally better tolerated during mask induction. Therefore some practitioners induce using sevoflurane and then maintain anesthesia with the more cost-effective isoflurane.

Mask or Chamber Induction

Induction with inhalants is performed with either a mask or an induction chamber. Commercially available masks for dogs and cats can be used, but appropriate-sized masks and nose cones are also available or can be fashioned from syringe cases or other materials (see Fig. 37.2A). The mask should have minimal dead space and a diaphragm so that a seal can be achieved on the animal's nose or neck, and a piece of suture can be placed around the upper incisors and through the breathing circuit for security during maintenance (see Fig. 37.2B–C). Commercially available induction chambers can be used, especially for very stressed patients that may resist facemask induction. Advantages of appropriately-sized chambers are less waste gas and shorter induction times. In stressed patients, darken the chamber by covering it with a towel. Disadvantages of induction chambers are the inability to assess the patient, gas pollution when the chamber is opened, and trauma during the excitement phase of anesthesia. Pad the chamber and minimize its size to reduce movement and trauma. Adjust gas flow rates to chamber size to provide an optimum rate of rise of the anesthetic concentration. The flow rate can be calculated by the formula: $f = V/t \ln (S/(S - C)$, where f = the O_2 flow rate, V = chamber volume, t = time to reach the desired concentration, S = concentration being put out by the vaporizer, and C = desired concentration.[68] The patient is promptly removed after the righting reflex is lost. The final phase of induction is accomplished using a mask to facilitate monitoring.

Airway Access

Endotracheal intubation provides a patent airway, reduces dead space, and facilitates positive-pressure ventilation. Disadvantages are potential laryngeal and tracheal mucosal trauma, increased airway resistance, and airway occlusion due to mechanical forces or secretions. Increased resistance is of greater importance in very small patients because it is inversely related to the fourth power of the tube radius. For example, decreasing the tube radius from 3 to 2 mm increases the resistance 8-fold, whereas a decrease from 2 to 1 mm increases it 16-fold. Increased resistance can be overcome by positive pressure ventilation.

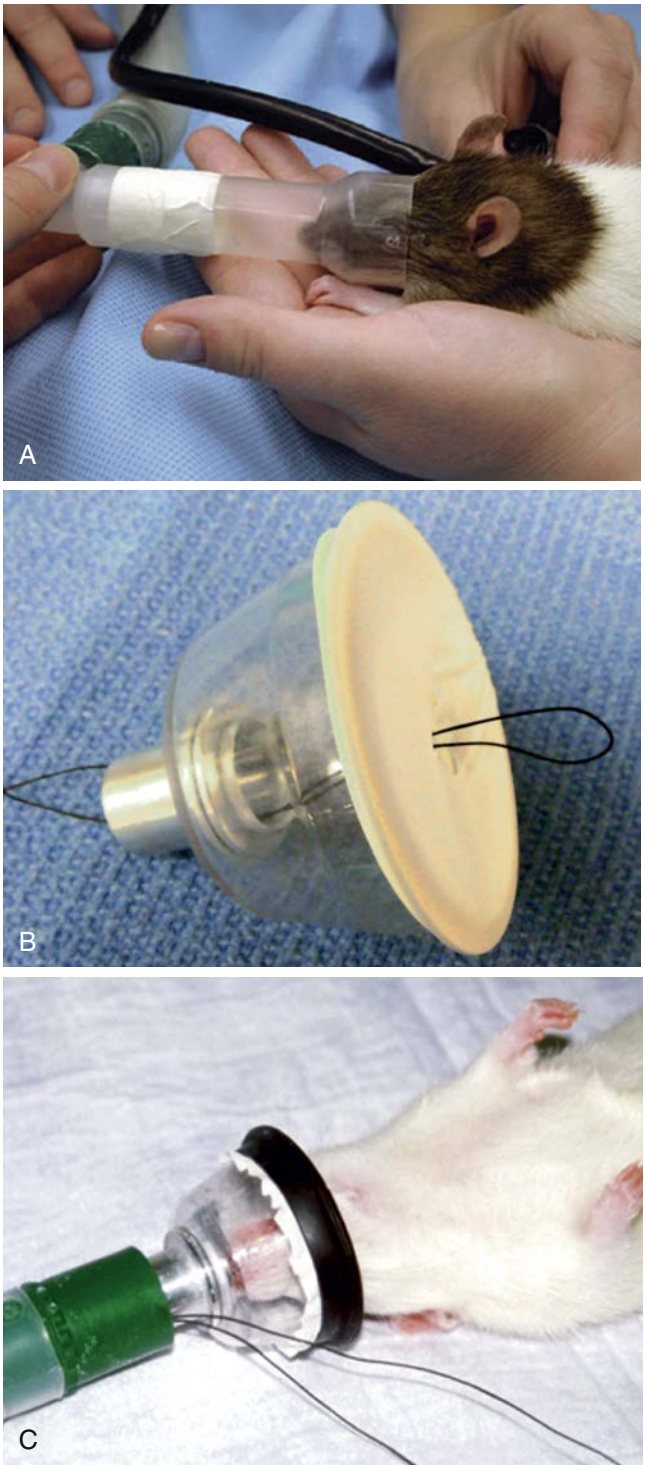


Fig. 37.2 (A) Appropriate-sized masks and nose cones are commercially available or can be fashioned from syringe cases or other materials to induce and to maintain anesthesia. The mask should have minimal dead space and a diaphragm so that a seal can be achieved on the animal's nose or neck (B). A piece of suture can be placed around the upper incisors and secured between the mask and breathing circuit (B,C).

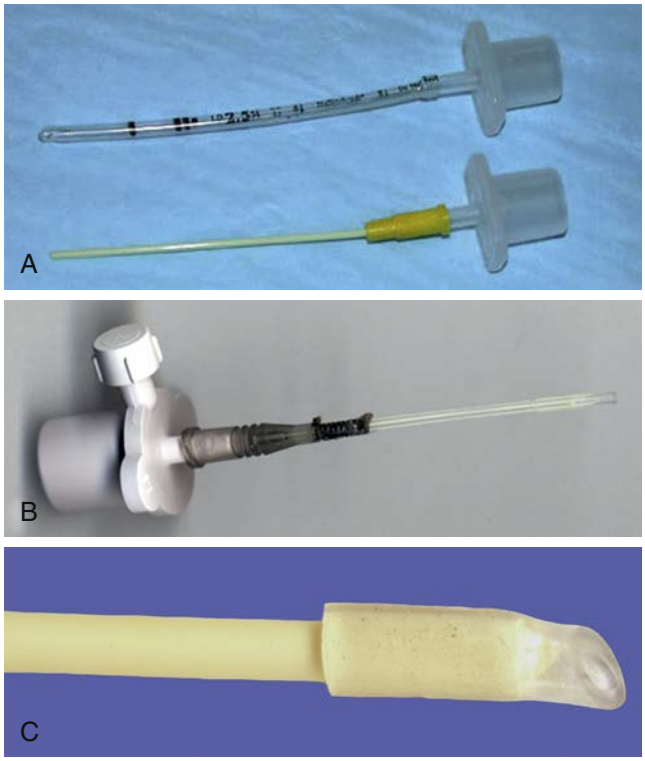


Fig. 37.3 (A) Commercial endotracheal tubes are useful for large mammals, but Teflon intravenous, red rubber, and urinary catheters are often necessary to intubate very small mammals. A small piece of silicone tubing can be glued over the end of the intravenous catheter to minimize sharp edges (B, C).

Specialized endotracheal tubes and light sources are available to aid intubation of small mammals. The smallest commercial uncuffed tubes have an internal diameter (ID) of 1 mm. However, tubes of less than 2 mm ID are often highly flexible and kink easily. The smallest-diameter cuffed tube is 2 mm ID (Mila International, Florence, KY). Uncuffed tubes do not provide a sealed airway, so clean the oral cavity before intubation, elevate the head, and monitor during the procedure. If a cuffed tube is used, the cuff is carefully inflated with just enough air to prevent leakage when 10 to 15 cm H_2O pressure is applied to the rebreathing bag. Very small mammals may be intubated with IV, red rubber, or urinary catheters (see Fig. 37.3A). Take care to ensure that no sharp edges are present at the tube end. This can be achieved by using a small piece of silicone tubing over the end of the catheter (see Fig. 37.3B–C).

Endotracheal tube obstruction is detected by monitoring for a prolonged expiratory phase. Anticholinergics reduce mucus production and plug formation but also increase viscosity, making it harder to clear secretions. The use of an endotracheal tube with a Murphy eye decreases the potential for mucus occlusion. Humidifying the gases reduces mucus plug formation. Commercial endotracheal tube humidifiers are available (Humidi-vent Mini Agibeck Product; Hudson RCI, Temecula, CA). Disadvantages of their use include increased dead space and plugging of the filter with secretions.

Take care to minimize head and neck movement in intubated patients because movement of the tube and changes in positioning may induce tracheal mucosal trauma. Always disconnect the endotracheal tube from the anesthetic circuit before moving an intubated animal. Sublaryngeal tracheal injury, ulceration, and postintubation tracheal strictures have been described in rabbits from several institutions that were intubated with both cuffed and uncuffed endotracheal tubes.[54,100] Other factors that predispose to mucosal injury include ventilation technique and endotracheal tube disinfection protocols.

Ferret intubation is straightforward and can be performed routinely, as in the cat. Rabbit intubation is challenging without prior training. Rabbits have large incisors, long narrow oral cavities, and thick tongues, making laryngeal visualization more difficult, and laryngospasm is easily induced. Several tracheal intubation techniques have been advocated for use in rabbits: direct visualization of the larynx with a laryngoscope and intubation; blind intubation with the neck in extension; endoscope-guided intubation; and nasotracheal intubation. Apply a topical local anesthetic spray onto the larynx 60 seconds before intubation to decrease laryngospasm. Regardless of which intubation technique is used routinely, it is important to also learn the direct intubation technique for use during emergency protocols for respiratory arrest in an unintubated patient. For the direct technique, gently grasp behind the rabbit's head and extend the head and neck so that they are in a straight line. This helps align the larynx and will aid in visualization. Using a No. 1 laryngoscope blade, gently "walk" the blade down the center of the tongue. The blade can be used to gently disengage the soft palate if extension alone does not do it. Use a commercial topical lidocaine spray, or draw up 0.1 to 0.2 mL of 2% lidocaine into a 1-mL syringe and fill the rest of the syringe with air. Once the larynx is visualized, spray the lidocaine onto the larynx by using a tomcat catheter. Wait 1 to 2 minutes, then use the same positioning for intubation. Placement of the tube is confirmed by visualizing the movement of water vapor in the tube, by the rabbit coughing, by auscultation of breath sounds in the lungs, and definitively by attaching a capnograph and seeing a characteristic capnographic trace. For routine rabbit intubation, we use the blind technique (see Fig. 37.4). Using the same positioning as for direct intubation, guide the tube down the center of the tongue to the larynx and either listen for the loudest breath sounds or visualize the movement of water vapor in the tube. Back the tube out just slightly (1–2 mm) and spray lidocaine onto the larynx as above. Wait 1 to 2 minutes, then use the same approach for intubation. Placement of the tube is confirmed as with the direct technique. A further technique has been described using a capnograph on the end of the endotracheal tube and using the presence of a capnographic trace to guide the placement of the tube.[86] Rabbits are obligate nasal breathers, so oxygen can be provided by using a small mask over the rabbit's nose while intubating. Monitor the heart/pulse rate during intubation and stop the procedure if the heart rate decreases significantly. Further attempts should not be made until the heart/pulse rate has recovered. Placing a Doppler crystal on a forelimb is a very good way to monitor the animal, because the person intubating the animal can hear a change in pulse rate immediately. A stethoscope over the thorax can also be used but requires a second person to monitor the animal. The patency of both nares must be carefully assessed after extubation, especially

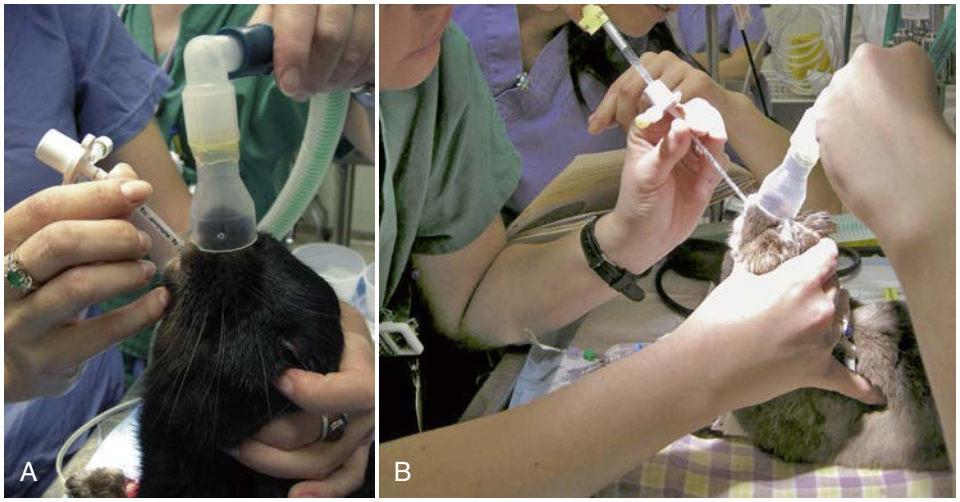


Fig. 37.4 Intubation of the rabbit by using the blind technique. Provide fresh oxygen and anesthetic gas through a nasal mask during the procedure. Guide the tube to the larynx, listen for louder breaths and/or visualize water vapor in the tube (A), place one drop of 2% lidocaine via tomcat catheter through the endotracheal tube directly onto the larynx (B), wait 60 seconds, then use the same approach for intubation. Correct placement is confirmed by visualizing movement of water vapor in the tube, by the rabbit coughing, by auscultation of breath sounds in the lungs, and definitively by attaching a capnograph and seeing a characteristic capnographic trace.

if the animal has been in dorsal recumbency. Reported complications include postextubation obstruction, respiratory arrest, and tracheal mucosal injury.[54,100] Intranasal intubation or catheterization can be used in the rabbit if endotracheal intubation cannot be performed or for complicated oral procedures, such as extensive dental procedures.

Recently a supraglottic airway (SGA) device has been developed for rabbits (V-gel; Docsinnovent Ltd., London, United Kingdom). This has been manufactured with close attention to the anatomy of the rabbit and is simple to place (Fig 37.5). The use of an SGA device will minimize the risks of creating laryngotracheal trauma associated with endotracheal intubation. There are six sizes of this SGA for different rabbit weights. The SGA device is slid into place, and the presence of a clear airway is confirmed with capnography and assessment of the pattern of ventilation. If excessive effort is observed during inspiration or expiration, the SGA device should be gently manipulated until the effort is reduced. The capnographic waveform should appear relatively normal, and the capnograph should be monitored throughout the anesthesia. It is relatively easy to displace an SGA device and end up with a blocked airway. Although it is possible to get enough of a seal with an SGA device to ventilate an animal at low pressures (<16 cm H_2O), there can be a leak even at low pressures (6 cm H_2O).[125] Placement of an endotracheal tube is recommended if positive-pressure ventilation is required during the procedure.[18]

Rodents also have a long narrow oral cavity, but equipment and techniques for intubating rodents have been developed.[96] In guinea pigs and chinchillas, orotracheal intubation is complicated by the fusion of the soft palate to the base of the tongue, creating the palatal ostium, which is highly vascular and easily traumatized (see Fig. 37.6A). Endotracheal tubes of 1.0 to 2.5 mm ID are most often needed for rodents. Very small rodents



Fig. 37.5 Supraglottic airway devices (V-gel, Docsinnovent Ltd., London, UK) for use in rabbits. Two different sizes are shown.

(<100 g) may be intubated with IV catheters, but occlusion with mucus plugs, due to the small internal diameter of these tubes, occurs frequently. An otoscopic cone, modified pediatric laryngoscope blade, commercially available rodent work stands and intubation packs, or endoscopy can help facilitate intubation. A stylet placed first may help facilitate endotracheal tube placement (see Fig. 37.6B–C). Endoscopy provides the best visualization of the epiglottis and minimizes trauma during tube placement.

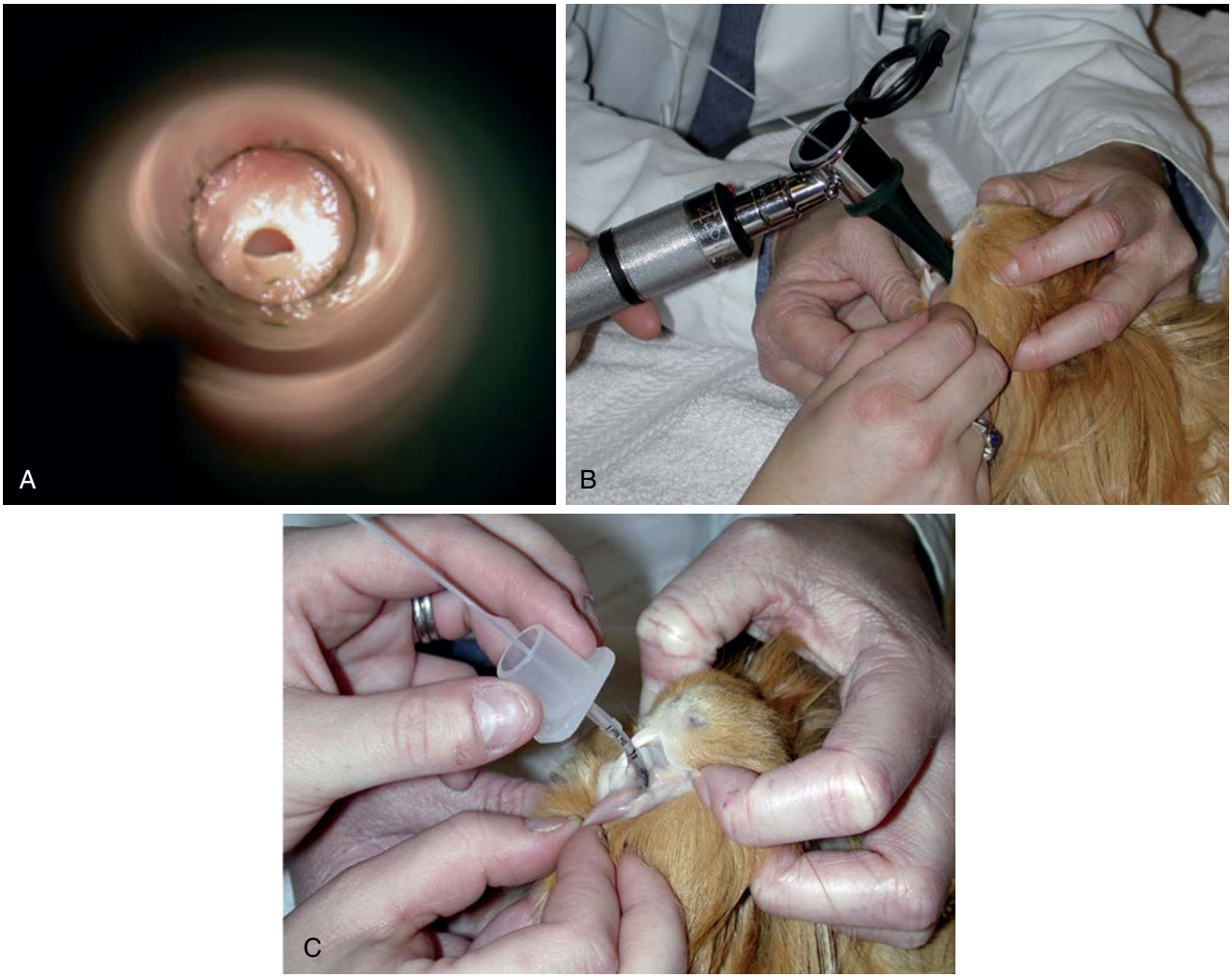


Fig. 37.6 In guinea pigs and chinchillas, orotracheal intubation is complicated by the fusion of the soft palate to the base of the tongue, creating the palatal ostium, which is highly vascular and easily traumatized (A). Intubation can be accomplished with the use of an otoscope or endoscope and placement of a stylet (B), then threading the endotracheal tube over the stylet (C).

LOCAL AND REGIONAL ANESTHESIA

Local anesthetics are ideal for use in preemptive analgesic combinations. Although local anesthetics provide sufficient analgesia for some procedures without the addition of another anesthetic, the stress of handling and restraint generally precludes their sole use when used topically.

Intraoperative CRIs and local or regional nerve blocks are commonly used, as are epidural or spinal administration, and can provide distinct benefits both during and after surgery.[3,74,79] Sciatic-femoral block with 2% lidocaine or lidocaine/bupivacaine was successful in rabbits, and motor responses were consistent with those reported in dogs after successful nerve location.[19,79] Ultrasound guidance of regional anesthesia has the potential to optimize local delivery and distribution of the local anesthetic agent, thereby reducing the amounts of the agent that must be administered.[41] This technique was successful for performing brachial plexus blocks in rabbits for forelimb surgery.[41] Dental nerve blocks may be useful in performing dental extractions. Intratesticular blocks can be used for castration; we use 0.25 mg/kg of 0.5% bupivacaine per testicle. A new, long-acting local anesthetic formulation of bupivacaine (bupivacaine liposome–encapsulated formulation, [Nocita]; Aratana Therapeutics, Leawood KS), with effects for up to 72 hours, has been licensed for tissue infiltration in dogs and may be useful for similar purposes in small mammals. In rats, antinociception was evident for 4 days after wound infiltration with this bupivacaine formulation.[75]

The toxic dose of local anesthetics in small mammals appears to be similar to that in cats and dogs. Toxic signs may include depression, drowsiness, muscle tremors, vomiting, hypotension, and arrhythmias, as well as central nervous system signs such as ataxia and nystagmus. Toxicity is prevented by using appropriate concentrations and volumes. For example, the commercial lidocaine (2%) solution often must be diluted to achieve a suitable injection volume while not exceeding a total dose of 4 mg/kg. Dilution can decrease duration of action and drug effectiveness, but clinical studies are lacking on dilution limits in small mammals. Bupivacaine is used conservatively because of concerns that its toxic effects may take longer to resolve, and it has been associated with significant ventricular arrhythmias, decreased myocardial contractility, convulsions, and cardiac arrest during

TABLE 37.4 Injectable Preservative-Free Drugs Used for Epidural Anesthesia/Analgesia in Small Mammals[a]

	Ferret	Rabbit	Guinea Pig	Chinchilla	Rat
Buprenorphine	12 µg/kg	12 µg/kg	12 µg/kg	12 µg/kg	
Bupivacaine	1 mg/kg	1 mg/kg	1 mg/kg	1 mg/kg	1 mg/kg
Morphine	0.1 mg/kg	0.1 mg/kg	0.1 mg/kg	0.1 mg/kg	0.1 mg/kg

[a]These are suggested doses based on published information and our clinical experience. Species and individual variation in response to a drug or combination of drugs may be uncertain, and doses should be adjusted for the needs of each patient. All doses are in milligrams per kilogram unless specified otherwise. All drugs should be diluted with preservative-free saline solution only. Total volumes for epidural administration should not exceed 0.33 mL/kg regardless of drug or drug combination. Opioid and local anesthetics can be administered in combination, and the dose recommended above for bupivacaine is a decreased dose used with opioids compared with the dose used with bupivacaine alone.



Fig. 37.7 Landmarks for epidural injections are the wings of the ileum bilaterally and the depression between the last lumbar and first sacral vertebrae (A). Sterile technique is used throughout. Appropriately sized spinal or hypodermic needles are introduced with a firm rotating motion until a "pop" is felt (B). Placement is confirmed by lack of resistance to air introduced with a glass syringe (C) before analgesics are delivered (D). Only one-quarter the calculated dose is delivered if spinal fluid is identified in the needle hub.

accidental intravenous administration. Ropivacaine is a local anesthetic with actions similar to bupivacaine and mepivacaine and is sold as the (S) isomer. It has reduced cardiovascular adverse effects when compared with equipotent doses of bupivacaine.

Epidural Anesthesia/Analgesia

Epidural anesthesia and analgesia can be a very useful adjunct to a balanced anesthetic protocols and can significantly reduce the concentration of inhalant anesthetics for surgical procedures (see Table 37.4). Anesthetic and analgesic effects are achieved with little to no systemic drug effects, thus further reducing the use of other cardiopulmonary depressant anesthetics in the protocol. Epidural anesthesia is more commonly used in rabbits, guinea pigs, chinchillas, and ferrets, but it can be performed in smaller species as well.[74,92] The lumbosacral junction site is most commonly used, and the techniques for administration are similar to those in dogs and cats (see Fig. 37.7A–D). In rabbits, injection into the lumbosacral space may result in subdural

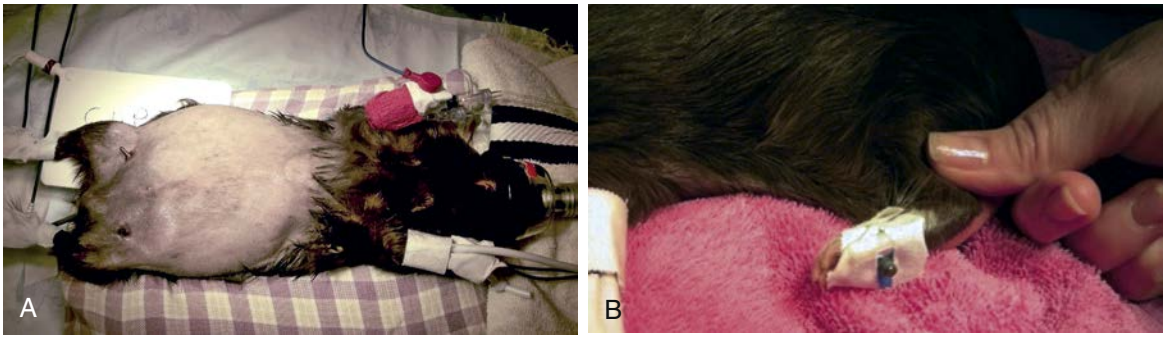


Fig. 37.8 Monitoring and supportive care equipment for surgery including Doppler and noninvasive blood pressure equipment, capnography, electrocardiography (ECG), esophageal/rectal temperature probes, intravenous catheters, and temperature support with pads and forced-warm-air blankets can be used even on small patients (A). The ECG pads can be cut and taped to the footpads of many rodents (B).

injections because the dural sac extends into the sacrum.[52] A shielded needle and electrical stimulation has been used successfully to help define entry to the subarachnoid space, with a twitch at 0.3 mA indicating successful needle placement.[97] If cerebrospinal fluid is visualized in the needle, the volume of injectate should be decreased to one-quarter of the epidural dose to prevent excessive spread of the drugs.

Morphine at 0.1 mg/kg is the most commonly used opioid for epidural administration because it has a high potency and long duration of analgesic action (18–24 hours), but hydromorphone and buprenorphine (0.012 mg/kg) have similar effects and duration. An epidural dose of 0.1 mg/kg of preservative-free morphine administered to ferrets before surgery decreased both physiologic and behavioral manifestations of surgically induced pain.[115] Bupivacaine (1 mg/kg) at concentrations ≤0.125% appears to have the least motor effect while producing good sensory block, which is important for minimizing recovery stress and potential trauma. In rabbits, lidocaine at 3 mg/kg provided a block that lasted 72 ± 34 minutes.[5] There appears to be synergism in the epidural space between local anesthetics and opioids; drug combinations reduce doses and minimize potential adverse effects of each drug. In general, the total epidural administration volume for all drugs combined should be ≤0.33 mL/kg, and all drugs should be diluted with preservative-free saline solution only.

ANESTHETIC MONITORING AND SUPPORTIVE CARE

Effective monitoring requires minute-to-minute patient assessment. Regardless of the anesthetic used, the eyes should be well lubricated often to prevent corneal dessication and ulceration. Covering the eyes with damp gauze sponges helps maintain the moisture provided by the eye lubrication.

Withdrawal reflexes that are used in small mammals include toe pinch, stimulation of the interdigital tissue, tail pinch, and rectal pinch. The toe pinch does not always reliably measure anesthetic depth in guinea pigs because involuntary leg movements sometimes occur under anesthesia. Slight corneal and palpebral reflexes are commonly maintained at a surgical plane of anesthesia; absence of these reflexes indicates an excessively deep plane of anesthesia.

Heart rates vary widely between species. Base knowledge of expected heart rates for the species is important, but absolute trends in rate during anesthesia are of the utmost importance. The anesthetic gas concentration is decreased with any sudden heart rate reduction. Because of the rapid heart rate of many small rodents, electrocardiographic (ECG) complexes can be difficult to assess at the standard sweep speed of 25 mm/sec. Sweep speeds of 100 and 200 mm/sec are available on some ECG machines and can allow for a more accurate assessment. Needle ECG leads are ideal for small rodents, as they provide excellent conduction without the use of gels. Alternatively, metal alligator clips attached to a hypodermic needle or a saline solution–soaked cotton ball or adhesive pad can be used (see Fig. 37.8). Peripheral pulse quality can be subjectively assessed by changes in pulse loudness gauged with a Doppler ultrasound probe placed over an artery. This is quite insensitive, but a change in Doppler loudness should alert the anesthetist to reevaluate the patient. Noninvasive blood pressure monitoring can be performed by using a Doppler probe, a pressure cuff, and a sphygmomanometer (Fig 37.8). The width of the blood pressure cuff should approximate 40% of the limb circumference. Cuffs that are too large can give falsely decreased pressures, and cuffs that are too small may give falsely increased pressures. The cuff is placed over the radius/ulna, humerus, tibia, or femur, or a tail cuff can be placed over the base of the tail. Special tail cuffs have been developed for rodents and are used extensively in research animals. The Doppler probe is placed between the carpal/tarsal pad and pads of the feet, above the carpus on the ventromedial aspect, or on the ventral surface of the tail over the ventral tail artery; shaving of these areas is sometimes necessary. Standard oscillometric machines do not work well in animals weighing less than 2 kg and can be especially unreliable in the small hypotensive or hypothermic patient with a high heart rate. In rabbits, oscillometric readings from the forelimb correlated well with arterial blood pressures at low and normal pressures, but hind-limb readings did not.[128] The pressures determined with a Doppler and sphygmomanometer are taken as systolic pressures, whereas oscillometric devices can provide systolic, diastolic, and mean arterial pressures.[61] Normal systolic blood pressure measurements in awake animals obtained with the Doppler range from 90 to 120 mmHg. Perfusion is assessed by evaluating the color and capillary refill time of the oral, rectal,

or vaginal mucous membranes, femoral pulse quality, heart rate, and blood pressure. Fluid types, uses, and volume calculations are discussed in Chapter 41.

Respiratory rate and character should be monitored closely. Visual monitoring of the respiratory rate can be complicated by surgical drapes, especially in small rodents: clear drapes are preferred. Ventilation is monitored by watching the frequency and degree of movement of the chest or movement of the reservoir bag on the anesthesia machine. Small reservoir bags, such as balloons, can be used to visualize small movements. High respiratory frequency can be misleading and does not mean that the patient is necessarily light and hyperventilating. High respiratory rates can be associated with small tidal volumes, resulting in more dead-space ventilation than pulmonary ventilation. Lighten the plane of anesthesia and institute manual ventilation for any period of apnea greater than 10 to 20 seconds. Respiratory monitors that are triggered by a thermistor in the airway function well in patients weighing more than 500 g, but they may not respond to small respiratory movements and lower tidal volumes in animals weighing less than 200 g. In general, normal ventilation produces little to no noise. Whistling, wheezing, or harsh sounds may indicate airway obstruction.

Both injectable and inhalant anesthetics cause dose-dependent respiratory depression; this and the increased resistance to breathing imposed by the endotracheal tube provide compelling reasons to ventilate these animals. Sick or debilitated patients may not be able to accommodate these physiologic changes and thus require intermittent positive-pressure ventilation. We recommend initial inspiratory pressures of 5 to 10 cm H_2O and rates of 10 to 20 breaths/min. Thoracic excursions are assessed and the tidal volume is adjusted to achieve appropriate thoracoabdominal expansion. In general, the average tidal volume for most species is 8 to 10 mL/kg. Inspiration should take 1 to 1.5 seconds. If a mechanical ventilator is not available, hand ventilation delivered from the reservoir bag provides assisted ventilation.

End-tidal carbon dioxide monitoring using a capnograph is useful to assess ventilation with the expectation that end-tidal CO_2 is closely correlated with partial pressure of CO_2. Evaluation of the capnograph tracing can provide important information regarding trends in end-tidal carbon dioxide. Mainstream capnographs read directly from the gas in the airway, whereas sidestream capnographs pull gas along a tube to the measuring device in the machine. Mainstream capnographs may add an unacceptably large dead space in small patients (<500 g), and the weight of the detector on the end of the endotracheal tube may predispose to inadvertent extubation. With sidestream sampling, the port should be located inside the endotracheal tube; but it is important that this not take up excessive volume and lead to an increased resistance to breathing. Endotracheal tube adapters with a built in sidestream port can be used to minimize changes in dead space. Sidestream capnographs draw samples at a rate of 50 to 200 mL/min. Instruments with a sample rate of 50 mL/min provide more accurate measurements in small patients.[102]

Pulse oximetry is used in many species to evaluate arterial hemoglobin oxygen saturation, but the high normal heart rates in these species may exceed the upper limits of standard monitors. Pulse oximeters that can detect high heart rates and low signal strengths are now available. The pulse oximetry probes are placed on the tongue, ear, toe, tail, or vaginal/rectal mucous membranes. Smaller probes are available through laboratory animal supply companies.

To reduce potential anesthetic-associated morbidity and mortality rates, it is mandatory to monitor core body temperature and to provide thermal support. Most anesthetics depress thermoregulatory function, and this is exacerbated in small patients prone to heat loss because of their high body surface-to-volume ratios. Hypothermia certainly depresses cardiopulmonary function, and arrhythmias and disturbances of coagulation can occur with deep hypothermia in mammals (<86°F [<30°C]). Hypothermia decreases anesthetic requirement and metabolism and prolongs recovery. Supplemental heat sources should be used regardless of the length of the procedure. Core body temperature is most accurately monitored with an esophageal temperature probe, but rectal temperatures can also be obtained if necessary. Most heat is lost via radiation, so the most effective technique to prevent heat loss is to minimize the temperature gradient between the patient and the room. This can be done by increasing room temperature; insulating the patient with clear plastic drapes, bubble wrap, or foil; and wrapping nonsurgical fields. Surgical time and the time the body cavities are open are minimized, as are the time for hair clipping and alcohol/saline solution use for skin preparation. Latex gloves, empty fluid bags, or plastic bottles can be filled with water, warmed in a hot-water bath, and placed next to the patient. Water bottles are wrapped in a towel to prevent burns. Gel-packs can be prewarmed in a warming cabinet or heated in a microwave—these will generally hold their heat longer than a water container, and so the animal can be placed on top of the gel-pack immediately after induction and remain on this during the procedure. Circulating-warm-water blankets insignificantly diminish the rate of heat loss in small patients, but resistive polymer pads such as the Hot-Dog system (Augustine Medical, Eden Prairie, MN) can maintain normothermia if the animal is insulated from above. Forced-air warmers are more effective at minimizing hypothermia during anesthesia than other methods and are particularly effective when set up to have warm air rising around the patient either by wrapping the patient in the blanket or by using a perforated table. Lubricate the eyes well to prevent corneal ulceration due to drying from the warm air. Warm the replacement fluids before administration. Heated, humidified anesthetic gases also help to reduce or prevent the development of hypothermia.[93] Inspired gases can be warmed simply by running the breathing circuit through hot (40°C) water. Commercial humidifiers are available (Humidivent Mini Agibeck Product; Hudson RCI, Temecula, CA) that can be placed in the anesthetic circuit.

MANAGEMENT OF HYPOTENSION

Decreased blood pressure is common during anesthesia. In most mammals, the autoregulation of blood flow to vital organs is thought to begin to become pressure dependent at around a mean arterial pressure of 70 mmHg, which roughly correlates to a systolic pressure of 90 mmHg. These two points have been used clinically as the cutoff values to define hypotension during anesthesia. The three main steps used to treat anesthetic-induced

hypotension are (1) decrease the amount of anesthetic, (2) increase the circulating volume, and (3) use a positive inotrope to reverse the effect of the anesthetic

The first step is only possible if the animal is in a deeper plane of anesthesia than is needed for the current level of stimulation, but decreasing the amount of anesthetic should always be considered first in order to reduce the negative inotropic effect of the anesthetic. If this is not possible, then consider adding a drug that has minimal effect on the cardiovascular system while reducing the need for the main anesthetic (see Balanced Anesthesia above). The second step is to increase circulating volume, usually by administering a bolus of fluids. Most commonly this involves using balanced electrolyte solutions, with the aim to increase blood volume by at least 5%. Because only about one-third of the administered dose is going to remain in the vascular space, the dose needs to be three times the volume needed. We use boluses of 10 to 20 mL/kg, depending on the species. Several veterinary and human studies now suggest that crystalloids may not be very effective at restoring blood pressure under these circumstances and that colloids such as hydroxyethyl starch or polygelatins are more effective because they are retained in the circulation—doses range from 2 to 5 mL/kg as a starting point. These solutions are more expensive than crystalloids, and in the human literature there are concerns about renal damage ensuing from their use. The last step is the use of positive inotropes such as dobutamine or dopamine. These are administered as CRIs starting at 2 to 5 µg/kg per minute. If the starting rate is not effective, it is worth progressing to an increased infusion rate to see if a higher dose would work. Vasoconstrictors, like phenylephrine, norepinephrine, and ephedrine, are usually only used if there is a significant vasodilatory contribution to the hypotension (e.g., as evidenced by low diastolic pressures). Rabbits tend to become profoundly hypotensive during anesthesia, with mean pressures in the 40 to 50-mmHg range.[51,63] The mechanism for this hypotension is unclear, although a persisting hyporeactivity of vascular smooth muscle has been demonstrated in rabbits after halothane anesthesia, but it is not just a function of inhalant anesthesia.[63] Dopamine appears to be ineffective in this species; in one study, neither blood pressure nor cardiac output increased even at doses as high as 30 µg/kg per minute.[51] Phenylephrine only increased blood pressure at high doses (2 µg/kg per minutes), but cardiac output did not change, and heart rate decreased by about 10%.[51] In rabbits, norepinephrine may be more effective because it is both a positive inotrope and vasoconstrictor, but doses may again need to be high (e.g., 1–2 µg/kg per minute). In a sepsis model, doses of 5 to 7 µg/kg per minute were needed to maintain blood pressure.[129]

EMERGENCIES

Emergencies during anesthesia should be anticipated and planned for in advance. Most are averted by careful monitoring of heart rate, respiratory rate, blood pressure, and body temperature. Endotracheal tubes, oxygen, IV catheters and materials for securing them, ventilatory support, and emergency drugs should be close by and ready for use. Emergency drug doses should be calculated and predrawn before induction (see Table 37.5). Treat respiratory depression and arrest by turning off the anesthetic vaporizer and controlling ventilation. The standard approach of maintaining airway, breathing, and circulation should be followed. Cardiac massage can be performed, and in many of these small species, in which the heart is palpable through the thoracic wall, the resuscitator should be able to feel the heart during each compression. The rate of compressions should be as high as can be achieved, to maintain blood flow (150–300 beats/min depending on the species). If external cardiac compression is not immediately successful, then administration of epinephrine IV, IO, or tracheal/endobronchial is recommended (in that order of preference). Treat severe

TABLE 37.5 Emergency and Cardiopulmonary Resuscitative and Supportive Drug Dosages Commonly Used in Small Mammals[a]

Drug	Dose[b]	Route of Administration	Indications
Atropine	0.04–0.1 mg/kg	SC, IM, IV, IO, IT	In all small animals except the rabbit where much higher doses are required (0.2–1.0); bradycardia, CPR
Dobutamine	0.12–0.6 mg/kg/ h	IV CRI	Nonhypovolemic hypotension during surgery
Dopamine	0.3–1.2 mg/kg/h	IV CRI	Nonhypovolemic hypotension during surgery. Does not work well in rabbits
Doxapram	1–10 mg/kg	IV, sublingual	Ineffective during cardiac arrest or severe hypoxia
Epinephrine (1:1000)	0.01–0.1 mg/kg	IM, IV, IO, IT	Cardiac arrest; dilute to 1:10,000 before IV use
Glycopyrrolate	0.01–0.05 mg/kg	IM, IV	Bradycardia; slower onset than atropine but may provide longer benefit
Lidocaine	1–2 mg/kg	IV	Antiarrhythmic
Midazolam	0.1–2.0 mg/kg	IM, IN, SC, IV	Seizures, sedation
Norepinephrine	0.03–0.12 mg/kg/h	IV	May be the best option for hypotension in rabbits
Vasopressin	0.8–1.2 U/kg	IV, IO, IT	The higher dose should be used for IT administration diluted in 0.2–0.5 mL/kg of saline solution

[a]Note that these are suggested doses based on the authors' clinical experience. Species and individual variation in response to a given drug can be uncertain, so adjust the dose based on clinical response.
[b]All doses are in milligrams per kilogram unless specified otherwise.
CRI, Constant rate infusion; *IM,* intramuscular; *IN,* intranasal; *IO,* intraosseous; *IT,* intratracheal; *IV,* intravenous; *SC,* subcutaneous.

bradycardia, assuming that it is due to increased parasympathetic tone, with atropine/glycopyrrolate (see Chapter 41).

RECOVERY

One of the most important ways to reduce the potential for complications during anesthesia and recovery is to minimize anesthetic time. Postprocedural recovery should have the patient connected to the circuit or on a face mask with 100% O_2 for as long as possible, in a quiet area. If the animal is wet from the procedure, gently dry it with a loose towel or with warm air. Always monitor the character of respiration during towel restraint to ensure that chest movement is not impaired. Once recovery is considered to be of minimum potential for self-trauma, place the patient in a warm, quiet, darkened, well-oxygenated environment for continued recovery. Respiratory depression can continue into the postanesthetic period, so continue with supplemental oxygen. Use thermal support in the recovery area, but do so with caution, because many small mammals are susceptible to heat stress. Chinchillas are particularly prone to be stressed by temperatures greater than 75°F (24°C) and should be monitored closely.

Provide food and water as soon as the patient has recovered to a point of minimal to no ataxia. Gastrointestinal (GI) transit times are very rapid for most small mammals; therefore carefully consider the patient's nutritional plane in advance. To minimize the potential for GI stasis after the anesthetic period, administer nutritional support to small mammals exhibiting anorexia of concerning duration. Replacement fluid therapy plays a role in nutritional support, as the GI tract must be hydrated to facilitate motility and function. If IV fluids were not provided during surgery, administer warm SC fluids at this time. If voluntary food intake has not resumed within the first few hours after anesthetic recovery, initiate syringe feeding of appropriate products.

ANALGESIA

Recognition and alleviation of pain are an essential component of every animal's evaluation. Surveys evaluating veterinarians' use of analgesics in companion exotics have shown that many small mammals are still undertreated and are less likely to receive analgesics than are dogs or cats.[77,82]

Analgesic therapy is limited by the reliability of pain assessment, which remains highly subjective in these species. The assessment and management of pain include behavioral, physiologic, clinical, and psychologic indicators. Pain assessment is complex because it requires consideration of differences in age, sex, species, breed, individual behaviors, and environment. One must also consider the different types and sources of pain, such as acute versus chronic pain and visceral versus somatic pain.

Standardized scales create a more accurate way to assess a patient's response to therapy. Pain scales and score sheets are increasingly being used to assess an animal's pain level but are highly variable among species and models studied. Rabbits and rodents are prey species, and often hide signs of pain or distress. Recent studies have evaluated behavioral assessments of pain in rabbits,[59,84] ferrets,[115] guinea pigs,[50] and rats.[76] Facial expressions have been examined in rodents and rabbits as a means to evaluate pain (i.e., grimace scores).[33,59,66] Many other behaviors and clinical signs have been associated with pain, including changes in temperament (either aggressive or passive), restlessness, reduced mobility or reluctance to stand, lethargy, hunched appearance, constipation/GI stasis, increased respiratory rate, and lameness. Reduced food consumption or fecal production often occurs with small mammals in pain.[50] Rabbits, ferrets, and some rodents will often grind their teeth. As with other species, small mammals with abdominal pain may exhibit abdominal tensing with a "tucked up" or "hunched" appearance to the abdomen; rats show a characteristic abdominal twitch with abdominal pain.[103] Animals may avoid a painful area of the body, or they may bite or chew at the site. Decreased grooming in small mammals may be exhibited by a dull or greasy appearance, or, conversely, the animal may overgroom a painful site. Some species respond to strong pain stimuli with tonic immobility.

Another clinical manifestation of pain is hyperalgesia, or an abnormally heightened response to a noxious stimulus. This is caused by central and peripheral sensitization of nociceptive pathways and inflammation at the site of tissue damage, such as at a surgical incision.

There is still tremendous room for error in assessing pain in these species. To provide some standards for determining whether to provide analgesics, a set of universal questions is used to determine whether a patient is in pain: (1) Would the lesion or procedure be painful in any species? (2) Is the lesion or procedure damaging to tissues? (3) Does the patient display any abnormal behavioral responses? If the answer to any of these questions is yes, one must assume that the patient is in pain and that an analgesic plan must be developed. There is still a paucity of pharmacokinetic and pharmacodynamic information for many of the drugs used clinically in small mammals; thus dosages are often extrapolated from experience in other species. Published doses and dosing frequencies should be critically evaluated for each patient before clinical use. Sustained-release formulations of many analgesics reduce the frequency of dosing in many small laboratory mammals; studies in these species will provide guidelines for use in pet animals.

Balanced or multimodal analgesia has become part of analgesic best practices in small mammal medicine. The process of nociception and pain involves many steps and pathways, so one analgesic agent is unlikely to completely alleviate pain. Multimodal analgesic plans include drugs of different classes that act at differing parts of the nociceptive pathways. For example, patients can be premedicated with an opioid medication and a tranquilizer to modulate pain and stress; ketamine used as a part of the induction protocol can reduce central facilitation; local anesthetic blocks can be added to inhibit nociceptive transmission; and nonsteroidal antiinflammatory drugs (NSAIDs) can be added before or after surgery to reduce inflammation and pain. This approach allows smaller dosages of each drug to be used, as analgesic effects can be additive and may reduce undesirable adverse effects from larger doses of individual drugs.

ANALGESIC DRUGS

Opioids

Opioids are most commonly used for moderate to severe pain, such as fractures and traumatic or surgical pain. The most

common adverse effects reported with opioids are respiratory or cardiac depression and constipation/GI dysmotility. Changes in GI motility are concerning but can be overcome by providing excellent hydration and assisted feeding during drug administration. Emesis can occur in ferrets with μ-opioid agonists such as morphine.

The effects of opioids can vary between and within species at the same dose. Most opioids are used parenterally because of their poor oral bioavailability associated with the first-pass effect. Morphine, methadone, hydromorphone, and oxymorphone are μ-receptor agonists with similar durations of action. In ferrets, μ-opioid agonists cause profound sedation, making assessment of analgesia difficult. Morphine reduced isoflurane MAC by 30% and 50% when administered IM to rats at 3 and 10 mg/kg, respectively.[17] Hydromorphone at 2 mg/kg in chinchillas, but not at 0.5 or 1 mg/kg, resulted in analgesia for less than 4 hours in a thermal nociception model, and a dose-dependent effect on fecal output and food intake was observed.[31]

Fentanyl citrate has an effect for only 30 minutes after a single IV injection and is thus most commonly used as a CRI during the perianesthetic and postoperative periods (see above and Table 37.3). As with all μ-receptor agonists, fentanyl can cause respiratory depression, so the dose must be titrated to provide analgesia with minimal effect on respiration, or a secure airway and ability to ventilate are required when using it as a CRI. Systemic uptake of transdermal fentanyl in rabbits with the 25-μg/h patch was highest, with the longest duration of activity (3 days) when the hair was clipped at the patch site, and no systemic concentrations were identified when hair was present at the patch site.[39] Although extrapolated effective therapeutic plasma concentrations were obtained, loss of body weight occurred in this study.

Buprenorphine is a partial μ-opioid agonist that can antagonize the effects of other pure μ agonists and is also described as a κ-receptor agonist and antagonist. It is the preferred opioid in small mammals for postoperative analgesia because of its reportedly longer duration of effect (see Table 37.6). Gastrointestinal effects are the most commonly reported adverse effects, but in rabbits buprenorphine increased activity in the foregut without prolonging transit time through the GI tract.[21] "Pica behavior" may occur when rats are housed on certain types of bedding, especially sawdust or wood chips, while on this analgesic. Buprenorphine can be administered SC, IM, IV, or oral transmucosally. Buprenorphine is considered safe and effective when administered at 0.01 to 0.05 mg/kg to dogs, but higher doses are often necessary in smaller mammals. For example,

TABLE 37.6 Analgesic Drug Dosages Recommended in Small Mammals[a]

Drug	Ferret	Rabbit	Guinea Pig	Chinchilla	Rat	Comments
NSAIDS						
Carprofen	2.0–5.0 PO, SC q 12–24 h	1.5–5.0 PO, SC q 12–24 h	—	—	2.0–5.0 PO, SC q 12–24 h[35,103,104]	
Ketoprofen	1.0–3.0 SC or IM q 12–24 h[37]	1.0–3.0 IM q 12–24 h[37]	1.0–2.0 SC, IM q 12–24 h	1.0–2.0 SC, IM q12–24 h	2.0–5.0 SC, IM q12–24 h[35,103]	
Meloxicam	0.2–0.3 PO, SC q 24 h[14]	1.0 PO, SC q 24 h[22,45]	0.3–0.5 PO, SC q 24 h[50]	0.3–0.5 PO, SC q24 h	0.5–2.0 PO, SC q 24 h[105,108]	
OPIOIDS						
Buprenorphine	0.01–0.03 SC, IM, IV q 6–12 h	0.01–0.05 SC, IM, IV q 6 h[34,72]	0.1–0.2 SC, IM, IV q 7 h 0.2 mg/kg OTM q 4 h[107]	0.1–0.2 mg/kg q 4–6 h[43]	0.05–0.5 SC, IM q 6 h[72,104]	
Buprenorphine sustained release		0.3 SC q 48–72 h[116,23]	0.3–0.6 SC q 48–72 h[130]	—	1.2 SC q 48–72 h[15]	
Butorphanol	0.05–0.5 SC, IM, IV q 2–4 h	0.2–2.0 SC, IM, IV q 2–4 h[64,101,122]	0.5–2.0 IM, SC, IV q 4h	0.5–2.0 IM, SC, IV q 2–4 h	1.0–5.0 SC, IM, IV q 2–4 h[37]	Lower doses used in premedication combinations
Hydromorphone	0.05–0.3 SC, IM q 6–8 h	0.05–0.3 SC, IM q 6–8 h	1.0–2.0 SC, IM q 6–8 h	1.0–2.0 SC, IM q 2–4 h [31]	0.4 SC < q 2 h	—
Methadone		0.2 SC[120]			0.5–3.0 SC	
Morphine	0.05–1.0 SC, IM q 2–4 h	0.5–2.0 SC, IM q 4 h[120]	2.0–5.0 SC, IM q 2–4 h[38]	2.0–5.0 SC, IM q 4 h	4.0–10.0 SC, IM, q 4 h[46]	
Nalbuphine HCl	0.5–1.5 IM, IV q 2–4 h	1.0–2.0 IM, IV q 2–4 h	1.0–2.0 IM q 2–4 h[37]	—	1.0–2.0 SC, IM q 2–4 h[37]	
Naloxone	0.01–0.1 SC, IM, IV	0.01–0.1 SC, IM, IV	0.01–0.1 SC, IM, IV	0.01–0.1 SC, IM, IV	0.01–0.1 SC, IM, IV[36]	Opioid antagonist
Oxymorphone	0.02–0.05 SC, IM q 6–8 h	0.05–0.2 SC, IM q 6–8 h	1.0–2.0 SC, IM q 6–8 h	1.0–2.0 SC, IM q 6–8 h	1.2–1.5 SC	
Tramadol	—	—	—	—	5.0–20.0 PO, SC[20,37,56]	

[a]These are suggested dosages based upon published information and our clinical experience. Species and individual variation in response to a given drug can be uncertain, so the dosage should be adjusted depending upon the clinical response of the animal. Although there are no good data available for hamsters and gerbils, extrapolation from rat doses clinically appears to be appropriate. Many published doses are based upon laboratory animal data; differences in pet breeds of these animals are unknown. Doses are in milligram per kilogram unless specified otherwise.
IM, intramuscular; *IV,* intravenous; *OTM,* oral-transmucosal; *PO,* by mouth; *q,* every; SC, subcutaneous.

0.5 mg/kg provided 6 to 8 hours of analgesia in rats, while 2 mg/kg provided 3 to 5 hours of analgesia in mice.[46] Dosing of oral transmucosal buprenorphine every 4 hours was required in guinea pigs to maintain a target plasma concentration of 1 ng/mL.[107] Recently, a compounded, sustained-release formulation of buprenorphine (Bup-SR) and a commercially available high-concentration buprenorphine (HCB) product for use in domestic cats (Simbadol 1.8 mg/mL; Zoetis, Florham Park, NJ) have become available. It is important to differentiate between these two products, because the compounded formulation uses a vehicle for sustained release, whereas HCB primarily allows once-daily dosing to be provided as a single-injection SC and relies on slow release from the injection site to provide lasting analgesia. Therefore, dosing of the two products can be dramatically different, and published data should not be extrapolated between formulations. Bup-SR has been evaluated in rats, guinea pigs, rabbits, and prairie dogs.[12,23,114,116] In guinea pigs, administration of Bup-SR at 0.3 to 0.6 mg/kg SC resulted in target plasma concentrations being maintained for 48 to 72 hours, and a dose-dependent decrease in fecal output occurred.[130] Rats dosed with 1.2 mg/kg SC of compounded Bup-SR showed evidence of analgesia for 72 hours,[15] and target plasma concentrations of 1 ng/mL were maintained for 72 hours after a single dose.[40] Prairie dogs administered doses of 0.9 and 1.2 mg/kg Bup-SR maintained plasma concentrations therapeutic for other species for greater than 72 hours.[12] In rabbits, effects were comparable between Bup-SR at 0.3 mg/kg SC administered once and standard buprenorphine adminstered at 0.05 mg/kg every 12 hours for 48 to 72 hours.[23,116] Very little work has been done to date to evaluate HCB in small mammals. In rats, standard buprenorphine, Bup-SR, and HCB at clinical doses showed some antinociception with all three formulations, but adverse behaviors such as self- and cage-biting were evident with both Bup-SR and HCB, and pica behavior highest with Bup-SR.[4] Additional studies are warranted to evaluate the safety and efficacy of these formulations in small mammals.

Butorphanol is a mixed agonist/antagonist with low intrinsic activity at the μ receptor and strong agonist activity at the κ receptor. Butorphanol is commonly used in small mammals for mild pain, and the half-life of butorphanol in rabbits administered 0.5 mg/kg IV was shown to be 1.6 hours and 3.2 hours when given SC, consistent with results from other pharmacokinetic studies of this drug. In rabbits administered 0.4 mg/kg butorphanol SC, ketamine/medetomidine anesthesia was prolonged, but only minor anesthetic-sparing effects were seen,[64] and butorphanol 0.4 mg/kg IV reduced the MAC of isoflurane only by 7.5%.[122] Butorphanol 5 mg/kg intraperitoneal reduced sevoflurane MAC by approximately 30% in rats.[2]

Most opioids can be reversed with antagonists, but this will also terminate analgesia. Pure antagonists such as naloxone and naltrexone at high doses are most effective in small mammals. These antagonists compete for the receptor but have minimal effects at the receptor themselves. They reverse both μ- and κ-receptor agonists but will also reduce or eliminate any analgesic effect of the agonist. Nalbuphine is a κ agonist; it can be used to reverse μ agonists and has some residual analgesic effect via the κ receptors. Butorphanol can be used in the same way, but it is a much weaker antagonist and may increase sedation. Administer antagonists carefully, preferably titrating the dose slowly IV to the desired effect.

Tramadol

Tramadol hydrochloride is a synthetic analgesic used to treat moderate and severe acute and chronic pain. It demonstrates central and peripheral mechanisms of action and is active at opiate receptors and decreases the reuptake of noradrenaline and serotonin.[113] Tramadol is a very weak μ agonist, and its main metabolite O-desmethyl metabolite is more potent. Conversion to the O-desmethyl metabolite varies among species, but it is produced in rats and rabbits, and pharmacokinetics have been established for these species.[98,117,126] The analgesic effects of tramadol in small mammals are controversial and likely vary by species, dose, and route of administration. Clinically insignificant isoflurane-sparing effects have been shown in both rats and rabbits administered 10 and 4.4 mg/kg tramadol PO, respectively.[20,29] Results of several studies in rats have shown that tramadol can be an effective analgesic for acute pain.[13,56,58,118] In rats with neuropathic pain, its efficacy decreased with increased duration of pain, and its anti-nociceptive mechanism changed over time, which may partially explain its inconsistent efficacy in patients with chronic pain.[58,123] In chinchillas, tramadol at 10, 20, and 40 mg/kg SC did not significantly reduce thermal nociception and demonstrated dose-dependent reductions in fecal output.[32] Doses above 40 mg/kg resulted in acute transient neurologic adverse effects.

Tapentadol

Tapentadol is also a novel atypical opioid medication with μ-agonist properties and is a norepinephrine reuptake inhibitor. It is equivalent in analgesic activity in humans to morphine, but has a 50-fold lower affinity for μ receptors. To date, there are few studies evaluating this analgesic in small mammals. When administered at 5 mg/kg PO in rabbits as a premedication for orchiectomy, tapentadol elicited a good analgesic plane that resulted in rapid recovery and no complications.[48] Tapentadol showed antinococeptive/antihyperalgesic activity in models of acute and chronic inflammatory pain in rats and mice, and it was antagonized completely with naloxone and yohimbine.[110]

Nonsteroidal Antiinflammatory Drugs

Nonsteroidal antiinflammatory drugs are the most commonly prescribed analgesics in veterinary medicine. Reported adverse effects include GI ulceration and renal damage. Cyclooxygenase-2 (COX-2) has been shown to be constitutively expressed in the kidney in all mammalian species studied and is highly regulated in response to alterations in intravascular volume. In conditions of relative intravascular volume depletion and/or renal hypoperfusion, such as dehydration, hemorrhage, hemodynamic compromise, heart failure, and renal disease, interference with COX-2 activity can have deleterious effects on maintenance of renal blood flow and glomerular filtration rate. Generally, NSAIDs are well absorbed after PO, SC, and IM administration. All NSAIDs are highly protein bound, some greater than 99%, which explains their extended therapeutic activity in inflamed tissues. Plasma half-life therefore may not be the most important factor in determining NSAID dosing intervals, and plasma concentrations may have very little to do

with activity in inflamed tissues. For example in a rat model, the mean residence time for robenacoxib was three times longer in exudate than in plasma.[78]

Meloxicam is a COX-2 selective NSAID (see Table 37.6). Meloxicam is the most widely used antiinflammatory medication in small mammal practice. It is currently available as an oral suspension, tablets, and an injectable form. Single-dose meloxicam at 0.2 mg/kg SC in ferrets produced plasma concentrations similar to those considered analgesic in other mammals. Drug elimination was faster and plasma concentrations were lower in female ferrets than in male ferrets. Ferrets are sensitive to the gastrointestinal effects of NSAIDs, and thus further evaluation in ferrets receiving repeated dosing of meloxicam is warranted before dosing can be recommended.[14] In African pygmy hedgehogs, the pharmacokinetics of 0.2 mg/kg of meloxicam PO and SC suggest that every-12-hour dosing is necessary for the SC route and that the PO route requires a higher dose, because plasma concentrations achieved after PO administration were not considered sufficient.[1] In rabbits, a dose of 1 mg/kg PO is necessary to achieve clinically effective concentrations, and the administration of this dose every 24 hours for 29 days or 1.5 mg/kg for 5 days was found to be safe in healthy rabbits.[22,45,121] In guinea pigs, pharmacokinetic data indicate that a dose of 1.5 mg/kg every 12 hours is required to achieve plasma levels considered analgesic in other species, and oral bioavailability of meloxicam is low (54%) compared with other herbivores.[91] Because no safety data on the use of this dosage in guinea pigs are available, use of this dosage cannot be recommended at this time. Meloxicam at a lower dose (0.5 mg/kg PO) produced significant analgesia in guinea pigs in visceral pain tests,[73] but in a different study, the same dose SC did not prevent physiological and mechanical postoperative changes after orchiectomy.[50] In rats, meloxicam at a dose of 1 mg/kg SC reduced acute postlaparotomy pain behaviors, but a dose of 0.5 mg/kg SC was not effective.[105] Plasma concentrations of meloxicam in prairie dogs were maintained within the therapeutic range identified in other species for less than 24 hours when administered at 0.2 mg/kg SC but for greater than 72 hours when administered at 4 mg/kg.[12] In another study in prairie dogs, the administration of 1 mg/kg SC resulted in plasma concentrations considered excessive in other species. These studies suggest that significant differences in the pharmacokinetics of meloxicam between different rodent species exist, making extrapolation challenging.

Ketoprofen is a potent nonselective COX inhibitor (see Table 37.6). Ketoprofen is used parenterally in small mammals because of limited oral pharmacokinetic data and difficulty in accurately dosing oral formulations. Ketoprofen administered at 5 mg/kg SC before surgery in rats undergoing exploratory laparotomy showed an effect for at least 5 hours, but this dose was not effective PO, suggesting that higher doses may be needed for PO administration.[35] In another study using laparotomy in rats, SC doses of 15 and 25 mg/kg were needed to show evidence of analgesia using the grimace scale.[124]

Carprofen is available in both injectable and PO forms. It is a weakly nonspecific COX inhibitor and may achieve its therapeutic effects, at least partially, through other pathways. The half-life of carprofen varies considerably among mammalian species, which may affect dosing intervals. Carprofen administered at 5 mg/kg SC provided postlaparotomy analgesia for at least 5 hours in rats, but an equivalent effect was found using only 2.5 mg/kg in another study.[105] Postoperative food and water consumption were improved when rats were administered 5 mg/kg SC but not PO, suggesting that higher doses may be necessary with PO dosing.[35] Carprofen at 5 mg/kg SC did not alter facial expression scores in buprenorphine-treated rabbits after maxillary sinus surgery.[66]

Gabapentin

Gabapentin is used to treat a variety of conditions in both human and veterinary medicine, including seizures, neuropathies, and chronic pain. Gabapentin was poorly active against mechanical hyperalgesia in both rats and guinea pigs after a single oral dose (100 mg/kg), although it produced up to 70% and 90% reversal in rats and guinea pigs, respectively, with repeated administration.[42] In small mammals, the effects of gabapentin appear to be significantly enhanced when multimodal analgesia is used.[16] Gabapentin administered to rats at 10 mg/kg IP provided some antihyperalgesia in a model of neuropathic pain, but the effects were significantly enhanced when gabapentin was combined with tramadol at 3.2 mg/kg[16] or meloxicam 1 mg/kg IP.[30]

ACUPUNCTURE

Acupuncture has become more popular and accepted in veterinary medicine because of a recent increase in scientific studies investigating its mechanism of action and documenting results. The main mechanism of action for analgesia appears to be an increased release of endogenous opioids, and the analgesic effects of acupuncture are reversible with naloxone. Many of these studies have been performed in rodents.[69,81,127,131]

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38

Diagnostic Imaging

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Veterinary radiology continues to expand in both technological and interpretative capabilities. The replacement of film-based radiographs with digital radiography by many veterinary practices has improved image dissemination, archiving, and overall quality. The greater availability of ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) gives practitioners an enormous armamentarium of diagnostic options. This chapter touches on advantages and limitations of the different imaging modalities available in small mammal practice. The chapter ends with a few comments on advanced treatment modalities related to radiation therapy and interventional radiology.

GENERAL CONSIDERATIONS

Some radiographic technical principles are ubiquitous regardless of the species involved. These include proper restraint, maintenance of radiation safety, practical considerations for unstable patients, and proper positioning.

Chemical restraint is recommended for most small mammal radiographic examinations. Isoflurane or sevoflurane delivered by facemask is convenient and safe. In excitable or fractious animals, induce anesthesia in an induction chamber and use a facemask for maintenance. In other instances, injectable agents can be used for short examinations. Sedative protocols are detailed in Chapter 37. For lengthy procedures, intubating the animal is preferable, but this can be difficult or impossible in small species.[36]

Depending on local and state laws, manual patient restraint techniques can sometimes be implemented for making radiographs, primarily with tractable rabbits and guinea pigs. Whether the patient is manually or chemically restrained, always maintain strict adherence to radiation safety principles. The basics of radiation safety can be boiled down to *time, distance,* and *shielding*.[39] Efforts should be made to reduce the patient and restrainer's *time* exposed to ionizing radiation. Lower exposure settings and reduced number of retakes are effective ways to reduce time of exposure. Increasing the *distance* from the primary source of radiation is the single most effective method to reduce exposure to the restrainer. If a patient is properly positioned without manual restraint, for example, with the use of foam troughs, wedges, or both and taping the limbs in position, there is no reason for anyone to be close to the radiology table during exposure, even if a lead apron is worn (Fig. 38.1). Even one step back from the table exponentially reduces one's exposure to the radiation.[6] Barriers *(shielding)*—such as lead gloves, aprons, and walls—are effective means of radiation protection. However, lead gloves will not protect the restrainer from the primary beam radiation (the area outlined by the collimator light). Leaded garments will protect only from the scatter radiation emanating from the tube, patient, and table (Fig. 38.2A–B).

Proper restraint allows for proper positioning. Improper positioning is a common source of radiographic misinterpretation. In radiography, orthogonal (90-degree) projections allow us to pinpoint the exact location of an abnormality (e.g., is it on the patient's skin or in the body?). The more views we obtain, the more confident we can be of the presence of a radiographic abnormality (Fig. 38.3). Obliquity should be minimized, especially for ventrodorsal or dorsoventral projections. Properly positioned ventrodorsal and dorsoventral radiographs are ideal for assessing symmetry from left to right and are crucial when performing standardized measurements on radiographic images.[8,12,36,37] Symmetry is also crucial for interpreting cross-sectional imaging modalities such as CT and MRI.



Fig. 38.1 Appropriate positioning of this guinea pig is facilitated by chemical restraint (sedation), as well as mechanical restraint (tape). Other tools for restraint can include foam wedges or troughs, sandbags, or lead gloves. This enables optimal visualization of the body region of interest while concurrently minimizing the radiation dose to staff who need not be present during the exposure, as well as to the patient due to decreased retake images.

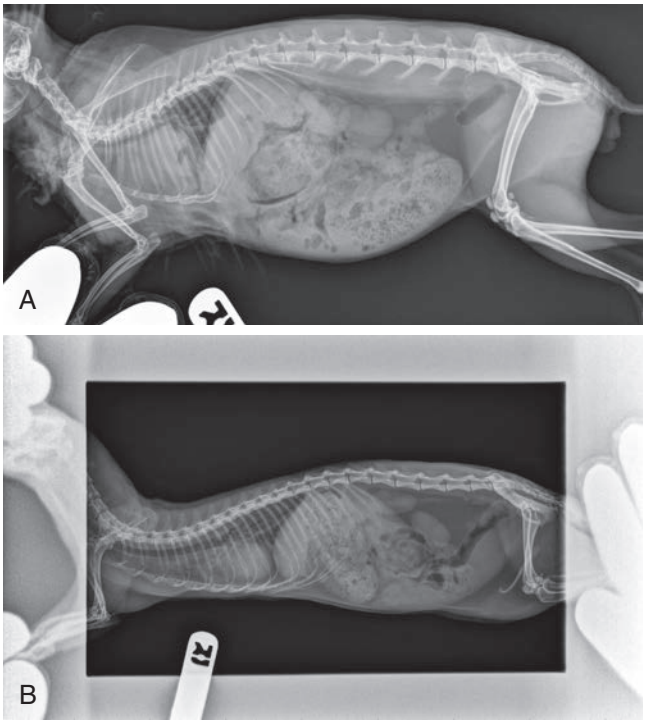


Fig. 38.2 (A) Lateral projection of a rabbit. A gloved hand is within the primary beam, in violation with radiation safety. Leaded shielding does not protect the restrainer from primary beam radiation within the confines of collimation. (B) A lateral projection of a ferret with a field of view that is beyond the confines of collimation (removed border mask). The gloved hands are visible because of off-focus and scatter radiation, not from the primary beam. This demonstrates proper use of a leaded glove to protect from lower-energy scatter radiation and not the high-energy primary beam.

WHICH IMAGING EXAMINATION TO PERFORM

Uncommon species presented for evaluation can pose diagnostic challenges. Facing this challenge, the radiologist and primary care veterinarian work as a team to determine which imaging examination will provide the most useful information. A review of the advantages and drawbacks of various imaging modalities is presented below to illustrate this decision-making process.

Practical considerations such as anesthetic requirements, cost, and availability must all be prioritized for each patient and facility. Other factors that may not be readily obvious are the objective criteria used to assess image resolution (Table 38.1).

Image Resolution

Contrast Resolution

Contrast resolution refers to the ability to distinguish between shades of gray in an image. For example, MRI, which has exquisite contrast resolution for soft tissues, is the modality of choice for identifying subtle changes in gray and white matter of the brain (Fig. 38.4).

Spatial Resolution

Spatial resolution refers the ability to distinguish two small, closely spaced objects as separate. Small animals can have small changes in anatomy when they are diseased. If the modality can resolve only 5 mm of tissue, disease processes smaller than 5 mm will be averaged as part of the surrounding tissues and appear indistinct or invisible. Spatial resolution is perhaps the greatest challenge posed to radiologists seeking to improve lesion detection and image quality in small patients.

Temporal Resolution

An imaging modality's ability to record anatomy in real time is termed *temporal resolution*. This is best depicted with ultrasonography—for example, in assessing cardiac contraction.

The Modalities

Radiography

Radiography is the most common imaging modality used by veterinarians because of its high availability, low cost, and greatest familiarity regarding technique and interpretation. Additionally, whole-body assessments are easy to obtain in small mammals, allowing for complete imaging of the thorax, abdomen, and musculoskeletal system without excessive geometric distortion.

A few points should be made regarding the radiographic imaging of very small patients. In all veterinary patients but particularly in small mammals with increased respiratory rates, motion during exposure is a problem. Therefore radiography equipment capable of producing 300 milliamperes (mA) in 0.008 second is a minimum requirement.[34,36] Most radiographs can be exposed for 0.008 to 0.016 second with excellent results. An x-ray unit's focal spot can be thought of as an adjustable narrowing of the beam of radiation emanating from the x-ray tube. A small focal spot allows for better spatial resolution and is optimal for small anatomic regions, generally under 10 cm in thickness.[4,34] Radiography of small patients scatters fewer x-rays and is therefore not constrained by anti-scatter techniques like grids. Horizontally directed x-ray beams are helpful in evaluating gravity-dependent (fluid and sediment) and non-gravity-dependent (gas) structures in both large and small patients (Fig. 38.5). A horizontally directed beam can also provide safe, effective restraint for small, fractious patients, such as ferrets being "scruffed" during x-ray exposure or birds and reptiles that can remain standing during an exposure.[14,42]

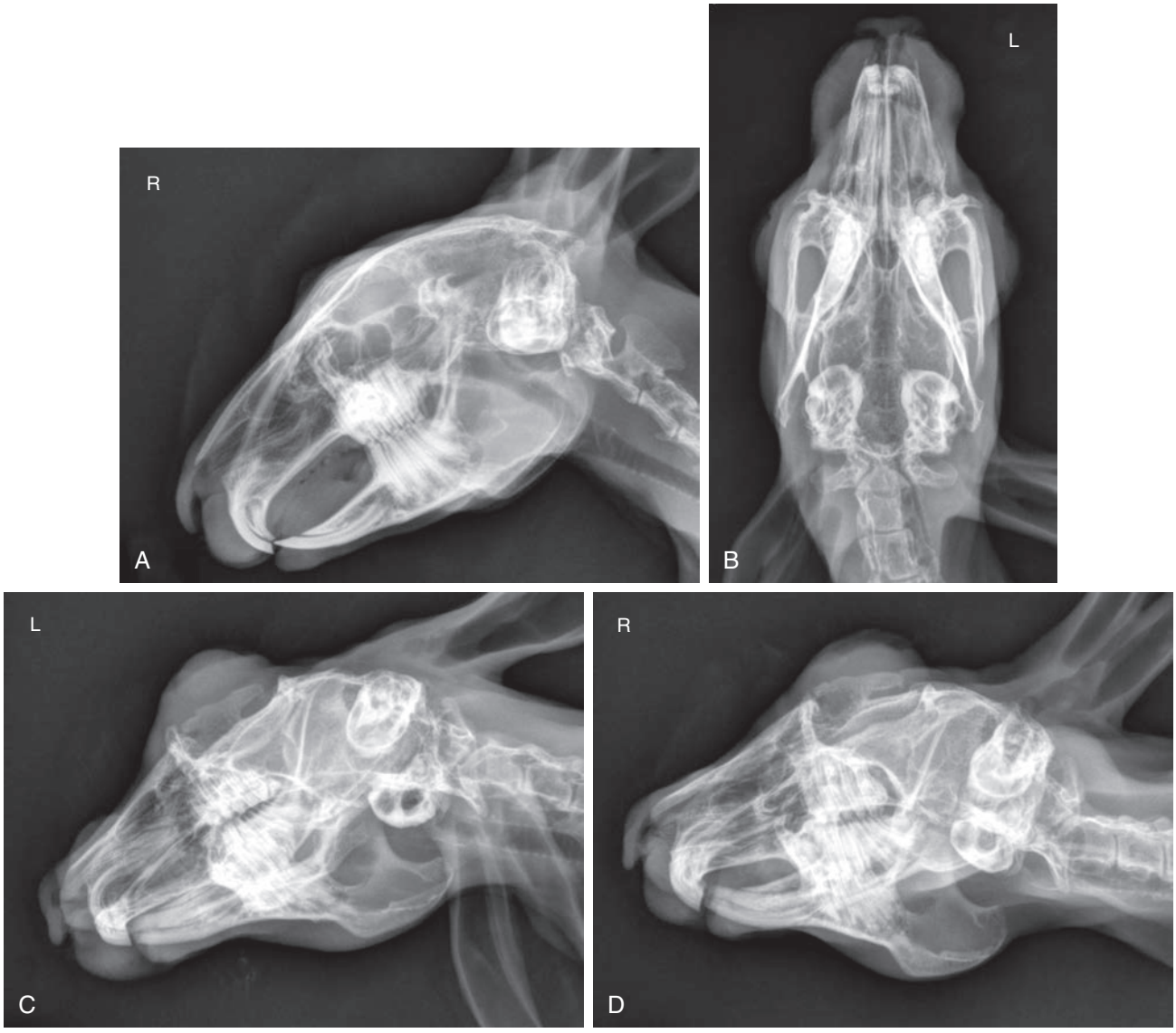


Fig. 38.3 Lateral (A), ventrodorsal (B), and lateral oblique (C, D) projections of the skull of a rabbit. The ventrodorsal view allows for direct comparison of the tympanic bullae on one projection. The marker on the oblique views denotes the more ventrally directed bulla. Oblique projections should be positioned similarly (in this case, 40 degrees ventral-laterodorsal) to make the comparisons. Despite slight differences in obliquity, the additional views (including the lateral projection) support mild sclerosis and thickening of the left tympanic bulla relative to the right.

TABLE 38.1 Comparison of the Common Imaging Modalities Available to Small Mammal Practitioners

	Cost	Availability	Anesthesia/Sedation	Radiation Production	Spatial Resolution	Contrast Resolution
Radiography	+	++++	±	++	++	++
Mammography	+	+	±	+	+++	+++
Ultrasound	+(+)	+++	Seldom	None	+++(+)	++
CT	+++	++	Usually	+++(+)	+++(+)	+++
MRI	++++	+	Always	None	++(+)	++++
Scintigraphy	+	+	±	++	+	+

Strategies for optimizing spatial resolution in film-based radiography focus on appropriate film-screen combinations. Digital radiography spatial resolution strategies are based on a multitude of factors (pixels, size of detector elements, software manipulations, to name a few). The inherent spatial resolution of film-based radiography is actually greater than that of digital radiography, but this difference is not clinically relevant. The image quality benefits of digital radiography over film are

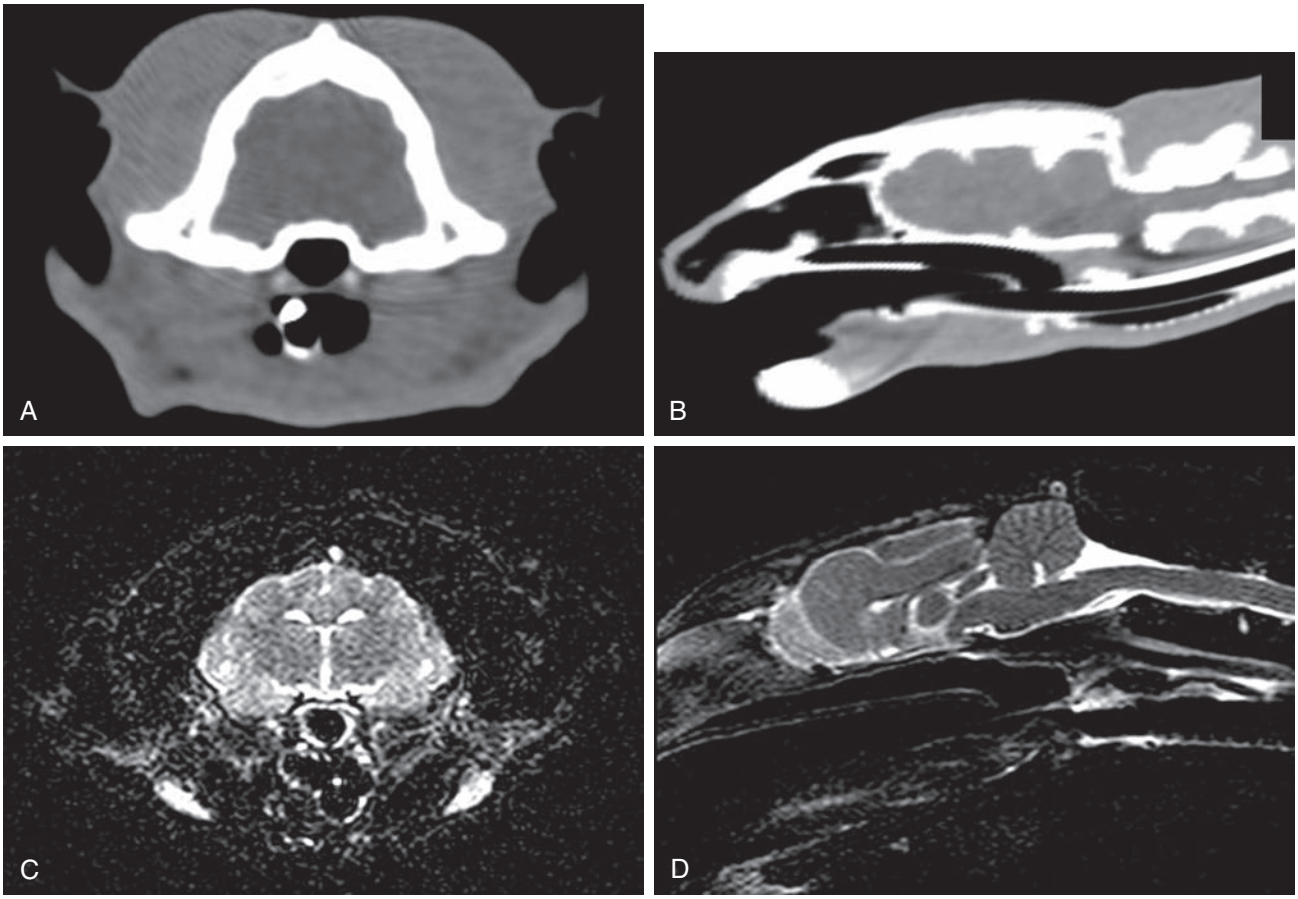


Fig. 38.4 Transverse and sagittal reformatted computed tomography (CT) images (A, B) compared with T2-weighted transverse and sagittal magnetic resonance imaging (C,D) of a normal ferret's brain. Notice the excellent contrast resolution in the MRI relative to the CT image, differentiating gray matter, white matter, and ventricles. MRIs are acquired in different planes, whereas CT images are usually acquired in a single plane (transverse) and then reformatted to produce other planes, like the sagittal view in B.

mainly related to improved contrast resolution and larger exposure latitude (acceptable image quality over a large range of exposure settings).[15,17,26,31,38] Mammography (either film-based or digital) is not as available as general radiography but has superior spatial and contrast resolution (see Table 38.1).[34,36,39]

Digital radiography is available in three general forms: computed radiography, flat panel direct digital radiography, and charged-coupled device digital radiography (CCD). Computed radiography can be simply referred to as "cassette-based," wherein a cassette captures the image, is removed from the table, and is processed in a separate reader. Manipulations are like that of film-based radiography (the reader replaces the dark room). Flat panel direct digital radiography and CCD generate an image automatically on a computer screen soon after the exposure.[39] Obvious advantages of flat panel and CCD include faster image acquisition and less manipulation of hardware that can break. However, some exotics-only practices prefer computed radiography for the ease of horizontal beam imaging, table-top acquisitions (without a grid), and exquisite image quality, often better than flat panel and almost always better than CCD. Because technology has advanced and pricing has come down, we now do not recommend CCD for veterinary practices investing in digital radiography, especially practices looking to optimize resolution of very small patients.

Contrast Radiography

An important strategy for improving contrast resolution is the use of a contrast medium (such as barium- and iodine-based compounds). Barium studies are important for assessing the anatomy and motility of the esophagus and gastrointestinal tract. Barium has excellent coating properties for evaluating mucosal abnormalities. The barium gastrointestinal (GI) series can yield important information regarding the origin of a mass, mass effect, or obstruction.[19] A contraindication of barium for GI studies is in cases of suspected viscous rupture. Barium leakage into the peritoneum can have catastrophic consequences.[11] Iodine-based contrast medium is less effective orally for evaluating the GI tract but is crucial for urogenital imaging. Intravenous urography increases the conspicuity of the kidneys, ureters, and urinary bladder. Direct injection through the urethra is useful for assessing the urethra (positive contrast urethrogram) and urinary bladder (positive-contrast or double-contrast cystograms) (Fig. 38.6).[3,7] Iodinated contrast has also historically been used for myelography to assess extradural spinal cord lesions and may still be used in cases where MRI or CT is not available.[41]

Readers are encouraged to follow proper technique in performing contrast studies.[19,33] Common mistakes include (1) forgetting to make survey radiographs (radiographs made

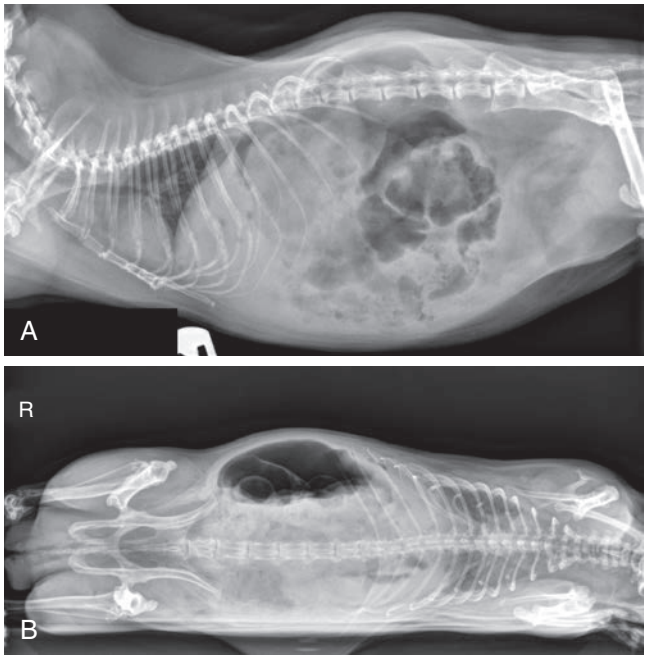


Fig. 38.5 Lateral (A) and ventrodorsal (B) projections, the latter a horizontally directed projection with the patient in left lateral recumbency. The patient is an adult male guinea pig with anorexia and abdominal distention. The horizontally directed beam allows for confirmation of pneumoperitoneum, a surgical emergency for a ruptured viscus. In this case the stomach was ruptured. Notice the gas cap and air-fluid interface in the nondependent portion of the abdomen in B. This type of radiograph must be made with the patient in left lateral recumbency and not right lateral recumbency, where a gas-cap could be confused with normal fundic gas.

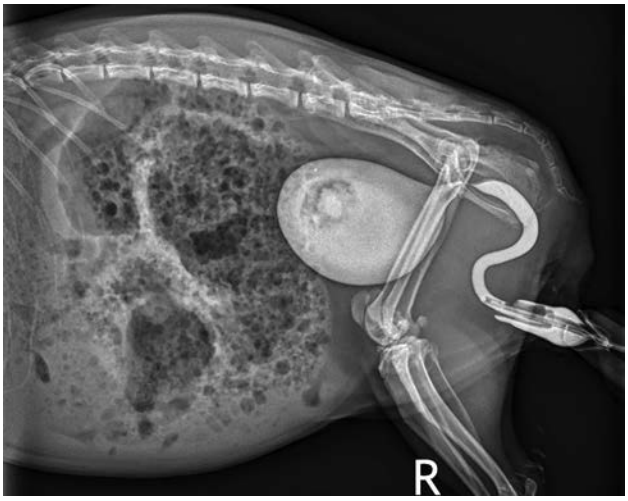


Fig. 38.6 Right lateral positive-contrast cystourethrogram of a clinically normal sedated castrated adult male guinea pig. This study can be performed easily by a general practitioner to determine the position of filling defects (calculi or masses) in the lower urogenital tract (distal ureters, urinary bladder, urethra, seminal vesicles, accessory sex glands), as well as to assess for rupture/perforation of these structures.

immediately before contrast administration); (2) too little contrast medium administered; and (3) too few radiographic views made after the contrast medium is added.

Ultrasonography

Ultrasonography provides an enormous amount of diagnostic information while at the same time being safe, seldom requiring sedation or anesthesia, and not producing any ionizing radiation. Additionally, ultrasonography allows real-time evaluation of important physiological processes such as cardiac contractility and organ perfusion.

The components that influence the image quality of ultrasound for small patients include high-frequency, broad-bandwidth transducers, electronic focusing/beam steering, tissue harmonics, and spatial compounding capabilities. Higher-frequency transducers provide better spatial resolution at the cost of diminished depth penetration. Inability to image tissues deep to the skin is generally not a problem with small mammals. A high-frequency transducer can have a large, bulky footprint (surface that touches the patient's skin), which may be impractical on very small patients. A broad-bandwidth transducer allows the operator to switch to lower frequencies when deeper structures are being imaged. Broad-bandwidth technology and electronic focusing/beam steering also provide the capabilities for image optimization with harmonics and spatial compounding, the details of which are described elsewhere.[23]

Ultrasonography provides the best images of organs that are largely composed of fluid and soft tissue. The abdomen is ideally suited to this. Gas and bone ineffectively reflect ultrasound waves, decreasing overall image quality. As a result, lung and gas-filled bowel are common barriers to lesion identification. In general, the ferret gastrointestinal ultrasound examination can provide relatively better image quality and potentially more diagnostically useful information than the largely gas-filled rabbit abdomen.

An additional important application of ultrasound is needle guidance for aspirating fluid or masses and for biopsy (Fig. 38.7B). Aspirates can be critically diagnostic for distinguishing inflammatory or infectious conditions from neoplastic processes.[2] A caveat to this is the thick, caseous material within some abscesses, which can be extremely difficult to pull into a thin needle. Neoplastic processes that exfoliate well include round cell tumors and some carcinomas. Peritoneal and pleural fluid aspirates can help to identify a cause of the fluid accumulation.[2,20] Definitive histopathologic diagnoses can be made with an ultrasound-guided biopsy sample, but this requires chemical restraint and operator skill.

Computed Tomography

Computed tomography has become more available in exotic animal veterinary practice; correspondingly, more literature is available to substantiate its diagnostic utility.[7,16] The process of acquiring CT images has traditionally required general anesthesia. Newer multidetector CT technology has increased acquisition speed to a point where immobilization devices alone may be used for some acquisitions.[24] Older CT technology (one- to four-detector CT) is still fairly common in veterinary referral practices, producing excellent images but generally requiring anesthesia because of slower image acquisition.

With CT, a beam of ionizing radiation opposite a detector rotates around a patient. The result is a computer mapping of the different x-ray-attenuating characteristics of tissues. With radiography, the three dimensions of the patient are summated to produce a two-dimensional shadow of x-ray attenuation characteristics. With CT, the third dimension (slice thickness) is

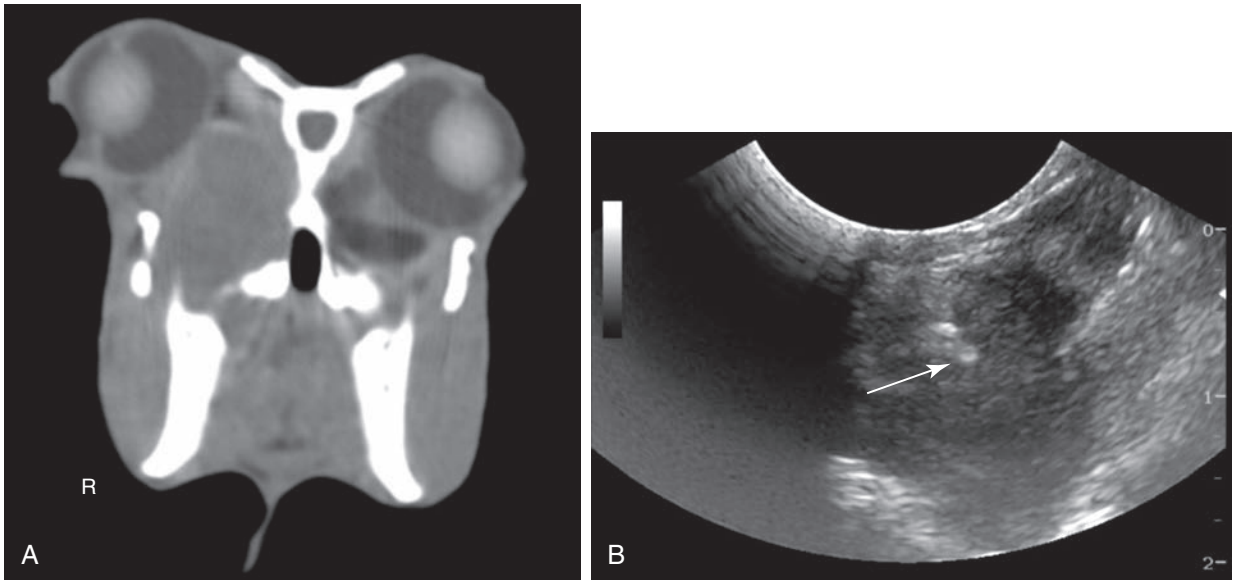


Fig. 38.7 A rabbit presenting with right-sided exophthalmos, confirmed on contrast-enhanced computed tomography (CT) (A). A rim-enhancing retroorbital mass related to a tooth root abscess was suspected from the CT exam. Color Doppler ultrasound confirmed that the mass was mainly fluid-filled with a peripheral vascular supply. Most importantly, ultrasonography aided in directing an 18-gauge needle into the mass for cytologic confirmation of an abscess (B). The *arrow* denotes the needle in the center of the mass.

thin and minimally contributes to the summed image. A major advantage of CT over standard radiography is removal of superimposed tissues that would obscure anatomy (Fig. 38.8).

A CT image includes more shades of gray (greater contrast resolution) than a radiograph. Whereas radiography provides five shades of gray (gas, fat, fluid/soft tissue, bone, metal), CT can distinguish between thousands of shades of gray, including a distinction between soft tissue and fluid. Contrast resolution is further improved with the addition of an intravenous contrast medium, increasing the conspicuity of lesions with greater blood flow or capillary permeability (see Fig. 38.7A).[5,6,16]

Clinicians can use CT for a variety of clinical situations. Subtle bone fractures are better defined with CT than with other modalities, and micro-CT examination can further shorter scan times while maintaining improved spatial resolution compared with radiography.[30] Also, CT defines extent of disease and the effect of disease on surrounding normal anatomy.[5,7,16] A well-documented benefit of CT lies in evaluating dental disease in rabbits (see Chapter 36).[2,16] The anatomy of the rabbit's mouth limits oral examination and radiography lacks sensitivity for ruling out dental disease. A CT scan can help differentiate which specific tooth root is affected in cases of severe tooth root abscessation and osteomyelitis (Fig. 38.9). Images can be reformatted into different scan planes other than the transverse plane. This allows the observer to appreciate disease, because it is oriented relative to surrounding normal tissues. Three-dimensional and multiplanar reformatting help the radiologist to communicate with surgeons, owners, and other veterinarians and help to orientate surgeons for surgical planning, including approach and regional vasculature.[1,5,7,32] At our institution, CT is an important tool for surgical planning in adrenalectomies (to assess tumor thrombus) and any thoracic surgery (to determine surgical approach and vascular environment in mediastinal masses, such as thymomas).

Cone beam CT has proved particularly clinically useful in the field of human dentistry, although its utility in veterinary medicine has only begun to be explored. This technology is more modest in terms of cost and space requirements than conventional CT; potentially permits faster scan times, as well as lower radiation dose; and does not have specific electrical power requirements.[13,27,29,35] Of further diagnostic relevance, the 360-degree scanning geometry and uniformly sized units of data acquisition of cone-beam relative to conventional (including multidetector) CT confers improved spatial resolution (as low as 0.15-mm slice thickness) in not only the transverse plane (as with conventional CT) but also in all reconstructed planes, as well as volume-rendered models.[13,27,35] Use of this technology in rabbits has already revealed numerous common dental diseases that are not apparent on routine physical examination.[28] However, the image quality of soft tissues (vasculature, etc) with cone beam CT is inferior to that of conventional CT.

Magnetic Resonance Imaging

Clinical use of MRI in small mammals is limited, despite the enormous library of literature dedicated to MRI of rabbits and rodents in research settings. Availability, cost, and long scan times are the major limiting factors. Exquisite spatial resolution of very small patients is possible with high-field-strength magnets (7 Tesla and up).[4] However, these magnets are primarily used in research settings. Most veterinary clinics practice with 1.5 T magnets or lower.[22,25] With all magnets, image quality tends to be proportional to scan time. Scanning protocols try to strike a balance between image quality and scan time. Notice that the MRI scan in Fig. 38.3 has a stippled appearance caused by a low signal-to-noise ratio. Longer scan time can improve on this.

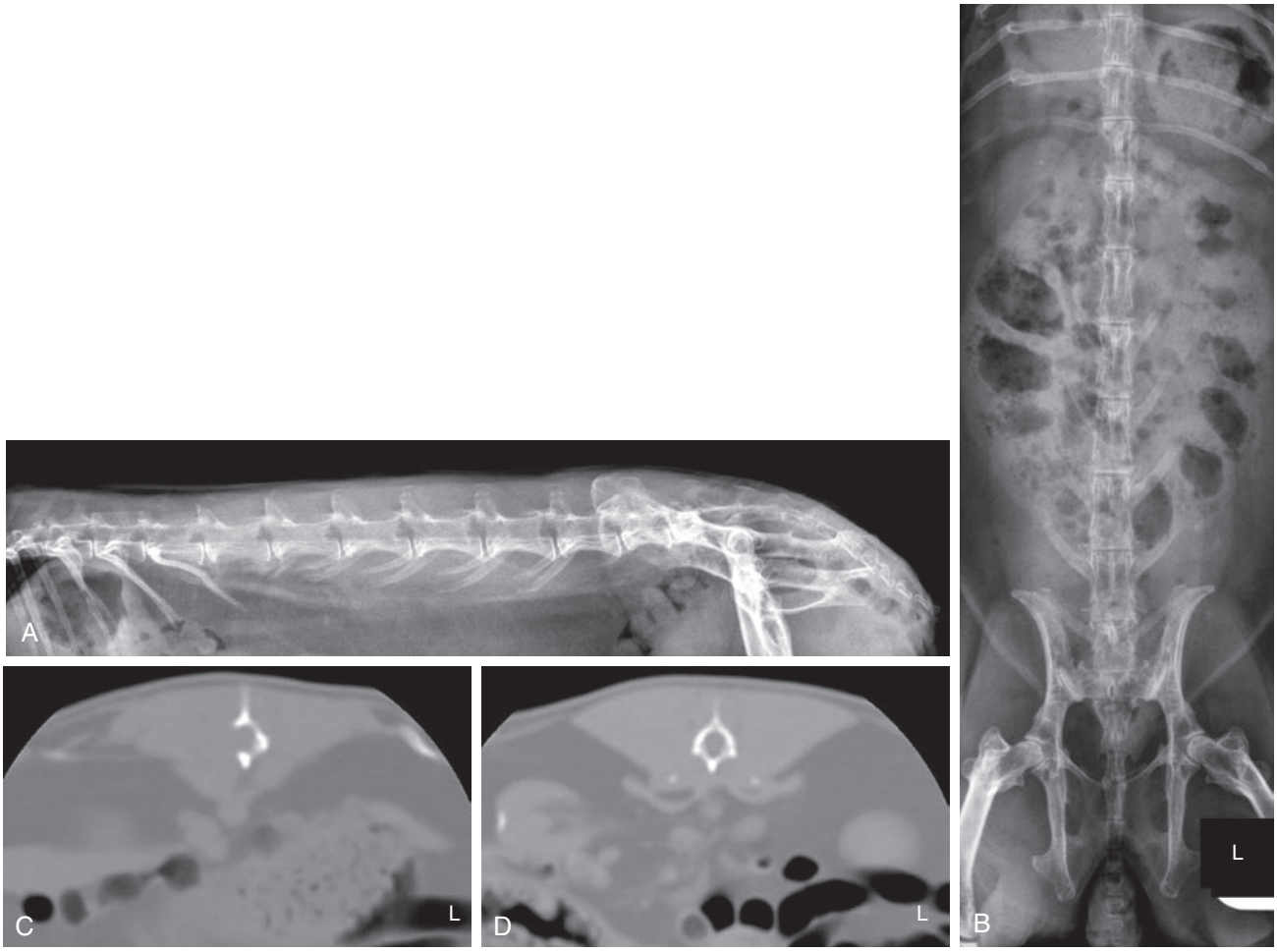


Fig. 38.8 Lateral (A) and ventrodorsal (B) projections of the lumbar vertebral column in a rabbit with progressive lumbar pain and a previous diagnosis of uterine carcinoma. Compare the radiographs with the transverse computed tomography (CT) image at the level of the last thoracic vertebral body (C). Notice the extensive bony lysis and associated soft tissue mass of the right pedicle and body. Compare this with the normal L1 vertebra caudally (D). CT removes superimposed structures that would otherwise obscure changes in anatomy on radiographs.



Fig. 38.9 A common indication for computed tomography is to assess dental disease in rabbits. From left to right, transverse, dorsal, and parasagittal images of a rabbit with expansile bony lysis of the right hemimandible secondary to tooth root abscess. (Images courtesy Dr. Peter V. Scrivani, Cornell University, Ithaca, NY.)

Magnetic resonance imaging takes advantage of the resonance properties of protons within organs, allowing for subtle differentiation in the contrast of soft tissues. Assessment of the brain and spinal cord by MRI has revolutionized the practice of veterinary neurology. As with CT, MRI also has the advantage of reducing superimposition with thin scan slices. Unlike CT, MRI scans can be acquired in different planes. As a result, MRI has a similar or even superior capacity to assess disease in relation to surrounding anatomy and to aid surgical planning.

Nuclear Scintigraphy

With nuclear scintigraphy, a radioactive substance is injected into the patient; this then localizes to a tissue of interest and emits radiation. Tissue localization of a radionuclide or radiopharmaceutical gives this modality an important advantage over all other modalities: assessment of physiological processes. For example, technetium pertechnetate, the most common radionuclide used, has similar physiological properties to negatively charged ions in the body, like iodine. Technetium can localize into tissues like the thyroid lobes, which take up iodine, to assess ion-trapping as a step in thyroid hormone production (Fig. 38.10). Radionuclides can also be bound to molecules that mimic physiologic processes. Renal scintigraphy with technetium bound to diethylenetriamine pentaacetic acid can quantitatively assess glomerular filtration rate from each kidney. Methylene diphosphonate–labeled radiopharmaceuticals localize in areas of increased bone metabolism, pinpointing areas of bone metastasis and sources of orthopedic lameness. Nuclear scintigraphy has been used clinically to evaluate tissue ischemia and necrosis of the extremities of a ferret.[9] A limitation of nuclear scintigraphy is poor contrast and spatial resolution relative to other imaging modalities, as well as the limited availability of facilities that handle radionuclides for these studies. Newer CT protocols may even begin to complement or subsume the role of scintigraphy in providing functional data, such as the use of contrast CT in evaluating glomerular filtration rate in rabbits.[43]

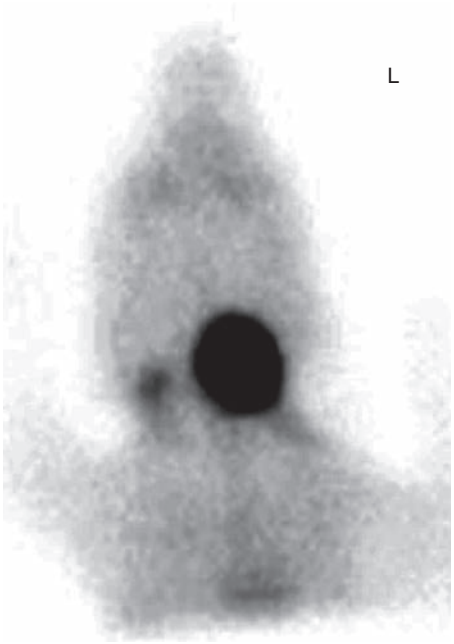


Fig. 38.10 One-year-old male guinea pig evaluated for a neck mass that was palpated on physical examination. This ventral image of the neck was obtained after technetium pertechnetate was injected intravenously (the patient's nose is at the top of the image). Pertechnetate localizes to areas of iodine uptake, as in the thyroid lobes. Notice the large amount of uptake in the area of the left thyroid lobe relative to the right. A left thyroid adenoma was diagnosed histologically. (Image courtesy Drs. Federica Morandi and Silke Hecht, University of Tennessee, Knoxville, TN.)

ADVANCED TREATMENTS

Thus far, our discussion has been limited to the use of radiation in imaging for diagnostic and prognostic purposes. Radiation oncology and interventional radiology are two veterinary specialties that work closely with diagnostic imaging to provide novel treatment options.

Radiation Therapy

Radiation therapy targets high-energy radiation at diseased tissue to destroy cancerous or other space-occupying masses. Radiation therapy has been described alone or in conjunction with surgery for the treatment of various tumors in ferrets.[10,18,21] At our institution, the most common application of radiation therapy in small mammals is in treatment of thymomas in rabbits (Fig. 38.11).

Interventional Radiology

Interventional radiology uses diagnostic imaging to direct minimally invasive procedures for diagnosis and treatment. Small needles, guidewires, catheters, and other tiny instruments are guided to areas of interest primarily by using fluoroscopy (to obtain a real-time radiographic image). Treatments are generally focused on providing an opening (e.g., stenting) or a closing (e.g., embolization) for diseased organs with a lumen. Interventional radiology has long been used by veterinary cardiologists to treat congenital heart anomalies and place pacemakers. A recent report describes the extraction of heartworms from a ferret with caval syndrome.[40] The specialty is gaining momentum for many other applications, including those in small mammals, such as the placement of stents in animals with urethral blockage and pyloric stenosis (Fig. 38.12).

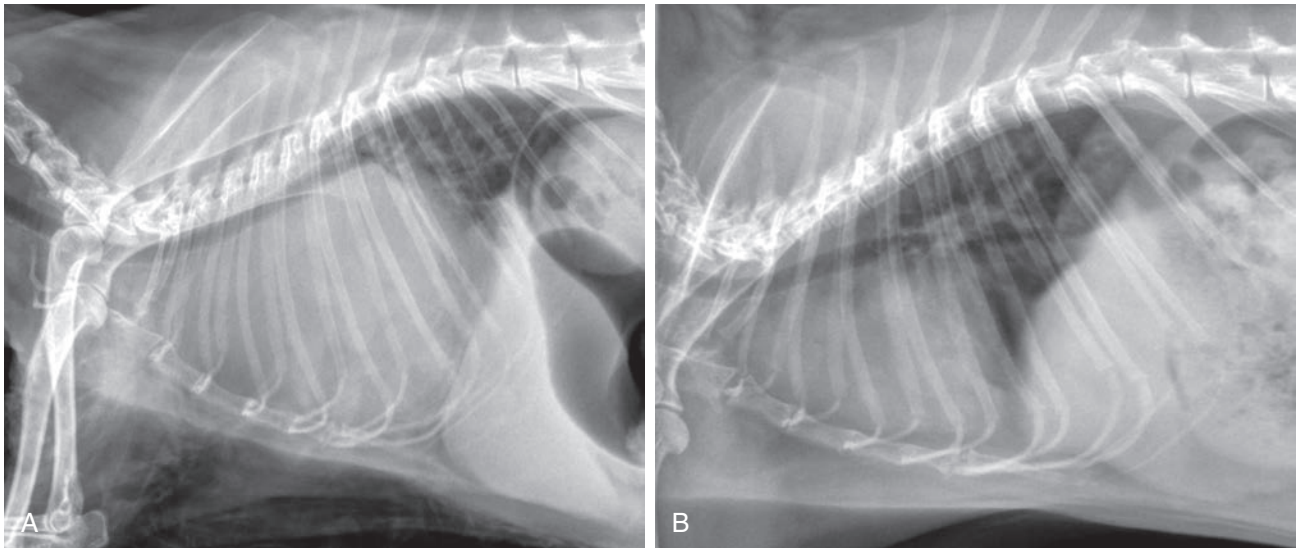


Fig. 38.11 Pre- (A) and post- (B) radiation therapy (RT) in a rabbit with a large thymoma. Radiation therapy reduced the tumor size by approximately 80% and greatly improved the patient's clinical signs of dyspnea. Notice the severe dorsal and caudal displacement of the trachea before RT and the improvement of this mass effect after treatment. (Images courtesy Dr. John Farrelly, The Animal Medical Center, New York, NY.)

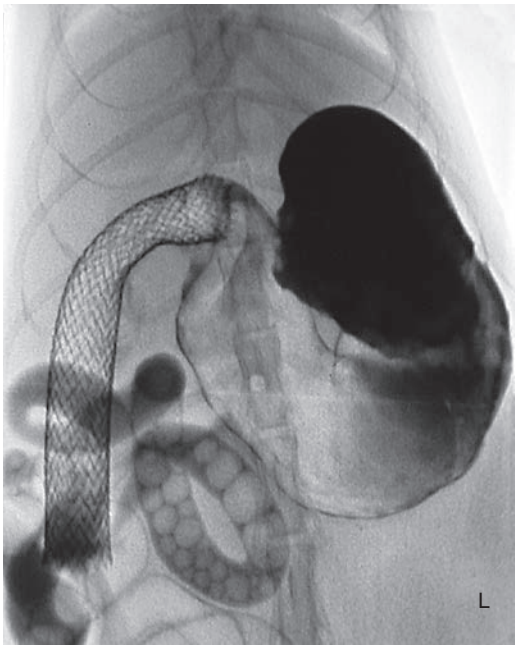


Fig. 38.12 Ventrodorsal fluoroscopic image of a ferret after a stent was placed in the pyloric sphincter and duodenum. Contrast medium outlines the stomach and intestines with most of the contrast medium settled in the fundus. The stent provides a lumen for a stenosis, caused by lymphoma, at the pyloroduodenal junction. (Image courtesy Dr. Chick Weisse, The Animal Medical Center, New York, NY.)

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39

Hematology and Biochemistry of Small Mammals

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SMALL MAMMAL HEMATOLOGY

Blood cell morphology of small mammals resembles that of domestic animals. However, establishing representative population-based hematologic reference intervals (RIs) is difficult because of the limited numbers of healthy individuals within studies, intra-species variations (age, breed, sex, diet, reproductive status), and variations in blood collection techniques and laboratory procedures.[11,78] Therefore RIs should be used as a tool rather than a sole guide for result interpretation.[13] Hematologic parameters derived from inadequate RIs may yield false-positive or false-negative results.[43] Using values from a single individual (subject-based; see Biochemistry below) to establish health and to help detect a pathologic state may be valuable for some small mammal species in which having large sample of individuals for RI studies is not feasible.[14,78]

Blood Collection and Handling

Blood collection techniques and handling are described in various chapters of this publication and other references.[10,11,80] Because of the small sample volume that can be obtained from one animal, a single lithium heparin (anticoagulant) microtainer tube is generally used in small mammals to perform both hematologic and biochemical testing.[81] Ideally, blood smears should be made from blood without added anticoagulants.[80] Additionally, submitting a properly made blood smear at the time of venipuncture prevents artifacts related to *in vitro* aging of blood cells.

General Hematologic Features of Small Mammals

Evaluation of Erythrocytes

Erythrocytes of mammals are small, anucleated, and biconcave (discocytes) cells that function to carry hemoglobin.[33] The red

blood cell (RBC) life span also varies and correlates positively with the species longevity and body mass. Thus small mammals have shorter RBC life spans when compared with larger species because of higher rates of oxidative metabolism.[15]

Rats and Mice. Hematologic parameters and reference intervals of mice and rats are influenced by many preanalytic factors such as strain, sex, age, exercise, circadian cycle, and nutrition.[2,3,43] Reference intervals for mice and rats are available in this textbook and other publications.[13,64,76]

Mature erythrocytes of rats and mice are round and biconcave with central pallor and a diameter between 5 to 7 µm.[64] Polychromasia (proportion of erythrocytes that stain more basophilic than mature erythrocytes) and anisocytosis are pronounced because of the high numbers of reticulocytes (2%–7% in adults, 10%–20% in young), which is directly related to the short erythrocyte half-life of 45 to 60 days for rats and 40 to 50 days for mice.[10,11] Low numbers of Howell Jolly bodies (nuclear chromatin remnants) and nucleated RBCs are common in normal rats and mice.[46,64] Rouleaux formation (stack-of-coins of RBCs) is rarely seen, even with inflammatory disease.[10]

Hamsters and Gerbils. The golden or Syrian hamster is the most popular research and pet hamster. Hematologic values of hamsters and gerbils can be found in this textbook and other publications.[36,49,64] While castration lowers the RBC count by 25% to 30% because of testosterone decrease, pseudohibernation in the hamster causes the red cell mass to increase because of prolongation of the erythrocyte life span.[36,46] Polychromatophilic cells and basophilic stippling are common in young and adult gerbils, likely because of the shorter erythrocyte life span (RBC half-life, 9–10 days) compared with that of other laboratory rodents.[3a,49] As in other rodents, RBC concentration is higher in males than in females.[80] Gerbils less than 8 weeks old have a red cell mass of less than 50% of the adult value and larger erythrocytes.[36]

Guinea Pigs. Guinea pigs have larger erythrocytes and a lower RBC count than do other small mammals.[80] Unlike other rodents, hematologic sex differences are not reported, and rouleaux formation is normally seen on blood smears.[49] Reference values are reported in this text and from other references.[80,84,86]

Chinchillas. Hematologic features of chinchillas resemble those of rats and mice.[62] Affinity of hemoglobin for oxygen is higher in chinchillas than in other rodents and rabbits, likely as an adaptation to their natural high-altitude environment.[57]

Rabbits. In contrast to rodents, erythrocyte parameters do not differ significantly between male and female rabbits.[80] Polychromatophilic erythrocytes as well as a few nucleated red cells and occasional Howell Jolly bodies (basophilic nuclear remnants) are seen in blood smears because of the high erythrocyte turnover rate.[50] Likewise, high numbers of circulating reticulocytes are present in adult (2%–4%) and young (3%–11%) rabbits.[53,80] Normal hematologic parameters are reported in this and other publications.[50,53,80]

Ferrets. Hematologic reference values of adult ferrets are similar to those of dogs and cats except for higher hematocrit values, hemoglobin concentration, and RBC and reticulocyte counts.[24,72] Inhalant anesthesia in ferrets may significantly and rapidly decrease the RBC mass because of splenic sequestration and hypotension.[11] Normal hematologic values have been reported for ferrets.[23,69,83,85]

Hedgehogs. There are minimal data from healthy African hedgehogs to establish true reference intervals.[35,56a] Values (mean and standard deviation) of a mixed population of healthy and ill animals have been published.[39] High numbers of nucleated RBCs, Howell Jolly bodies, and reticulocytes were found in a study of healthy juvenile European hedgehogs.[69]

Interpretation of Abnormal Erythrocyte Parameters

Most disease processes causing anemia in other species also cause anemia in small mammals. The number of circulating reticulocytes (young erythrocytes) is a useful indicator of the bone marrow's response to anemia and the most practical approach to classify anemia.[34] Reticulocytes stain basophilic (polychromatophilic), are larger, and contain less hemoglobin than mature erythrocytes. Therefore, if reticulocytes are present in sufficient numbers, a high mean corpuscular volume and a low mean corpuscular hemoglobin concentration are expected. However, polychromasia should not be overinterpreted, because most small mammals, especially gerbils, normally have high percentages of polychromatophilic cells due to the short erythrocyte life span.[49] Anisocytosis, basophilic stippling, and Howell-Jolly bodies are other indicators of a bone marrow response to anemia. Nucleated RBCs can be associated with regenerative responses or secondary to alterations in the blood/bone marrow barrier when reticulocytosis is not present (inappropriate metarubricytosis). In rabbits, increased numbers of nucleated RBCs have been associated with acute infectious processes, possibly related to endothelial damage and regeneration. Causes of regenerative anemia are blood loss and hemolysis, whereas nonregenerative anemia is the result of defective or decreased erythropoiesis and is nonspecific.[11] A maximal bone marrow response may be seen approximately 4 days after the inciting cause of hemolysis or blood loss. Therefore anemia may be initially classified as nonregenerative or preregenerative until enough time has elapsed.[34]

Interpreting the hematocrit along with the total protein concentration is also recommended. A hematocrit below the reference interval with a low total protein concentration suggests blood loss, while a mild normocytic, normochromic, nonregenerative anemia and normal total protein concentration may indicate anemia of chronic disease.

Other clinicopathologic parameters such as neutrophil count, platelet count, and total bilirubin level may provide useful information to determine the underlying cause of the anemia. In general, panleukopenia (nonregenerative anemia,

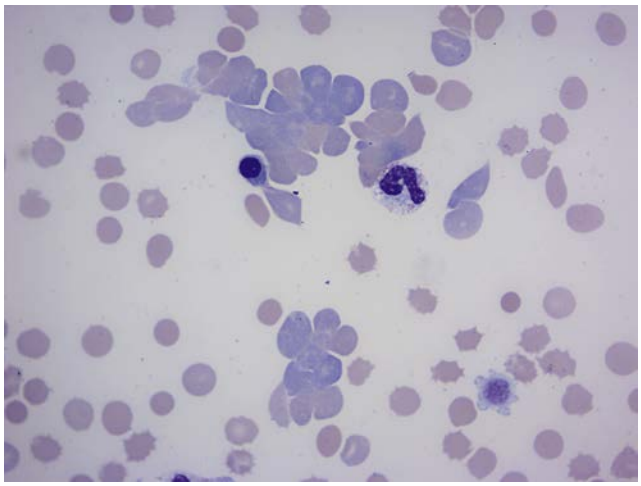


Fig. 39.1 Autoagglutination (clumping) of erythrocytes in the blood film of a guinea pig with immune-mediated hemolytic anemia. A nucleated RBC, polychromatophilic erythrocytes and a neutrophil displaying toxic change (cytoplasmic basophilia) (left to right) are present. (Wright-Giemsa, magnification ×100.)

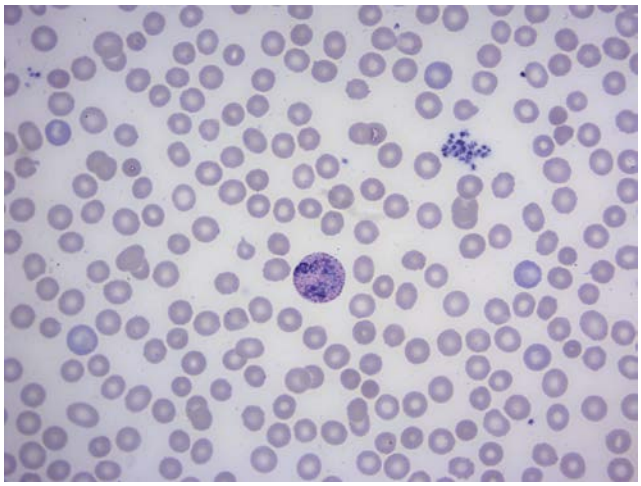


Fig. 39.2 Hypochromic erythrocytes showing increased central pallor in the blood film of a rabbit. A heterophil (middle) and a small platelet clump (top right) are also present. (Wright-Giemsa, magnification ×100.)

neutropenia, and thrombocytopenia) indicates bone marrow hypoplasia. In intact female ferrets, high levels of estrogen due to prolonged estrus may cause bone marrow suppression.[72] An animal with a mild nonregenerative anemia and an inflammatory leukogram likely has anemia of chronic disease, including malignant neoplasia and infectious disease. Pasteurellosis, dental disease, pneumonia, pododermatitis, and pyometra are potential causes of anemia of chronic disease in rabbits.[53] Anemia of chronic inflammation may be seen in ferrets with endocrinopathy, gastrointestinal disease, neoplasia (lymphoma), and, to a lesser degree, infectious diseases.[11] In general, regenerative anemia and hyperbilirubinemia suggest hemolysis, whereas anemia and hypoproteinemia may indicate blood loss. Immune-mediated hemolytic anemia has been reported in laboratory rabbits with lymphoma,[51] and occurs in rare cases of small mammal species in clinical practice (Fig. 39.1). Fisher rats with large granular lymphocyte leukemia may have associated immune-mediated anemia, which, as in other species, is characterized by numerous spherocytes (see below, Interpretation of Abnormal Leukocyte Parameters).[13] A diagnosis of hemolytic anemia will grant a blood smear examination to search for erythrocytic hemoparasites.[49] However, hemoparasites are rarely seen in pet rodents.[62]

Microcytic hypochromic regenerative anemia suggests chronic blood loss, especially due to gastrointestinal parasites (Fig. 39.2).[49] Heavy lice infestations, occasionally seen in rats and guinea pigs, can also cause chronic blood loss.[62] Ectoparasitic and endoparasitic infestations with secondary blood loss anemia are common in wild European hedgehogs admitted in rehabilitation centers.[69] In ferrets, *Helicobacter*-associated duodenal ulcers are a common cause of regenerative anemia secondary to blood loss.[11,23] Trauma, severe flea infestation, hematuria, bleeding uterine adenocarcinomas, and endometrial hyperplasia are causes of regenerative anemia in rabbits.[51,53] Regenerative anemia with increased numbers of

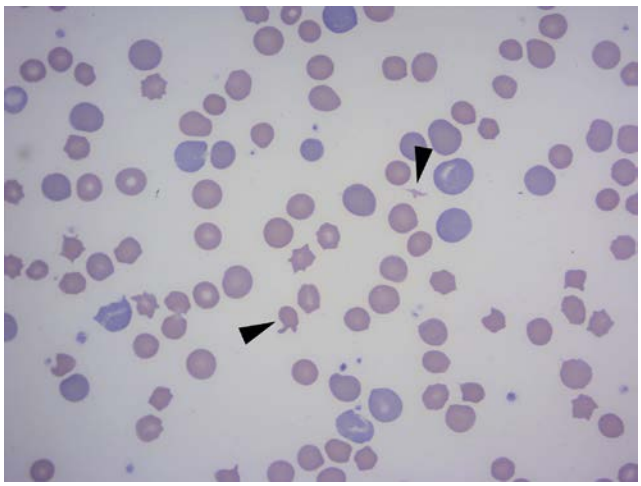


Fig. 39.3 An acanthocyte *(left arrowhead)* (erythrocyte with unevenly spaced projections of different lengths) and schistocyte *(right arrowhead)* (erythrocyte fragment) in the blood film of a rabbit. (Wright-Giemsa, magnification ×100.)

nucleated RBCs, hypochromasia, and basophilic stippling could suggest lead toxicosis.[51]

Morphologically, abnormal erythrocytes (poikilocytes) documented in domestic animals may be also observed in small mammals and are generally associated with the same physiopathologic mechanisms. For example, Heinz bodies may be seen with oxidant injury, whereas acanthocytes may be present in animals with severe liver disease (Fig. 39.3).[13]

Erythrocytosis, which is a combination of a high hematocrit, RBC count, and hemoglobin concentration, is generally relative and secondary to dehydration. A high serum protein concentration is expected.

Evaluation of Leukocytes

Leukocytes are relatively similar in appearance and function across most mammal species with some differences.[17] Nevertheless,

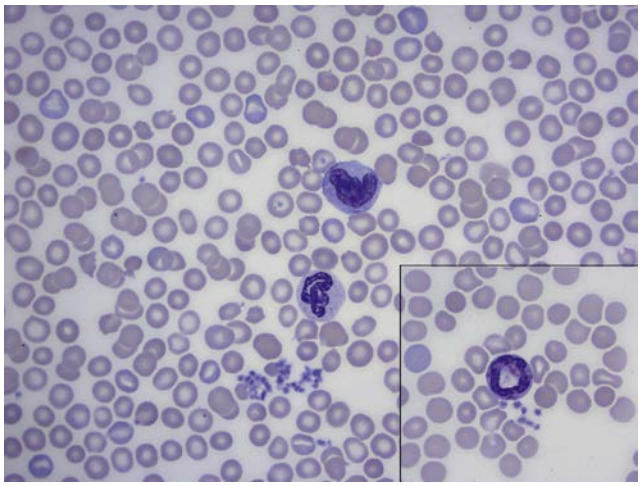


Fig. 39.4 Monocyte (top), neutrophil (bottom), and ring eosinophil (insert) in the blood film of a rat. (Wright-Giemsa, magnification × 100.)

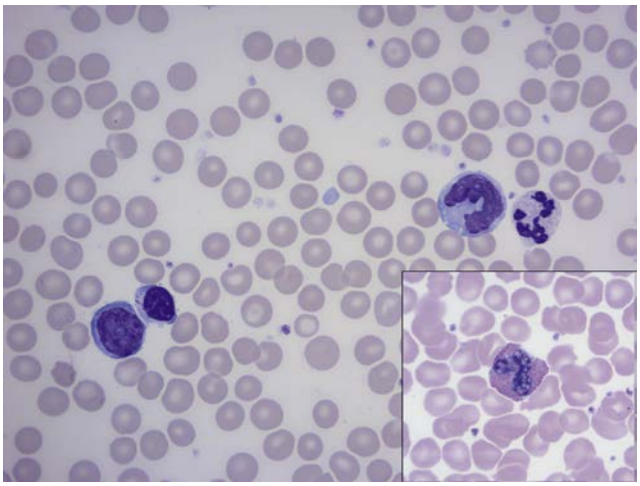


Fig. 39.5 Two lymphocytes (large and small), monocyte, and neutrophil (left to right) and eosinophil (insert) in the blood film of a guinea pig. (Wright-Giemsa, magnification ×1000)

numbers, composition, and staining properties of neutrophil granules vary between species. Basophils are very uncommon in rats, mice, and hamsters but may account for up to 30% of rabbit leukocytes.[53] Evaluation of leukocytes should include a total white blood cell (WBC) count, as well as a differential count, with percentages and absolute numbers of each type of leukocyte.[17,64]

Rats and Mice. Lymphocytes are the most common white blood cell (approximately 75%), followed by neutrophils.[64] As rodents age, the proportion of lymphocytes decreases whereas that of neutrophils increases.[46] Small or large lymphocytes with slightly increased amounts of cytoplasm and large granular lymphocytes can be present.[64] Neutrophils may have dust-like eosinophilic cytoplasmic granules.[11] Granulocytes of mice and rats occasionally have a doughnut-shaped, nonlobed nuclei (ring forms).[46] These ring forms may be present in normal animals but generally reflect accelerated granulopoiesis (Fig. 39.4).[46] Eosinophils comprise up to 7% of the WBC differential and contain numerous small, eosinophilic intracytoplasmic granules.[11]

Hamsters and Gerbils. Leukocytes of hamsters and gerbils are similar in structure and proportions to those of rats and mice.[11] In hamsters, lymphocytes, predominately small with fewer large forms, are the main leukocyte, comprising 60% to 80% of the WBCs. The leukocyte count decreases to 2500 cells/μL in Syrian hamsters during pseudohibernation.[11] A nocturnal increase in the WBC count and proportions of neutrophils has been observed.[11] Neutrophils in hamsters are frequently referred to as *heterophils* and resemble eosinophils because of eosinophilic rounded or rod-shaped cytoplasmic granules.[11,46] Hamster eosinophils normally are seen in very low numbers and contain rod-shaped rather than rounded granules present in other rodents.[46] In gerbils, lymphocyte numbers are higher in males than in females, resulting in a 6:1 lymphocyte to heterophil ratio.[36]

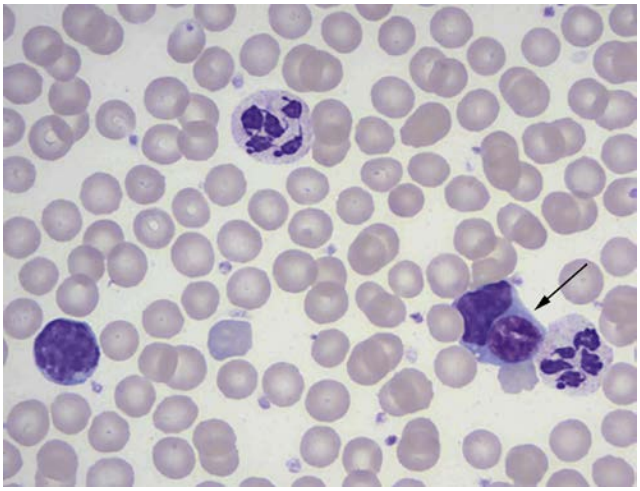


Fig. 39.6 Kurloff cell *(arrow)* with a large intracytoplasmic eosinophilic inclusion body in the blood smear of a guinea pig. A lymphocyte (left) and two heterophils (middle and bottom right) are also present. (Wright-Giemsa, magnification × 1000)

Guinea Pigs. In normal guinea pigs, lymphocytes and fewer numbers of heterophils, the equivalent of the neutrophil in other species, comprise most of the WBCs.[66] Heterophils (pseudoeosinophils) have eosinophilic cytoplasmic granules.[11] Eosinophils are larger than heterophils, with less segmented nuclei and round, bright red cytoplasmic granules (Fig. 39.5).[11,84] Small lymphocytes are more numerous than large lymphocytes, which may contain azurophilic granules.[84]

The Kurloff cell is a mononuclear cell unique to guinea pigs and capybaras that contains a single large cytoplasmic inclusion body and may account for up to 3% to 4% of the leukocytes.[11,84] The inclusion is comprised of eosinophilic, finely granular mucopolysaccharides and is located within a vacuole in the cytoplasm, displacing the nuclei (Fig. 39.6).[11,86] Kurloff cells are seen in increased numbers in adult females, pregnant females, and in males and females after exogenous estradiol and testosterone administration.[49,63,82] Kurloff cells have natural killer and natural cytotoxic activity.[63]

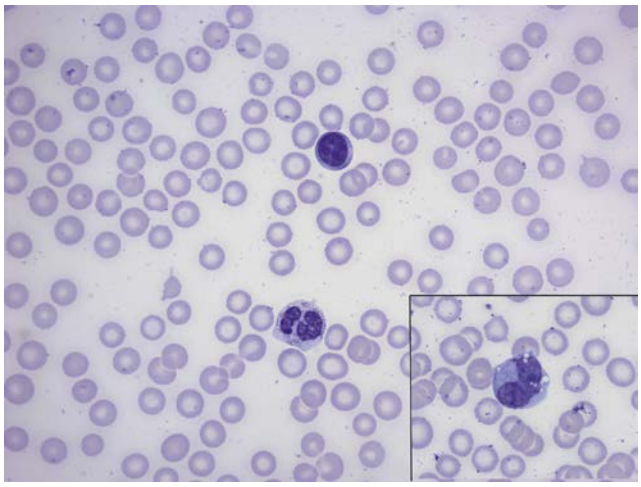


Fig. 39.7 Neutrophil with faint eosinophilic cytoplasmic granules (middle), lymphocyte (top), and monocyte (insert) in the blood smear of a chinchilla with anemia. Note hypochromic erythrocytes in the background. (Wright-Giemsa, magnification × 1000)

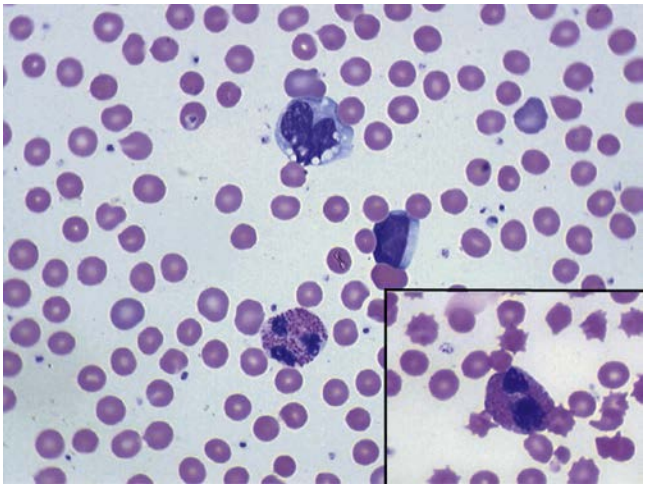


Fig. 39.8 Monocyte, lymphocyte, heterophil (top to bottom), and eosinophil (insert) in the blood smear of a rabbit. (Wright-Giemsa, magnification × 1000)

Chinchillas. Lymphocytes are the predominant leukocyte, followed by neutrophils.[67] Mature neutrophils of chinchillas may be hyposegmented and contain faint eosinophilic cytoplasmic granules (Fig. 39.7).[11] Monocytes, eosinophils, and basophils are present in low numbers.[67]

Rabbits. Many factors, including circadian cycles, nutrition, age, and breed, affect the WBCs of rabbits.[53] Leukocyte numbers are lower in newborns and juveniles younger than 6 to 12 months of age.[64] Neutrophil-to-lymphocyte proportions vary with age, from 1:2 in 2-month-old rabbits to 1:1 in adults, with the highest neutrophil numbers present in old rabbits.[11] Lymphocytes are reported as the predominant leukocyte.[50,53] Most lymphocytes are small (RBC size), with occasional large lymphocytes, which occasionally display cytoplasmic azurophilic granules.[17,51] The main granulocytes are often referred to as *heterophils* because of their large cytoplasmic granules that stain dark pink with Romanowsky stains.[11,64] Nevertheless, rabbit heterophils are functionally equivalent to neutrophils in other mammals.[11] Eosinophils can be differentiated from heterophils by their larger rounded granules that tend to fill the cytoplasm and are bright red to pink-orange staining (Fig. 39.8).[11,17,50] Unlike other mammal species, basophils are common in rabbits and may comprise up to 30% of the WBC differential but generally account for 2% to 5% of the WBCs.[50] The cytoplasm of basophils contains numerous purple to black granules (Fig. 39.9).[64]

Ferrets. Hematologic parameters of ferrets are similar to other domestic carnivores, with some differences, including a slightly lower WBC count with a reference interval that ranges from 3000 to 16,700 cells/μL.[37,71] Neutrophils are the predominant leukocyte, with the exception of ferrets younger than 5 to 7 months, in which lymphocytes are the main leukocyte.[11,71,85] However, in a recent study of 111 healthy ferrets, lymphocytes comprised 53% of the WBC differential,

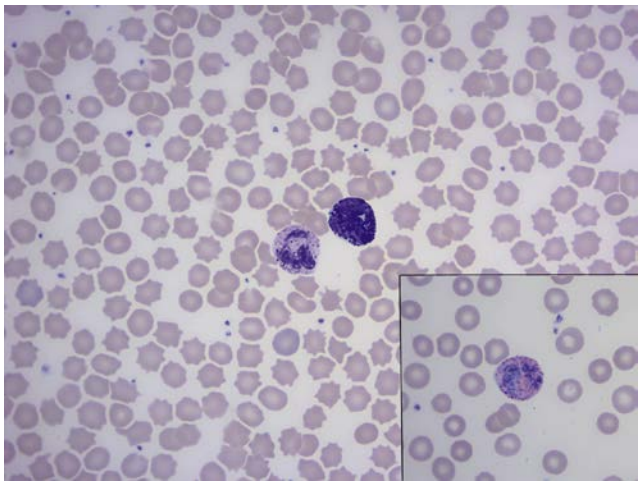


Fig. 39.9 Heterophil showing toxic change (basophilic granules and hypogranulation) (left) and basophil (right) in the blood film of a rabbit. Note the normal heterophil (insert) for comparison. (Wright-Giemsa, magnification × 1000)

closely followed by neutrophils (43%).[37] Eosinophil granules are rounder and more numerous than those of neutrophils (Fig. 39.10).[85] Small and large lymphocytes are reported in ferrets.[85]

Hedgehogs. Leukocyte morphology of African hedgehogs is similar to other domestic carnivores (Fig. 39.11).[11] A study of European hedgehogs found that lymphocytes were the predominant leukocyte, and basophils were increased in numbers compared with other species.[69]

Interpretation of Abnormal Leukocyte Parameters

In general, neutrophil/heterophil numbers increase with inflammation associated with invading bacterial microorganisms.[11] Similar to other mammals, an acute inflammatory response is characterized by a neutrophilia with increased numbers of bands (left shift) and often a monocytosis.[62] However,

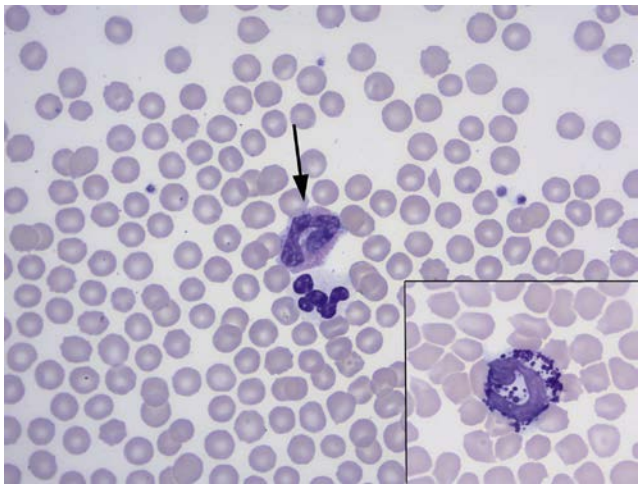


Fig. 39.10 Eosinophil *(arrow)*, neutrophil, and basophil (insert) in the blood film of a ferret. (Wright-Giemsa, magnification ×1000)

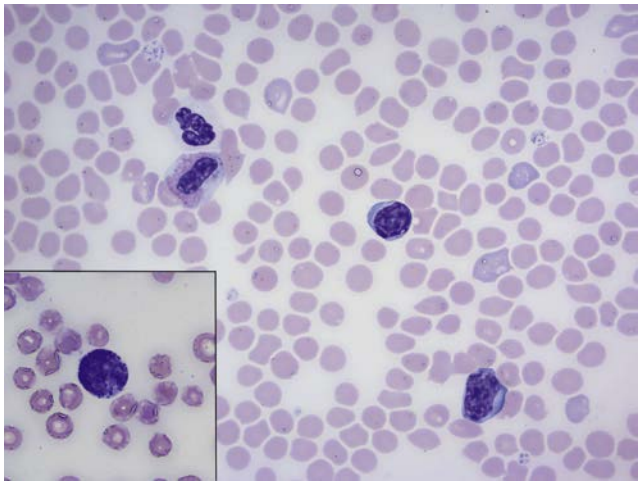


Fig. 39.11 Neutrophil, eosinophil, two lymphocytes (top left to bottom right), and basophil (insert) in the blood film of a hedgehog. (Wright-Giemsa, magnification × 1000)

some small mammals like chinchillas and guinea pigs may have only increased proportions of heterophils (reverse of the normal distribution) without a leukocytosis in early inflammatory stages. Likewise, significant leukocytosis (>15,000 cells/μL) or a left shift is not common in rabbits with acute systemic inflammation.[17] Instead, a leukopenia with a normal differential or a normal WBC count with a heterophil-dominated differential may be observed.[62] In ferrets, leukocyte numbers above 20,000 cells/μL and a left shift are not commonly seen with inflammatory disease,[11] and chronic inflammation may result in leukopenia.[83] In mice and rats, circulating bands are uncommon, and the degree of the inflammatory response is less pronounced; even mild increases in neutrophils may be significant in these species.[64] Thus, in small mammals, the presence of immature cells like bands and toxic changes or a change in the neutrophil/lymphocyte ratio are more reliable indicators of inflammation than the total WBC and differential counts.[11]

Illness, handling, or trauma may cause a leukocytosis characterized by a neutrophilia and lymphopenia due to endogenous glucocorticoid release.[17] This may occur simultaneously with a compensated inflammatory response, making interpretation difficult. In rats and mice, cathecholamine release (fight/flight response) increases both lymphocytes and neutrophils because of the demargination of neutrophils.[13,64]

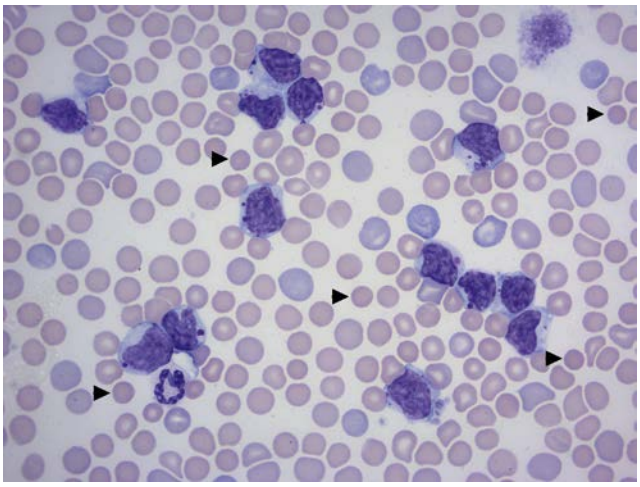


Fig. 39.12 Marked leukocytosis characterized by large granular lymphocytes in a Fisher rat with large granular lymphocyte leukemia. Numerous smaller erythrocytes without a central pallor, spherocytes *(arrowheads)*, and polychromatophilic erythrocytes are also present in the background. (Wright-Giemsa, magnification × 1000)

Large granular lymphocyte (LGL) leukemia is a common cause of death in aging Fisher 344 rats and has been occasionally reported in Wistar-Furth rats.[70,75] There is a single report of LGL leukemia in ferrets.[6] This leukemia likely originates in the spleen and is characterized by large lymphocytes with natural killer activity and prominent cytoplasmic azurophilic granules (Fig. 39.12).[13,75] In Fisher rats, LGL leukemia is often associated with immune-mediated hemolytic anemia with spherocytosis and reticulocytosis, as well as thrombocytopenia.[75] Myeloid leukemia is rare in rats.[13] Cavian leukemia (acute lymphoblastic leukemia) occurs rarely in young adult guinea pigs and presents with leukocyte counts that range from 25,000 to 500,000 cells/μL, lymphadenopathy, and hepatosplenomegaly with neoplastic infiltrates.[82] Ferrets with lymphoma may have a lymphocytosis and occasionally neutropenia and thrombocytopenia.[71]

Similar to other mammals, differential diagnoses for eosinophilia are hypersensitivity responses and tissue parasites rather than parasites in the intestinal lumen.[73] Moderate to severe eosinophilia may be seen in ferrets with eosinophilic gastroenteritis or heartworm disease.[71]

Monocytosis, usually with neutrophilia or a left shift, generally reflects increased demand of tissue macrophages, whereas a mild monocytosis combined with a mild neutrophilia and lymphopenia may be present with a glucocorticoid response.[10]

Neutropenia may result from overwhelming acute inflammatory response (usually with a left shift) or secondary to decreased neutrophil production resulting from primary bone marrow disease.[62] Leukocyte counts as low as 3000 to 4000 cells/μL occur in normal ferrets and should not be interpreted as leukopenia.[71]

Evaluation of Platelets

Platelets are small (1–3 μm) rounded to oval to elongated, pale, basophilic anucleated cell fragments derived from the cytoplasm of megakaryocytes that prevent bleeding and have a major role in inflammation.[34] Compared with other species, platelet counts in mice and rats are higher, with reference intervals as high as 1600 × 10^3 cells/μL and 1450 × 10^3 cells/μL, respectively.[11] Mouse and rat platelets may spontaneously activate or aggregate in response to stimuli, resulting in platelet clump formation.[64] Therefore platelet counts of rats and mice are often inaccurate due to clumping and the underestimation of platelet counts by some hematologic analyzers because of the small size of rodent platelets.[64] Thrombocytopenia occurs in female ferrets in estrus as well as in females with hyperestrogenism exhibiting severe anemia and marked thrombocytopenia.[64]

Interpretation of Abnormal Platelet Numbers

Thrombocytopenia is a common laboratory finding in small mammals and is often spurious because of blood collection difficulties and platelet clumping.[64] Therefore blood smear evaluation and platelet estimation are recommended to confirm low automated platelet counts. True thrombocytopenia may be caused by decreased production (hypoplastic bone marrow) or secondary to destruction or consumption of platelets.[34] Marked thrombocytosis, without significant leukocytosis, may be the only evidence of inflammation in some small mammal species like chinchillas.[67] Iron deficiency anemia due to chronic hemorrhage and accelerated erythropoiesis are other conditions that may result in thrombocytosis.[34]

BIOCHEMISTRY

Reference Intervals: Test Interpretation

All laboratory data are compared to a "normal" set of values or RIs that are considered representative of health. In the absence of RIs, laboratory data are meaningless. Data interpretation in veterinary laboratory medicine has traditionally used cross-sectional, population-based RIs that can prove problematic in exotic species medicine given the large sample numbers necessary for generating representative RIs. Current recommendations for establishment of RIs ideally require 120 healthy individuals, although 40 is the minimum acceptable number.[25] With many exotic pet species, biochemical RIs are lacking, and those that are available may be inappropriate. Using these sets of RIs for test interpretation can be misleading and result in either not detecting or falsely identifying disease states. The risk of clinical misinterpretation of patient values outside of RIs is mitigated if the clinician is fully informed as to how the intervals were generated and therefore how representative they truly are. Selected biochemical values for rodents, rabbits, ferrets, and hedgehogs are available in this and other publications.[37,38,50,54]

Subject-based RIs derived from longitudinal data may provide a viable alternative to population-based RIs for exotic species.[78] Subject-based RIs allow data from a sick animal to be compared with values obtained from that individual in health. Changes between two consecutive values in an individual patient can be identified as significantly different by using a reference change value (RCV) or critical difference value, expressed as a percentage change. The RCVs can be calculated from biological variation data that can be obtained from relatively few animals over time. Once more data on biological variation are published for exotic species, RCVs will be available to assist in data interpretation in the absence of RIs. Nondomestic species with published biological variation data include Dumeril's monitor lizards, rats, and bald eagles.[5,14,41]

Preanalytical Variation

Preanalytical variation in small mammals occurs as a result of differences in sampling sites, anesthesia, stress, diet, age, pregnancy, sex, fasted or nonfasted state, and seasonal variation. Information regarding these variables are useful in data interpretation. The more characteristics shared by your sample and the samples used to generate the data for the RI used for test interpretation, the more accurate will be the interpretation. Some known preanalytical effects are listed below.

Blood Collection Site

Test values differ as a result of how the blood sample was obtained. In mice, samples collected from the retroorbital venous sinus have lower concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), protein, albumin, triglycerides, total cholesterol, and creatinine and higher glucose values compared with samples from the submandibular vein.[16,21] In rats, creatine kinase (CK) and AST concentrations are higher in blood samples taken from the retroorbital sinus than from the heart.[4] Using a consistent site for blood collection in a given species will help to mitigate the effects of preanalytical variation due to collection site. Different blood collection methods also result in varying degrees of hemolysis, which can cause spurious results for multiple analytes.

Anesthetics

In rabbits, isoflurane and halothane produce changes in some analytes relative to preinduction concentrations. In one study, halothane administration significantly increased serum glucose, ALT, AST, urea nitrogen, and creatinine levels; isoflurane resulted in similar effects, although ALT level was not significantly impacted. In some cases, the increases resulted in values above the population-based RI for rabbits. The effects persisted up to 120 minutes after anesthesia was discontinued.[29] Ketamine-xylazine and ketamine-diazepam injections in rabbits caused increases in urea nitrogen and creatinine above the upper limit of the RI up to 24 hours after injection; significant increases in ALT and AST relative to baseline were also reported. In contrast, fentanyl-droperidol sedation produced no effects on the parameters measured (AST, ALT, alkaline phosphatase [ALP], gamma glutamyl transpeptidase [GGT], urea nitrogen, creatinine, phosphate, and potassium).[30]

Pregnancy

In pregnant New Zealand white rabbits, total protein, albumin, glucose, cholesterol, calcium, urea nitrogen, and creatinine levels decreased significantly during the middle or late periods of gestation.[52] Relative to nonpregnant females, mean and/or

median RI values for pregnant Wistar Hannover and Sprague-Dawley strains of rats were below the lower limit of the RI for glucose, sodium, and chloride and above the upper limit of the RI for total bilirubin, triglycerides, and cholesterol.[45]

Fasted or Nonfasted

The need to fast species that feed mainly at night is controversial, because a fast contradicts the normal circadian pattern of the rodent. Fasted samples are usually recommended for laboratory analysis to decrease lipemia that can interfere with many laboratory tests. Moreover, lipemia enhances hemolysis, compounding assay interference. In rats, a minimum of 16 hours fasting is necessary to produce a nonabsorptive state characterized by triglyceride, glucose, and ALP concentrations that are significantly lower than nonfasted samples.[79] The fasted state may mask mild elevations in ALP associated with cholestasis.

Analytical Variation

The importance of test validation for different species cannot be overstated; blood samples should be submitted to veterinary reference laboratories that have validated assays for particular veterinary species. The use of point-of-care biochemical analyzers or handheld glucometers that have not been validated for the species in question will lead to laboratory results of questionable accuracy or poor reproducibility that could affect test interpretation. A methodology that is adequate for one species may be inappropriate for another as a result of interspecies structural differences in any given analyte.[77] Moreover, assays may not be accurate for some species if reference values for a particular analyte fall below or above the analytical range or detection limit of the analyzer.

Often there are generalized statements about the spurious effects of hemolysis, icterus, or lipemia on biochemical values. Species differences exist in the effects of interferences caused by serum lipid, hemoglobin, or bilirubin on analyte measurements.[40] Reported interferences may or may not be applicable to the species being evaluated. One cannot assume that hemolysis will universally result in spurious hyperkalemia, for example. For species with high potassium content erythrocytes, this is often true, but erythrocyte potassium content varies considerably between species. Because the effects of hemolysis or lipemia on the accuracy of biochemical tests are unknown in many nondomestic species, avoidance of these interferences is crucial to accurate test interpretation.

Rodents

The CBC and serum biochemical analyses in adult mice and other small rodents requires roughly 10% to 15% of total blood volume. While this amount of acute blood loss is usually well tolerated in healthy animals, taking blood from animals that are already ill can exacerbate dehydration and azotemia and cause significant decreases in body temperature and activity. Pretreatment with intraperitoneal fluid therapy has been shown to mitigate some of the deleterious effects of blood loss in ill mice.[48] Splitting a blood sample from a single animal into two different tubes for a CBC and biochemical evaluation may result in inadequate sample volume to perform the desired tests or may introduce inaccuracies if the ethylenediaminetetraacetic acid (EDTA) tube is underfilled. A plasma sample provides more volume relative to serum and can be used for both the CBC and biochemical evaluations. The largest plasma volume can be extracted from a blood sample by using a lithium heparin separator tube with a gel plug.[81] Lithium-heparinized plasma is recommended whenever electrolytes are evaluated, because plasma collected in potassium EDTA or sodium heparin may have inaccurate potassium and sodium results, respectively.

Liver

Mice, hamsters, gerbils, and chinchillas are similar to rats with respect to markers of hepatocellular and hepatobiliary injury and their interpretation. A minimum of two appropriate tests is recommended for hepatocellular evaluation. Hepatocellular tests appropriate in most rodents include ALT, AST, and sorbitol dehydrogenase (SDH).[7] For hepatocellular evaluation, ALT and SDH are highly specific cytosolic liver enzymes; SDH correlates slightly better than ALT with the presence of histopathologic hepatic lesions. Hepatic causes of increased serum ALT and SDH activity are hepatocellular necrosis, injury, or regenerative/reparative activity. Nonhepatocellular increases in ALT activity may be attributed to muscle injury, which can cause increases in both AST and ALT activity. Generally, levels of AST are higher than ALT when both are concurrently increased with muscle injury.

Aspartate aminotransferase is a cytosolic and mitochondrial-associated enzyme that, because of its presence in cardiac and skeletal muscle, is less sensitive and specific for hepatocellular evaluation. Hepatocellular injury usually results in a greater magnitude of increase in ALT than in AST levels, in part due to AST being bound to mitochondria. Large elevations in AST relative to ALT activity would be interpreted as either severe hepatocellular damage or as muscular, not hepatic, injury. Lactate dehydrogenase (LDH) is less sensitive and specific than AST, and use of LDH as a biomarker for hepatocellular injury is not recommended.[7]

In contrast to other rodents, ALT is neither sensitive nor specific in guinea pigs as a hepatocellular biomarker; SDH is used in lieu of ALT. Because AST is less specific for liver disease than SDH is, AST should ideally be assessed with SDH. If SDH is not an available test choice, AST should be interpreted with CK to exclude muscle injury as a cause of increased AST activity.

Bile acids serve to assess hepatic function.[47] Bile acids measurement is less sensitive than hepatocellular and biliary enzymes to evaluate hepatocellular injury and cholestasis. Decreases in concentrations of analytes synthesized in the liver, such as glucose, albumin, urea nitrogen, cholesterol, and bilirubin, are highly insensitive in detecting hepatic dysfunction, and many are also nonspecific.

Tests assessing biliary injury include ALP, GGT, and total bilirubin. Pathologic increases in ALP are most often associated with hepatobiliary disease and bone injury. In most species, increases in ALP precede increases in total bilirubin with hepatobiliary disease.[7] Nonpathologic factors affecting increased ALP concentrations are feeding, fasting, sex, and age. Because intestinal ALP is the predominant source of circulating isoenzyme in rats and mice, serum ALP concentrations

may transiently increase postprandially, whereas they decrease within 8 hours of fasting in males and 16 hours in females.[42,79] Concentrations of ALP tend to be significantly higher in male rats than in females.[38,42] In contrast to rats, ALP concentrations in some strains of mice may be significantly higher in females than in males.[58] Young growing rats and mice have higher ALP concentrations than adults due to bone growth.

In rats, GGT is a canalicular enzyme that is associated with cholestasis, but can also be increased secondary to glucocorticoids. Because most ALP is of intestinal origin, increases in both ALP and GGT provide stronger evidence of biliary disease. Total bilirubin concentrations may be increased as a result of bile retention subsequent to impairment of intrahepatic or extrahepatic bile flow (cholestasis), increased production associated with marked erythrocyte destruction (prehepatic), or altered bilirubin metabolism (e.g., Gunn rats).

Kidney

Urea nitrogen and creatinine will increase with decreases in glomerular filtration, but similar to dogs and cats, these are neither sensitive nor specific tests of renal function in rabbits and rodents. Prerenal causes of increased urea nitrogen are high-protein diet, protein catabolism, dehydration, gastrointestinal hemorrhage, and fever. Creatinine is a more specific biomarker than urea nitrogen, and levels do not tend to increase with protein catabolism or gastrointestinal bleeding, but will increase with dehydration. Creatinine is an end product of muscle metabolism; thus, relatively higher and lower concentrations may be attributable to well-muscled and muscle-wasted animals, respectively. Accordingly, body condition should be considered when interpreting creatinine concentrations. Creatinine can be less sensitive as a marker for decreased glomerular filtration in a poorly muscled or markedly muscle-wasted animal. Creatinine may be determined by either an enzymatic method or the Jaffe method. Values can differ significantly depending on the method used, especially in mice.[60]

Electrolytes

Rodent electrolytes are interpreted as for domestic species. Sodium and chloride typically increase and decrease in tandem. Pure water loss (dehydration) or decreased water intake are common causes of hypernatremia and hyperchloridemia. In rodents, sodium and chloride loss occurs most often from diarrhea, osmotic diuresis (diabetes mellitus), and renal disease. Hypotonic fluid administration or polydipsia may result in dilutional hyponatremia and hypochloridemia. Sodium concentrations have been reported to be slightly higher in mice than in other rodent species, largely based on one study that reported values in mature male C57BL-6J mice to be as high as 174 ± 23 (SD) mEq/L.[22] However, a recent study using adult C57BL-6J mice (aged 90–135 days) generated sodium reference intervals of 139 to 155 mEq/L.[58] Other reports in mice have slightly higher upper limits with reference intervals of 132 to 162 and 155 to 161 mEq/L.[65]

Common causes of hyperkalemia in rodents are acute renal failure, postrenal urinary obstruction, marked tissue necrosis, and rhabdomyolysis. Potassium is often spuriously increased due to leakage from high potassium–content erythrocytes or marked thrombocytosis. Only species with high potassium–content erythrocytes will have hyperkalemia associated with hemolysis or leakage from erythrocytes during clotting. Rats, mice, and hamsters have high potassium–content erythrocytes, resulting in hyperkalemia associated with hemolysis or leakage from intact erythrocytes during clotting.[9,19,20] Information for the other species is not available, and whether hemolysis results in hyperkalemia is not known. Marked thrombocytosis may result in sufficient release of potassium during the clotting process to produce hyperkalemia; use of plasma samples will obviate this effect. Spurious hyperkalemia can be avoided by using nonhemolyzed plasma that is immediately spun after collection so that potassium leakage from erythrocytes does not occur. Hypokalemia is often caused by decreased intake or renal or gastrointestinal loss.

Serum phosphorus is principally regulated by the kidneys. Increased dietary intake, decreased glomerular filtration, and increased parathyroid hormone secretion are associated with hyperphosphatemia. Vitamin D oversupplementation and cholecalciferol toxicosis result in hyperphosphatemia and hypercalcemia. As in other species, young mice and hamsters have higher phosphorus concentrations relative to adults due to bone growth.[9,65] Hypophosphatemia is less common and may be seen with hyperparathyroidism. In dogs, significant transient hypophosphatemia may be associated with respiratory alkalosis caused by panting/hyperventilation; studies are not available to determine whether this applies to tachypneic rodents.

Calcium concentration in serum or plasma represents both ionized and protein-bound calcium; thus, hypoalbuminemia is expected to decrease total calcium. Other causes of hypocalcemia in rodents are magnesium-deficient diets, chronic renal failure, and hypoparathyroidism.[65] Common differential causes of hypercalcemia are paraneoplastic syndromes, hyperparathyroidism, osteolytic lesions, and hypervitaminosis D/cholecalciferol toxicosis. Hyperproteinemia may also result in increased total, but not ionized calcium concentration.

Protein

Protein may be measured as total protein or divided into its components by electrophoresis. A new capillary methodology for electrophoresis permits evaluation of serum protein fractions with as little as 2 µL, and it has been shown as a viable alternative to conventional agarose gel electrophoresis for protein electrophoresis in mice, rats, and marmosets.[18] Albumin is measured independently of total protein. Unless electrophoresis is performed, globulin concentrations are calculated values that are the result of subtracting albumin from total protein values.

Total protein can be determined with a chemical reaction (biuret method) or by using a handheld refractometer. Refractometry is a total solids-based protein measurement technique that is influenced by the total dissolved solids in the sample. The light refraction index is converted to total protein either via the refractometer scale or published tables. American medical refractometers are designed by using a conversion factor, and their built-in scales report total protein, *not* total solids. Nonprotein solutes in serum and plasma that contribute to

refraction include electrolytes, lipid, urea, and glucose. Total protein estimates from refractometers may be inaccurate when there is marked hyperglycemia (>600 mg/dL), hyperlipidemia, and azotemia (urea nitrogen 273 mg/dL). Sodium concentrations required to significantly affect a refractometer reading are incompatible with life. Hemolysis and icterus do not cause inaccurate refractometer readings, although hemolysis can result in the loss of a readable demarcation line.[27]

Interpretation of protein changes in rodents is similar to that in domestic animals. In general, increases in total protein are associated with hemoconcentration or hyperglobulinemia, whereas decreases may be attributable to hypoalbuminemia, hypoglobulinemia, or both (panhypoproteinemia). Panhypoproteinemia is usually caused by acute blood loss or protein-losing enteropathy. Increases in globulin concentration are related to chronic antigenic stimulation or neoplasia (i.e., monoclonal gammopathy). Hypoalbuminemia may be due to glomerular disease, loss or decreased absorption in the gastrointestinal tract, or decreased production due to liver insufficiency.

Glucose and Lipids

In veterinary medicine, blood glucose concentration increasingly is being measured by using portable glucometers. However, accuracy of portable glucometers varies widely in veterinary species (see below, Ferrets). Only portable glucometers that have been validated for a particular species should be trusted for glucose measurement.

Glucose is synthesized by the liver but is influenced by preanalytical factors and many extrahepatic factors such as hormones (insulin, glucagon, glucocorticoids, epinephrine, and thyroxine); thus it is not a specific indicator of hepatic function. Delayed separation of serum or plasma from blood is a common cause of spurious hypoglycemia and can be mitigated by using collection tubes containing sodium fluoride to inhibit glycolysis. Hypoglycemia may be attributable to fasting, liver insufficiency, and tumors secreting insulin and insulin-like growth factor (i.e., insulinoma, leiomyosarcoma, etc.). In contrast to dogs and cats, induced sepsis in rats did not produce hypoglycemia in one study.[1] Hyperglycemia is associated with diabetes mellitus, stress, blood collection site, anesthetics (see Preanalytical Variation), and certain neoplasms such as glucagonoma, functional adrenocortical tumors, and pheochromocytoma.

In veterinary species, cholesterol and triglycerides are the most commonly assessed lipids. Cholesterol concentrations in health tend to be highest in hamsters relative to other laboratory rodent species. In rats, postprandial hyperlipidemia is common and may be seen in at least a third of unfasted rats; a fast of 16 hours minimum is required to reach a nonabsorptive state.[79] Pathologic hyperlipidemia is most often attributable to endocrine disorders (diabetes mellitus; hypothyroidism), diet, cholestasis, and nephrotic syndrome; Syrian hamsters with renal amyloidosis and hypoalbuminemia may be hypercholesterolemic.[9] Thyroidectomy in rats and diabetes mellitus in Chinese hamsters are associated with hypercholesterolemia.[9,47] Diets high in cholesterol produce hypercholesterolemia in rats, hamsters, and mice.[9,47,65] Concurrent chronic hepatitis and biliary disease in hamsters are associated with increased cholesterol, likely as a result of cholestasis.[8]

Muscle

Biomarkers of skeletal and cardiac injury include CK, AST, and LDH. In rodents, CK and AST are most often used to assess skeletal muscle injury. Because AST is present in muscle and liver and is less specific than CK for muscle, evaluating AST in conjunction with hepatocellular markers (ALT or SDH) increases specificity and may help to distinguish between skeletal muscle and hepatic disease. Given the small size of the heart relative to the skeletal muscle mass, these enzymes have poor sensitivity for cardiac disease. Cardiac troponin-T and cardiac troponin I are highly sensitive and specific markers for traumatic, ischemic, and toxic cardiac injury, which are validated for use in mice and rats.[55,56]

Rabbits

Changes in biochemical values in rabbits are generally similar as those as discussed above for rodents. However, some specific analytes have variations in rabbits.

Liver

In the rabbit, ALT is not liver specific although it is used commonly for liver evaluation, whereas SDH is liver specific but the assay is not available in all diagnostic laboratories. Because ALT and AST are present in liver and muscle, concurrent evaluation of CK is helpful in localizing the source of enzyme elevation. Markers of cholestasis include GGT, ALP, and total bilirubin. Blood ALP includes bone isoforms; thus levels are increased in young, growing animals, as well as with bone lesions associated with osteoblastic activity.[24]

Kidney

Creatinine, urea nitrogen, and phosphorus are of similar sensitivity and specificity as other species as markers for glomerular filtration. A unique feature in the rabbit is the fluctuation of urea nitrogen through the day, with highest concentrations occurring in the late afternoon and evening.[24]

Electrolytes

Interpretations of sodium, chloride, or potassium abnormalities in rabbits are as in other mammals. Potassium shows diurnal variation in rabbits; highest concentrations occur in the morning and lowest concentrations at night.[24] Rabbits are a species with high erythrocyte potassium content, thus hemolysis will produce spurious hyperkalemia. Increased phosphate is often a result of decreased glomerular filtration in rabbits and can be associated with bone disease (healing fractures; metabolic bone disease), muscle trauma, or rhabdomyolysis. Total calcium concentrations in rabbits are higher than in many species. Because intestinal absorption of calcium does not depend on vitamin D if dietary levels are high, high-calcium diets may result in hypercalcemia.[51] Similar to horses, renal failure is associated with hypercalcemia as a consequence of the importance of renal excretion in maintaining calcium balance. Other causes of increased total calcium are lytic bone disease and neoplasia. Total calcium in rabbits is protein-bound, and decreases are observed with hypoalbuminemia. Marked demand for calcium in late pregnancy and early lactation can result in hypocalcemia in does.

Protein

Increases in total protein concentration are associated with hemoconcentration or hyperglobulinemia. Decreases may be attributable to hypoalbuminemia, hypoglobulinemia, or both (panhypoproteinemia). Panhypoproteinemia is usually caused by acute blood loss. A common cause of hypoalbuminemia in pet rabbits is chronic malnutrition (poor diet or severe dental disease), whereas protein-losing enteropathy and glomerular disease are uncommon. Reduced cecotrophy can produce hypoproteinemia, specifically hypoalbuminemia.

Lipids and Glucose

Rabbits have the propensity to develop marked cholesterolemia within days of beginning a high-cholesterol diet.[50] Both glucose and cholesterol concentrations decrease significantly during the middle or late periods of gestation in pregnant New Zealand white rabbits.[52]

Rabbits have a constant supply of food in the form of cecotrophs, which precludes obtaining a fasted blood sample. Blood samples taken after 96 hours of food deprivation can show little change in blood glucose levels. Differential causes for hyperglycemia are stress/excitement, hyperthermia, and anesthetics (see Preanalytical Variation). Diabetes mellitus has been reported in laboratory rabbits,[68] although it appears to be rare in the pet population. Significant increases in blood glucose concentration occur with active signs of stress, and marked hyperglycemia was found to be a poor prognostic factor in nondiabetic ill rabbits.[32] Hypoglycemia has been associated with liver insufficiency, insulinoma, and prolonged anorexia.

Muscle

Primary biomarkers for muscle injury are AST and CK. Levels can increase after physical restraint, especially if rabbits are fractious or unfamiliar with handling. Rhabdomyolysis may also result in hyperkalemia or hyperphosphatemia.

Ferrets

Most biochemical parameters in ferrets are interpreted as for dogs and cats, although differences exist in the characteristics of some analytes.

Liver

Hepatocellular biomarkers in ferrets are similar to most species. Although ALT and SDH are sensitive and specific for the liver, ferret erythrocytes are rich in SDH, and marked elevations occur as an artifact associated with hemolysis.[44] Increases in AST along with ALT concentration are noted in hepatic lipidosis. Little information is available regarding tissue distribution of AST in ferrets, but if present in muscle as with many species, evaluation of AST in conjunction with a specific hepatocellular marker and with CK is useful to distinguish between hepatic and muscular disease.

Biliary markers include total bilirubin, GGT, and ALP. Ferrets possess a bone isoenzyme of ALP, and age-related decreases in ALP are presumably due to the cessation of rapid bone growth as in other species. Cholestasis in ferrets may be associated with increases in total bilirubin, ALP, GGT, and cholesterol. In general, increased ALP activity is uncommon, and increased total bilirubin concentration is rare. Likely as a result of efficient renal clearance, marked hyperbilirubinemia in the ferret is rarely associated with jaundice, even when total bilirubin is as high as 6.2 mg/dL.[31]

Kidney

Whereas creatinine, urea nitrogen, and phosphate concentrations are inversely related to glomerular filtration in ferrets, creatinine concentrations in health are considerably lower than for most species, and increases are often well within the reference limits of most other small mammals. Similar to other small mammals, increases in urea nitrogen may be nonspecific; creatinine is more kidney specific than urea nitrogen but is affected by dehydration. Increases in two or all three of these indexes are highly supportive of decreased glomerular filtration but do not distinguish between prerenal (dehydration), renal, or postrenal (obstruction) causes.

Electrolytes

Changes in sodium, chloride, phosphorus, and calcium concentrations are interpreted conventionally. Common causes of hyperkalemia in ferrets include acute renal failure, postrenal urinary obstruction, marked tissue necrosis, rhabdomyolysis, and hypoadrenocorticism, which may occur as an iatrogenic complication of bilateral adrenalectomy for hyperadrenocorticism. Causes of spurious hyperkalemia in ferrets are similar to those described in rodents; however, hyperkalemia is not reported with hemolysis in ferrets, suggesting that intraerythrocyte potassium concentration is low in this species.[44]

Protein

Interpretation of protein fractions in ferrets is similar to most species. Two distinctive causes of moderate to marked hyperglobulinemia in ferrets are Aleutian disease virus and systemic coronavirus-associated diseases.

Lipids and Glucose

Hypoglycemia is most often associated with insulinoma in ferrets, especially ferrets older than 4 years of age. Spurious and nonpathologic causes of hypoglycemia include delayed separation of blood from plasma or serum and prolonged fasting (>6 hours). Given the relatively high prevalence of insulinoma in ferrets relative to other small mammals, accurately assessing glucose levels in ferrets is important. The growing attraction of handheld glucometers for glucose measurement is based on ready availability, low expense, and rapid results requiring relatively small amounts of capillary blood. Recent studies illustrate the variability in accuracy for glucose measurement using different glucometers in ferrets and underscore the need for verification with a laboratory analyzer.[74] Much of this variation may be attributable to species-specific matrix properties such as hematocrit, RBC count, mean corpuscular volume, proportion of glucose bound in RBC versus plasma (species differences), and plasma water content.[28] In one study with ferrets, a veterinary glucometer coded for use in dogs correlated best with a laboratory analyzer.[61] Differential causes of hyperglycemia are diabetes mellitus and excitement or

stress. Hyperadrenocorticism in ferrets is not typically associated with hypercortisolemia; thus hyperglycemia is not characteristic of this disease. Transient hyperglycemia may develop after surgical excision of pancreatic islet cell tumors and usually resolves within 1 to 2 weeks.[12]

Common causes of increases in cholesterol and triglycerides in ferrets do not include hypothyroidism and hypercortisolemia, because these diseases are rare in this species. In ferrets, hypercholesterolemia is reported with diabetes mellitus and with marked cholestasis associated with cholelithiasis.[31]

Muscle

Commonly used biomarkers of skeletal and cardiac muscle are CK and AST. With severe muscle injury, ALT may also increase. Although CK and AST appear to be appropriate muscle biomarkers in ferrets, neither are significantly increased in most reported cases of disseminated myofasciitis, which is a multifocal inflammatory myopathy. Increases in ALT have been reported in some of these cases, although whether the increase was due to concurrent suppurative hepatitis or to the myopathy is not clear.[26]

Cardiac troponin-T (cTnT) is a biomarker for cardiac muscle in the ferret, but its sensitivity in disease has not been adequately evaluated. Increases in cTnT values were associated with cardiac puncture in ferrets, although values were highly variable and a second cardiac puncture did not cause further increases, suggesting that most of the increase was attributable to direct tissue contamination rather than to release of cTnT into blood.[55]

Hedgehogs

The African hedgehog, a nonhibernating species, is the most common hedgehog species kept as a pet in the United States. Most available biochemical and hematologic information is derived from the European hedgehog, and data for juvenile European hedgehogs rescued from the wild were recently published.[69] Limited RI data have been reported for African hedgehogs,[54,56a] and until more studies have been done, biochemical data should be interpreted in these species as for omnivorous domestic species.

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40

Ophthalmologic Diseases of Small Mammals

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OUTLINE

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Ophthalmic examination of small mammals follows the same principles as in other species. Ophthalmic examination starts with evaluation of symmetry of globes and orbits. Evaluation of vision can be challenging because not all small mammals will have a consistent menace response. Evaluation of eyelids, conjunctiva, cornea, iris, and lens is best performed using a source of magnification and illumination. A slit-lamp biomicroscope is best suited for this, but use of an otoscope can provide magnification and illumination as well. The fundus is evaluated by direct or indirect ophthalmoscopy.

Tear production can be challanging to measure, depending on the species and size of the animal. In addition, a low tear production is present in some small mammals, leading to the use of different methodology to measure tear production. In larger animals, tear production can be determined by inserting a Schirmer tear test strip between the cornea and lower eyelid for 1 minute. However, the width of the strip is 5 mm, which is longer than the palpebral fissure in many small mammals. In the phenol red thread tear test, a 75-mm–long cotton thread, impregnated with pH-sensitive phenol dye, is inserted in the ventral conjunctival fornix.[71] After 15 seconds, the part of the thread that has changed to a red color is measured. This test is well tolerated and can be performed in species with very small eyes or low tear production.[47] The endodontic adsorbent paper point tear test measures the aqueous fraction of the tear film.[43] It uses sterile standardized paper cones or tips, originally developed for endodontics. The cones or tips are placed in the lower conjunctival fornix, and the amount of wetting is measured after 1 minute.[43] This test also is suitable for animals with small eyes or low tear production.

Intraocular pressure is measured by either applanation tonometry (MacKay-Marg®, Tono-Pen XL® [Reichart Technologies, Dewpew, NY], Tono-Pen AVIA® [Reichart Technologies]) or rebound tonometry (TonoVet®, TonoVet Plus®, TonoLab® [Icare, Vanta, Finland]). The Tono-Pen XL® is widely used. It needs to be calibrated frequently. The Tono-Pen AVIA has a more ergonomic design, can be used in any position, and does not require calibration.[67] The advantage of the Icare TonoVet is that application of topical anesthetic to the eye is not required before use, and measurements can be obtained faster than with the Tono-Pen. Disadvantages are the need for the instrument to be in a vertical position and lack of calibration for certain species. Reference values for various diagnostic tests can be found in Table 40.1.

RABBITS

Ophthalmic examination of rabbits can be performed easily.[90,91] The eyes are laterally located and have a round pupil. Evaluation of a menace response is difficult, but most rabbits will react to bright light by squinting. The dorsal rectus muscle can usually be seen as a large striated band of tissue under the conjunctiva. Some rabbits do not respond to topical application of mydriatic agents because of the natural presence of atropinase. In these rabbits, adding topical 10% phenylephrine may help to obtain mydriasis. Rabbits have a merangiotic fundus. The well-myelinated optic nerve is present above the visual axis and has a deep optic cup (Fig. 40.1A). Retinal blood vessels are present in a linear streak medial and lateral to the optic nerve. An extensive venous plexus is present in the orbit.

The nasolacrimal system of rabbits has a single nasolacrimal punctum, which is located in the ventral eyelid 3 mm from the eyelid margin, near the medial canthus, and ventral to the lacrimal caruncle (Fig. 40.2).[11,50] The lacrimal sac is immediately rostral to the punctum and caudal to the nasolacrimal duct aperture. The nasolacrimal duct extends from the orbit to the nasal fossa and runs within the part of the maxilla that forms the lateral wall of the maxillary sinus.[50] Approximately 5 to 6 mm within the maxilla, the duct curves sharply and decreases

TABLE 40.1 Reference Values for Ophthalmic Diagnostic Tests in Small Mammals

Species	Intraocular Pressure (mmHg)	Schirmer Tear Test (mm/min)	Phenol Red Thread Tear Test (mm/15 sec)	Endodontic Paper Point Tear Test (mm/min)
Chinchilla	2.9 ± 1.8 (TonoVet)[61] 17.7 ± 4.2 (Tono-Pen XL)[47]	Not reliable[61] 1.1 ± 0.5[47]	14.6 ± 3.5[61]	—
Ferret	22.8 ± 5.5[77] 14.5 ± 3.3[58]	5.3 ± 1.3[58]	—	—
Guinea pig	16.5 ± 3.2 (Tono-Pen XL)[97]	3.8 ± 1.3[97] Not possible[84]	—	—
Hamster	—	—	6.8 ± 2.5[71] 5.1 ± 1.2 male[71] 8.5 ± 2.3 female[71]	—
Mouse	19.3 ± 0.4[94]	—	—	4.4 ± 1.5[43]
Rabbit	9.5 ± 2.6 (TonoVet)[67] 15.4 ± 2.2 (Tono-Pen Avia)[67] 9.7 ± 2.7 male (TonoVet)[93] 9.5 ± 2.2 female (TonoVet)[93]	5.2 ± 1.0[47] 5 ± 2.4[1]	—	13.8 ± 1.5[47]
Rat	18.4 ± 0.1[94]	—	—	6.2 ± 2.1[43]

in diameter.[11] At the level of the palatine bone, the nasolacrimal duct leaves the bony nasolacrimal canal and makes a sharp turn at the nasolacrimal duct flexure, which is located just caudal to the caudal limit of the incisor tooth roots. The nasolacrimal duct narrows at this flexure in normal rabbits. The duct then follows the ventral margin of the nasoturbinates and exits on the ventromedial aspect of the alar fold just caudal to the mucocutaneous junction of the nares.

Conjunctivitis and Epiphora

Conjunctivitis in rabbits is common. In normal rabbits with no ocular or respiratory disease, the most frequently isolated organisms from the conjunctival cul de sac are *Staphylococcus, Micrococcus*, and *Bacillus* species. *Pasteurella multocida* is a recognized cause of conjunctivitis, epiphora, nasolacrimal duct obstruction, and dacryocystitis in rabbits.[25] Less common organisms include *Bordetella*, *Stomatococcus, Neisseria*, *Pasteurella*, *Corynebacterium, Streptococcus,* and *Moraxella* species.[16] Other infectious agents that have been associated with conjunctivitis in rabbits are *Staphylococcus aureus, Pseudomonas* species, *Haemophilus* species, *Treponema paraluiscuniculi,* mycoplasmas, chlamydiae, and myxoma virus.[79] In New Zealand white rabbits with conjunctivitis, upper respiratory disease, and pneumonia, bacterial isolates consisted of *Bordetella bronchiseptica, P. multocida, S. aureus*, and *Pseudomonas alcaligenes*.[63] Mucopurulent conjunctivitis and blepharitis with corneal ulceration have been associated with *S. aureus* infection in a rabbit.[57] Treatment with topical gentamicin ophthalmic ointment and systemic gentamicin was curative. We have isolated a methicillin-resistant *S. aureus* in a rabbit with severe bilateral conjunctivitis. The strain isolated was identified as hospital acquired; the owner was a nurse in an urban hospital setting. Other causes of conjunctivitis in rabbits are foreign bodies, entropion, distichia, trichiasis, and high ammonia or dust content in the environment. Dental disease, including root elongation and dental abscesses, is also associated with conjunctivitis.

Unilateral or bilateral epiphora can be present in rabbits without conjunctivitis. The discharge often has a white, gritty appearance and may be intermittent and resistant to treatment with topical antibiotics. Root elongation of the maxillary incisors is a common underlying cause.[25,33] The elongated roots can cause an obstruction of the nasolacrimal duct at its flexure just caudal to the roots of the incisors. Radiographs or computed tomography (CT) scan of the skull are needed to assess the incisors; excess curvature of the incisor roots is abnormal. Dacryocystorhinography using contrast material injected into the nasolacrimal system can help localize the site of obstruction, differentiate between a complete and partial obstruction, and identify any dilation. In one report describing 2 affected rabbits and 13 normal rabbits, radiographs revealed a cystic dilation of the nasolacrimal duct immediately caudal to the duct flexure, and the incisors were more arched than in normal rabbits.[50] Irrigation of the nasolacrimal duct in affected rabbits yielded opaque, white, gritty fluid that, on cytologic examination, showed numerous macrophages, lipid-laden mesothelial cells, lipid droplets, and small numbers of bacteria and erythrocytes. Occlusion of the ducts was presumed to be attributed to fat droplets. Bacteriologic culture of fluids used to irrigate the nasolacrimal ducts of both normal and affected rabbits yielded similar bacterial isolates; therefore microorganisms may not be important in the pathogenesis of epiphora in rabbits. The most common bacterial isolates were *S. aureus,* coagulase-negative *Staphylococcus* species, *Moraxella* and *Neisseria* species, *Oligella urethralis,* and *Streptococcus viridans.* In a study of 28 cases of dacryocystitis in rabbits, 89% of cases were unilateral.[25] Of all cases, 50% were determined to be caused by dental malocclusion, 7% by rhinitis, 4% by both rhinitis and dental malocclusion, and 4% by panophthalmitis; no apparent cause was found in 35% of cases. Other ophthalmic abnormalities included conjunctivitis, nasal discharge, keratitis, periorbital swelling, and panophthalmitis. Bacterial culture of the fluid revealed the presence of one pathogen in four rabbits, two pathogens in two rabbits, and no growth was present in two rabbits. Most animals (98%)

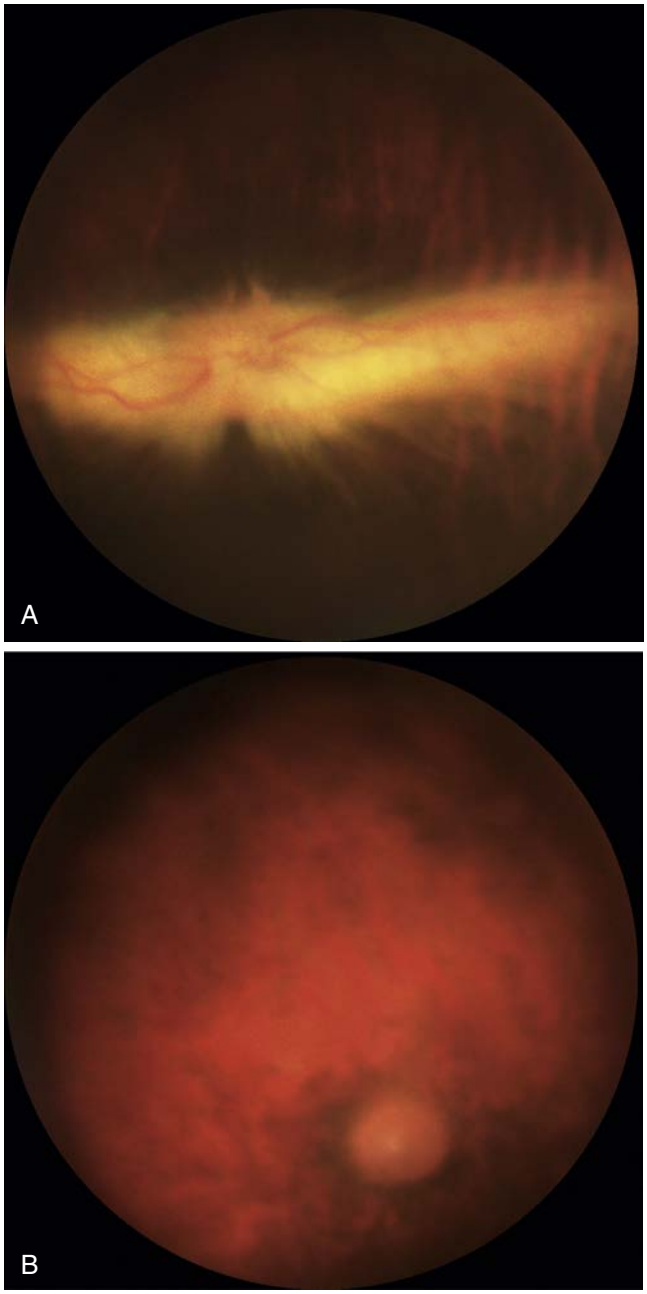


Fig. 40.1 Fundus examination of the rabbit and the guinea pig. (A) The fundus of the rabbit is merangiotic. A horizontally ovoid disc is present with a horizontal zone of major vessels on both sides. The optic disc lies above the posterior pole of the eye. (B) The fundus of the guinea pig is classified as paurangiotic. It appears avascular in most animals.The optic disc is white to gray. The fundus is a mottled red-brown in pigmented guinea pigs and appears diffusely reddish in white guinea pigs.

were treated with topical or oral antibiotics or both, with or without topical nonsteroidal antiinflammatory medications, with a mean duration of 5.8 weeks. Flushing of the nasolacrimal system with 0.9% NaCl solution was performed in most rabbits. The duct was patent in 12 rabbits and obstructed in 14 rabbits. Whether the nasolacrimal duct was patent or obstructed did not affect the disease outcome. In this study, 43% of rabbits improved with the obstruction resolved in an average of 2.9 weeks of treatment, 28% were euthanized, 11% died of unrelated causes, 11% were lost to follow-up, and 7% had chronic dacryocystitis. The prognosis of animals with severe dacryocystitis requiring systemic therapy is guarded. The prognosis is also poor if any complications arise.

Treatment of epiphora in rabbits can be frustrating. The primary treatment is irrigation of the nasolacrimal duct, and this can be performed easily in rabbits. After instilling a topical ophthalmic anesthetic, insert a 23-gauge lacrimal cannula or a 22- to 24-gauge Teflon intravenous catheter into the nasolacrimal puncta in the medial aspect of the lower eyelid to flush the duct (Fig. 40.3). Recurrence of the obstruction is common, and duct irrigation may need to be repeated every 2 to 3 days or weekly until a few consecutive clear irrigations are obtained. If topical antibiotic therapy is used, a broad-spectrum medication such as triple antibiotic solution is recommended. Topical nonsteroidal, antiinflammatory ophthalmic medications, such as 0.03% flurbiprofen or 0.1% diclofenac, may help minimize irritation caused by the procedure. In rabbits with chronic or severe infections, concurrent topical ophthalmic and systemic antibiotic therapy may be needed. Suggested combinations include a systemic fluoroquinolone such as enrofloxacin or marbofloxacin and topical ciprofloxacin or gentamicin ophthalmic solution. In rabbits with evidence of underlying incisor root abnormalities or infection, removing the incisors can be considered in severe cases.

Cornea

Corneal dystrophy is the accumulation of cholesterol or lipid crystals in the cornea.[4] This may develop spontaneously, as has been reported in American Dutch belted rabbits,[59] or be associated with high dietary cholesterol. It also occurs in breeds that are predisposed to hypercholesterolemia, such as the Watanabe rabbit with heritable hyperlipidemia.[26,42] In Watanabe rabbits, yellowish-white granules can develop along the corneal-scleral junction and in the iris. In rabbits without systemic lipid abnormalities, spontaneous corneal dystrophy is usually bilateral and symmetric and does not progress to visual impairment. In any rabbit with corneal dystrophy, carefully evaluate the fat content of the diet.

Progressive occlusion of the cornea with a conjunctiva-like membrane is occasionally seen in rabbits.[3,21,75,78] Membranous corneal occlusion, or pseudopterygium, is a pain-free condition that may affect one or both eyes (Fig. 40.4). Ophthalmic examination reveals a circular membrane that originates at the limbus (the junction of the cornea and sclera) and gradually advances over the cornea. In severe cases, only a small central opening is present, allowing visibility of an otherwise normal globe. The membrane does not adhere to the cornea. The cause of this condition is unknown, although trauma has been suggested. Progressive membranous occlusion in rabbits has been compared with pterygium in people. However, in people the membrane is triangular and adherent to the cornea, whereas in rabbits it is nonadherent and circumferential from the limbus. Treatment with topical antibiotic or antibiotic-steroid medications has no effect. The membrane can be resected surgically and treated with topical antibiotics; this usually results in quick recurrence of the membrane. However, if the membrane is resected a few millimeters beyond the limbus and the eye is then treated with a topical antibiotic-steroid combination, recurrence

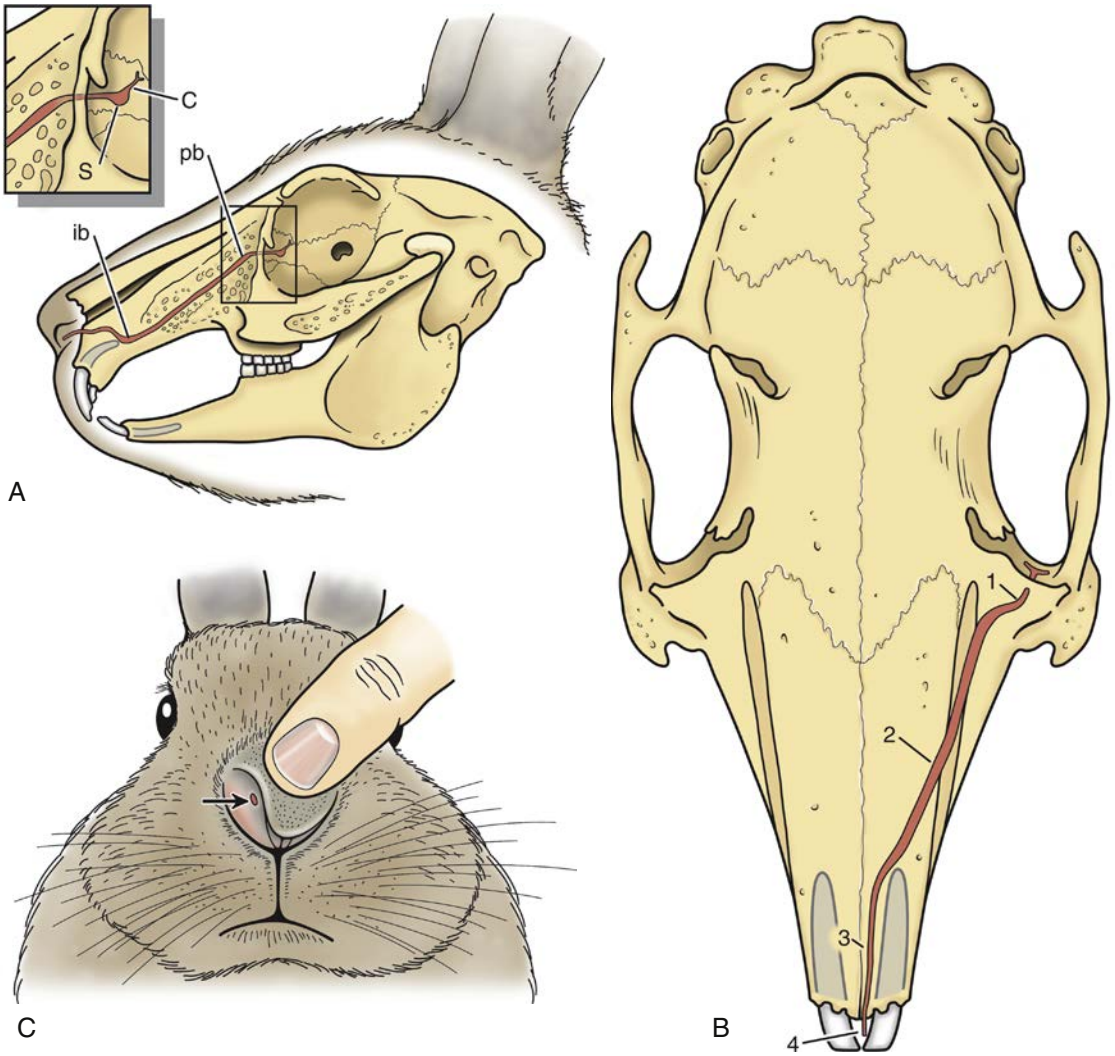


Fig. 40.2 Diagram of the rabbit nasolacrimal duct (A) Lateral view with inset. The two sharp bends, the proximal maxillary bend *(pb)*, and the bend at the incisor tooth *(ib)*, are indicated. The inset shows the canaliculus *(C)* and the lacrimal sac *(S)*. (B) Dorsoventral view. *(1)* Proximal portion of the duct extending from the punctum through the proximal maxillary curve; *(2)* portion of the duct extending from the proximal maxillary curve to the base of the incisor tooth; *(3)* portion of the duct extending from the base of the incisor tooth to the end of the lacrimal canal; *(4)* distal portion of the duct extending from the end of the lacrimal canal to the nasal meatus. (C) The nasal meatus of the nasolacrimal duct *(arrow)*. The opening is enlarged for diagrammatic purposes. (From Burling K, Murphy DJ, da Silva Curiel J, et al: Anatomy of the nasolacrimal duct and its clinical implications. *Prog Vet Comp Ophthalmol* 1991;1:33–40.)



Fig. 40.3 Irrigation of the nasolacrimal duct in a rabbit with a 24-gauge Teflon intravenous catheter. Rabbits have a single nasolacrimal punctum in the ventral eyelid.



Fig. 40.4 Progressive occlusion of the cornea with conjunctiva-like tissue. This tissue is not adherent to the cornea. The disease is not painful. (Courtesy David Wilkie, DVM, MS.)

may be prevented. Good results have also been obtained with surgical resection and the use of topical cyclosporine with or without corticosteroids.[75] Another described surgical technique is to incise the membrane into four to six quadrants and suture each quadrant of the membrane to the inside of the eyelid.[3,78] With this technique, recurrence may be prevented for at least 1 year.

Superficial, nonhealing corneal ulcers are occasionally seen in rabbits. Clinical signs are usually mild and include epiphora, conjunctival hyperemia, and blepharospasm. The ulcer is usually located in the paracentral cornea, is very superficial, and has redundant epithelial edges. The clinical appearance is that of an indolent ulcer, as seen in boxer dogs. If an ulcer is present, carefully examine the eye to eliminate potential causes such as abnormal hairs, lagophthalmos (inability to fully close the eyelid), facial nerve paralysis, or a foreign body. Treatment with a topical antibiotic solution or ointment usually fails to resolve the ulcer. Additional therapies such as corneal debridement, grid keratotomy, use of topical serum, application of corneal glue, tarsorrhaphy, or superficial keratectomy are usually necessary for the ulcer to heal.

Keratomycosis is described in rabbits. A corneal ulcer with white stromal infiltrates and a stromal abscess with dense hypopyon was reported in a 2-year-old female dwarf rabbit.[9] Fungal culture of the ulcerated area grew *Aspergillus fumigatus*. Treatment with 1% terbinafine ointment and 2% povidone iodine solution resulted in resolution of the ulcer and abscess in 8 weeks.

Eosinophilic keratitis is an inflammatory disease of the cornea that is most commonly diagnosed in cats. This condition was described in two rabbits that were presented with discharge, dacryocystitis, blepharitis, conjunctivitis, white plaques in the conjunctiva and cornea, and corneal vascularization. Cytologic examination and biopsy revealed the presence of eosinophils. Treatment of eosinophilic keratitis consists of a topical antibiotic-steroid combination (neomycin-polymyxin-dexamethasone) four times a day until the lesions resolve, followed by a slow taper.[31]

Uveitis and Diseases of the Lens

Encephalitozoon cuniculi causes granulomatous encephalitis and renal lesions in rabbits. Many rabbits infected with *E. cuniculi* are asymptomatic, but neurologic signs can include convulsions, tremors, torticollis, paresis, and coma (see Chapter 18). *Encephalitozoon cuniculi* infection has also been associated with phacoclastic uveitis.[23,28,82] Most affected rabbits are young (less than 2 years of age), and dwarf rabbits appear predisposed to this disease. Clinically, a white mass is often seen protruding into the anterior chamber (Fig. 40.5). Careful examination of the anterior segment of the eye with slit-lamp biomicroscopy may reveal a break in the anterior lens capsule. The break is frequently hidden by inflammatory material, and it may appear as if only the iris is involved in the inflammatory process. A focal cataract is often present in the area of the anterior lens capsule break. Signs of a severe pyogranulomatous anterior uveitis are usually present, such as conjunctival hyperemia, a swollen



Fig. 40.5 Rabbit infected with *Encephalitozoon cuniculi*. A white lesion is present in the iris, protruding into the anterior chamber. Lens involvement with cataract formation is present underneath the iridial lesion.

hyperemic iris, miosis, aqueous flare, and low intraocular pressure. The posterior segment of the eye is initially normal; however, if left untreated, severe uveitis and cataract formation can lead to blindness and possible phthisis bulbi or glaucoma. An abscess in the iris caused by *P. multocida* initially may resemble phacoclastic uveitis. Measurement of serum antibody titers for *E. cuniculi* and *P. multocida* may aid in the differential diagnosis. The treatment of choice is surgical removal of the lens by phacofragmentation. If an artificial lens is implanted, a 13-mm diameter, 58-Diopter intraocular lens is recommended.[76] Systemic treatment of *E. cuniculi* with albendazole (30 mg/kg orally every 24 hours for 30 days, then 15 mg/kg orally every 24 hours for an additional 30 days) has been reported.[82] Fenbendazole (20 mg/kg every 24 hours for 28 days) has proved effective in both preventing experimental *E. cuniculi* infection in rabbits and treating naturally infected seropositive rabbits.[83] If the lens is not removed surgically, control of the uveitis with topical steroidal (such as 1% prednisolone acetate) or nonsteroidal antiinflammatory medications, as well as systemic fenbendazole or albendazole, is necessary. Enucleation may be indicated if the uveitis cannot be controlled medically and a chronically painful eye is present.[28,98]

Cataract and subsequent glaucoma often can develop subsequent to ocular trauma, such as cat-scratch injury. Laceration of the cornea and anterior lens capsule by a sharp object results in formation of cataract often within weeks after the traumatic event. Exposure of the normally sequestered lens proteins may result in anterior uveitis. Secondary glaucoma or phthisis bulbi is common. However, spontaneous cataract formation is rare in rabbits. One report describes a low incidence of juvenile cataracts in laboratory New Zealand white rabbits.[62] Another report describes a high incidence of cataract in an inbred strain of New Zealand white rabbits. Virtually all inbred rabbits developed cataract after the age of 37 months, whereas no rabbits of an outbred strain developed cataract.[66] Keratitis caused by Shope fibroma virus has been reported in one rabbit.[39] Cataracts developed 3 months after the keratitis, which may have been hereditary in origin and unrelated to the virus.



Fig. 40.6 Measurement of the intraocular pressure in a rabbit using a Tono-Pen. Compression on the neck and eyelids during restraint can artificially raise the intraocular pressure and should be avoided during measurement.

Persistent hyperplastic tunica vasculosa lentis with persistent hyperplastic primary vitreous was reported in a 3-month-old wild rabbit that presented for evaluation of cataract. This is a congenital abnormality.[8]

Intraocular sarcomas have been described in three adult rabbits; two had a nonvisual eye associated with chronic inflammation, and the second had chronic uveitis, cataract formation, and glaucoma.[19,53] In all rabbits, intraocular spindle cell neoplasms closely associated with lens and lens capsular fragments were described. The histologic features of the tumors closely resembled posttraumatic ocular sarcomas in cats; chronic inflammation and trauma were considered as probable causes.

Glaucoma

Congenital glaucoma is inherited as an autosomal recessive trait in rabbits. In rabbits with this condition, the intraocular pressure is high as early as 3 months of age.[12] With increasing age, progressive buphthalmos with a markedly enlarged cornea, structural abnormalities of the iridocorneal angle, atrophy of the ciliary processes, and excavation of the optic nerve develop. Topical glaucoma medications used in dogs, such as 0.5% timolol maleate and 2% dorzolamide, may be used in rabbits. Because response to therapy is unpredictable in rabbits, carefully monitor the intraocular pressure during treatment (Fig. 40.6). Enucleation, insertion of an intrascleral prosthesis, and laser cycloablation with a diode laser have also been used to manage glaucoma in pigmented pet rabbits. However, laser cycloablation cannot be used in albino rabbits. If left untreated in chronic cases, pressure-induced atrophy of the ciliary body may cause the intraocular pressure to return to normal.

Orbit

Retrobulbar disease processes are occasionally seen in rabbits. Clinical signs are progressive exophthalmos, protrusion of the third eyelid, and inability to retropulse the globe. Exposure keratitis may be present if the ability of the eyelids to close properly has been affected. Abscesses are the common cause of retrobulbar disease in rabbits; dental disease with tooth root abscessation is often a predisposing factor (see Chapter 36). Infection is caused by both aerobic and anaerobic bacterial species. A thorough dental examination and skull radiographs are indicated in any rabbit with a suspected retrobulbar mass. If available, a CT scan is especially helpful in diagnosis. Abnormalities affecting the orbital bones and anterior ocular structures are predictive of neoplastic disease. Retrobulbar neoplasia is uncommon in rabbits. Malignant B-cell lymphoma of the Harderian gland was diagnosed on postmortem examination in a rabbit with exophthalmos.[89] Abnormalities of extraconal fat and skin are suggestive of inflammatory disease.[44] In one report, *Taenia serialis coenurus* formation caused exophthalmos in a pet rabbit. Surgical removal was curative.[64]

An abscess in the retrobulbar space of a rabbit can be very difficult to treat. Because of the thick nature of the abscessed material and the anatomy of the alveolar bulla, drainage of the abscess through the mouth, as performed in dogs and cats, may or may not be successful. A CT scan of the head is indicated to determine if tooth root abscessation is the underlying cause. If the abscess is caused by an abscessed tooth root, the tooth or teeth must be extracted to allow drainage, and the rabbit must be treated with long-term systemic antibiotic therapy. In some cases, aggressive surgical debridement is necessary. This may include exenteration of the orbit and sacrifice of a sighted eye. Even with aggressive surgical and medical management, the prognosis for recovery is always guarded. Stomatoscopy-aided dental trimming, tooth removal, and debridement successfully treated a retrobulbar abscess in a rabbit.[51] Anecdotal reports suggest that some rabbits with retrobulbar abscesses respond to medical therapy with long-term (3-month) administration of benzathine/procaine penicillin G (for rabbits <2.5 kg, 75,000 U per rabbit subcutaneously every 48 hours; for rabbits >2.5 kg, 150,000 U per rabbit subcutaneously every 48 hours).[74]

Bilateral exophthalmos in rabbits is commonly associated with compromised vascular drainage of the head. Periodic exophthalmos is common in rabbits with thymomas (see Chapter 20).[41,68,87] In one report, a localized myasthenia gravis associated with the thymoma was suggested as a cause.[87] More probably, the presence of a large intrathoracic mass, such as a thymoma, causes cranial vena caval syndrome, in which the mass compresses vessels in the cranial thorax.[54] This compression impedes blood flow in the right and left cranial vena cava as well as the external jugular veins and causes decreased vascular drainage from the head. Exophthalmos was also reported in a rabbit after the long-term placement of an external jugular catheter,[36] and bilateral exophthalmos can develop with thrombosis of both jugular veins. The external jugular veins are the largest vessels draining the head, whereas the internal jugular veins of rabbits are relatively small and primarily drain the brain, throat, and neck regions. Therefore occlusion of the external jugular veins will

compromise vascular drainage of the head. In clinical cases, exophthalmos secondary to venous thrombosis often resolves spontaneously, presumably after the jugular veins become patent again. Exophthalmos in obese rabbits may be caused by excessive fat deposition in the orbit. Simultaneous retropulsion of both globes should be avoided during ophthalmic examination, as a decrease in heart rate can occur in conscious rabbits.[27]

Rabbits have several glands in the orbit. The lacrimal gland is located dorsolaterally, and the accessory lacrimal gland, divided into three lobes, is located along the caudal and ventral orbital margin. The superficial gland of the third eyelid is a small gland located near the third eyelid's cartilage. The deep gland of the third eyelid, also known as the Harderian gland, consists of two parts: dorsal (white) and ventral (pink) lobes.[34] Enlargement of the Harderian gland may occur in orbital disease because of inflammation of the gland or obstruction of the excretory ducts.[34] Prolapse of the deep gland of the third eyelid has been described in rabbits. Surgical correction with a pocket technique, as has been described in dogs, was successful in reducing the gland in one rabbit.[38]

FERRETS

Ferrets have prominent globes placed laterally in the skull; they have very limited binocular vision.[29] The ferret's pupil is a horizontal slit that quickly responds to light. Topical 1% tropicamide may need to be applied to evaluate the fundus. Like dogs and cats, ferrets have a holangiotic retinal vascular pattern. The projection of retinal ganglion cells from the temporal area of the retina in albino ferrets differs from that of pigmented ferrets.[60] In pigmented ferrets, 6000 retinal ganglion cells project ipsilaterally to the brain, whereas in albino ferrets, only 1500 retinal ganglion cells project ipsilaterally. The significance of this difference has not been established.

Conjunctivitis in ferrets can be caused by viral or bacterial infection. Ocular signs of canine distemper virus, a fatal disease in ferrets, are mucopurulent oculonasal discharge, blepharitis, corneal ulcers, and keratoconjunctivitis sicca.[40] Conjunctival swelling and a proliferative lesion of the nictitans caused by infection with *Mycobacterium genavense* have been described in two ferrets. Other clinical signs in these ferrets included peripheral lymph node enlargement.[49]

Degeneration of corneal endothelial cells leading to progressive corneal edema and cloudiness of the cornea is seen in older mink (8–11 years of age).[32] Royal pastel females are predisposed. Unlike the disease in dogs, these mink do not develop corneal ulceration, pigmentation, or vascularization. There is no specific treatment for this condition, but symptomatic treatment with 5% sodium chloride solution or ointment two to four times a day may or may not improve corneal clarity.

A lymphoplasmacytic keratitis has been reported in a ferret with lymphoma.[73] An infiltrative lesion resembling corneal lesions reported in mink with Aleutian disease was present in the cornea.

Cataracts are common in ferrets.[86] Progressive cataract formation has been reported in two genetically unrelated populations of laboratory ferrets.[55] In 1-year-old ferrets in one population, cataracts were observed in 47% of animals examined. Severity ranged from clinically insignificant, small cataracts in the posterior cortex of the lens to blinding, complete cataracts. By 18 months of age, cataracts were detected in virtually every animal, and in animals previously diagnosed, the cataracts had progressed. A genetically separate group had a combination of blinding cataract, microphthalmos, abnormal iris formation, and retinal detachment. In another ferret colony, microphthalmos, cataract, retinal dysplasia, and a persistent hyperplastic primary vitreous-type membrane were shown to be inherited as an autosomal dominant defect.[20] Dietary factors may play a role in the development of cataracts in ferrets. A diet high in fat or deficient in vitamin E or protein may promote cataract formation.[55] In ferrets with cataracts, monitor the eyes regularly for the onset of secondary complications. Lens-induced uveitis can usually be controlled with topical 1% prednisolone acetate applied once or twice daily. Other complications caused by cataracts are lens subluxation or luxation and glaucoma. Ferrets that are blind because of cataracts usually adjust well in a home environment. However, cataract surgery can be performed successfully in ferrets. The lenses can be removed by phacofragmentation or by an extracapsular technique. Artificial lenses are not available in a size suitable for ferrets. Before cataract surgery, make sure the ferret becomes accustomed to frequent application of eye medications to facilitate easy treatment after surgery.

Retinal degeneration is seen in ferrets. Clinical signs are progressive loss of vision, which may not be noticed until the disease is advanced. Ophthalmic examination reveals mydriasis with a very poor pupillary light reflex. Cataracts may or may not be present. Retinal vascular attenuation and tapetal hyperreflectivity are seen in the fundus. There is no treatment for retinal degeneration.

Exophthalmos can develop in ferrets from several causes. Lymphosarcoma is a common disease in ferrets, and although orbital involvement has been reported in only two ferrets,[53] it is occasionally seen clinically. Exophthalmos is often the presenting complaint. Ophthalmic examination reveals unilateral or bilateral exophthalmos, decreased retropulsion of the globe, and protrusion of the third eyelid. Lagophthalmos may result in exposure keratitis with corneal ulceration and vascularization. In clinical cases, lymphosarcoma is usually present in other areas of the body. In the two ferrets described,[42] peripheral lymph nodes were affected in one ferret and involvement of the liver, spleen, intestines, kidneys, and adrenals was present in the other. Retrobulbar adenocarcinoma has been reported in one ferret,[52] and we have seen this clinically as a rare cause of unilateral exopthalmos.

In ferrets with exophthalmos, a CT scan of the head is the best method of diagnosing a retrobulbar mass and determining the extent of the lesion. Cytologic examination of a sample from the retrobulbar area obtained by ultrasound-guided fine-needle aspiration can confirm the diagnosis of neoplasia. However, this procedure can be difficult because of the limited size of the retrobulbar space. Instead, in cases of suspected orbital lymphosarcoma, diagnosis may be confirmed by obtaining samples



Fig. 40.7 Conjunctivitis and keratitis in a guinea pig. Note the abundant mucopurulent discharge, corneal vascularization, and fibrosis.

for diagnostic tests elsewhere in the body, such as a fine-needle aspirate or wedge biopsy of an enlarged lymph node. In ferrets with lymphosarcoma, therapy is directed at treating the disease systemically with prednisone or chemotherapeutic agents. While treating the ferret for lymphosarcoma, temporary tarsorrhaphy may be necessary to protect the cornea if pronounced exophthalmos is present. If the corneal epithelium is intact, protect the eye with lubricating ophthalmic ointment applied two to four times daily. If an ulcer is present, treat with an antibiotic ophthalmic ointment, such as triple antibiotic or gentamicin ointment, applied three to four times daily. In cases of retrobulbar adenocarcinoma, treatment may include exenteration and radiation therapy.[52] Zygomatic salivary gland mucocele is another reported cause of exophthalmos in ferrets.[56] Fine-needle aspiration of a soft fluctuant swelling dorsotemporal to the eye yields a tenacious, blood-tinged fluid. Surgical excision is usually curative.

GUINEA PIGS

Guinea pigs have a paurangiotic retina that appears avascular on examination (Fig. 40.1B). Their eyelids are open from birth, and they have a rudimentary third eyelid. Guinea pigs produce a very small amount of tears, and measurement of tear production by using commercially available strips is not possible.[84] The phenol red thread tear test is a better option to assess tear production in guinea pigs.

Conjunctivitis is common in guinea pigs (Fig. 40.7). One common cause is *Chlamydia caviae* (previously classified as *Chlamydia psittaci*),[40] which causes a self-limited disease manifesting as mild chemosis, ocular discharge, and follicle formation. Cytologic examination of a specimen from a conjunctival scraping may reveal intracytoplasmic inclusion bodies in epithelial cells. Treatment is generally considered unnecessary. Vitamin C deficiency in guinea pigs causes conjunctivitis with a flaky discharge. Treatment is directed at correcting the dietary deficiency.

Other causes of conjunctivitis are varied. A spontaneous outbreak of listerial keratoconjunctivitis has been reported in hairless guinea pigs.[15] Clinical signs ranged from serous lacrimation with hyperemic conjunctiva to purulent, ulcerative keratoconjunctivitis with corneal neovascularization. *Listeria monocytogenes* was cultured from the ocular discharge. Treatment was not attempted. Blepharitis caused by dermatophyte infection may be seen in young guinea pigs.[5] Topical antifungal therapy is usually effective. Irritation from abnormal hairs causes conjunctivitis, irritation, and possibly corneal ulceration. Surgical resection is curative.

Causes of infiltrative or nodular disease of the eye are also varied. Lymphosarcoma is rare in guinea pigs but has been reported to infiltrate the cornea.[81] Lymphosarcoma should also be considered as a differential diagnosis of conjunctival masses in guinea pigs.[2] Another differential diagnosis for conjunctival nodules in guinea pigs is a syndrome known as "pea eye." These nodules are protrusions of portions of the lacrimal or zygomatic glands and appear pale or pink. Treatment is not necessary because animals are usually not bothered by this condition. A large palpebral liposarcoma was diagnosed in a guinea pig. Treatment was not attempted.[70] A dermoid is a congenital lesion in which skin-like tissue is present in an abnormal location. Corneal and conjunctival dermoids have been reported in guinea pigs.[65,92]

Cataracts have been reported in guinea pigs.[97] Cataracts can be removed surgically, but the procedure is difficult because of the small size of the globe, the large size of the lens, and the difficulty of intubating a guinea pig for general anesthesia.

Osseous metaplasia of the mesectodermal trabecular meshwork occurs in guinea pigs (Fig. 40.8).[10,30] Clinically, an arc of white, opaque material is visible in the anterior chamber, covering the iridocorneal angle. Vessels may be present overlying the osseous choristoma. Hematopoietic active bone marrow is present. This is usually an incidental finding and no specific treatment is necessary.

As in other rodents and rabbits, exophthalmos in guinea pigs may be related to dental disease. A tooth root abscess of a molar may result in maxillary sinusitis and orbital disease. Careful examination of the teeth and a CT scan of the skull are indicated in any guinea pig with exophthalmos.

CHINCHILLAS

Chinchillas have a vertical slit pupil and an anangiotic retina without a tapetum.[45,61] The optic disc can be myelinated or nonmyelinated, and focal cupping of the optic nerve is a normal finding. Most chinchillas do not have a menace or dazzle response. The orbit is shallow, and the globe proptoses easily. The third eyelid is rudimentary. Chinchillas have a Harderian gland, Meibomian glands along the length of both eyelids, a lacrimal gland in the temporal canthus, and two lacrimal puncta on the inner conjuctival surface of both eyelids near the medial canthus.[88] Cataracts and asteroid hyalosis have been reported in older animals.[40] Epiphora and conjunctivitis are commonly seen and often related to husbandry (see Chapter 22). The most common isolates from normal conjunctiva include *Streptococcus,* coagulase-negative *Staphylococcus* species, and *Staphylococcus aureus.*[45]

The premolar, molar, and incisor teeth in chinchillas, as in guinea pigs, continue to grow and erupt throughout the animal's life. Insufficient wear can result in elongated roots of the premolar and molar teeth, resulting in progressive orbital disease including epiphora, decreased retropulsion of the globe, and proptosis (see Chapter 36).[18] Computed tomography is more



Fig. 40.8 Ophthalmologic conditions in guinea pigs. (A) protrusion from the inferior conjunctival sac or "pea eye." (B) Heterotopic bone formation characterized by white lesions at the limbus. (Courtesy C. Mans.)

sensitive than radiography in detecting early lesions.[17] The prognosis for advanced disease is poor. Exophthalmos secondary to an orbital *Taenia coenurus* has been reported. Surgical excision was curative.[35]

RATS, MICE, AND HAMSTERS

The retinas of rats, mice, and hamsters are holangiotic, with arteries and venules radiating from the optic nerve like spokes on a wheel.[24,96] Rats have three lacrimal glands: the intraorbital, extraorbital, and Harderian glands.

Inbred strains of rats and mice are commonly used in commercial laboratories to study naturally occurring ophthalmologic diseases. Diseases involving all parts of the eye have been described. Common abnormalities are retinal degeneration, as in the Royal College of Surgeons (RCS) rat strain[85]; microphthalmos; and cataracts. In addition to specific, genetically determined ocular abnormalities in inbred strains, other spontaneous abnormalities occur. Ophthalmic examination of 6000 Sprague-Dawley rats revealed a focal linear retinopathy in 3% and a fundic coloboma in 0.5%.[37] Spontaneous corneal degeneration has been described in Sprague-Dawley and Wistar rats,[7] and corneal dystrophy has been described in Fischer 344 rats.[48] Experimental infections also lead to ophthalmic abnormalities. Blepharitis with crust formation in the medial canthus and partial periocular alopecia were observed in mice experimentally infected with *Trypanosoma brucei*.[80]

Conjunctivitis in mice can be caused by numerous infectious agents, including *Pseudomonas aeruginosa, Pseudomonas pneumotropica, Salmonella* species, *Streptobacillus moniliformis, Corynebacterium kutscheri,* Lancefield group C streptococci, *Mycoplasma pulmonis,* mousepox or ectromelia virus, Sendai virus, and lymphocytic choriomeningitis virus.[6,40] Bacteriologic culture and sensitivity testing may be indicated in individual rats and mice with persistent conjunctivitis. Epiphora in rats and mice can be caused by dental problems. Nasolacrimal duct obstruction can result from overgrowth or malocclusion of the incisors.

Chromodacryorrhea, or "red tears," is red staining around the eyes seen in rats and mice. Inflammation of the Harderian gland causes secretion of tears pigmented with porphyrin. Sialodacryoadenitis virus is a highly contagious coronavirus that replicates in the respiratory tract epithelium, causing rhinotracheitis, bronchitis, and alveolitis. The virus also causes sialoadenitis of the submandibular and parotid salivary glands and necrotizing dacryoadenitis of orbital and Harderian lacrimal glands. Exophthalmos, epiphora, and keratoconjunctivitis may result. The infection usually resolves within 1 week in immunocompetent animals. In a study of athymic rats, infection persisted for more than 3 months, indicating that normal T-cell function is required for host defenses against the virus.[95] Infection with sialodacryoadenitis virus may also result in uveitis and multifocal retinal degeneration.[40] Complications from infection include corneal opacification, anterior and posterior synechiae, cataract, and glaucoma. Specific therapy is not available, and treatment is supportive only. Other causes for red tears are infection with parainfluenza virus type 3 or Sendai virus, as well as pain or stress. Ammonia vapor from soiled bedding can act as an ocular irritant, predisposing animals to secondary infection. Keeping the housing areas well ventilated is important in preventing infection with sialodacryoadenitis virus.

Of clinical significance is the effect of xylazine on the lens in rats and mice. A reversible cataract has been observed after systemic use of xylazine. Transcorneal water loss and altered aqueous humor composition caused by corneal exposure have been suggested as a pathogenesis of cataract formation.[14]

In hamsters, keratoconjunctivitis can result from ammonia vapor from soiled bedding. Dental problems including tooth root infection may result in facial or retrobulbar abscesses, with hemifacial swelling, proptosis, and exposure keratitis as common sequelae. Treatment with systemic antibiotics is often unrewarding, and such abscesses frequently lead to the animal's death.[40] A decrease in tear production was observed after systemic treatment with trimethoprim-sulfa for 14 days in hamsters.[72]

Insidious globe enlargement with loss of vision has been reported in four hamsters.[22] Ophthalmic examination of these hamsters revealed enlarged globes in both eyes, widely dilated pupils, lack of pupillary light reflex, a small optic nerve, and pale retinas. Histopathologic results suggested chronic open-angle glaucoma. Treatment of the suspected glaucoma was not attempted.

An intraocular signet-ring cell melanoma was diagnosed on histopathologic examination of an enucleated globe in a hamster. Enucleation was curative.[46]

SUGAR GLIDERS

Sugar gliders have an avascular retina. Only a small residual tuft of fluorescein-impermeable vessels projects from the optic disk into the vitreous.[13]

Sugar gliders have prominent globes that are susceptible to trauma. Corneal ulcers may result from intraspecies fighting.[69] A retrobulbar abscess can result from a bite wound to the face or a molar root abscess (see Chapter 27). Corneal lipid infiltration may form in juvenile sugar gliders when the mother is fed a diet that is too high in fat. Although not reported, cataract formation is seen clinically.

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41

Emergency and Critical Care of Small Mammals

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IDENTIFICATION AND TRIAGE OF THE CRITICALLY ILL PATIENT

Most exotic companion mammals do not show symptoms of illness in the early stages of disease. Thus patients with chronic disease often present as emergencies due to an innate ability to mask clinical signs of disease until the condition is severe. For these reasons, owners suspecting illness in their small mammal pets should be advised to present them as soon as possible for examination.

Identify critical patients as soon as they come into the veterinary hospital. Admit immediately to the hospital any patient demonstrating extreme respiratory difficulty or open-mouthed breathing, collapse, marked weakness, seizure, or uncontrolled bleeding. In many cases, complete physical examination is delayed in favor of emergency stabilization.

Treatment of critically ill exotic companion mammals is complicated by their small size, physiological diversity, and the lack of research and clinical data on response to therapy. Despite these impediments, the same principles and techniques used in dogs and cats can be applied to small mammals.

CARDIOPULMONARY RESUSCITATION (CPR) IN EXOTIC COMPANION MAMMALS

Cardiopulmonary arrest occurs frequently in critically ill small mammals presenting on an emergency basis. It is essential that clinicians are prepared to initiate effective, evidence-based, cardiopulmonary resuscitation (CPR) efforts to improve outcomes in these patients. In 2012, the Reassessment Campaign on Veterinary Resuscitation (RECOVER) initiative developed a set of clinical consensus CPR guidelines for small animals (dogs and cats) that represent the most current, evidence-based standards for veterinary CPR.[16] Although these guidelines do not specifically include exotic pet species, they offer a reasonable foundation for universal CPR efforts in most mammals. These recommendations outline both approaches to basic life support (BLS) and advanced life support and follow concise, clear guidelines for CPR efforts and postarrest care.[16] Many clinicians follow a similar approach to CPR in exotic companion mammals but modify it to the unique needs of these patients as detailed below (Fig. 41.1).

Begin CPR in any unresponsive, apneic patient or in any patient suspected of being in cardiopulmonary arrest (CPA), because the risk of injury due to CPR in patients not in cardiopulmonary arrest is low and time is of the essence. This is particularly true for smaller exotic patients where higher metabolic rates and increased oxygen demand likely contribute to poorer outcomes. In these patients, the use of pulse palpation to support a diagnosis of CPA before initiating CPR is not recommended. Ensuring that anesthetized exotic companion mammal patients are intubated and well monitored allows not only for early recognition of cardiopulmonary arrest but for provision of prompt and effective

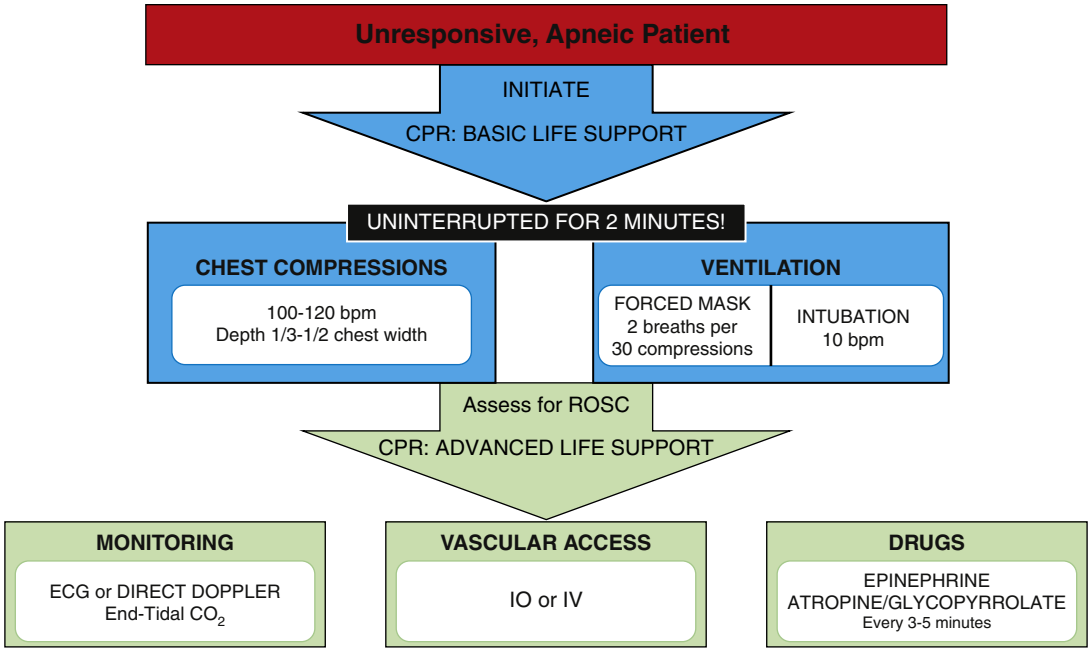


Fig. 41.1 Recommended cardiopulmonary resuscitation algorithm for both basic and advanced life support for exotic companion mammals. (Modeled after the small animal Reassessment Campaign on Veterinary Resuscitation guidelines.[16]) While not validated in exotic species, these guidelines represent a logical starting point and have been found clinically useful. This flow chart should be readily available along with the emergency resuscitation drug dosage list (Table 41.1) and should be maintained with emergency and critical care supplies (Box 41.1) for easy reference. *ROSC,* Return of spontaneous circulation.

CPR. Always attempt CPR in an anesthetized patient in cardiopulmonary arrest, because these patients typically have a better prognosis for survival and discharge from the hospital than the overall CPR survival rate.[8,16]

Basic Life Support

Basic life support consists of providing effective chest compressions and appropriate ventilation (Fig. 41.1). Perform chest compressions in lateral recumbency (although circumferential compressions may also be used) at a minimal rate of 100 to 120 compressions/min with a compression depth of ⅓ to ½ the width of the chest, while ensuring full chest wall recoil occurs between compressions.[16] Chest compressions should be uninterrupted for 2-minute cycles, after which compressors should rotate to reduce compromise of compression efficacy because of fatigue.[16] Continuous chest compressions with simultaneous ventilation are recommended for patients that are intubated and could be considered even in patients receiving forced mask ventilation. Likewise, following the RECOVER guidelines for mouth-to-snout ventilation,[16] some clinicians will deliver two rapid, forced-mask ventilation breaths for every 30 chest compressions. Recommended ventilation rates for dogs and cats with cardiopulmonary arrest is 10 breaths/min and is likely a good initial starting rate for exotic patients.[16]

The most challenging aspect of CPR in most exotic companion species relates to difficulties with patient intubation. Oral endotracheal intubation techniques and ventilation are covered in more detail elsewhere in this text (see Chapter 37). In apneic or critically ill patients with signs of imminent respiratory arrest, emergency intubation and positive-pressure ventilation is ideal. For the ferret, endotracheal intubation is similar to the cat and is relatively simple to perform even in an emergency setting. Ferret intubation can be performed with supplies routinely stocked in most emergency hospital crash carts. In rabbits and small rodents, oral endotracheal intubation is considerably more challenging and often time consuming. Blind techniques cannot be performed in rabbits experiencing respiratory arrest because this technique relies on breath sounds to accurately place the endotracheal tube.

Forced-mask ventilation with a tight-fitting face mask can be a life-saving means of providing positive-pressure ventilation during cardiopulmonary arrest in any patient that cannot be rapidly intubated (Fig 41.2). In a case report reviewing a successful CPR episode in a geriatric chinchilla, noninvasive positive-pressure face mask ventilation was used to provide effective ventilation.[15] In a retrospective study on cardiopulmonary arrest in rabbits, five of seven animals recovered when using only a tight-fitting mask during CPR for ventilation and oxygenation.[8] Species such as rabbits, guinea pigs, and chinchillas are unable to vomit, minimizing the risk of aspiration when using a tight-fitting face mask for ventilation. Progressive gastric distention caused by aerophagia commonly occurs and may require management once return of spontaneous circulation is established. In severe cases, passage of a nasogastric or orogastric tube may help relieve significant gastric distention contributing to cardiovascular compromise.

Another means of ventilation in rabbits is the use of a supraglottic airway device; various sizes have been developed for rabbits (V-gel for Rabbits; Docsinnovent Ltd., London United Kingdom). During CPR, however, these may become easily dislodged, and correct placement of these devices relies on end-tidal CO_2 ($ETCO_2$) measurements, which makes placement during CPR challenging. In some cases, emergency tracheostomy may be required for rapid airway management and ventilation (see Oxygen Therapy).

Advanced Life Support

Advanced life support consists of initiating patient monitoring, obtaining vascular access, and providing appropriate drug therapy. Advanced life support is performed after BLS has been initiated, until return of spontaneous circulation occurs (Fig. 41.1). Providing continuous electrocardiography (ECG) monitoring allows for assessment of underlying rhythm status. Evaluate the ECG after each 2-minute cycle of compressions, during the brief period of time when compressor rotation occurs (ideally <5–10 seconds). In very small mammal patients, ECG monitoring may not be practical during CPR; instead, place a Doppler crystal directly over the sternum during this brief pause to evaluate the heart (Fig. 41.3). Small mammal patients typically demonstrate asystole or pulseless electrical activity, which requires drug therapy including epinephrine, vasopressin, and anticholinergics (Table 41.1). For patients with ventricular fibrillation or pulseless ventricular tachycardia, prompt defibrillation is indicated but poses technical limitations and safety risks, given the small size of many exotic patients. Defibrillation in small patients requires the use of internal paddles and defibrillators capable of providing lower energy settings (1–5 Joules). The incidence of ventricular fibrillation in exotic companion mammals is unknown but is suspected to be quite low in most species, with the exception of rabbits.

In intubated patients, $ETCO_2$ monitoring during CPR is recommended as an early indicator of return of spontaneous



Fig. 41.2 Positive-pressure ventilation in a rabbit using a tight-fitting anesthetic mask. This form of ventilation may be effective in cases of respiratory arrest when intubation is not possible.



Fig. 41.3 Correct placement of a Doppler crystal over the sternum of a sugar glider for assessment of return of spontaneous circulation during a brief compressor rotation pause in cardiopulmonary resuscitation. Note the concurrent use of an IO catheter and forced mask ventilation.

TABLE 41.1 Cardiopulmonary Resusitation (CPR) Drug Dosages and Vasopressor Constant Rate Infusion (CRI) Dosing Suggested for Use in Exotic Companion Mammals

Drug (Concentration)	Dose (IV or IO)[c]	mL/50 g	mL/100 g	mL/kg	mL/2 kg
Epinephrine (1:1,000) (1 mg/mL)	0.01 mg/kg	0.0005	0.001	0.01	0.02
Atropine[a] (0.54 mg/mL)	0.04 mg/kg	0.004	0.008	0.08	0.16
Glycopyrrolate (0.2 mg/mL) (rabbits)	0.1 mg/kg	0.025	0.05	0.5	1
Vasopressin (20 U/mL)	0.8 U/kg	0.002	0.004	0.04	0.08
Naloxone (0.4 mg/mL)	0.04 mg/kg	0.005	0.01	0.1	0.2
Flumazenil (0.1 mg/mL)	0.01 mg/kg	0.005	0.01	0.1	0.2
Atipamezole[b] (5 mg/mL)	100 µg/kg	0.001	0.002	0.02	0.04
External defibrillation (monophasic)	4–6 J/kg	NA	NA	4	8

Increasing the dose of atropine increases the risk of severe tachycardia as well as the risk of ventricular arrhythmias. Use glycopyrrolate (onset of action 30–45 seconds) in rabbits.

[a]Atropine (onset of action 15–30 seconds) is not recommended in rabbits, as many possess serum atropinesterase and the dose is unpredictable.

[b]Reversal for 10 µg/kg dose of dexmedetomidine; for higher doses of dexmedetomidine, reverse with equal volume of atipamezole.

[c]Other routes including intramuscular and intratracheal could be considered, although efficacy is unknown.

Drug (Concentration)	Dose in CRI
Norepinephrine (1 mg/mL)	0.05–0.5 µg/kg/min IV CRI
Vasopressin (20 U/mL)	0.5–4.0 mU/kg/min IV CRI
Dopamine[d] (40 mg/mL)	5–10 µg/kg/min IV CRI
Dobutamine[e] (12.5 mg/mL)	1–20 µg/kg/min IV CRI

[d]Within a dose range of 5-30 µg/kg/min, dopamine was not effective in treating isoflurane induced hypotension in rabbits.[17]

[e]Inotrope.

circulation and is also helpful in measuring the efficacy of CPR in conditions of consistent minute ventilation. Measuring $ETCO_2$ is practical only in intubated patients weighing more than 50 grams.[14,21] Values greater than 15 mmHg suggest that chest compressions are adequate,[16] whereas values greater than 18 mmHg have been shown to consistently predict return of spontaneous circulation in dogs.[23]

Obtaining vascular access in debilitated, critically ill patients can be difficult. Intraosseous catheterization (IO) offers a rapid and effective means of vascular access (see Chapter 37), and IO catheters can be placed in the tibia of most patients without interfering with the provision of chest compressions. For drug therapy during CPR, intravenous (IV) or IO routes are preferred over intratracheal administration and are associated with improved survival from CPA in studied species. If IV or IO routes cannot be obtained, intratracheal administration can be attempted if the patient is intubated. Drugs delivered by this method are diluted with saline solution or sterile water and administered at higher doses via a catheter passed through the tube lumen and extending past the end of the tube.

Should CPA occur in anesthetized patients, immediately discontinue inhalant anesthesia and provide 100% oxygen via an endotracheal tube or tight-fitting face mask as previously described. Vascular access should be obtained before any anesthetic procedure; this allows one to rapidly administer anesthetic reversal drugs as indicated. Reversal agents include naloxone (to reverse opioids), flumazenil (to reverse benzodiazepines), and atipamezole (to reverse alpha-2 agonists) and should be provided at recommended doses during CPR as needed (Table 41.1).

The RECOVER CPR guidelines recommend the use of low-dose (0.01 mg/kg IV) epinephrine administered every 3 to 5 minutes (i.e., every other cycle of BLS) early in CPR.[16] A single high dose (0.1 mg/kg IV) of epinephrine may be considered after prolonged CPR (>10–15 minutes) but should otherwise be avoided; although higher doses have been associated with increased rates of return of spontaneous circulation, they have not been associated with increased survival to discharge.[16] Epinephrine is a catecholamine, predominately used for its alpha-1 vasopressor activity during CPR. However, epinephrine also has β_1 adrenergic activity and should be used judiciously to avoid exacerbating myocardial ischemia, which can predispose patients to arrhythmias after return of spontaneous circulation. Rabbit CPR studies have shown epinephrine to be effective in achieving return of spontanous circulation at doses as low as 0.015 mg/kg IV,[24] despite the wide dose range reported in a recent rabbit CPR retrospective study (0.006–0.26 mg/kg; median, 0.09 mg/kg), which likely reflects the lack of CPR standardization before the 2012 RECOVER guidelines.[8] In the case of successful CPR in a chinchilla, a much higher dose of epinephrine (0.2 mg/kg) with the addition of vasopressin (0.9 U/kg) was reported.[15] Because little evidence-based medicine exists in terms of epinephrine use during cardiopulmonary arrest in many exotic species, the RECOVER recommendations should be strongly considered as a reasonable range to initiate CPR drug therapy in exotic companion mammal species (Table 41.1).

Vasopressin is a vasopressor that mediates effects via a peripheral V1 receptor located on smooth muscle and therefore works independently of the adrenergic system. Vasopressin has no inotropic or chronotropic effects that could worsen myocardial ischemia, and its V1 receptors remain responsive in the face of an acidic pH, making this an ideal vasopressor in cardiopulmonary arrest patients. The RECOVER CPR guidelines recommend the use of vasopressin (0.8 U/kg IV) as a substitute or in combination with epinephrine every 3 to 5 minutes[16] (Table 41.1). Use in exotic species has been documented in several case reports and under experimental conditions. In a rat model of asphyxial cardiac arrest, low-dose vasopressin (0.4 U/kg) produced similar outcomes with no additional benefits when compared with a higher dose of vasopressin during or after CPR.[11] However, when a standard vasopressin dose (0.8 U/kg IV) was compared with high-dose epinephrine (0.2 mg/kg) in a rabbit model of asphyxia cardiac arrest, 13 of 24 epinephrine rabbits had return of spontaneous circulation compared with only 2 of 23 rabbits receiving vasopressin.[12] In the rabbit CPR retrospective study, 3 of the 15 reported cases received vasopressin within a wide dose range (0.15–1.5 U/kg; median 0.64 U/kg).[8]

Although anticholinergics such as atropine are commonly administered during CPR, the current literature supports no beneficial or detrimental effect.[16] The RECOVER CPR guidelines note that in cases of asystole or pulseless electrical activity associated with high vagal tone, the use of standard dose (0.04 mg/kg) atropine is reasonable (Table 41.1).[16] In some species such as dogs, higher doses (0.1, 0.2, and 0.4 mg/kg) have been associated with worse outcomes in experimental studies.[16] Glycopyrrolate has been recommended as an alternative to atropine in rabbits because of concerns that some rabbits have high levels of serum atropine esterase activity, potentially resulting in reduced efficacy and duration. Whether this is clinically significant in terms of CPR is not known. In a study evaluating the effects on heart rate in anesthetized rats and rabbits, both atropine and glycopyrrolate increased the heart rate in rats, while only glycopyrrolate (0.1 mg/kg) elevated the heart rate in rabbits.[37] Both atropine (0.015–0.18 mg/kg; median, 0.04 mg/kg) and glycopyrrolate (0.002–0.045 mg/kg; median, 0.01 mg/kg) were administered to rabbits in a recent retrospective CPR study, with no difference in outcome elucidated.[8] In the report of CPR in a geriatric chinchilla, return of spontanous circulation occurred rapidly with only epinephrine and vasopressin, and no anticholinergics were administered.[15]

CPR Preparedness

Crash carts or tool-boxes containing appropriate resuscitation equipment should be available in areas of the hospital such as the intensive care unit, operating room, and emergency triage areas (Box 41.1). They should be standardized and undergo regular audits of their location, storage, and contents.[16] Likewise, CPR cognitive aids including CPR algorithms and dosing charts should be displayed in these areas of the hospital. ProCPR training, including both didactic and "hands-on" simulation, should be provided to all staff members, with ongoing refresher courses offered on a regular basis to ensure continued competency in CPR techniques.[16]

BOX 41.1 Exotic Companion Mammal Emergency and Critical Care Crash Cart Inventory[a]

Mandatory Drugs
- Epinephrine (1:1000, 1 mg/mL)
- Vasopressin (20 U/mL)
- Atropine (0.54 mg/mL)
- Glycopyrrolate (0.2 mg/mL)
- Naloxone (0.4 mg/mL)
- Flumazenil (0.1 mg/mL)
- Atipamezole (5 mg/mL)

Additional Drugs
- Lidocaine 2%
- Hypertonic saline solution (7.3%)
- Dextrose (50%)
- Furosemide
  - Norepinephrine
  - Dobutamine
  - Dopamine
  - Calcium gluconate
  - Amiodarone

Supplies
- ET tubes (appropriate size for exotic mammals)[b]
- Laryngoscope with appropriate blades (±otoscope or endoscope)
- ET tube tie material (can also be used assist with oral cavity positioning)
- Tight-fitting anesthetic face masks (appropriate size for exotic mammals)[b]
- Ambu-bag (bag valve mask; infant sizes with pressure relief valve is ideal)
- Extra oxygen line
- Extra suction tubing
- Sterile cotton-tip applicators
- Syringes, needles, flush, catheters (appropriate size for exotic mammals)[b]
- Blades (No. 11, No. 15)
- Suture (sizes 5-0 to 2-0; absorbable and nonabsorbable)
- Blood gas syringes
- Intraosseous catheters (25- to 18-gauge hypodermic needles; spinal needles with stylet)[b]
- ECG with atraumatic clips or small ECG pads
- Capnograph (portable ideal)
- Warmed fluids (replacement crystalloids such as LRS or saline solution)
- Tracheostomy kit (no. 11 blade, 25G × 1 mL syringe, <20G IV catheter, ET tube adapter)
- Thoracocentesis kit (three-way stop cock, 25G butterfly catheter, small syringe)
- Bandaging supplies (basic vetwrap, rolled gauze, cast padding, tape-cut to size)
- Tourniquet (rubber band with a hemostat or small commercial product)

Ideal Equipment Available in ER/ICU
- Oxygen flow meter + humidifier
- Oxygen cage (with heat and humidity control)
- Multi-parameter monitor with ECG, BP, $ETCO_2$, pulse oximeter[b]
- Doppler unit (used to monitor heart directly or for BP with appropriate cuff sizes)[b]
- Lactate meter, glucometer, hematocrit tubes, slides for blood smear
- Point-of-care ultrasound unit
- Vacuum suction unit with suction tubing
- Defibrillator (monophasic with capability of 1–5 J and small internal paddles)

[a]Drugs and supplies should be stored together and readily available in one or more designated locations. Contents should be checked regularly to be sure all items on the list are present and drugs are within use date.
[b]Refer to Chapter 37 (Anesthesia, Analgesia, and Sedation of Small Mammals) for more details.
BP, blood pressure; *ECG,* electrocardiographic unit; *ER/ICU,* emergency room/intensive care unit; *ET,* endotracheal; *$ETCO_2$,* end total CO_2.

OXYGEN THERAPY IN EXOTIC COMPANION MAMMALS

Providing oxygen to emergency and critically ill patients is an essential and often life-saving intervention. The small body weight of many exotic patients is associated with high metabolic and oxygen consumption rates, leading to a relatively low tolerance to even brief hypoxemia.[21] Irreversible CNS injury can occur rapidly (≤30 seconds) after respiratory arrest in rodents.[21] Oxygen supplementation is provided to patients to increase arterial oxygen content and decrease the risk of tissue hypoxia.

Unless animals are presented apneic or with signs of imminent respiratory arrest, most critically ill small mammals benefit from noninvasive oxygen supplementation before a complete physical examination. Patients in severe respiratory distress may require ongoing oxygen supplementation during a brief, limited examination.

The simplest way to provide noninvasive oxygen therapy to emergency and critically ill patients is by using an oxygen chamber or cage. Commercial oxygen cages, found in many emergency hospital settings, that regulate oxygen concentration, humidity, and temperature and monitor carbon dioxide levels are ideal. These units are often large enough to accommodate smaller transport cages to minimize stress associated with handling (Fig. 41.4). These oxygen cages can provide fraction of inspired oxygen (FiO_2) levels up to 60% in some units, although they typically supply levels around 40% to 50%. Small Plexiglass induction units or plastic containers supplied with oxygen via tubing or anesthesia machine circuits require openings to allow venting or scavenging of carbon dioxide but can be effective alternatives to commercial units. Oxygen analyzer devices (i.e., MiniOX; Ohio Medical, Gurnee, IL) can be used to determine supplied FiO_2 levels in constructed oxygen chambers.



Fig. 41.4 A rabbit with respiratory disease hospitalized in a commercial oxygen chamber. Chambers able to regulate oxygen concentration, humidity, and temperature and monitor carbon dioxide levels are ideal.

Other means of supplying oxygen therapy include both noninvasive and invasive strategies. While flow-by oxygen



Fig. 41.5 Flow-by oxygen delivered to a critical guinea pig. While flow-by oxygen supplementation is one of the simplest methods of providing oxygen to emergent patients, the oxygen supply tubing must be held within 2 cm of the patient's nostril to be effective.

supplementation is one of the simplest methods of providing oxygen to emergent patients, the oxygen supply tubing must be held within 2 cm of the patient's nostril to be effective (Fig. 41.5).[33] Tight-fitting face masks at flow rates of 8 to 12 L/min can provide a FiO_2 of up to 50% to 60% in small animals.[33] Face masks for small rodents can be fashioned from adapted syringe cases, and small diaphragms can be constructed from glove material for an improved fit. Stressed, dyspneic, and relatively conscious patients will often not tolerate these methods. Nasotracheal oxygen/intubation, oral endotracheal intubation, and laryngeal masks/supraglottic airway devices are covered elsewhere in this text (see Chapter 37).

Because many exotic species are obligate nasal breathers, using wet gauze sponges to clean away any nasal discharge obstructing the nares is beneficial. In rabbits with very thick nasal discharge that presents risk of imminant asphyxiation, consider emergency nasal irrigation. Sedate the patient by using a drug combination administered rapidly by intramuscular injection (see sedation below), and induce anesthesia by using an IV induction agent or facemask/chamber induction with an inhalant agent, depending on the patient's predicted ability to tolerate stress and handling. Intubate the rabbit and then position it head down to promote egress of fluids. Gently irrigate the nasal cavities with warm saline solution until the flush solution is clear. Monitor the patient carefully for dyspnea after extubation. One author (A.M.L.) has used this technique successfully in several rabbits; in one case, there was no improvement at extubation. The rabbit was reinduced and irrigation repeated, which resulted in significant improvement.

Percutaneous emergency airway access and tracheostomy are rarely used but can be performed in cases where the inability to provide oxygenation becomes life threatening. With the exception of rabbits with a large dewlap, transtracheal oxygen catheters (an appropriately sized over-the-needle IV catheter smaller than the tracheal lumen) can be placed under emergency conditions in a manner similar to other companion animals. In guinea pigs, chinchillas, and small rodents, transtracheal oxygen catheters can provide a rapid means of oxygenation, and in some cases manual ventilation, most notably in patients presenting in respiratory arrest. If indicated, tracheostomy can be performed after a transtracheal oxygen catheter is placed, which allows the clinician to place larger-diameter tubes, including small cuffed endotracheal tubes. This provides more effective positive pressure ventilation than percutaneous catheter techniques. Although well tolerated in dogs, experience with this technique in exotic species is very limited.

Pulse oximeters are inexpensive and readily available, and probe placement is generally well tolerated in conscious veterinary patients. In ferrets, pulse oximetry was closely related to oxygen saturation measured by blood gas analysis, with the most precise measurements obtained when the oxygen saturation was between 90% and 100%.[36] Pulse oximetry has been validated in rabbits (accurate at hemoglobin saturation values >85%) and rats (at values >70%).[21] Depending on level of consciousness and willingness to tolerate monitoring, pulse oximeter transmission sensors can be placed on the tongue, buccal mucosa, ears, paws, proximal tail, and vulva/prepuce, and reflectance probes can be placed against the carotid artery in the cervical region or used in the esophagus or rectum.[21]

FLUID RESUSCITATION OF CRITICALLY ILL EXOTIC COMPANION MAMMALS

Shock and Fluid Therapy

Shock is defined as inadequate tissue perfusion and is often classified based on the driving cause; hypovolemic, distributive, obstructive, or cardiogenic. Depending on the extent and duration of the underlying cause, patients can present in compensated or decompensated shock.

In our experience, exotic mammals rarely present in compensated shock, but instead are more likely to have signs of decompensated shock on arrival to the hospital. Studies in rabbits and rats show baroreceptor response to hypovolemia begins at 30% loss of blood volume, and continued loss of blood volume after this point results in hypovolemic shock and hypotension. Clinical signs are hypothermia (i.e., cool limbs and skin), tachycardia, normal or decreased blood pressure, pale mucous membranes, prolonged capillary refill time, and mental depression.[2] Aggressive fluid therapy using crystalloids and possibly colloids to support blood pressure and heart rate is required at this stage.

When a larger volume of blood or plasma is lost, the neuroendocrine responses to hypovolemia become ineffective and irreversible organ failure begins. This is the final common pathway of all forms of shock in all species.[2] Clinical signs are bradycardia with low cardiac output, severe hypotension, pale or cyanotic mucous membranes, absent capillary refill time, weak or absent pulses, hypothermia, oliguric to anuric renal failure, pulmonary edema, and a stuporous to comatose state. Cardiopulmonary arrest commonly occurs at this stage.[2]

Types of Fluids

Fluid choices include crystalloids and colloids. Individual characteristics of fluids influence the type and volume of fluid administered.[19] Isotonic crystalloid replacement solutions are commonly used in the resuscitation phase and can

BOX 41.2 Flow Chart for Treatment of Hypovolemic Shock in Exotic Companion Mammals[a]

Treatment of Decompensatory Shock	Dosage
Obtain STAT diagnostics: PCV, TSS, glucose, lactate, indirect BP, ECG, POCUS, +/- acid-base panel (ideally rule out cardiogenic shock/congestive heart failure with POCUS before proceeding)	
Administer warmed crystalloid solutions IV or IO 1–2 boluses as needed	10–15 mL/kg
Begin external and core body temperature warming	
Begin crystalloids at maintenance rate	3–4 mL/kg per hour
If hypoglycemic, administer 50% dextrose IV or IO	1 mL/kg diluted 1:4
Add 5% dextrose as needed to additional fluids based on serial blood glucose measurements	
For trauma patients with suspected head trauma or pulmonary contusions, consider administering hypertonic saline solution 7.2%–7.5% IV or IO in lieu of initial crystalloid boluses for a small-volume resuscitation approach	3–4 mL/kg slowly over 10 min
↓	
When patient is warmed to minimum 98°F (36.6°C), begin correction of hypovolemia using crystalloid boluses IV or IO	10–15 mL/kg
Monitor indirect systolic blood pressure and/or other clinical markers including mm/capillary refill time, HR, pulse quality, mentation, serial lactate; repeat 2–3 boluses until blood pressure >90 mmHg and there is improvement in clinical markers	
Positive response: indirect BP >90 mmHg	
↓	
Replace fluid losses to correct dehydration (Box 41.3)	3–4 mL/kg per hour
Replace ongoing losses	
Add maintenance fluids	
Negative response (indirect blood pressure <90 mmHg) after total volume 60–70 mg/kg crystalloids	
↓	
Add inotrope or vasopressor support (Table 41.1) especially if sepsis is suspected	10–20 mL/kg
If PCV < 20%, consider whole blood transfusion	3–5 mL/kg
If TSS <4–5 g/dL, consider synthetic colloid boluses to effect *or* administered as a constant rate infusion	10–20 mL/kg per 24 hours

[a]A flow chart and emergency resuscitation drug dosage list (Table 41.1) should be maintained with emergency and critical care supplies (Box 41.2) for easy reference.
BP, blood pressure; *ECG,* electrocardiographic unit; *HR,* heart rate; *IO,* intraosseus; *IV,* intravenous; *PCV,* pack cell volume; POCUS, point-of-care ultrasound; *TSS,* toxic shock syndrome.

be used in combination with colloids.[19] Isotonic replacement cystalloids include 0.9% saline solution and balanced electrolyte solutions such as lactated Ringer's solution, Plasma-Lyte A, or Normosol-R. Hypertonic saline solution (7.2%–7.5%) is a hyperosmolar crystalloid solution that draws fluid into the intravascular space from all body compartments rapidly; therefore this can be extremely useful in selected cases.[46] Natural colloids are blood, plasma, or albumin. The most commonly used synthetic colloids are hydroxyethyl starch (hetastarch [HES]) solutions, primarily used for acute intravascular volume expansion and intravascular colloid osmotic pressure maintenance. These solutions are characterized by their average molecular weight, concentration, degree of molar substitution, and C2:C6 ratio. Commercially available HES solutions include 6% HES 600/0.75 (HESpan; B. Braun Medical Inc., Bethlehem, PA) and 6% HES 130/0.4 (VetStarch; Zoetis, Kalamazoo, MI). The use of HES solutions in both human and veterinary medicine has been a source of recent controversy, because concerns have developed over the potential risk of acute kidney injury (AKI) with the use of these products.[20,35]

Warm all fluids to the body temperature of the patient regardless of the route of administration (see "Maintenance of Normothermia," below). Fluids can be warmed to 100°F to 103°F (38°C–39°C) without affecting their composition.[19] Dextrose solutions may be added to crystalloid solutions (1.25%–5%) and adminstered IV or IO for treatment of hypoglycemia confirmed via blood glucose measurement.

Fluid Resuscitation Strategies

Fluid therapy is used to correct life-threatening abnormalities in volume, electrolyte, and acid-base status. The goals of fluid therapy are resuscitation (correction of perfusion deficits), rehydration (correction of interstitial deficits), and maintenance.[19] Administering the least amount of fluids necessary to reach the desired endpoints of resuscitation is important. Resuscitation implies an urgent need to restore tissue perfusion and oxygenation. The type, quantity, and rate of fluid administration required to reach the desired resuscitation endpoints are determined based on the phase of shock. As mentioned above, exotic mammals typically present in the decompensatory phases of shock. Single-product fluid regimens and fixed administration volumes based on simple milliliter-per-kilogram formulas are, in most instances, outdated and often inadequate. Appropriate fluid therapy, based on rational product choice, combined with frequent patient evaluation and periodic blood pressure monitoring (where applicable), can greatly improve patient response to therapy and survival rates (Box 41.2).

The ideal approach to fluid resuscitation in critically ill small mammals is not known and likely varies based on their underlying condition. However, it is reasonable to consider similar protocols to those used in dogs and cats. These are based on titrating fluid therapy to effect, using measurable resuscitation end-points. In larger species, such as ferrets and rabbits, this includes the serial assessment of STAT diagnostic tests (see below) including pack cell volume (PCV)/total solids (TS), lactate, acid-base panels,

blood pressure, ECG, and point-of-care ultrasound (POCUS)-based volume assessments. For smaller patients such as rats and other rodents species, clinical markers are often more appropriate determinants of response to therapy and include restoration of normal mentation, mucous membrane color, capillary refill time, and establishment of normothermia, normovolemia, and normal heart rate and urine output.[19]

The total blood volume for most small mammals can be calculated as approximately 6% to 7% of normal body weight, or about 60 to 70 mL/kg. Thus providing crystalloid fluid boluses of 10 to 15 mL/kg while assessing response to therapy is a reasonable approach for the initial resuscitation of most critically ill, hypovolemic patients (Box 41.2). For those presenting moribund or with more advanced stages of decompensated shock from profound fluid losses or hemorrhagic shock due to trauma, the use of colloids or hyperosmolar therapy may be indicated. Infusion of 7.2% to 7.5% hypertonic saline solution (3–4 mL/kg IV or IO as a slow bolus over 10 minutes) allows for marked increases in intravascular volume by using smaller resuscitation volumes. The rapid effects of hypertonic saline solution can be maintained with the addition of the synthetic colloids (HES), which can be given in bolus aliquots of 3 to 5 mL/kg IV or IO over 5 to 10 minutes. In large, critically ill patients, indirect systolic blood pressure should be checked frequently (see below). In hypothermic patients, once pressure is greater than 40 to 60 mmHg systolic or there is improvement in other clinical markers of shock, administer maintenance isotonic crystalloids while aggressively rewarming the patient (see below). In many species, once rectal temperature approaches 98°F (36.7°C), adrenergic receptors begin to respond to catecholamines and fluid therapy.[38] Temperatures during this rewarming phase must be checked frequently in all patients to prevent inadvertent hyperthermia. Blood pressure is rechecked when the temperature is greater than 98°F (36.7°C). Isotonic crystalloids (10–15 mL/kg) or synthetic colloids in increments of 3 to 5 mL/kg can be repeated over 15 to 30 minutes until the systolic blood pressure rises above 90 mmHg or there is again improvement in clinical markers (Box 41.2). When the systolic blood pressure is above 90 mmHg, the rehydration phase of fluid resuscitation begins.

If the patient is known to be hypoproteinemic, a constant-rate infusion (CRI) of synthetic colloids may help maintain oncotic pressures in the intravascular space. If improvement is not seen after three to four boluses of HES and crystalloids, the patient is evaluated and treated for causes of nonresponsive shock (i.e., excessive vasodilation or vasoconstriction, hypoglycemia, electrolyte imbalances, acid-base disorder, cardiac dysfunction, hypoxemia). If cardiac function is normal and glucose, acid-base, and electrolyte abnormalities have been corrected, consider treatment for other causes of nonresponsive shock, including sepsis. For refractory hypotension, a dobutamine CRI (inotrope support) should first be provided before considering the use of vasopressor agents. Vasopressors such as dopamine or norepinephrine can then be added to further manage refractory hypotension (often associated with sepsis) as is common practice in traditional pet species (Table 41.1).[38] If PCV and total protein are low (e.g., PCV < 20%), whole blood may be required (see below).

BOX 41.3 Correction of Dehydration Deficits

- Estimate percent dehydration:
  4%–5% Dry MM
  5%–7% Mild skin tenting, dry MM
  7%–9% Moderate skin tenting, dry MM
  >10% Sunken eyes, altered mentation, significant skin tenting, dry MM
- Calculating deficits: % dehydration × kg × 1000 mL = fluid requirements (mL)
- Add maintenance requirements: 3–4 mL/kg/hour plus on-going losses (diarrhea, etc.)
- Replacing losses based on CV status:
  Acute loss of <24 hours, unstable CV status: replace deficit over 4–6 hours.
  Chronic loss >24 hours, stable CV status: replace over 12–24 hours.
  Assess response to rehydration with serial body weight and urine output.

CV, cardiovascular; *MM,* mucous membranes.

Determine hydration status after successful resuscitation. As in dogs and cats, dehydration is often indicated and losses estimated by decreased skin turgor and dry mucous membranes; however, this method is somewhat insensitive (Box 41.3).[18] Rehydration is best accomplished by using an isotonic replacement crystalloid solution. The rate of fluid administration depends primarily on the rate of fluid losses and clinical status of the animal, as indicated by the physical examination and laboratory parameters. For animals with evidence of interstitial dehydration on physical examination but stable cardiovascular parameters, replace fluid deficits over 12 to 24 hours. If the interstitial volume was lost rapidly, replace the interstitial fluid deficit rapidly (4–6 hours). Fluid requirements for dehydration are calculated as percent dehydration × kilogram × 1000 mL = fluid deficit (mL) (Box 41.3). Serial weight determinations are helpful in determining when appropriate fluid volumes have been replaced. An objective way to assess whether the fluid volume is adequate is to evaluate body weight regularly throughout the day. Acute weight loss is commonly associated with fluid loss and can be used to determine whether the patient is at risk of becoming dehydrated again.[19]

Maintenance fluids should be administered to meet metabolic demands and restore intracellular water balance until the animal is eating and drinking on its own.[19] Maintenance requirements are higher in smaller patients because of their higher metabolic rate. Some clinicians use a maintenance rate of 3 to 4 mL/kg per hour for most exotic mammals, which is double that used in cats and dogs.[28] Likewise, allometric calculations of resting energy requirement (weight [kg] 0.75×70) can be used to approximate daily maintenance fluid requirements in small mammals weighing less than 5 kg. Critically ill animals that are relatively inactive and not eating have reduced daily maintenance fluid requirements.

Special conditions may warrant adjustments to fluid replacement, including ongoing fluid losses, and conditions such as AKI. The volume of ongoing losses (polyuria, diarrhea, vomiting) are estimated and added to maintenance fluids. Whereas urinary catheterization and measurement of urine can be used to objectively determine urinary output, this is not usually practical in small mammals. An alternative approach is to weigh bedding or towels before and after placing them into the cage

(1 mL urine = 1 g). Baseline and serial monitoring of body weight every 6 to 8 hours may also assist in assessing ongoing fluid shifts. It is important to avoid fluid overloading patients, especially AKI patients because this is associated with worse clinical outcomes in dogs and cats and likely applies to small mammals as well. An increase in weight of greater than 10% of initial body weight is consistent with fluid overload, and fluid adjustments should be made to avoid this in critically ill patients.

For patients with AKI and significant polyuria (urine output >2–3 mL/kg per hour), fluid rates should be adjusted based on measured urine output and serial body weights. For anuric/oliguric (urine output <0.5 mL/kg per hour) AKI patients that have been adequately fluid resuscitated, fluid rates should replace insensible losses only (20–30 mL/kg per day), until polyuria returns. Total fluid adminstration, including parenteral medications and catheter flush volumes, must be monitored. In dogs and cats, CRIs of furosemide and fenoldopam (selective dopamine DA-1 agonist) have been used in an effort to manage oliguric AKI states with variable success, and CRIs could be considered in small mammal patients, given that renal replacement therapy (diuresis) is not practical in most species. Close monitoring of renal values, urine output, body weight, and electrolyte status is key to succesfully managing fluid therapy in AKI patients.

Routes of Fluid Administration

Placement of IV or IO catheters in exotic companion mammals is discussed elsewhere in this text (see Chapters 2, 12, and 37). Ideally, oral or subcutaneous fluids should be reserved for stable, standing patients that are suspected to be less than 5% dehydrated. In reality, the risks of catheter placement in some patients may outweigh its benefits. Therefore in these select patients it may be beneficial to administer subcutaneous fluids while gently rewarming the patient before catheterization. Oral fluids should not be administered if there is significant risk of aspiration or evidence of gastrointestinal dysfunction.

BLOOD TRANSFUSIONS

Administer blood products when albumin, coagulation factors, platelets, or red blood cells are required.[19] Most fluid-responsive shock patients will tolerate acute hemodilution to 20% PCV. Most animals can tolerate an acute blood loss of 10% to 15% blood volume without requiring a blood transfusion. Acute hemorrhage exceeding 20% of blood volume often requires transfusion therapy in addition to initial fluid resuscitation. When promoting cardiac output is the first priority in the management of acute hemorrhage, blood is not the ideal resuscitation fluid. Blood products do not promote blood flow, as well as acellular fluids; therefore blood is rarely used for initial resuscitation, unless the patient is exsanguinating, there is a coagulopathy, or there is severe trauma. The density of erythrocytes impedes the ability of blood products to promote blood flow (viscosity effect). Crystalloids and HES solutions are less viscous and therefore promote blood flow. As in other species, continued blood loss, severe anemia with a PCV <12%–15%, and clotting disorders (such as rodenticide toxicosis) are typical indicators used to determine the potential need for a whole-blood transfusion. Whole blood can be administered at 10 to 20 mL/kg (IV or IO).

The availability of blood products in sufficient quantities to meet the needs of exotic patients is often the limiting factor in survival. Commercial blood banks do not carry blood products for small mammals, with the possible exception of the ferret. Current options for overcoming this limitation are maintaining a relationship with a local rescue for small mammals and keeping a list of other clients willing to bring in their pets for blood donation in exchange for clinic credit. Blood is collected in the carefully restrained or sedated patient via the cranial vena cava or another large, accessible vein by using a needle or butterfly catheter and syringe. Be aware that isoflurane can cause a reduction in PCV in the ferret and should be avoided. A large needle size prevents red cell hemolysis; therefore we prefer to use a 22-gauge needle in rabbits and ferrets. Anticoagulant products typically used in small animals can be used for exotic species as well. The most common anticoagulant available at most clinics is citrate-phosphate-dextrose-solution with adenine (CPDA), typically used at a ratio of 7:1 (7 mL blood to 1 mL CPDA). Citrate-phosphate-dextrose and acid-citrate-dextrose solutions are also available and can be used at similar ratios. Heparin can be used at 1 to 10 IU per 1 mL of blood, but collected blood must be used within 24 hours because it lacks preservatives. Collect blood into syringes with an appropriate anticoagulant and use immediately because ideal storage conditions are unknown for many species. One study showed that ferret blood preserved with CPDA at a ratio of 6:1 (6 mL of ferret blood to 1 mL CPDA) was safely stored short term at 39°F (4°C) in plastic polyethylene terephthalate blood collection tubes for up to 7 days.[38]

Ferrets are unique in that they appear to have a single blood type; therefore multiple donor transfusions are possible and commonly performed.[39] Blood groups have not been identified in most other exotic companion mammals. A simplified cross match can be performed in these small patients by mixing two drops of plasma from the recipient with one drop of whole blood from the donor on a slide at room temperature.[19] The development of macroscopic agglutination within 1 minute would suggest incompatibility. A successful major cross match does not imply that reactions will not occur, but it helps to minimize potential complications resulting from agglutination.

The blood-administration set must include a filter to remove most of the aggregated debris. The most practical solution for small blood volumes is to use an in-line 18-µm pore blood filter (Hemo-nate; Utah Medical Products, Midvale, UT) attached to a syringe. Administer donor blood by slow bolus or by infusion with a syringe pump into a catheter placed in the jugular, saphenous, or cephalic vein or into an IO catheter. In cases of massive hemorrhage, administer blood more rapidly, within minutes. Otherwise, administer blood transfusions within 4 hours of collection, according to standards set by the American Association of Blood Banks, to prevent the growth of bacteria.



Fig. 41.6 A constant-read-out thermometer (Electronic Thermometer; Veterinary Specialty Products, Mission, KS) with a flexible temperature probe used in a rabbit. The probe should be secured with tape to the tail to prevent it from slipping out.

MAINTENANCE OF NORMOTHERMIA

All small animals experience some degree of hypothermia in the early decompensatory stages of shock. Body temperature is easily recorded in most species by using a standard rectal thermometer, a constant-readout temperature probe, or an esophageal temperature probe (for anesthetized patients only) (Fig. 41.6). New methods using infrared thermometry methods have been developed and tested in human patients and are currently under investigation for small mammals.[9,22,27]

The normal body temperature of exotic companion mammals varies. Some species such as guinea pigs and chinchillas easily experience heat stress; therefore rewarming should proceed cautiously in these species.[43] Monitor temperature constantly during the rewarming process, because severely depressed animals may not be able to move away from the heat source in case of overheating.

External rewarming methods include the use of warming blankets and pads (Hot Dog Warming Unit, Augustine Biomedical and Design, Eden Prairie, MN), circulating-warm-air blowers (Bair Hugger; Arizant Healthcare, Eden Prairie, MN; or Thermacare; Gaymar Industries, Orchard Park, NY), or hot-water-filled examination gloves (with careful monitoring) (Fig 41.7). Warming of core body temperature is accomplished through warming of the IV or IO fluids with an intravenous fluid warmer (Meditemp III, Gaymar Industries; or Hotline Fluid Warmer; Smiths Medical PM, Inc., Waukesha, WI) or by running the IV line under warming devices or through hot water. Inspired oxygen can be warmed by placing warmed fluid bags directly on top of the oxygen line. In severely hypothermic patients, attempts to rewarm via external methods only can result in the shunting of colder blood to the body core, causing rebound hypothermia.[38]

NUTRITIONAL SUPPORT

Enteral nutrition should be delivered as rapidly as possible to prevent negative consequences of prolonged anorexia. Anorexia causes breakdown of the tight junctions between gastric and intestinal cells, leading to bacterial overgrowth and possible sepsis.





Fig. 41.7 Hospitalized patients. (A) Rabbit. (B) Ferret. Both animals are catheterized with fluids delivered via a pediatric infusion pump, intravenously in the cephalic vein. Note measurement of indirect systolic blood pressure in each. Rewarming with a warm-air circulating device (Thermacare; Gaymar Industries, Orchard Park, NY) (A) and a flexible heating blanket (Hot Dog Warmer; Augustine Biomedical and Design, Eden Prairie, MN) (B).

Nutritional support is a vital component of treatment and is crucial to resolve and prevent gastric stasis, especially in herbivores. Fluid replacement therapy must also play a role in nutritional support, as the gastrointestinal tract must be hydrated to facilitate motility and function. Many small mammals tolerate syringe feeding well in general, but when syringe feeding is refused, consider placing a nasogastric or esophagostomy tube (see Chapters 12, 21, 22).

Support feeding diets are available from Oxbow Pet products (Critical Care, and Carnivore Care; Oxbow Animal Health, Murdock, NE) and the Lafeber Company (Emeraid; Lafeber, Cornell, IL). Both companies provide detailed instructions for use of diets in various exotic species.

Perform syringe feeding slowly and carefully to avoid aspiration, especially in animals in respiratory distress. Oxbow

Critical Care Fine Grind is suitable for delivery via a nasogastric tube. All diets should be fed as recommended by the manufacturers.

CRITICAL CARE STAT DIAGNOSTIC TESTING AND MONITORING

There are several key STAT diagnostic tools available for traditional small animal veterinarians that are historically underutilized in exotic animal medicine. These tests allow rapid assessment and ongoing monitoring of key parameters while minimizing stress, handling, and required blood sample volumes. These point-of-care assessments span from bedside laboratory tests to emergency ultrasound assessments and show promise for the management of critically ill exotic patients.

CLINICAL PATHOLOGY

It is extremely important that hematologic and biochemical data be available as soon as possible to help guide decision making for the critical care patient. For this reason, in-house testing is preferred. Several manufacturers produce equipment that enables in-house analysis of relatively small blood samples. One biochemical analyzer can produce a panel with 0.13 mL of high-quality whole blood (VetScan; Abaxis, Union City, CA). Other point-of-care analyzers (i-STAT; Abbot Point of Care Inc, Abbott Park, IL; NOVA Stat Profile Critical Care Xpress; Nova Biomedical, Waltham, MA) also require small sample volumes. Although reference ranges have not been established for all exotic species, values can often be extrapolated using guidelines similar to those used in traditional small animal species.[1,13]

Even very small samples, for example those obtained from the hub of the IV catheter, may be used to determine manual PCV/total solids, lactate, blood smear, and glucose determination, which can provide important information. Although trends in glucometer values may be useful, a recent study in ferrets demonstrated that results from handheld glucometers varied markedly and should be compared with those obtained from analyzers validated for ferrets.[44]

LACTATE MONITORING

Blood lactate concentrations are considered by some to be accurate indicators of inadequate tissue perfusion in humans and traditional pet species.[5] Lactate monitoring is especially important in critically ill patients presenting in shock. Assessing and interpreting baseline and serial blood lactate levels not only serve as indicators of tissue hypoperfusion but are often used to guide therapy in critically ill animals.[40] Changes in serial lactate values in response to therapy can be potential prognostic indicators in emergent patients presenting with several serious conditions. [40] Lactate values become increased (i.e., >2.5 mmol/L) in many domestic animals when perfusion parameters are poor (e.g., heart rate, blood pressure, temperature, and capillary refill time). Lactate and perfusion parameters often return to baseline values with effective fluid therapy. Hyperlactatemia also commonly develops in patients with anemia, hypoxemia, sepsis, systemic inflammatory response syndrome, and septic shock.[40] Peritoneal-fluid to blood lactate comparisons are also used to assess small animal patients presenting with acute abdomen and abdominal effusion to help determine if septic peritonitis is present and if surgical intervention is warranted.[40]

Blood lactate values in exotic species may provide clinicians with a key clinical assessment tool when stabilizing emergent cases. However, lack of reference ranges for these species warrants clinician discretion when extrapolating from traditional pet species. A recent evaluation of blood lactate values in rabbits revealed baseline lactate values in healthy rabbits were considerably higher than those established in dogs and cats.[26] In one study comparing commonly available analyzers, lactate values reported for rabbits were 7.0 (± 2.6) mmol/L for the Nova analyzer (Nova Biomedical), 7.3 (± 2.9) mmol/L for the IDEXX analyzer (IDEXX Veterinary Chemistry Analyzer, Westbrook, MA), and 6.6 (± 3.7) mmol/L for the Point of Care Lactate Analyzer (Point of Care Portable Lactate; Arkray, Kyoto, Japan).[42] Although references ranges have not yet been published in ferrets, in one author's experience (J.G.), they tend to follow similar trends noted in dogs and cats.[40]

COAGULATION TESTING

Coagulopathy is not commonly reported in exotic species, although without routine testing and established references ranges, the true incidence remains unknown. In ferrets, prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen ranges measured by use of a photooptical clot detection system (ACL 3000 Coagulation nalyzer; Beckman Coulter, Brea, CA) have been published and reported as PT, 10.9 ± 0.3, range 10.6 to 11.6 seconds; PTT, 18.1 ± 1.1, range 16.5 to 20.5 seconds; and fibrinogen concentration, 107.4 ± 19.8 mg/dL, range 90.0 to 163.5 mg/dL.[4] Unpublished data (M. Lichtenberger and Z. Schwartz, personal communication; 2004) for normal ferrets comparing reference laboratory values (Antech Diagnostics, Irvine, CA) for PT and PTT with values derived from the commonly used in-house SCA2000 (Synbiotics Corporation, Kansas City, MO) gave results of 12 ± 1.5 seconds from the reference laboratory and 20 ± 1 seconds for the SCA2000 device. The PTT was 18 ± 2 seconds from the reference laboratory and 52 ± 19 seconds for the SCA2000. Correlation was good between results from the two different testing methods for PT but not for PTT.

The use of coagulation parameters in small-animal critical care medicine is very important, as coagulopathies frequently occur with liver disease, toxicoses, and disseminated intravascular coagulation. One author (J.G.) has managed cases of anticoagulant rodenticide toxicosis in several species, including ferrets and rabbits. Cases frequently presented with signs consistent with coagulopathy and had PT values out of range of common analyzers.

POINT-OF-CARE ULTRASOUND (POCUS) IN EXOTIC COMPANION MAMMALS

Emergency ultrasound scanning offers rapid real-time information that assists in urgent patient care and clinical decision making. Numerous studies have shown that emergency ultrasound scanning is an expedient and sensitive tool for the rapid diagnosis of life-threatening conditions in dogs and cats.[6,7,30–32,34] Ultrasound scanning evaluates patients more objectively than survey radiographs alone, while minimizing patient stress and handling. Recent reports of ultrasound use in critically ill rabbits have shown great benefit, including rapid identification of occult liver lobe torsion and characterization of severe thoracic disease, including thymomas.[18,25]

Although complete diagnostic ultrasound techniques have also been reported for other species, including rabbits, ferrets, and even rats, emergency POCUS techniques appear underreported in exotic species.[3] One author (J.G.) routinely performs emergency POCUS examinations (including evaluation of the abdomen, lung/thoracic cavity, and cardiac views) to rapidly assess emergency conditions in exotic companion mammals. Results from experimental studies suggest that typical ultrasound lung artifacts used in bedside lung ultrasound examination techniques can be visualized in rabbits, including the glide sign and the presence of pleural effusion.[48] Emergency POCUS cardiac evaluation is often useful in determining if the cause of respiratory distress in patients is cardiac in origin. A recent study describing diagnostic echocardiography in rabbits determined that the median values for the left atrium to aorta ratio and percent fractional shortening in the study rabbits were very similar to those previously determined in dogs and cats, making the subjective assessment of these parameters on POCUS cardiac evaluation relatively straightforward.[10] Relative mastery of POCUS cardiac assessments in dogs was shown to be feasible after minimal training of inexperienced sonographers, with 97% of participants in a recent study able to correctly identify right parasternal short-axis views.[45] Participants were also able to correctly identify pleural effusion (90%) and pericardial effusion (95%), and discriminate between normal atrial size and atrial enlargement (86%).[45] A full discussion of POCUS techniques is beyond the scope of this section but has been well described for traditional pet species in several published articles and a recent text book.[6,7,30,31,34]

INDIRECT MEASUREMENT OF SYSTOLIC BLOOD PRESSURE

Indirect measurement of systolic blood pressure is commonly used in veterinary medicine. In general, to ensure adequate organ perfusion in both the conscious and anesthetized patient, mammalian diastolic pressure should be above 60 mmHg and systolic pressure above 90 mmHg. Methods for detection include use of a sphygmomanometer with an ultrasonic Doppler scanner and newer oscillometric blood pressure measurement techniques.[47] Advantages of the Doppler method are relatively low cost and portability. New developments in oscillometric methods may eventually make this a reasonable alternative for use in exotic companion mammals as well.

To obtain blood pressure using the ultrasonic Doppler, place the patient in lateral or sternal recumbency. Place a pneumatic cuff above the carpus or tarsus or on the tail (Fig. 41.8). The cuff size should ideally be about 40% of the circumference of the limb or tail. Finger cuffs used in human medicine are available (Parks Medical, Aloha, OR). Shave the hair on the ventral carpus, tarsus (not in rabbits), or medial midshaft of the radius-ulna or tail. Place the transducer probe crystal on the shaved area in a bed of ultrasonic gel and tape or hold it in place. Inflate the cuff to a suprasystemic pressure until the Doppler signal is extinguished. The first sound heard as the cuff is deflated denotes the systolic pressure. This technique requires practice and becomes more difficult with decreasing patient size.

Studies on the use of blood pressure measurement in exotic companion mammals are lacking. One study indicated that the forelimb was more reliable than the pelvic limb for measuring indirect blood pressure in rabbits.[47] Another study in ferrets showed that larger-sized cuffs resulted in a decrease of 28 to 30 mmHg in indirect systolic pressures when compared with direct systolic pressures.[36]

Studies in many species demonstrate some degree of disagreement between indirect and direct systolic blood pressure measurement; this is attributed to variations in cuff sizes and sensitivities as well as variations in arterial waveforms between anatomic sites. For this reason, the greatest benefit of blood pressure measurement may be as a trend monitor. We routinely use indirect blood pressure measurement along with other parameters to gauge response to therapy in the patient in hypovolemic shock and as part of monitoring during anesthesia. We have found indirect systolic blood pressures in normal exotic companion mammals to range between 80 and 120 mmHg.

SEDATION AND ANESTHESIA OF THE CRITICALLY ILL SMALL MAMMAL

Anesthesia should be avoided in the critically ill patient; however, some diagnostic testing and procedures can produce discomfort and stress, negatively affecting patient survival. The risk of sedation or anesthesia should be weighed against the risk of foregoing diagnostic tests and treatments or attempting procedures in the conscious animal. Correct hemodynamic abnormalities (shock, hypovolemia) and hypothermia before administering sedatives or anesthetic agents. Many minor procedures (catheterization, sample collection, diagnostic imaging) can be done in ill small mammals with the use of sedation alone or with the addition of local analgesia, if indicated. For example, for IV or IO catheterization, we prefer a combination of low-dose midazolam (0.25 mg/kg IM) plus an opioid, with topical application or infiltration of lidocaine over the catheterization site.

Isoflurane induction via face mask has historically been favored by exotic mammal practitioners. While isoflurane and sevoflurane have a wider margin of safety than many older anesthetic agents, they can produce apnea and hypotension, especially at the higher concentrations required when they are

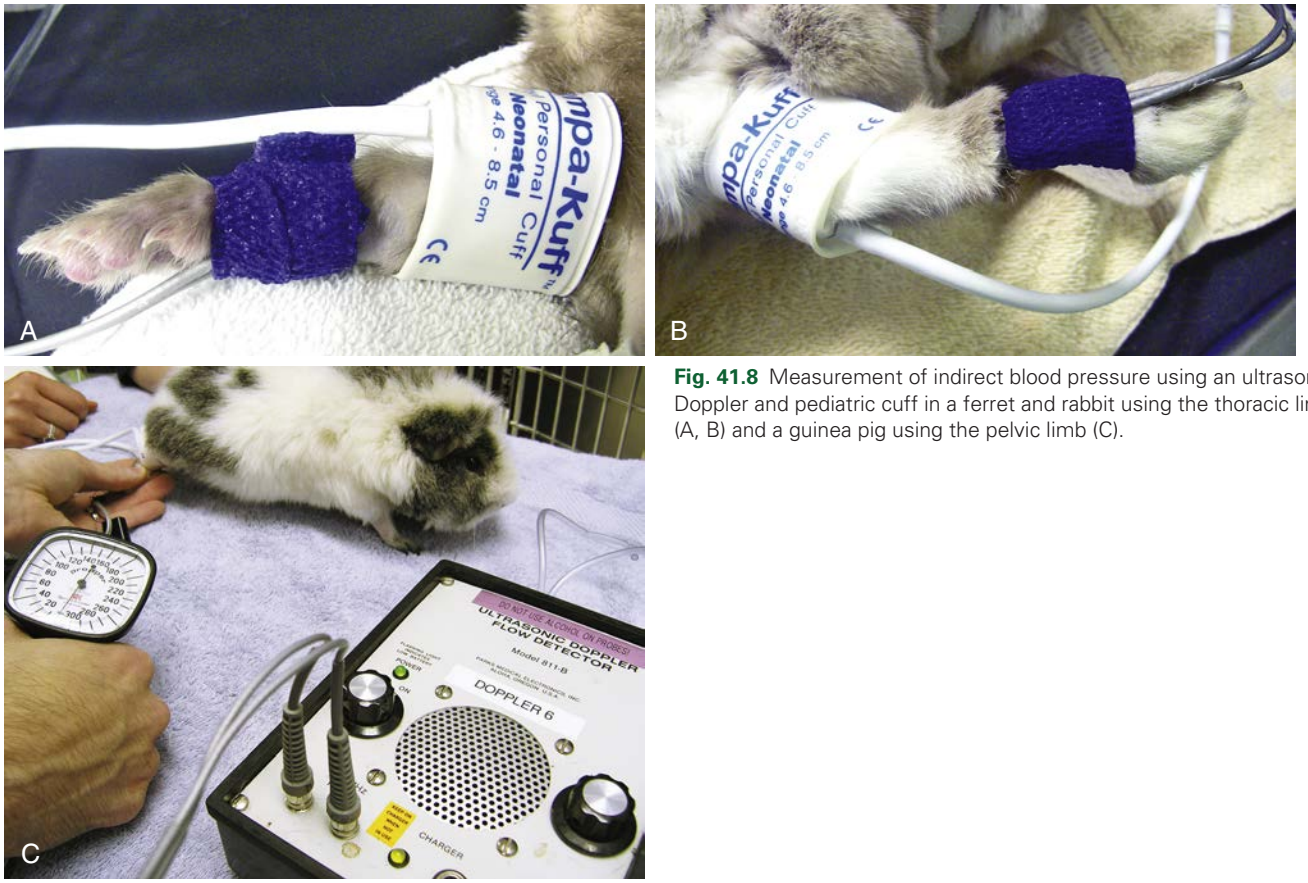


Fig. 41.8 Measurement of indirect blood pressure using an ultrasonic Doppler and pediatric cuff in a ferret and rabbit using the thoracic limb (A, B) and a guinea pig using the pelvic limb (C).

used as sole agents. Multimodal analgesic and anesthetic protocols greatly reduce the needed amount of any single agent, thus enhancing patient safety and survival.[29] When using any sedation or anesthesia protocol in critically ill exotic patients, be prepared for complications including cardiopulmonary arrest and have all reversal drugs drawn up and nearby (Table 41.1) to quickly antagonize any adverse effects, should they occur.[14]

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Zoonotic Diseases Associated With Small Mammals

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Small exotic mammals are relatively inexpensive pets that often do not require the intensive care or attention that is required of dogs and cats. Because of these perceived advantages, ferrets, rabbits, and rodents are frequently purchased as a child's initial pet. Unfortunately, most pet owners are unaware of the zoonotic risks associated with owning these animals. However, this lack of knowledge also extends to medical and veterinary professionals, who also are often unfamiliar with the common zoonotic agents associated with small exotic mammals. Specific reports of zoonotic diseases attributed to nontraditional species are rare. However, because of their increasing popularity and the amplified exposure to children and individuals with compromised immune systems (e.g., those who have undergone organ transplantation or immunosuppressive drug therapy or who have immunosuppressive diseases), the incidence of zoonotic diseases correlated with small mammal ownership may increase.

Most disease conditions associated with nontraditional mammalian pets are related to allergies, bites, and scratches. Dander from these nontraditional species can cause cutaneous and respiratory allergies in susceptible individuals. Many bite and scratch wounds inflicted by these pets can become infected with bacterial organisms. Pet owners can avoid bite injuries if they understand the behavior of their pets. These animals should be primarily handled during peak activity hours. Certain rodents, such as hamsters, will assume a defense posture by rolling on their backs and will vocalize to ward off any perceived dangerous advances from people. Most bite injuries are related to nocturnal/crepuscular species, such as hamsters and sugar gliders, and can be avoided if owners are educated about the most appropriate times to handle their pets.

This chapter focuses on the zoonotic potential of disease transmission to the typical companion animal owner. Individuals who work with large collections of ferrets, rabbits, and rodents in laboratory animal settings or breeding facilities have a higher potential for exposure.

BACTERIAL DISEASES

Bordetella bronchiseptica is a gram-negative rod to which high morbidity and mortality rates in guinea pigs have been attributed.[36] Hamsters and mice are not as susceptible to this pathogen as other rodents.[50] *Bordetella bronchiseptica* can be isolated from clinically normal rodents and lagomorphs. Clinical signs in affected animals are generally associated with the respiratory system and are characterized by nasal and ocular discharge, coughing, sneezing, and pneumonia. This pathogen is associated with respiratory tract infections in people. Although rodents and lagomorphs pose minimal risk in the zoonotic dissemination of this bacterium, at-risk individuals should take specific precautions to reduce exposure. Pet dogs are a greater risk than nontraditional mammals for *B. bronchispetica* transmission to humans through increased mouth-to-face contact.

Campylobacteriosis is a serious zoonotic disease responsible for the annual expenditure of millions of dollars in medical expenses. Although contaminated food (e.g., poultry) and water are the primary methods of exposure to *Campylobacter* species in the United States, infected pets (e.g., dogs, cats, horses, hamsters) may also be a source of exposure.[36] A very small percentage of the nearly 2 million confirmed cases a year of campylobacteriosis in the United States are attributed to pet exposure.[36] Although nontraditional small mammals may harbor *Campylobacter jejuni* or *Campylobacter pylori,* the risk that they will transmit this organism to their owners is low. A pet animal with diarrhea is a risk factor for shedding of *Campylobacter* species, which resulted in 6.3% of the cases of campylobacteriosis reported in a 1993 study.[36] Incubation of *Campylobacter* species is approximately 2 to 5 days, and the disease is generally self-limiting (10–14 days)

in the immunocompetent host.[36] Ferrets that have recovered from campylobacteriosis may shed the bacteria for more than 140 days.[36] Biomedical research suggests that ferrets orally inoculated with, *C. jejuni* may pose a special threat to individuals working with ferret colonies, as these animals were found to shed the organism for 144 days post-inoculation.[21a] Although no cases of ferret-associated campylobacteriosis have been reported, the prevalence of *Campylobacter* species in these ferrets suggests that they may serve as a source of infection. People usually suffer from a mild, self-limiting gastroenteritis with infection, but the disease may develop into a generalized septicemia that can result in death.

Chlamydia caviae is an obligate intracellular bacterium that can cause upper and lower respiratory disease in guinea pigs. Historically, this bacterium has not been considered an important zoonotic pathogen, as it was only associated with conjunctivitis[31]; however, a recent report describing respiratory failure in three human cases suggests that the zoonotic potential for this pathogen may be greater than originally thought.[44] One guinea pig was reported by the owner to have exhibited clinical signs consistent with respiratory disease before the owner's illness. Because the pathogen requires specific testing (e.g., polymerase chain reaction [PCR] testing), it is underdiagnosed. Veterinarians treating guinea pigs should consider it in their differential disease diagnoses when managing animals with upper and lower respiratory tract disease and educate their clients as to the potential risks associated with *Chlamydia caviae*.

Corynebacterium kutscheri is a gram-positive bacillus that is routinely isolated from the nasopharynx of rats. This microbe has also been isolated from clinically normal mice and hamsters. Most rodents that harbor this microbe are asymptomatic; however, acute clinical disease has been reported in susceptible animals. Affected rodents are generally in poor condition and may develop cutaneous abscesses, nasal and ocular discharge, and arthritis. Because this pathogen has been isolated from a human case of chorioamnionitis, rodents should be considered a potential reservoir for the disease.

Francisella tularensis is the causative agent of rabbit fever, or tularemia. This gram-negative coccobacillus is primarily a pathogen of wild rodents and lagomorphs. Captive rodents and lagomorphs generally are not considered important reservoirs for this microbe. The domestic cat is actually more likely to serve as a reservoir than other domestic species because of possible contact with infected wildlife. *Francisella tularensis* can be transmitted by aerosolization, direct contact, or ectoparasites (fleas and ticks). Affected individuals may develop cutaneous lesions, respiratory disease, or meningitis.

Leptospira interrogans is frequently isolated from wild rodents; however, a recent report suggests pet rodents, such as rats and mice, may also serve as a source of exposure to people.[37] Six human cases were identified in Belgium and France over a 7-year period. These cases represented individuals that developed severe disease, so the actual number of cases was likely much higher. In most cases, the pet rodent does not exhibit clinical signs; thus owners should be reminded to practice strict hygiene when handling their pets or the feces or urine of their pet. Veterinarians must also consider these potential risks. A veterinarian contracted leptospirosis from a pet rat through contamination of a hand abrasion.[3] Handwashing was not protective; this illustrates the importance of using examination gloves when handling patients. If leptospirosis is diagnosed in a person, testing the urine of the pet rodent by using a *Leptospira*-specific PCR assay is recommended. Individuals working with wild rodents or in areas where high densities of wild rodents are concentrated may also be at risk of contracting leptospirosis. *Leptospira interrogans, Leptospira grippotyphosa,* and *Leptospira icterohaemorrhagiae* have been isolated from ferrets. Individuals who have contact with ferrets used for hunting may also be predisposed to leptospirosis. The bacteria are shed in the urine, and transmission may occur from direct contact or aerosolization of urine-contaminated food, water, bedding, or soil. Affected individuals may have chills, fever, and malaise or septicemia and generalized organ dysfunction. The incubation period from exposure to infection is 2 days to 4 weeks,[12] and the initial clinical signs are a sudden fever, chills, headaches, vomiting, myalgia, and/or diarrhea.[12] People can recover from the initial disease with no other problems. If more severe disease problems develop after the initial recovery, this is also called Weil's disease (i.e., the development of kidney or liver failure or meningitis).

Listeria monocytogenes is a gram-positive, non-spore-forming rod. Ferrets may serve as a source of the *Listeria* organism because it has been isolated from the liver and lung tissue of infected animals. Listeriosis was also identified in ferrets experimentally infected with canine distemper virus. The common finding in many cases is that the infected ferrets were immunocompromised animals. Because adrenal gland disease is often diagnosed in geriatric ferrets and *L. monocytogenes* is ubiquitous in the environment, caretakers should take appropriate precautions to minimize their animals' exposure to this pathogen.

Ferrets are extremely sensitive to mycobacteriosis. *Mycobacterium avium, Mycobacterium bovis,* and *Mycobacterium tuberculosis* have all been isolated from ferrets. Most mycobacteriosis cases reported in ferrets are from Europe and New Zealand, where ferrets are used for hunting and are often fed uncooked meat and meat by-products. However, a recent case of *M. avium* subspecies *hominissuis* was reported in a pet ferret in Spain.[6] *Mycobacterium* species can be transmitted to people from ferrets through aerosolization of contaminated respiratory or gastrointestinal secretions or direct skin contact. Ferret owners should be instructed to offer only cooked meat to their animals, thereby reducing the likelihood of introducing pathogens to their colony. This disease should especially be a concern for clients with immunodeficiencies.[6]

Mycoplasma pulmonis is one of the most common diseases reported in pet rats. Affected rats present with a range of upper and lower respiratory signs, including sneezing, nasal discharge, hemoptysis, tachypnea, rough hair coat, anorexia, and crackles. This is a chronic disease that can eventually lead to debilitating disease for the pet rat. Historically, this bacterial pathogen was not considered a risk to humans; however, a recent study suggests persons who are exposed to this bacterial pathogen of rats and can develop significant titers.[40] A quarter of veterinarians and pet rat owners were found to be PCR positive on oropharyngeal swabs, and more than 65% of those tested were

seropositive for immunoglobulin G based on an enzyme-linked immunosorbent assay diagnostic test. Because serologic titers were high for several *Mycoplasma* species, the authors suggested there could be active infection. Although there is still much to learn about the effects of this pathogen in people, the high prevalence of disease in rats suggests it should be investigated further.

Pasteurella multocida, a gram-negative rod, is an opportunistic pathogen of lagomorphs and rodents. In rabbits, *P. multocida* can cause multisystemic disease and is difficult to eradicate. Because this organism is ubiquitous in the environment, inoculation into bite injuries or scratches received from lagomorphs or rodents can occur. In people, *P. multocida* has also been associated with multisystemic disease. Susceptible individuals, including young children and immunocompromised adults, should practice strict hygiene after handling these animals. Bite or scratch injuries should be immediately disinfected, and a physician should be contacted for additional information for wound management.

Pseudomonas aeruginosa, a gram-negative bacterium, is ubiquitous in the environment. Although many exotic small mammals are considered commensal hosts, few studies have characterized the prevalence of this opportunistic pathogen. A 2010 study in chinchillas reported the prevalence of *P. aeruginosa* to be nearly 42% in animals maintained as pets or in the laboratory setting.[36] The *P. aeruginosa* isolated from chinchillas showed patterns of resistance to antibiotics commonly used to treat these animals in captivity. Because this organism is a common cause of nosocomial infections in people, routine disinfection methods should be practiced after handling or cleaning small mammals and their cages to minimize the potential of exposure to this organism.

Rat-bite fever (RBF) is a rare but serious zoonosis caused by both *Streptobacillus moniliformis* and *Spirillum minus* (Fig 42.1). These gram-positive microbes are considered indigenous flora in rats and may be isolated from the nasal and oropharyngeal areas.[41] Laboratory and pet rats are the primary reservoirs, although wild rats and mice may also serve as competent reservoirs. These bacteria are primarily transmitted from a bite. The incubation for streptobacillary RBF in people is approximately 3 to 10 days, whereas it is 1 to 6 days for spirillary RBF. The clinical signs attributed to RBF are generally observed at about the same time the bite wound is healing; these include relapsing fever, chills, vomiting, myalgia, and regional lymphadenopathy. Persons infected with *S. moniliformis* frequently have a maculopapular rash on their extremities. This rash does not occur with spirillary RBF. In 2003, two cases were reported of previously healthy adult women dying from S. *moniliformis* septicemia 2 to 3 days after the initial onset of disease symptoms (i.e., headache, diarrhea, lethargy, myalgia, lymphadenopathy).[23] In another case reported in 2004, a 24-year-old male pet shop employee died after becoming infected through a superficial skin wound that occurred from contact with a contaminated rat cage.[36] Clinical signs were similar to those described for the women in the earlier report, although endocarditis and multiorgan failure ultimately led to the demise of the male patient. Rat-bite wounds should be immediately disinfected to reduce

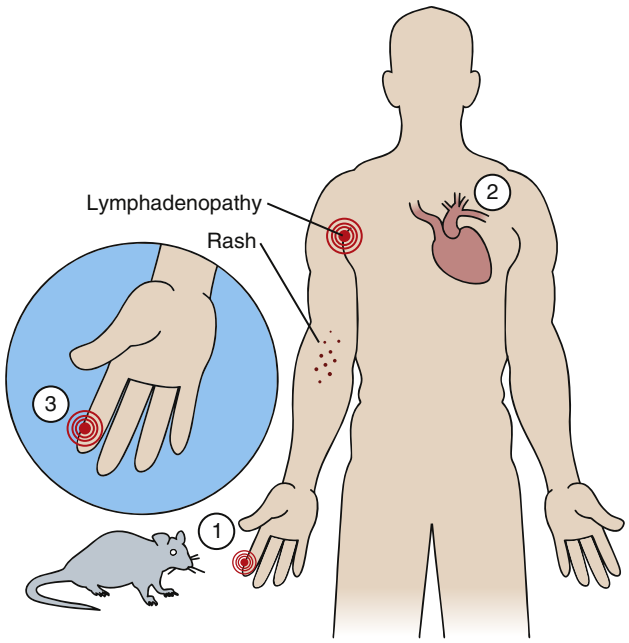


Fig. 42.1 Rat-bite fever in people is initiated with a bite that compromises the protective epithelial barrier. *1,* Entry wound (rat bite); *2,* spread of infection; *3,* disease ulceration at entry site.

the likelihood of transmitting these pathogens, and care should be taken in working around enclosures with positive animals. Affected individuals should seek medical attention and report their exposure history.[41] Physicians should be informed of a patient's exposure to a rat if an owner is being examined for an unexplained febrile illness or sepsis.[23,36] Although the disease is called rat-bite fever, approximately 30% of the patients confirmed with RBF have not reported being bitten or scratched by a rat.[23,36] Wearing gloves, handwashing after handling a rat, and avoiding hand-to-mouth contact with the animal or when cleaning its cage will help reduce the risk of being infected with organisms causing RBF or other potential rodent-transmitted zoonotic infections.[41]

Salmonella species, which are gram-negative facultative anaerobes, are ubiquitous in the environment. This microbe has been associated with both enzootic and epizootic outbreaks in captive rodent and lagomorph colonies.[24,36] *Salmonella* have also been isolated from other nontraditional small mammals, including sugar gliders, African hedgehogs, and ferrets.[51] All vertebrate species should be considered susceptible to *Salmonella* infection. There are more than 2400 different *Salmonella* serotypes, and all are potentially pathogenic, although most infections in people and animals are caused by fewer than 12 serotypes. *Salmonella enterica* ser. Enteritidis *(S. enteritidis)* and *S. enterica* ser. Typhimurium are the two most common serotypes isolated from rodents and lagomorphs, whereas *S. enterica* ser. Tilene appears to be the most common serotype isolated from sugar gliders and hedgehogs.[26,51] *Salmonella enterica* serovars Typhimurium, Hadar, Kentucky, and Enteritidis have been isolated from ferrets.[26,51] Most rodents and ferrets appear to be subclinical reservoirs for this microbe, except for guinea pigs, which can develop life-threatening septicemia. *Salmonella* infections are primarily transmitted by the fecal-oral route or

from contaminated fomites, but they also can be transmitted by aerosol through the conjunctiva in some species.[36] Affected vertebrates may have anorexia, weight loss, enteritis, lymphadenopathy, or septicemia. Reproductive disorders, including abortions and premature birth, have also been associated with *Salmonella* infections in rodents and lagomorphs. Persons who contract salmonellosis from these animals may have headaches, nausea, vomiting, abdominal pain, enteritis, or septicemia.[36]

People can acquire *Salmonella* from either direct or indirect exposure to mammal reservoirs, and the incubation period is approximately 6 to 48 hours. In 1994, a case of hedgehog-associated salmonellosis in a 10-month-old girl from Washington was attributed to indirect contact with the family's breeding colony of hedgehogs.[36] From December 2003 through October 2004, 28 cases of multidrug-resistant *S. enterica* ser. Typhimurium matched by pulsed-field gel electrophoresis to isolates from rodents (e.g., hamsters, mice) purchased at retail pet stores were reported in the United States.[48] The median age of those affected was 16, and many affected individuals (40%) were hospitalized. In addition to having been isolated from people and rodents, the organism was also found in rodent cages and transport boxes. Recently, an outbreak of *S. enterica* ser. Enteritidis was reported in guinea pigs, and a *Salmonella* Typhimurium outbreak was reported in hedgehogs.[2,5] The outbreak in guinea pigs was tracked over eight states, and 10 cases were identified.[5] The median age for the affected individuals was 9.5 years, which is slightly younger than those reported for the earlier outbreak. Younger children may be more likely to keep small mammals such as guinea pigs, so it is important for veterinarians to remind their clients to be aware of these risks when they clean their pet rodents and cages. In the hedgehog outbreak, 26 cases were reported over 12 states, and one death was associated with the outbreak.[2] Interestingly, most cases were in females, which is different from what is reported with reptile-associated salmonellosis. Hedgehogs remain an important reservoir of *Salmonella* species, with prevalence rates that can rival reptiles. For this reason, the authors educate all hedgehog clients by using the same hygiene recommendations they provide reptile clients. Frozen rodents intended as food for reptiles also have been found to serve as a potential zoonotic source of *S. enterica* Typhimurium.[10,36] One concern identified by Cartwright et al.[10] during their investigation of a 2008 to 2010 *Salmonella* outbreak associated with feeder mice was how few of the human patients (13%) realized that there was a potential risk for zoonosis from mice and rats. Because of the inherent zoonotic risks associated with ownership of small rodents and other animals, pet ownership should always involve adult supervision. Strict hygiene, including handwashing with soap, should be practiced to reduce the risk of exposure. The recommendations formulated by the Association of Reptile and Amphibian Veterinarians and the Centers for Disease Control and Prevention for reducing the risk of reptile-associated salmonellosis are appropriate to distribute to owners of companion exotic mammals.[36]

Streptococcus pneumoniae, a gram-positive cocci, has been isolated from several different mammalian species. However, rats and guinea pigs appear to be the most susceptible to this pathogen. Several different serotypes affect rats (II, III, VIII, XVI, and XIX) and guinea pigs (III, IV, and XIX); some of these serotypes can also infect people. Transmission of this pathogen is generally through aerosolization of contaminated respiratory secretions or by direct contact. Affected rodents may have pneumonia and torticollis. Persons infected with *S. pneumoniae* may have respiratory and meningeal disease.

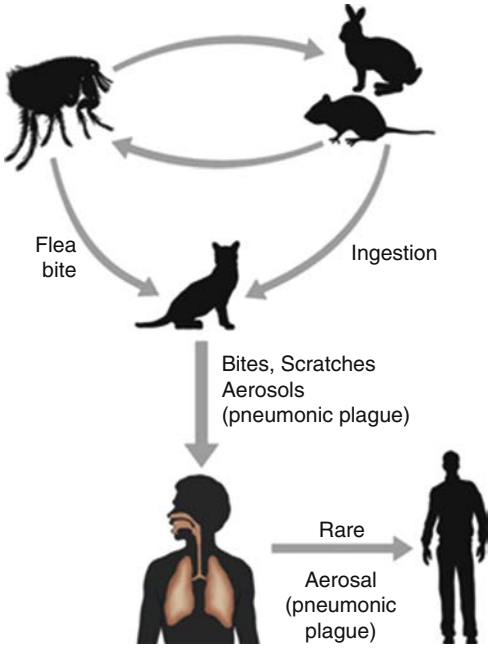


Fig. 42.2 Diagram of human plague exposure. (Courtesy Veterian Key.)

There have been three known major historic pandemics of plague. *Yersinia pestis*, the causative agent of plague, is generally transmitted by flea-borne vectors, although it can also be spread by contaminated respiratory secretions with the pneumonic form and direct contact with infected tissues or fluids from handling sick or dead animals (Fig 42.2). The three forms of disease associated with *Y. pestis* infection in people are (1) bubonic plague (enlarged sensitive lymph nodes, fever, chills), (2) septicemic plague (fever, chills, prostration, shock, and bleeding into the skin and other organs), and (3) pneumonic plague (fever, chills, cough and difficulty breathing, rapid shock and death if not treated early).[13] The primary vector for *Y. pestis* is the rat flea *(Xenopsylla cheopis),* although other rodent fleas (*Thrassis, Diamanus, Hoplopsyllus, Oropsylla* species, and *Orchopeas sexentatus*) are also competent vectors. In the United States, *Y. pestis* is primarily a problem in southwestern states and may be spread by domestic species. Captive nontraditional pet mammals (e.g., chipmunks, prairie dogs) can also serve as competent hosts for many of the vectors reported for this pathogen; therefore precautions should be taken to prevent the introduction of flea vectors into the home. Although no cases of plague associated with nontraditional pets have been reported in the United States, guinea pigs have been associated with plague in Andean countries, where they are raised for food.[45]

Yersinia pseudotuberculosis and *Y. enterocolitica,* opportunistic gram-negative coccobacilli, are routinely isolated from clinically normal rodents and lagomorphs. *Yersinia pseudotuberculosis* has been associated with epizootics in guinea pig

colonies worldwide, in rats from Japan, and in hares from Europe.[36] Affected animals generally suffer from weight loss and enteritis. Mortality rates can approach 75%. Wild rodents play an important role in the transmission of this pathogen. Although captive rodents have not been identified as an important source of infection in people, these animals can potentially serve as competent reservoirs of the bacteria in the human environment.

Yersinia enterocolitica has been associated with epizootics in chinchillas from Europe, Mexico, and the United States.[36] Septicemia was a common finding, and affected animals had enteritis and weight loss. Studies evaluating the prevalence of enterocolitic yersiniosis in wild rodent populations from the Czech Republic, Slovakia, Scandinavia, and Chile suggest that the prevalence of this pathogen in wild rodents is low (4%–26%). Although pathologic lesions, including abscesses of the liver and intestinal lesions, have been reported in wild rodents, most animals screened for this pathogen are negative. The biotypes characterized in rodents are not the same as those that infect people. Even though rodents are not considered an important source of human enterocolitic yersiniosis, veterinarians and animal caretakers should practice strict hygiene and take appropriate precautions in working with infected rodents and lagomorphs.

VIRAL DISEASES

Type A and B influenza viruses from the family Orthomyxoviridae are common pathogens of both ferrets and people (see Chapter 6). These viruses can be transmitted by aerosolization and direct contact. The disease is characterized in both people and ferrets by a mucopurulent nasal and ocular discharge, sneezing, lethargy, fever, and inappetence. Pneumonia can develop in immunocompromised individuals. The influenza virus is apparently widespread in some ferret colonies. Although influenza virus transmission is typically from people to pet ferrets, infected ferrets should be isolated from people, and vice versa. Ferrets are commonly used as laboratory animal models in research in influenza epidemiology and developing human influenza vaccines.[49] In a 2009 report, a ferret tested positive for the H1N1 virus after exhibiting flu-like clinical signs.[20] The owner of the ferret had suffered from flu symptoms before the ferret became ill. The ferret's nasal secretions were tested, where the genetic markers for the strain of H1N1 influenza virus were identified.[20] Although uncommon, other small exotic mammal species also may be infected with influenza viruses. In 2009, H5N1, a highly pathogenic avian influenza virus, was isolated from wild pikas (*Ochotoma* species) in China.[52]

Hantavirus infections have been associated with epidemics in the United States, Japan, and Eurasia. There are at least 30 hantaviruses worldwide (genus *Bunyavirus*), many of which can cause a severe, often fatal illness in people. This virus is transmitted through direct contact and the aerosolization of infected rodent urine, droppings, and saliva. Infected rodents generally exhibit no clinical signs. Although this virus is generally related to wild rodent exposure, outbreaks have also been attributed to laboratory rodents in Europe and Japan. Infected persons reported flu-like symptoms, fever, myalgia, and oliguria. The Sin Nombre hantavirus was isolated from the Four Corners region of the southwestern United States in 1993.[36] This virus caused an acute respiratory disease, subsequently named *hantavirus pulmonary syndrome,* in people.[36] From 1993 to 1997, infection of otherwise healthy individuals with the Sin Nombre hantavirus had a mortality rate of 45%.[35] Rodents should be screened for the virus before they are incorporated into a colony.

In 2017, the Centers for Disease Control and Prevention investigated a seven-state outbreak that initially identified 17 people that tested positive for Seoul virus, a member of the hantavirus family.[11] As opposed to the Sin Nombre hantavirus whose natural host is the deer mouse (*Peromyscus maniculatus*), the Seoul hantavirus' natural host is the Norway rat (*Rattus norvegicus*) and the black rat (*Rattus rattus*) and is found worldwide. In the United Kingdom, an owner of two pet rats became infected due to exposure.[28] In the natural host, rats, the virus is shed for the life of the infected animal. However, if other rodent species are infected that are not natural hosts, the animals will not develop chronic disease and shed the virus. Rats become exposed to the virus through contact with viral-laced urine and feces or bite wounds from infected conspecifics. In most human cases, Seoul virus infection is less severe than that documented with Sin Nombre hantavirus, having only a 1% to 2% mortality rate.[11] Hemorrhagic fever with renal syndrome can occur with severe infections in human patients. Therefore there is a significant zoonotic concern because, at this time, there is no effective treatment for Seoul virus.[11] Fortunately, most people who become infected exhibit mild to no symptoms of disease. The incubation period of the virus is usually 1 to 2 weeks after exposure.[11] Typical human symptoms of Seoul virus are fever, headache, chills, nausea, blurred vision, rash, back and abdominal pain, flushing of the face, and inflammation or redness of the eyes.[11] Antibody serologic testing is recommended to test rats for this virus, although PCR testing is also available but has not been validated for accuracy at this time.[11] The IDEXX serologic (antibody) test (Opti-Spot; IDEXX BioAnalytics, Westbrooke, ME) and PCR test have performed in a similar manner to Centers for Disease Control and Prevention testing for Seoul virus in rats.[11] Charles River Laboratories (Wilmington, MA) has a serologic test (EZ-Spot) that may also be effective in evaluating rats for Seoul virus infection.[11] Again, only serologic testing for viral antibodies in a rat patient can be used to determine whether that animal is infected with the Seoul virus. Rats will not exhibit clinical signs of the disease; therefore serologic testing is required to confirm the carrier status of the animal.

Lymphocytic choriomeningitis (LCM) is caused by an RNA arenavirus. The house mouse (*Mus musculus*) is the primary reservoir for LCM, although the hamster and guinea pig are also competent reservoirs. This virus is transmitted by horizontal and vertical routes in rodents.[36] Affected rodents generally exhibit no clinical disease signs, although weight loss, photophobia, tremors, and convulsions may occur.[26] People may become infected with the LCM virus from exposure to contaminated feces, urine, aerosolized dust or droplets, or nesting material, or from a bite. People with normal immune systems may have no symptoms with LCM viral infection.[32] Affected

persons frequently report clinical symptoms consistent with a flu, including malaise, headaches, fever, myalgia, and arthritis. Pregnant women who become infected with LCM virus can pass the infection to their fetuses.[32] Fatal aseptic meningitis or meningoencephalitis is rare. In a serologic study, about 5% of adults had a positive blood test showing that they were infected with LCM virus at some time in their lives.[36] In 1973 to 1974, an epidemic of LCM with more than 181 human cases was reported from 12 states; morbidity was associated with hamsters being produced by a single facility in Alabama.[36] Persons working closely with large populations of domestic rodents or wild rodents should practice strict hygiene and wear protective clothing to reduce the likelihood of exposure. Although the risk of infection from LCM virus is low, any woman who is pregnant or planning to become pregnant should avoid contact with rodents, including pet rodents (e.g., hamsters, guinea pigs) and rodent droppings.[32]

Rabies is caused by a negative-strand RNA lyssavirus. All mammals should be considered competent reservoirs for this virus; however, most (more than 90%) reported cases are associated with wildlife.[38] Rabies has been isolated from ferrets, lagomorphs, and various rodent species, including rats, squirrels, and woodchucks. Although lagomorphs and pet rodents are not considered important reservoirs for rabies, a report of rabies in seven domestic rabbits and a guinea pig suggests that pet owners and veterinarians should take appropriate precautions when animals show clinical signs associated with rabies infection.[18] The pet rabbits and guinea pig were exposed and infected with the raccoon variant of rabies virus in the northeastern United States. An inactivated rabies vaccine (Imrab 3; Merial, Athens, GA) has been approved for use in ferrets but not rabbits or rodents. Veterinarians should strongly recommend vaccinating ferrets against rabies. Although the risk of contracting rabies is extremely low, an unvaccinated ferret that bites a person must be confined for a 10-day period to be evaluated for signs of disease. If no disease signs are observed after the 10-day confinement period, the animal is released back to the owner.[18] At this time, there is no known shedding period or clinical signs of rabies infection in pet rabbits and rodents.[18] If an owner is bitten and the owner is unsure of potential rabies exposure by that animal, a recommendation for definitively determining the animal's rabies status through euthanasia should be given.[18] Pet owners should take the appropriate precautions to prevent contact between pets housed outdoors and wildlife, especially in the northeastern United States.

Reoviruses are found in several different vertebrate hosts. Mouse reovirus type 3 has been associated with morbidity and death in suckling mice. Affected animals may be jaundiced, stunted, develop oily hair, and have diarrhea. This virus is spread through both horizontal and vertical routes. Reovirus type 3 has been associated with disease in people, causing enteritis in susceptible and particularly immunocompromised persons who come into contact with infected mice. Immunocompromised individuals should therefore avoid contact with reovirus-infected mice.

In 2003, a rare zoonotic viral disease outbreak occurred in the United States. Monkeypox virus (MPV), a member of the orthopoxvirus group, was responsible for the outbreak. Monkeypox virus infection has similar clinical manifestations as smallpox and primarily occurs in the rainforest countries of central and west Africa (Fig 42.3).[22] This was the first report of the disease in the United States, and community-acquired MPV infection had never been reported outside of Africa.

Until the latest MPV outbreak, most of the concerns for zoonotic infection have been in primate research and laboratory animal facilities, especially those housing Asian macaques.[36] Human-to-human transmission has been reported but rarely occurs.[36] In the 2003 U.S. outbreak, most people who contracted clinical illness were exposed through close contact with sick captive prairie dogs (*Cynomys* species). The prairie dogs were believed to have become infected after they were exposed to MPV-positive animals from a group of about 800 animals imported from Ghana to Texas.[15] The animals were transported



Fig. 42.3 Lesions on human patients attributed to monkey pox virus infection. (Courtesy the Centers for Disease Control and Prevention.)

to an Iowa animal vendor and subsequently to a Chicago-area pet distributor; they included at least one MPV-positive African giant pouched rat (*Aterurus* species), two rope squirrels (*Funisciurus* species), and three dormice (*Graphiurus* species).[15] Monkeypox virus was also transmitted from a diseased prairie dog to a rabbit at a veterinary clinic in the 2003 U.S. outbreak.[15] The rabbit was considered the source of MPV infection in a person, confirming the transmissibility of the virus from a common pet mammal to humans.[15] Animal species that are potential carriers of MPV or are showing disease signs of a nonspecific nature should be quarantined, stabilized, and reported to state public health officials.

The clinical signs of MPV infection reported in animals during the 2003 U.S. outbreak included fever, cough, sneezing, blepharoconjunctivitis, lymphadenopathy, and nodular rash. Traditionally, MPV has been associated with high morbidity rates and a low to variable mortality rate in people (1%–10% case fatality rate in African outbreaks). There were 81 reported cases of MPV infection in the 2003 U.S. outbreak with no fatalities.[15] Persons can be exposed from direct contact with body fluids of or bite wounds from an infected animal.[22] There are currently no proven treatments for human MPV infection.[15] Morbidity and mortality rates for animals are variable regarding this disease.

If MPV infection is suspected in an animal, the clinic should be contacted before its arrival. The owners should protect themselves against potential exposure by quarantining the animal and wearing masks and gloves when the animal is handled. Currently, all animals suspected of being infected with MPV or exhibiting clinical illness should be euthanized and submitted for necropsy. If the animal is not exhibiting clinical signs, there is no recommendation by the Centers for Disease Control and Prevention for euthanasia, even with the knowledge of an animal's possible exposure to a confirmed case of MPV infection.

The 2003 MPV outbreak is an example of a rare emerging viral disease in the United States. Veterinarians should be aware that they are often the first line of defense when an unusual form of morbidity and death in animals is encountered. Communication with local, regional, state, and national public health officers is important in trying to identify a series of unusual animal disease presentations and conditions.

In 2009, four human cases of cowpox virus (CPV) infection were reported in France. The source of infection was exposure to infected pet rats purchased at the same pet store.[39] The rats had been purchased from a rat breeder in the Czech Republic.[39] All four patients reported being scratched by their rats but not bitten.[39] Clinical signs included cutaneous pustular lesions and lymphangitis (Fig 42.4). All of the patients recovered from the CPV infection with no apparent complications. Also in 2009, another cluster of persons infected with CPV associated with exposure to pet rats was identified in Germany.[8] At the breeding facility where the rats were obtained, 31 rats tested positive for orthopoxvirus. The German patients had similar clinical signs as those described in the French report. As with MPV, the CPV infections reemphasize the possibility of unusual infectious diseases being transmitted from animals to people.

PARASTIC DISEASES

Cryptosporidiosis is a common zoonotic disease. *Cryptosporidium parvum* is not host-specific and may infect a wide range of mammals.[9] The infective dose is low (1–10 oocysts), and oocysts are immediately infective when excreted in the feces. The oocysts are very stable within the environment, which can lead to contamination of food and water supplies.[9] A 6-month study evaluating three serial fecal samples from a group of ferrets being received at a biologic research facility found that 66% of the animals had cryptosporidiosis.[36] Ferrets with cryptosporidiosis generally develop a subclinical infection, although postmortem examination has revealed mild pathologic changes in some clinically normal animals. A recent study evaluating the prevalence of *Cryptosporidium* species shedding in pet chinchillas from China found that 14 of 140 animals were PCR positive on feces.[42] *Cryptosporidium ubiquitum* and *C. parvum* were identified. *C. ubiquitum* appears to be an emerging parasitic zoonotic disease. Diagnostic testing using PCR and sequencing should be performed for those cases where cryptosporidiosis is diagnosed to determine whether the organism is potentially zoonotic. Individuals with compromised immune systems, such as children and those with acquired immunodeficiency virus, should limit their contact with *Cryptosporidium*-positive ferrets. Fatal intestinal cryptosporidiosis has also been reported in African hedgehogs, suggesting that these animals may also pose a zoonotic threat.[36] Recent reports appear to indicate that because household pets have rarely been implicated as a source of human infection, they may not serve as an important reservoir for *Cryptosporidium* species infection.[9] Animals with clinical



Fig. 42.4 Cowpox lesions on the leg of a rodent (A) and neck of humans (B), (C). From Campe H, Zimmermann P, Glos K, et al. Cowpox virus transmission from pet rats to humans, Germany. *Emerg Infect Dis* 2009;15:777–780.

signs usually develop gastrointestinal disease problems such as decreased appetite and subsequent weight loss and diarrhea.[47] Symptoms of cryptosporidiosis in people are a low-grade fever, headache, and gastrointestinal disease problems (e.g., nausea, vomiting, abdominal cramps, and diarrhea).[47]

The two main *Giardia* species that infect rodents are *Giardia duodenalis* and *Giardia muris*.[30] *Giardia duodenalis* has also been isolated from ferrets.[1] Although both of these parasites have been isolated from pet animals, limited epidemiologic investigations have been performed to determine the prevalence of this parasite in this group of animals. A 2010 study in chinchillas from Belgium found that 66% of animals tested shed *G. duodenalis* cysts. Shedding was more common in young animals and animals participating in shows. These results suggest that the risk to people may be greatest in those animals experiencing a form of physiologic stress. In China, chinchillas were also found to routinely harbor *G. duodenalis*, with 38 of 140 chinchillas shedding the parasite in their feces.[43] Clinical signs vary depending on the species of *Giardia* and the species of animal infected but may include either no outward signs of clinical disease or severe dehydration and diarrhea. The clinical disease in people primarily affects the gastrointestinal tract, but other body systems may be involved, including the joints, specifically the synovial surfaces; there may also be hypersensitivity reactions.[36] Transmission is direct through fecal-oral contamination of the trophozoite and cyst form of the organism, primarily in water. Diagnosis and treatment of the affected animals to prevent further shedding and proper hygiene after handling animals will prevent the spread and transmission of this protozoal parasite to people.

Hymenolepsis is a cestode that infects rodents. *Hymenolepsis diminuta* has been identified in rats, hamsters, and mice, whereas *Hymenolepsis nana* is found mainly in mice and rats. People can become infected with this parasite by ingesting contaminated feces. Indirect infection can occur when insects ingest the tapeworm eggs, which then develop into cysticercoid larvae in the indirect host's body (Fig 42.5). In a survey of pet stores in southern Connecticut, a fecal flotation analysis revealed a 9% overall prevalence of *H. nana* in 110 samples collected weekly from cages holding group-housed small exotic mammals from three stores for 4 weeks.[17] Only cages holding rats, mice, and prairie dogs were positive.[17] Necropsies were performed on 38 rats (32% prevalence, mean worm load 66), 72 domestic mice (22% prevalence, mean worm load 14), and 39 golden hamsters (10% prevalence, mean worm load 15) purchased from nine different pet stores.[17] *Hymenolepsis nana* has also been found to be common in the feces of mice housed in pet stores in Japan, with 8/28 animals testing positive.[27] The findings of the pet store surveys indicate the need for pet owners of small exotic mammals to practice good hygiene after handling their pets and the potential of public health significance of *H. nana*. Although most infected persons are asymptomatic, particularly with *H. diminuta,* clinical disease can occur with heavy infections because of the absorption of metabolic waste produced by a heavy worm burden and gastrointestinal irritation.[29] Children are more likely to be clinically affected than adults. Affected individuals may have abdominal cramping, nausea, vomiting, and diarrhea. The cestodes *Taenia taeniaeformis* of rats and mice and *Taenia serialis* in rabbits can cause clinical illness in people when infected animals are consumed.

Sarcoptic mange, caused by *Sarcoptes scabiei,* affects many mammalian species. Affected animals often have severe, intense pruritus, scales, crusts, erythema, and generalized alopecia. Pododermatitis and self-mutilation are common findings in ferrets. Humans who become infected with sarcoptic mange may develop wheals, vesicles, papules, and intense pruritus. Infected animals should be quarantined from other animals and handled only with gloves to reduce exposure. Imidacloprid/moxidectin may be used to treat affected animals.

Trixacarus caviae is an ectoparasite of guinea pigs. In general, guinea pigs infested with these mites exhibit no clinical disease signs. However, animals that are maintained in poor conditions or are stressed may have generalized clinical signs, including alopecia, intense pruritus, scales, crusts, and hyperkeratosis. Pet owners, especially children, may become infected with *T. caviae* from direct contact with infected guinea pigs. Affected individuals generally have mild dermatitis. *Trixacaris* is very difficult to eliminate in affected guinea pigs. Intensive environmental cleaning and management along with therapeutic treatment with imidacloprid/moxidectin can be effective.

Ornithonyssus bacoti, the tropical rat mite, will bite humans. Although this parasite mainly feeds on the rat host and lives within the animal's bedding, it is the transfer of other infectious diseases through the bite of the mite that is of medical concern. Tropical rat mites can transmit murine typhus, Q fever, and *Y. pestis*.[26] Treatment and prevention follow the same environmental and therapeutic protocols as described for other skin mite species.

Cheyletiella parasitovorax is an ectoparasite that infests domestic rabbits (Fig 42.6). This mite is generally found on the hair shaft and in the keratin layer of the skin. Infested rabbits may be subclinical or have alopecia and scaling. In severe cases, rabbits with cheyletiellosis appear to have "walking dandruff." The life cycle of this mite is 35 days, and the parasite generally does not survive for more than 10 days off of the rabbit host. Persons who become infested with this mite generally develop focal to multifocal dermatitis. Papular and pruritic eruptions on the arms, thorax, waist, and legs have been described. The mite does not reproduce on the human host; therefore, the infestation is generally self-limiting. Pet owners should be instructed to limit contact with infected rabbits during the treatment period, and gloves should be worn when contact is necessary.

MYCOTIC DISEASES

Trichophyton species (usually *T. mentagrophytes*) is an opportunistic fungal disease of mammals. "Ringworm" has been isolated from rodents, lagomorphs, sugar gliders, ferrets, hedgehogs, and marsupials. Affected animals may be subclinical or have focal to multifocal alopecia (Fig. 42.7). Depending on the degree of pruritus associated with the infection, crusts, scabs, and excoriations may also be present on all of the animals or groups of animals mentioned above. Approximately 25% of the human ringworm cases reported annually are attributed to animal contact.[36] Affected individuals may be asymptomatic or have alopecia and crusts, similar to the lesions identified in pet animals.

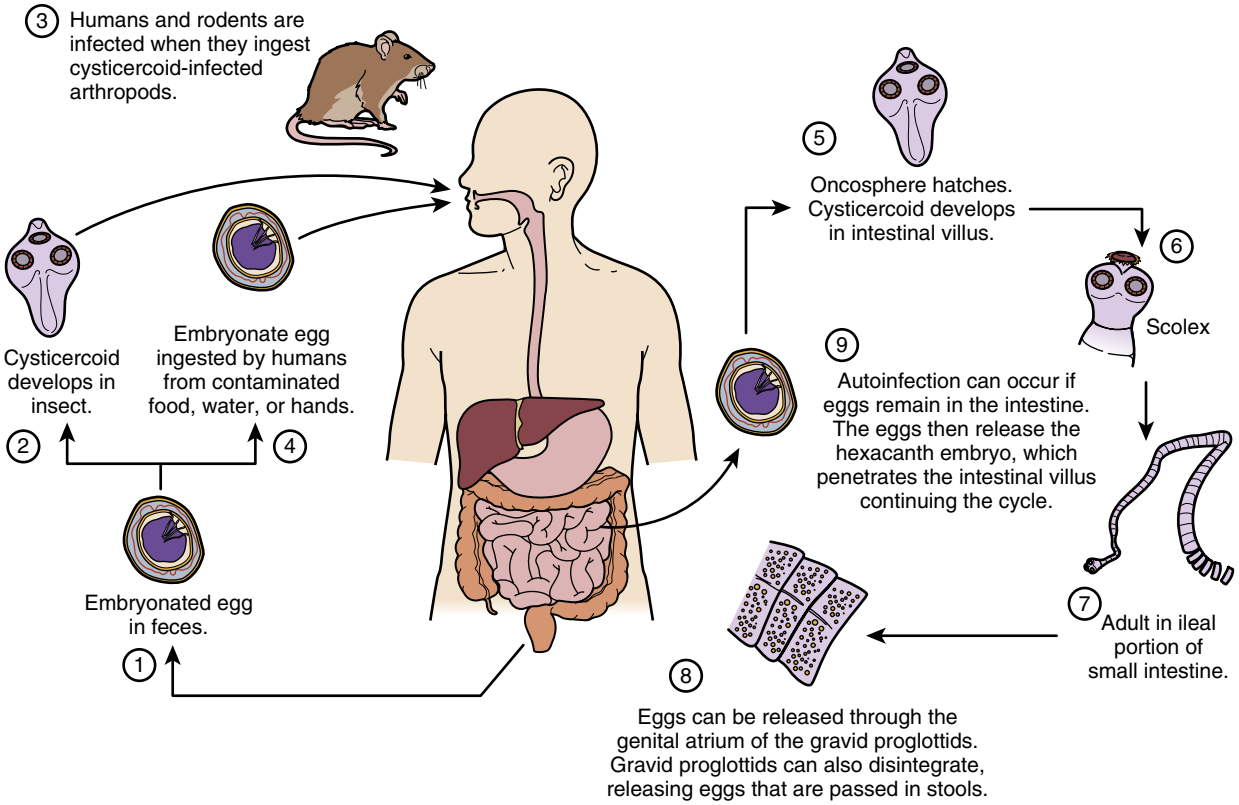


Fig. 42.5 Diagram of *Hymenolepsis nana* exposure in humans from infected rats and mice. (Courtesy parasitesinhumans.org.)



Fig. 42.6 Photomicrograph of the mite *Cheyletiella parasitovorax,* which commonly infests rabbits and can transiently infest humans. (Courtesy Bruce Williams, DVM.)



Fig. 42.7 Typical lesion associated with "ringworm," an opportunistic fungal disease diagnosed in rabbits that can be transmitted to humans resulting in similar dermal lesions. (Courtesy Frances Harcourt-Brown, DVM.)

To a lesser extent, *Microsporum canis* may affect rodents, with active lesions in people most often found on the scalp. A Wood's lamp may be used to diagnose *M. canis* through fluorescence of the fungal organism, whereas *M. gypseum* rarely fluoresce and *T. mentagrophytes* do not fluoresce.[33] *Trichophyton rubrum* and *T. mentagrophytes* produce mannans and other compounds that reduce cell-mediated immunity, thereby predisposing animals to recurrent infections.[33] Enilconazole 2% and chlorhexidine 2%/miconazole shampoo are dermatophyte treatment options.[19] Monitoring the small exotic animal patient is required with enilconazole use due to possible toxic reactions.[16] Itraconazole, ketoconazole, and griseofulvin are drugs that have been used with success to treat dermatophyte infections. The patient should have two negative fungal cultures, 4 weeks between submission, before medication is discontinued.[19] The risk of transmission and therefore exposure to humans is significantly reduced when

the infected animal is being treated.[19] During the treatment period, the animal's cage should be cleaned and disinfected at least once every 14 days. Only adults, wearing disposable gloves, should handle infected animals during the treatment period. Always check an exotic animal formulary for drug dosages and comments relating to treatment of a specific animal species with any therapeutic agent.

Paecilomyces species, saprophytic fungi, are ubiquitous in the environment.[46] Although these fungal organisms rarely cause clinical disease in mammals, infections have been reported in horses, dogs, cats, and reptiles.[14,21] A case of paecilomycosis has been described in an African pygmy hedgehog.[25] The animal presented for marked hyperkeratosis on the right side of the face. Treatment with itraconazole was curative. It is generally assumed that these infections are secondary to some immune-compromising event; however, this could not be determined in the hedgehog case. Human caretakers for exotic pet mammals should be reminded of the potential for exposure to fungal agents, especially when animals are being treated with immunosuppressant drugs or have an immune-compromising disease. The practice of strict hygiene should minimize the potential for exposure to this organism.

Although there are no serious zoonotic mycotic diseases that can be spread from rabbits to healthy people, immunocompromised (e.g., acquired immunodeficiency virus) patients may contract *Encephalitozoon* cuniculi, a primitive fungus.[36] In one report, three patients with human immunodeficiency virus had *E. cuniculi,* with one of these having clinical manifestations of disease with the fungus (severe interstitial pneumonitis).[9] The symptoms abated and excretion of the fungus ceased when these patients were treated with albendazole.

Enterocytozoon bieneusi is a microsporidian that has been found in people and several mammal species, including rabbits, guinea pigs, and chinchillas.[7,42] This pathogen is shed through the gastrointestinal tract. A 2-year-old child developed clinical disease associated with this organism, and the source was attributed to *E. bieneusi*-positive guinea pigs in the child's household.[7] A recent study in China found the prevalence of *E. bieneusi* in chinchillas to be 3.6%.[42] Although the prevalence of this organism in pet rodents and rabbits is low, the presence of this organism in these pet species and the case in a child suggests that they may serve as a source of exposure to their human caretakers. Albendazole appears to have good efficacy against this organism.[34]

ALLERGIC REACTIONS

It has been estimated that between 11% and 15% of people exposed to rodent and lagomorph species have or develop allergic reactions to antigens produced by these animals.[26] Human allergic reactions to small-mammal skin, dander, fur, urine, saliva, and fur antigens can present as respiratory (e.g., dyspnea, congestion), ocular (e.g., itchy tearing eyes), skin (e.g., dermal rash, pruritus), or anaphylactic clinical signs.[4] Many people are allergic to one animal's antigen, although multiple allergies involving small mammals may occur. The most common small-animal antigens are, in descending order, those of rats, guinea pigs, rabbits, mice, hamsters, and gerbils. Respiratory reactions to aerosolized rat urine are particularly severe because of the life-threatening pulmonary effects of the tissue response to the antigenic components of the urinary compounds.[26] Antihistamine treatment is recommended for people with allergic reactions; reducing exposure to the antigenic compounds by washing hands or wearing gloves and a face mask will help decrease hypersensitivity reactions.

SUMMARY

Although zoonotic diseases rarely result from our interactions with nontraditional small mammals maintained as companion animals, this is a topic of importance to veterinarians. Understanding the zoonotic potential of small-animal diseases is essential not only to protect the health of the veterinarians and staff but also to educate and inform their pet-owning clients and to serve as a source of information for the human medical community.

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APPENDIX: FORMULARY

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FORMULARY

This formulary presents the antimicrobial agents (Table A.1); antifungal agents (Table A.2); antiparasitic agents (Table A.3); chemical restraint, anesthetic, and analgesic agents (Table A.4); and miscellaneous agents (Table A.5) most commonly used in ferrets, rabbits, guinea pigs, chinchillas, gerbils, hamsters, rats, mice, hedgehogs, sugar gliders, and prairie dogs. There are many specific circumstances and drug types that cannot be included in this chapter. The reader is referred to other, more comprehensive references and the literature for more details of the drugs, dosages, indications, and precautions.[1,2] Additionally, specific chapters in this book may suggest dosages that are different or not mentioned in this chapter. The reader is strongly encouraged to refer to exotic pet formularies[1,2] for more details of the drugs, dosages, indications, and precautions.

Most dosages listed in this formulary are off-label and based on empiric data, observation, and experience. To date, very few drugs are approved by the Food and Drug Administration (FDA) for use in small mammals kept as nontraditional pets, such as the animals discussed in this book. The Animal Medicinal Drug Use Clarification Act (AMDUCA) enables veterinarians to use drugs approved for human and other animal use in animals other than those for which they are approved, if the medical reasoning is sound. This act requires that owners sign an informed consent form for off-label drug use. Because most drugs are not approved by the FDA for use in these animals, it may be warranted for the owners to sign a consent form in registering their pet. Rabbits are considered a minor species of food animal by the FDA, which means that some drugs, including metronidazole and the fluoroquinolones, are considered extra-label drug use and may be in violation of FDA regulations. It is the responsibility of the veterinarian prescribing these drugs to ensure that no part of the pet rabbit enters the human food chain to eliminate the public health risks associated with antibiotic resistance and residues. For more information, see the Food Animal Drug Residue Avoidance and Databank home page (www.farad.gov).

Because pharmacokinetic studies are lacking in these pet species, knowing some of the pharmacobiologic, physiologic, and anatomic characteristics of these animals is important. Drug uptake and use depend on many factors, including age, body fat, sex, physiology (gastrointestinal, hepatic, renal, etc.), illness, diet, fasting state, and others. For example, it is well known that hindgut fermenters, such as rabbits and guinea pigs, do not tolerate some oral antibiotics, such as penicillins, because these can cause a fatal enterotoxemia. The complete list of this information is beyond the scope of this chapter; the reader is referred to the chapters on anatomy and physiology of each species elsewhere in this book. Because dosages are often empirical, it is helpful to know, for maximum safety and efficacy, the basic pharmacologic features and side effects of the drugs being used. It is important to inform the owner or technical staff of clinical signs that may indicate toxicosis. This information is available in the drug inserts and with other references and formularies. Allometric scaling may also be helpful in prescribing drugs in this formulary to other species.

Most of the drugs given to these nontraditional pet species are administered parenterally or orally as a suspension. Little research has been done on the efficacy of various drug suspensions in these patients. Having a good working relationship with a licensed compounding pharmacist is essential for practitioners. Compounding pharmacists will ensure that the drug is placed in the appropriate medium to remain viable in suspension and can warn of potential risks associated with this medium.

Obtain a definitive diagnosis whenever possible to avoid the problems associated with empiric dosing and to improve efficacy in these species. Select an antibiotic based on culture and sensitivity results whenever possible. The use of more pathogen-specific antimicrobials will decrease the potential for resistant bacteria and often reduces the potential adverse effects.

We have attempted to verify all dosages presented in this formulary. However, despite these efforts, errors in the original sources or in the preparation of this chapter may have occurred. Therefore, all users of this reference should empirically evaluate all dosages to determine that they are reasonable before use. We assume no responsibility for and make no warranty regarding results obtained from the dosages listed.

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TABLE A.1 Antimicrobial Agents Used in Small Mammals

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Amikacin[a]	10–15 mg/kg SC, IM q12h	5–10 mg/kg SC, IM, IV divided q8–24h	16 mg/kg SC, IM, IV divided q8–24h	16 mg/kg SC, IM divided q8–24h	16 mg/kg SC, IM q8–12h	2.5–5.0 mg/kg IM q8–12h	3 mg/kg IM q12h	2.5 mg/kg SC, IM, IV q12h
Amoxicillin	20–30 mg/kg PO q8–12h	Do not use	Do not use	Do not use	20 mg/kg PO q12h	15 mg/kg PO, SC, IM q12h	30 mg/kg PO, IM divided q12h	Do not use
Amoxicillin/clavulanic acid	12.5–25 mg/kg PO q8–12h	Do not use	Do not use	Do not use	20 mg/kg PO q12h	12.5 mg/kg PO q12h	12.5 mg/kg PO, SC divided q12h	Do not use
Ampicillin	5–30 mg/kg SC, IM, IV q8–12h	Do not use	Do not use	6–30 mg/kg PO q8h (G); do not use (H)	20–100 mg/kg PO, SC, IM q8h	10 mg/kg IM q12h (use with caution)	—	Do not use
Azithromycin	5 mg/kg PO q24h	15–30 mg/kg PO q24h	15–30 mg/kg PO q24h	15–30 mg/kg PO q24h	30–50 mg/kg PO q12h-24h	—	—	15–30 mg/kg PO q24h
Cephalexin	15–30 mg/kg PO q8–12h	15 mg/kg SC q12h	Do not use	25 mg/kg SC q12h	60 mg/kg PO q12h (M); 15 mg/kg SC q12h (R)	25 mg/kg PO q8h	30 mg/kg PO, SC divided q12–24h	—
Chloramphenicol	25–50 mg/kg PO, SC, IM q12h	25–50 mg/kg PO, SC, IM q12h	30–50 mg/kg PO, SC, IM q8–12h	30–50 mg/kg PO, SC, IM q8–12h	30–50 mg/kg PO, SC, IM q8–12h	30–50 mg/kg PO, SC, IM, q12h	50 mg/kg PO, SC, IM q12h	50 mg/kg PO, SC, IM q12h
Ciprofloxacin	10–30 mg/kg PO q24h	5–20 mg/kg PO q12–24h	5–20 mg/kg PO q12–24h	5–20 mg/kg PO q12–24h	10 mg/kg PO q12h	5–20 mg/kg PO q12h	10 mg/kg PO q12h	—
Clarithromycin	12.5–25 mg/kg PO q12h	—	—	—	—	5.5 mg/kg PO q12h	—	Do not use
Clindamycin	5–10 mg/kg PO q12h	Do not use	7.5 mg/kg SC q12h; do not use PO	7.5 mg/kg SC q12h; do not use PO	7.5 mg/kg SC q12h; do not use PO	5.5–10 mg/kg PO q12h	—	—
Doxycycline	10 mg/kg PO q12h	2.5 mg/kg PO q12h	2.5–5.0 mg/kg PO q12h	2.5–5.0 mg/kg PO q12h	2.5–5.0 mg/kg PO q12h; 70–100 mg/kg SC, IM q7d (long-acting form)	2.5–10 mg/kg PO, SC, IM q12h	—	—
Enrofloxacin[b]	10–20 mg/kg PO, SC, IM q24h	5–10 mg/kg PO, SC, IM, IV q12h	5–20 mg/kg PO, SC, IM q12h	5–20 mg/kg PO, SC, IM q12h; 0.05–0.2 mg/mL drinking water	5–20 mg/kg PO, SC, IM q12h; 0.05–0.2 mg/mL drinking water	5 mg/kg PO, SC, IM q12h	5 mg/kg PO, SC, IM q12h	20 mg/kg PO, SC, IM q24h
Marbofloxacin	—	2–5 mg/kg PO, SC, IM q24h	4 mg/kg PO, SC q24h	4 mg/kg PO, SC q24h	4 mg/kg PO, SC q24h	—	—	—

Continued

TABLE A.1 Antifungal Agents Used in Small Mammals—cont'd

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Metronidazole	20 mg/kg PO q12h	20 mg/kg PO q12h	20 mg/kg PO q12h (GP); 10–20 mg/kg PO q12h (use with caution) (C)	20 mg/kg PO q12h	10–40 mg/kg PO q24h	20 mg/kg PO q12h	25 mg/kg PO q12h	20 mg/kg PO, IV q12h
Oxytetracycline	20 mg/kg PO q8h	15 mg/kg IM q8h; 50 mg/kg PO q12h	10–20 mg/kg PO q8h (GP); 50 mg/kg PO q12h (C)	10 mg/kg PO q8h (G); 20–25 mg/kg IM q8–12h (G, C)	10–20 mg/kg PO q8h	25 mg/kg PO q24h × 5–7 days	—	—
Penicillin G procaine	40,000 IU/kg SC q24h	60,000 IU/kg SC, IM q8h (use with caution)	Do not use (GP); 22,000 IU/kg SC, IM q24h (C) (use with caution)	22,000 IU/kg SC, IM q24h	22,000 IU/kg SC, IM q24h	40,000 IU/kg SC, IM q24h	22,000–25,000 IU/kg SC, IM q12–24h	25,000–50,000 IU/kg SC q3–5d
Tetracycline	25 mg/kg PO q12h	50 mg/kg PO q8–12h	10 mg/kg PO q8–12h (use with caution)	10–20 mg/kg PO q8–12h	10–20 mg/kg PO q8–12h	—	—	—
Trimethoprim/sulfa	15–30 mg/kg PO, SC q12h	30 mg/kg PO, SC q12h	15–30 mg/kg PO, SC q12h	15–30 mg/kg PO, SC q12h	15–30 mg/kg PO, SC q12h	30 mg/kg PO q12h	15 mg/kg PO q12h	30 mg/kg PO q12h
Tylosin	10 mg/kg PO, SC q8–12h	10 mg/kg PO, SC q12h	10 mg/kg PO, SC q12h (use with caution in guinea pigs)	2–10 mg/kg PO, SC q12h (use with caution)	10 mg/kg PO, SC q12h	10 mg/kg PO, SC q12h	—	Do not use or use with caution

[a]Most infectious disease clinicians recommend that aminoglycosides should be dosed q24h in most mammals. This dosing regimen yields higher peak levels with a resultant greater bacterial kill. However, incorporating this recommendation with the published dosages is at the discretion of the individual clinician. Aminoglycosides should be used with fluid support.
[b]The oral route of administration is preferable; avoid subcutaneous (unless the antibiotic is diluted) and intramuscular routes of administration because of potential tissue necrosis at the injection site.
C, Chinchillas; *d,* days; *G,* gerbils; *GP,* guinea pigs; *H,* hamsters; *h,* hours; *IM,* intramuscularly; *IV,* intravenously; *M,* mice; *PO,* orally; *q,* every; *R,* rats; *SC,* subcutaneous.

TABLE A.2 Antifungal Agents Used in Small Mammals

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Amphotericin B	0.4–0.8 mg/kg IV q7d (total dose, 7–25 mg)	—	—	1 mg/kg SC q24h × 5 days/ wk × 3 wk (H)	0.11 mg/kg SC; 0.43 mg/kg PO (M)	—	—	—
Enilconazole	—	—	Dip in 1:50 (0.2%) solution q7d	Dip in 1:50 (0.2%) solution q3–4d	Dip in 1:50 (0.2%) solution q3–4d	Dip in 1:50 solution q24h	—	—
Fluconazole	50 mg/kg PO q12h	38 mg/kg PO q12h	16 mg/kg PO q24h × 14 days	—	—	—	—	—
Itraconazole	15 mg/kg PO q24h	10 mg/kg PO q24h	2.5–10 mg/kg PO q24h	2.5–10 mg/kg PO q24h	2.5–10 mg/kg PO q24h (R); 50 mg/kg PO q24h (M)	5–10 mg/kg PO q24h	5–10 mg/kg PO q24h	5–10 mg/kg PO q24h
Ketoconazole	10–30 mg/kg PO q12–24h	10–40 mg/kg PO q24h	10–40 mg/kg PO q24h	10–40 mg/kg PO q24h	10–40 mg/kg PO q24h	10 mg/kg PO q24h	—	10 mg/kg PO q24h
Lime sulfur dip (2.5%)	Dip q7d	Dip q7d × 4 treatments	Dip q7d	Apply topically q7d	Apply topically q7d	Apply topically	—	—
Terbinafine	—	10–30 mg/kg PO q24h	10–30 mg/kg PO q24h × 4–6 wk	10–30 mg/kg PO q24h × 4–6 wk	10–30 mg/kg PO q24h × 4–6 wk	—	—	—

d, days; *H,* hamsters; *h,* hours; *IM,* intramuscularly; *IV,* intravenously; *M,* mice; *PO,* orally; *q,* every; *R,* rats; *SC,* subcutaneous; *wk,* weeks.

TABLE A.3 Antiparasitic Agents Used in Small Mammals

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/ Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Carbaryl powder (5%)	Apply topically q7d	Apply topically q7d	Apply topically q7d × 3 treatments	Apply topically q7d × 3 treatments	Apply topically q7d	—	Apply topically sparingly	Apply topically sparingly
Fenbendazole	20 mg/kg PO q24h × 5 days	20 mg/kg PO, q24h	20–50 mg/kg PO q24h × 5 days	20–50 mg/kg PO q24h × 5 days	20–50 mg/kg PO q24h × 5 days	10–30 mg/kg PO q24h × 5 days	20–50 mg/kg PO q24h × 3 days, repeat in 14 days	10–25 mg/kg PO q24h × 5 days
Fipronil	0.2–0.4 mL q30d; 1 pump of spray or ⅕–½ of cat tube q60d	Toxic; do not use	3 mL/kg topically (use with caution)	7.5 mg/kg topically q30–60d	7.5 mg/kg topically q30–60d	Apply 1 spray over dorsum, repeat in 10 days	—	—
Imidacloprid	0.1–0.4 mL or 1 cat dose topically q30d	10–16 mg/kg or 1 cat dose topically q30d	20 mg/kg topically q30d	20 mg/kg topically q30d	20 mg/kg topically q30d	½ kitten dose topically q30d	—	½ kitten dose topically q30d
Ivermectin	0.2–0.5 mg/kg PO, SC, repeat in 14 days; 0.05 mg/kg PO, SC q30d (heartworm prevention or microfilaricide)	0.2–0.4 mg/kg SC q7–14d	0.2–0.4 mg/kg SC q7–14d	0.2–0.4 mg/kg SC q7–14d, 0.2–0.3 mg/kg PO q24h (demodicosis)	0.2–0.4 mg/kg SC q7–14d	0.2–0.4 mg/kg PO, SC q7–14d × 3–5 treatments	0.2 mg/kg SC q7–14d	0.2–0.3 mg/kg SC q7–10d × 2–3 treatments
Lime sulfur dip (2.5%)	Dip 1:40 dilution q7d	Dip q7d × 4–6 wk	Dip q7d × 6 wk	Dip q 7d × 6 wk	Dip q7d × 6 wk	—	—	—
Lufenuron	30–45 mg/kg PO q30d	30 mg/kg PO q30d	—	—	—	½ kitten dose PO q30d	—	—
Metronidazole	15–20 mg/kg PO q12h	20 mg/kg PO q12h	10–20 mg/kg PO q12–24h (use lower dose in chinchillas)	20–50 mg/kg PO q12–24h	20–40 mg/kg PO q12–24h	25 mg/kg PO q12h	25 mg/kg PO q12h	—
Milbemycin oxime	1.15–2.33 mg/kg PO q30d	—	—	—	—	—	—	—
Moxidectin	0.17 mg SC once	0.3 mg/kg SC		—	—	0.3 mg/kg SC q10d	—	—

TABLE A.3 Antiparasitic Agents Used in Small Mammals—cont'd

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/ Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Praziquantel	5–10 mg/kg PO, SC, repeat in 10–14 days	5–10 mg/kg PO, SC, IM, repeat in 10 days	6–10 mg/kg PO, SC, repeat in 10 days	6–10 mg/kg PO, SC, repeat in 10 days	6–10 mg/kg PO, SC, repeat in 10 days	7 mg/kg PO, SC, repeat in 14 days	—	—
Pyrantel pamoate	4.4 mg/kg PO, repeat in 14 days	5–10 mg/kg PO, SC repeat in 14 days	50 mg/kg PO	50 mg/kg PO	50 mg/kg PO	—	—	—
Pyrethrin products	Topically as directed q7d	Topically as directed q7d	Topical powder q7d × 3 treatments	Topical powder 3×/wk; shampoo q7d	Topical powder 3×/wk; shampoo q7d	—	Topically as directed q7d	—
Selamectin	10 mg/kg topically	20 mg/kg topically q7d[b]	20 mg/kg topically	15–30 mg/kg topically	15–30 mg/kg topically	10–20 mg/kg topically	6–18 mg/kg topically	10–15 mg/kg topically
Sulfadimethoxine	50 mg/kg PO once, then 25 mg/kg q24h × 10 days	50 mg/kg PO once, then 25 mg/kg q24h × 10–20 days	25–50 mg/kg PO q24h × 10 days	25–50 mg/kg PO q24h × 10–14 days	10–15 mg/kg PO q12h	2–20 mg/kg q24h PO, SC, IM × 2–5 days, off 5 days, on 2–5 days	—	—
Sulfaquinoxaline	—	1 mg/mL in drinking water	1 mg/mL drinking water	1 mg/mL drinking water	1 mg/mL drinking water	—	—	—
Toltrazuril	—	2.5–10 mg/kg PO × 3 days, repeat in 7–10 days	—	10 mg/kg PO q24h × 3d, repeat in 5 days (H)	10 mg/kg PO q24h × 3 days	10 mg/kg PO q24h × 2 days, repeat q7d × 3 wk	—	—

[a] 0.1 mL/animal, using imidacloprid (10%)/moxidectin (1%) (Advocate/Advantage-Multi; Bayer, Shawnee Mission, KS).
d, days; *GP,* guinea pigs; *H,* hamsters; *h,* hours; *IM,* intramuscularly; *PO,* orally; *q,* every; *SC,* subcutaneous; *wk,* weeks.

TABLE A.4 Chemical Restraint, Anesthetic, and Analgesic Agents Used in Small Mammals

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Acepromazine	0.1–0.5 mg/kg SC, IM	0.25–1.0 mg/kg IM	—	0.5–1.0 mg/kg IM	0.5–1.0 mg/kg IM	0.1–1.0 mg/kg PO, SC, IM	—	—
Alfaxalone	5 mg/kg IV 5–15 mg/kg IM	1–4 mg/kg IV 4–6 mg/kg IM	5 mg/kg IM (GP) (may require a higher dose)	—	5 mg/kg IM (may require a much higher dose)	—	—	—
Atipamezole[a]	1 mg/kg SC, IM, IV	1 mg/kg SC, IM, IV	1 mg/kg SC, IM, IV	—	1 mg/kg SC, IM, IV, IP	0.3–0.5 mg/kg IM	—	—
Atropine	0.04–0.05 mg/kg SC, IM, IV	0.1–0.5 mg/kg SC, IM	0.05–0.2 mg/kg SC, IM, IV	0.04–0.4 mg/kg SC, IM	0.05–0.4 mg/kg SC, IM	0.01–0.04 mg/kg SC, IM	0.01–0.02 mg/kg SC, IM	—
Bupivicaine	1 mg/kg epidurally 1–1.5 mg/kg SC (local)	1 mg/kg epidurally 2 mg/kg SC (local)	1–2 mg/kg nerve block	—	1–2 mg/kg nerve block (R)	—	1–2 mg/kg SC (local)	—
Buprenorphine	0.01–0.05 mg/kg SC, IM, IV q8–12h	0.01–0.05 mg/kg SC, IM, IV q6–12h	0.1–0.2 mg/kg SC, IM q6h	0.1–0.2 mg/kg SC q2h (G); 0.5 mg/kg SC q8h (H)	0.02–0.1 mg/kg SC, IM, IP q6–12h (R); 0.05–2.5 mg/kg SC, IM, IP q6–12h (M)	0.01 mg/kg SC, IM q6–8h	0.01–0.03 mg/kg PO, SC q12h	0.03–0.05 mg/kg SC, IM, IV q8–12h
Butorphanol	0.05–0.4 mg/kg SC, IM q4–6h	0.1–1.0 mg/kg SC, IM, IV q2–6h (doses up to 2 mg/kg may be given)	0.2–2.0 mg/kg SC, IM q2–4h	1–5 mg/kg SC q4h	0.2–2 mg/kg SC, IM q2–4h (R); 1–5 mg/kg SC q4h (M)	0.05–0.4 mg/kg SC q6–8h	0.1–0.5 mg/kg SC, IM q6–8h	0.1–0.5 mg/kg SC, IM q6–8h
Butorphanol/ midazolam	(B) 0.2 mg/kg + (Mi) 0.2 mg/kg IM	(B) 0.25–0.5 mg/kg + (Mi) 0.5–1 mg/kg IM	—	—	—	(B) 0.4 mg/kg + (Mi) 0.25–0.5 mg/kg IM	—	(B) 0.5 mg/kg + (Mi) 0.5 mg/kg SC, IM
Carprofen	2–5 mg/kg PO, SC q12–24h	1–5 mg/kg PO q12–24h	2–5 mg/kg PO, SC q12–24h	5 mg/kg SC q24h	2–5 mg/kg PO, SC, IM q12–24h	1 mg/kg PO, SC q12–24h	—	—
Dexmedetomidine	0.04–0.1 mg/kg IM	0.035–0.05 mg/kg IM	See ketamine combination	—	—	0.02 mg/kg IM	—	—
Diazepam	0.5–2.0 mg/kg IM, IV	0.5–2.0 mg/kg IM, IV	0.5–3.0 mg/kg IM, IV	1–5 mg/kg IM, IP	1–5 mg/kg IM, IV	0.5–2.0 mg/kg IM	0.5–2.0 mg/kg PO, IM, IV	0.2–5.0 mg/kg PO, IM, IV q8h
Gabapentin	3–5 mg/kg PO q8–24h	3–5 mg/kg PO q12–24h	3–5 mg/kg PO q12–24h	50 mg/kg PO q24h (H)	—	—	—	—
Glycopyrrolate	0.01 mg/kg IM	0.01–0.02 mg/kg SC	0.01–0.02 mg/kg SC	0.01–0.02 mg/kg SC	0.01–0.02 mg/kg SC	—	0.01–0.02 mg/kg SC, IM, IV	—
Hydromorphone	0.1 mg/kg SC q1–2h	0.1–0.2 mg/kg SC, IM, IV q6–8h	1–2 mg/kg SC q4h (C)	—	0.4 mg/kg SC q2h (R)	0.1 mg/kg SC	—	—

TABLE A.4 Chemical Restraint, Anesthetic, and Analgesic Agents Used in Small Mammals—cont'd

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Ketamine	5–50 mg/kg SC, IM, IV	5–50 mg/kg SC, IM; 15 mg/kg IV	5–40 mg/kg SC, IM, IV	40–100 mg/kg IM (G); 50–100 mg/kg IM (H)	22–44 mg/kg IM	5–20 mg/kg IM	20 mg/kg IM	20–40 mg/kg SC, IM, IV
Ketamine/ dexmedetomidine ± midazolam	5 mg/kg (K)/0.03 mg/kg (De) IM	—	3–5 mg/kg (K)/0.05 mg/kg (De) SC, IM (GP); 4 mg/kg (K)/0.015 mg/kg (De) IM (C)	—	—	—	—	40 mg/kg (K) + 0.25 mg/kg (De) + 1.5 mg/kg (Mi) SC, IM
Ketamine/ midazolam	5–10 mg/kg (K)/0.25–0.5 mg/kg (Mi) IM, IV	25 mg/kg (K)/≤2 mg/kg (Mi) IM, IV	5–10 mg/kg (K)/0.5–1.0 mg/kg (Mi) IM	—	40 mg/kg (K)/1–2 mg/kg (Mi) IM, SC, IP	—	10–20 mg/kg (K)/0.35–0.5 mg/kg (Mi) SC, IM	—
Ketoprofen	1–3 mg/kg PO, SC, IM q12–24h	1–3 mg/kg IM q12–24h	1–2 mg/kg SC, IM q12–24h	5 mg/kg SC q24h	2–5 mg/kg PO, SC, IM q12–24h	—	—	2 mg/kg SC, IM q12h
Lidocaine	1–4 mg/kg SC infiltrate; 0.5–1.0 mg/kg IV q12h	1–4 mg/kg SC infiltrate 1–2 mg/kg IV PRN 50–100 µg/kg/min CRI	1–4 mg/kg SC infiltrate	1–4 mg/kg SC infiltrate	1–4 mg/kg SC infiltrate	1–4 mg/kg SC infiltrate	1–4 mg/kg SC infiltrate	1–4 mg/kg SC infiltrate
Meloxicam	0.2–0.3 mg/kg PO, SC, IM q24h	1 mg/kg PO, SC, IM q24h	≥0.5 mg/kg PO, SC q24h	≥0.5 mg/kg PO, SC q24h	1–2 mg/kg PO, SC q24h (R); 1–5 mg/kg PO, SC q24h (M)	0.5 mg/kg PO, SC q12h	0.2 mg/kg SC q12h; >0.2 mg/kg PO q12h	0.3–0.5 mg/kg PO, SC, IM q24h

Continued

TABLE A.4 Chemical Restraint, Anesthetic, and Analgesic Agents Used in Small Mammals—cont'd

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Midazolam	0.25–0.5 mg/kg SC, IM, IV	0.25–2 mg/kg SC, IM, IV	1–2 mg/kg SC, IM, IV	1–2 mg/kg IM	1.0–2.5 mg/kg SC, IM (R); 1–5 mg/kg SC, IM (M)	0.25–0.5 mg/kg IM	0.25–0.5 mg/kg IM	0.5 mg/kg SC, IM
Morphine	0.2–4.0 mg/kg SC, IM q2–4h	0.5–2.0 mg/kg SC, IM q2–4h	2–5 mg/kg SC, IM q4h	2–5 mg/kg SC q2–4h	2–5 mg/kg SC q4h (R); 2–10 mg/kg SC, IM q4h (M)	—	—	—
Oxymorphone	0.05–0.2 mg/kg SC, IM, IV q6–12h	0.05–0.2 mg/kg SC, IM q6–12h	0.2–0.5 mg/kg SC, IM q6–12h	0.2–0.5 mg/kg SC, IM q6–12h	1.2–1.5 mg/kg SC (R); 0.2–4.0 mg/kg SC (M)	—	—	—
Propofol	3–6 mg/kg IV	3–6 mg/kg IV	3–5 mg/kg IV	—	7.5–10 mg/kg IV (R); 12–25 mg/kg IV (M)	—	—	3–5 mg/kg IV to effect
Tramadol	5 mg/kg PO q12–24h	—	—	—	5–20 mg/kg PO, SC q12–24h (R); 5–40 mg/kg SC q12–24h (M)	—	—	—

A, Acepromazine; *B,* butorphanol; *C,* chinchillas; *d,* days; *D,* diazepam; *De,* dexmedetomidine; *G,* gerbils; *GP,* guinea pigs; *H,* hamsters; *h,* hours; *IM,* intramuscularly; *IV,* intravenously; *K,* ketamine; *M,* mice; *MAC,* minimum alveolar concentration; *Mi,* midazolam; *OTM,* oral transmucosal; *PO,* orally; *q,* every; *R,* rats; *SC,* subcutaneous; *wk,* weeks.

TABLE A.5 Miscellaneous Agents Used in Small Mammals

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Activated charcoal	1–3 g/kg PO	1 g/kg PO	1 g/kg PO	1 g/kg PO	1 g/kg PO	—	1–3 g/kg PO	—
Aminophylline	4 mg/kg PO, IM, IV q12h	—	50 mg/kg PO, SC (GP)	—	—	—	—	—
Benazepril	0.25–0.5 mg/kg PO q24h	0.25–0.5 mg/kg PO q24h	≤0.1 mg/kg PO q24h	≤0.1 mg/kg PO q24h	≤0.1 mg/kg PO q24h	—	—	—
Calcium EDTA	20–30 mg/kg SC q12h	27 mg/kg SC q6–12h	30 mg/kg SC q12h	30 mg/kg SC q12h (G)	—	—	—	—
Cimetidine	5–10 mg/kg PO, SC, IM, IV q6–8h	5–10 mg/kg PO, SC, IM, IV q8–12h	5–10 mg/kg PO, SC, IM, IV q6–12h	5–10 mg/kg PO, SC, IM, IV q6–12h	5–10 mg/kg PO, SC, IM, IV q6–12h	10 mg/kg PO q8h	—	—
Cisapride[a]	0.5 mg/kg PO q8–12h	0.5 mg/kg PO q8–12h	—	0.1–0.5 mg/kg PO q12h	0.1–0.5 mg/kg PO q12h	—	0.25 mg/kg q8–24h PO, IM	—
Dexamethasone	0.5–1.0 mg/kg SC, IM, IV	0.2–0.6 mg/kg SC, IM (use with caution)	0.5–2.0 mg/kg SC, IM, IV (use with caution)	0.5–2.0 mg/kg SC, IM, IV	0.5–2.0 mg/kg SC, IM, IV	0.1–1.5 mg/kg IM	0.1–0.6 mg/kg SC, IM, IV	—
Digoxin	0.005–0.01 mg/kg PO q12–24h	0.005–0.01 mg/kg PO q12–24h	—	0.05–0.1 mg/kg PO q12–24h (H)	—	—	—	—
Diltiazem	1.5–7.5 mg/kg PO q12h	0.5–1.0 mg/kg PO q8–24h	0.5–1.0 mg/kg PO q12–24h	0.5–1.0 mg/kg PO q12–24h	0.5–1.0 mg/kg PO q12–24h	—	—	—
Diphenhydramine	0.5–2.0 mg/kg PO, SC, IM q8–12h	2 mg/kg PO, SC q8–12h	1–5 mg/kg SC, prn; 2.0–7.5 mg/kg PO (GP); 1–2 mg/kg PO, SC q12h (C)	1–2 mg/kg PO, SC q12h	1–2 mg/kg PO, SC q12h	—	—	—
Doxapram	2–5 mg/kg IV, IM	5–10 mg/kg IV, IM	2–5 mg/kg IV, IM	5–10 mg/kg IV, IM	5–10 mg/kg IV, IM	—	2 mg/kg IV, IM	—
Enalapril	0.25–0.5 mg/kg PO q24–48h	0.25–0.5 mg/kg PO q24–48h	0.5–1.0 mg/kg PO q24h	0.5–1.0 mg/kg PO q24h	0.5–1.0 mg/kg PO q24h	0.5 mg/kg PO q24h	0.5 mg/kg PO q24h	—
Epinephrine	0.02 mg/kg SC, IM, IV, IT	0.2 mg/kg IV (cardiac arrest)	0.003 mg/kg IV prn (GP); 0.1 mg/kg IV (C)	0.1 mg/kg IV	0.1 mg/kg IV	0.003 mg/kg IV	0.003 mg/kg IV	—
Famotidine	0.25–0.5 mg/kg PO, SC, IV q24h	0.5–1.0 mg/kg PO, SC, IV q12–24h	0.4–0.5 mg/kg PO, SC q24h	—	—	—	—	—
Furosemide	1–4 mg/kg PO, SC, IM, IV q8–12h	1–3 mg/kg PO q8–24h; 1–4 mg/kg SC, IM, IV prn	2–5 mg/kg PO, SC, IM q12h	2–10 mg/kg PO, SC, IM q12h	2–10 mg/kg PO, SC, IM q12h	2.5–5.0 mg/kg PO, SC, IM q8h	1–5 mg/kg PO, SC q12h	—
Hydroxyzine	2 mg/kg PO q8h	2 mg/kg PO q8–12h	—	—	—	—	—	—
Insulin	0.5–6 U/kg SC (or to effect)	—	1–2 U/animal SC q12h (NPH) (GP); 1 U/kg SC q12h (C)	2 U/animal SC	1–3 U/animal SC (R)	—	—	—
Iron dextran	10 mg/kg IM once	4–6 mg/kg IM once	—	—	—	25 mg/kg IM	—	—
Lactulose syrup	0.15–0.75 mL/kg PO q12h	—	0.5 mL/kg PO q12h	0.5 mL/kg PO q12h	0.5 mL/kg PO q12h	—	—	—
Levetiracetam	—	20 mg/kg PO q8h	—	—	—	—	—	20 mg/kg PO q8h

Continued

TABLE A.5 Miscellaneous Agents Used in Small Mammals—cont'd

Agent	Ferrets	Rabbits	Guinea Pigs/ Chinchillas	Gerbils/Hamsters	Rats/Mice	Hedgehogs	Sugar Gliders	Prairie Dogs
Maropitant citrate	—	1 mg/kg SC q24h × 3–5 days, then q48h or 3× weekly if needed	—	—	—	—	0.2 mg/kg SC q24h	—
Metoclopramide	0.2–1.0 mg/kg PO, SC, IM q6–8h	0.5 mg/kg PO, SC q6–8h	0.2–1.0 mg/kg PO, SC, IM q12h	0.2–1.0 mg/kg PO, SC, IM q12h	0.2–1.0 mg/kg PO, SC, IM q12h	0.2–0.5 mg/kg PO, SC	0.05–0.1 mg/kg PO, SC, IM q6–12h prn	—
Oxytocin	0.2–3.0 U/kg SC, IM	0.1–3.0 U/kg SC, IM	0.2–3.0 U/kg SC, IM, IV	0.2–3.0 U/kg SC, IM, IV	0.2–3.0 U/kg SC, IM, IV	—	—	—
Phenobarbital	1–2 mg/kg PO q8–12h	1–2 mg/kg PO q12h	5–20 mg/kg PO, IV, IP (GP)	5–20 mg/kg PO, IP (G)	—	—	—	—
Pimobendan	0.5 mg/kg PO q12h	0.1–0.3 mg/kg PO q12–24h	0.2–0.4 mg/kg PO q12h	0.2–0.4 mg/kg PO q12h	0.2–0.4 mg/kg PO q12h	—	—	—
Potassium citrate	—	33 mg/kg PO q8h	10–30 mg/kg PO q12h (GP)	—	—	—	—	—
Prednisolone/ prednisone	0.25–2 mg/kg PO q12–24h	0.25–1 mg/kg PO q12–24h	0.5–2 mg/kg PO q12–24h	0.5–2 mg/kg PO q12–24h	0.5–1 mg/kg PO q12–24h	0.5–2 mg/kg PO q12–24h	0.2 mg/kg PO q12h	—
SAM-e (S-adenosyl methionine)	20–100 mg/kg PO q24h	—	20–100 mg/kg PO q24h	20–100 mg/kg PO q24h	20–100 mg/kg PO q24h	—	—	—
Sucralfate	25–125 mg/kg PO q8–12h	25 mg/kg PO q8–12h	25–100 mg/kg PO q8–12h	25–100 mg/kg PO q8–12h	25–100 mg/kg PO q8–12h	10 mg/kg PO q8–12h	—	—
Terbutaline	2.5–5.0 mg/kg PO q12–24h	—	5 mg/kg PO q12h	5 mg/kg PO q12h	5 mg/kg PO q12h	—	—	—
Vitamin B complex[b]	1–2 mg (thiamine)/kg SC, IM	0.02–0.4 mL/kg SC, IM	0.02–0.2 mL/kg SC, IM	0.02–0.2 mL/kg SC, IM	0.02–0.2 mL/kg SC, IM	1 mL/kg SC, IM	0.02 mL/kg SC, IM	—
Vitamin K	Use feline dose	1–10 mg/kg SC, PO q24h prn	1–10 mg/kg SC, PO q24h prn	1–10 mg/kg SC, PO q24h prn	1–10 mg/kg SC, PO q24h prn	—	2 mg/kg SC, PO q24–72h	—

[a]Not commercially available, must be compounded.
[b]Use concentration formulated for small animals.
C, Chinchillas; *d,* days; *G,* gerbils; *GP,* guinea pigs; *H,* hamsters; *h,* hours; *IM,* intramuscularly; *M,* mice; *PO,* orally; *prn,* as necessary; *q,* every; *R,* rats; *SC,* subcutaneous; *wk,* weeks.

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