veterinary

Emergency

Critical Care

manual

Karol A. Mathews

Veterinary Emergency and Critical Care Manual

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PREFACE

The second edition of the manual has kept the same format as the first edition as it is intended to anticipate all possible scenarios of a particular condition with the author guiding the reader through the diagnostic and management process. Key points and therapies are highlighted for easy accessibility. Hourly constant rate infusion charts for commonly used medications are also included to facilitate easy prescribing whether in the clinic or giving instructions over the telephone. The introduction to each chapter offers a brief background into the problem with a short discussion of relevant physiology and pathophysiology as it relates to the clinical signs, the diagnostic and management process. The pharmacology section at the end of each chapter discusses the important aspects (action, indications, contraindications and adverse effects) of the medications recommended as they relate to their use for the specific problem at hand and not necessarily other potential indications, which will be discussed in other chapters when indicated. The suggested reading material is a source of reference for a more in-depth understanding of the topic and not necessarily the source of all information within the chapter.

While some chapters are short with few potential scenarios, other chapters dealing with more complex problems and many scenarios (e.g., cardiopulmonary resuscitation, shock, fluid therapy requirements), are longer and require more detail. It is recommended that such areas be reviewed as early as possible, so the reader is familiar with the format, materials required and instructions prior to the emergent situation.

While every effort has been made to provide the latest information, the specialty of emergency and critical care in both human and veterinary medicine is very dynamic resulting in new and changing evidence and treatment regimens occurring continuously. This was experienced during the preparation of the manual, making it very difficult to stop!

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INTRODUCTION

The telephone personnel are frequently the first line of assistance for clients requiring emergency service. The receptionist should be trained to either deal with specific emergencies or to pass the call onto the trained animal health technician or veterinarian. Whoever is designated the first-line telephone personnel should have sufficient medical knowledge and a good understanding of emergency situations in order to direct owners appropriately. They should be able to distinguish between and recognize life-threatening situations that require immediate life-saving procedures by the owner, and critical scenarios in which owners are immediately directed to a veterinary clinic for assistance. Thus, telephone personnel should be familiar with life saving procedures (i.e., mouth to nose rescusitation, cardiopulmonary resuscitation, treatment for airway obstruction, massive hemorrhage). Staff should always remain composed during an emergency phone call and encourage owners to stay calm. Information should be gathered from the owner in as short a time period as possible, as well as imparted to the owners in a clear and concise manner. All phone calls should be assessed for life-saving needs, and the name and telephone number of the caller obtained, PRIOR to placing the caller on hold.

Telephone personnel should:

- Have medical knowledge to properly assess emergency calls.
- Get information about the condition of the pet in as short a time as possible.
- Remain calm and give clear, reassuring instructions.
- Know clear directions to the facility from all major highways entering the city.
- Treat all concerned clients as though a possible life-threatening situation exists.
- Advise owners NOT to administer any medications prior to arrival, unless the problem is associated with a previously diagnosed problem and appropriate medication is available (i.e., diazepam for seizures, furosemide for heart failure).

Have the owners answer the following questions regarding the type of accident or medical emergency:

- Is the animal breathing?
- Is the animal conscious?
- Is the animal bleeding?
- Is the animal able to move?
- Are there any open wounds or visible fractures?
- When did the accident occur?
- How far are the owners from the facility?

GENERAL INFORMATION

- Foremost, owners should be advised to avoid harm to themselves.
- Remind callers that all injured or seriously ill animals should be evaluated by a veterinarian, and that stress to the injured or sick animal should be minimized.
- Injured animals should be approached cautiously:
    - Injured dogs should be muzzled as they may bite in the face of pain and fear.
    - Cats should be covered with a blanket prior to handling.
- Animals should be transported with minimal restraint to avoid further injury:
    - Large dogs can be transported on a flat firm surface (plywood, board) or on a towel as a hammock.
    - Cats, rabbits, small rodents, reptiles and birds should be contained in a box or carrier.
    - Animals with possible spinal cord injury (i.e., trauma, paralysed) should be handled minimally and transported on a firm surface (i.e., plywood, cardboard, serving tray) and secured with duct or other tape or cloth strips. Speak calmly to the animal as struggling must be avoided. Generally animals are placed in lateral recumbency unless the animal resents this positioning (*see Spinal Injury p. 473*).

RECOMMENDATIONS FOR PARTICULAR SCENARIOS

If the animal:

1. **Is DYSPNEIC/having difficulty breathing.**
   - Keep the animal as calm as possible.
   - USE MINIMAL RESTRAINT and NO NECK LEADS.
   - Animals should avoid walking and be carried to the car.
   - Ensure a cool environment (turn the air conditioning on high in the car).

2. **Is CHOKING**
   - Apply the Heimlich manoeuvre (receptionist must be given the instructions for all size dogs).

3. **Is BLEEDING**
   - A clean cloth or towel should cover the hemorrhage with pressure applied to the area.
   - If bleeding is noted from a limb, apply the cloth or towel and elevate the leg.

4. **Has been exposed to a TOXICANT:** (*see Toxicological Emergencies p. 630*).
   - Advise the owners to bring the product container or the label that lists the ingredients.
   - Determine the time of exposure.
   - Determine if the animal has vomited.
   - Find out the time it will take for the owners to get to the hospital.
     - If this is less than 30 minutes, advise immediate departure.
     - If it is more than 30 minutes, and the animal is alert, the owners may be able to induce emesis (if the ingested toxin is not oil-based or caustic) at home to decrease toxin absorption. Discussion with a veterinarian prior to the owners departing is necessary (*see Toxicological Emergencies p. 630*).
     - If an external contact poison is involved
       - The animal should be bathed with water and mild soap.
       - The animal should not be allowed to groom (cover the body with a towel, or place an Elizabethan collar if available).

5. **Is RECUMBENT/SHOCKY**
   - Cover the animal for warmth.
   - Place the animal on a blanket or in a carrier or box for transport.

6. **Is SEIZING**
   - Advise the owners that the seizure should stop in 2 – 5 minutes.
   - Encourage the owners to stay calm and reassure the animal.
   - Recommend, if possible, that the owners move the animal away from stairs or objects that may injure the animal.
   - If it is a puppy recommend placing a small amount of corn syrup on the gums for possible hypoglycemia.
   - If it is a known diabetic patient and the animal is experiencing a diabetic insulin crisis then
     - If the animal is alert, offer a meal.
     - If the animal is minimally alert, apply a small amount of corn syrup to the gums.
   - Nothing should be placed in the mouth, and no attempt to pull the tongue out of the mouth, should be made, as the owner will get bitten.
   - Warn callers that the animal may have an altered mentation on recovering from the seizure.
   - Place cold wet towels on the animal for transport.
   - If the seizure has been longer than 5 minutes, rush the animal immediately to the facility. For large patients, transport them on a blanket. For small patient confine them to a box or carrier.

7. **Has a LIMB FRACTURE**
   - A visibly displaced limb can be splinted with any hard object (rolled newspaper, wood, hockey stick, pole) and secured with cloth strips, duct or other tape, etc. The joint above and below the fracture should be immobilized or the splint will cause more harm then good. Omit the splint if it is causing more injury or stressing the animal.
   - Move the fractured limb as little as possible, transport the animal with minimal handling to decrease movement and pain of the fractured limb.

8. Has an OPEN or PENETRATING WOUND
   - To the chest, place the animal in lateral recumbency with the affected side down.
   - Cover the wound with clean, water or saline moistened towels/cloths.
   - If a FOREIGN BODY is impaled LEAVE the object in place and place the animal with the impaled object side up.

9. Has a BURN
   - Apply cool water compresses.

10. Has HEATSTROKE
    - Cool the animal with a gentle spray from a garden hose, or wet, cool towels, cold packs, and wet the feet.
    - Offer water, or crushed ice if the animal is alert.
    - Maintain the animal in a cool environment (air condition the car).
    - Bring to the clinic – do not dry it.

11. Has an OCULAR injury (*see Ophthalmological Emergencies p. 520*)
    - If ocular exposure to an irritant has occurred, flush the eye with water or contact-lens saline solution
    - Cover the eye with a clean, water or saline moistened cloth

The following is a checklist that should be available at the reception area of any emergency facility:

- Clear, written directions to the facility from all major highways entering the city.
- The phone number to poison control for the area (*see Toxicological emergencies p. 630*).
- The phone numbers for police, ambulance and fire departments.
- The phone number to animal ambulance services (if available in the area) as well as local taxi services that transport animals.
- A list of acceptable forms of payment allowed by the clinic.

SUGGESTED READING

1. Fagella AM. First aid, transport, and triage. *Veterinary Clinics of North America, Small Animal Practice* 1994: 24 (6) 997-1014.
2. Many pet First Aid books.

NOTES

INTRODUCTION

Triage is the prioritization of critically ill or injured animals into those requiring immediate treatment. It may be necessary to triage many patients at the same time, and you will have to prioritize according to severity of illness. The following are examples of triage by a classification scheme, which may assist you in triage. Patients classified into **Class I**: Catastrophic and dying before your eye, must be attended to within seconds (cardiopulmonary arrest, respiratory failure, unconscious, seizures, severe trauma, gastric dilation-volvulus, penetrating thoracic wounds), **Class II**: Critical and most urgent, must be attended to within minutes (shock, multiple injuries but adequate ventilation, toxicity, pale mucous membranes, penetrating wounds to the abdomen, hemorrhage, dystocia), **Class III**, urgent, must be attended to within one hour (open fractures, blunt injuries without signs of shock or altered mentation, profuse diarrhea with depression and dehydration, actively vomiting, urethral obstruction). **Class IV** patients are less seriously ill but require attention within 24 hours (lameness, anorexia). Although not necessarily classified as urgent, animals that are vomiting, or have diarrhea or are bleeding (not life-threatening) should be removed from the waiting room, as this is disturbing to others. It is recognized that if the appropriate resuscitative therapy is instituted as soon as possible after the onset of the critical event, the better the outcome. **ALWAYS** discuss referral to a continuous care facility with the pet owner where continuous care is required to optimize outcome.

This section will not discuss definitive therapy but is a guide to triage and initial assessment. Once an emergency problem list is made, definitive therapy of the individual problems should be pursued. While emergency therapy for individual problems must be addressed, the reader is reminded to return to the secondary survey to ensure that other potential problems will not be missed. It is also recommended that all practices be prepared for any kind of emergency, supplies and equipment are well organized and labeled, and the staff is familiar with their location.

DIAGNOSIS

History

A detailed history can wait but ask what caused the injury or when the onset of signs occurred, the emergency care received prior to arrival, and questions regarding medications for current or non-related problem. Ask to what extent emergency or resuscitative procedures can be performed (e.g., blood products, open or closed chest CPR).

Clinical Signs/Physical Examination

PRIMARY SURVEY

Primary survey addresses **A**irway, **B**reathing, **B**leeding, **C**ardiovascular, **C**irculation, level of **C**onsciousness initially. Unnecessary noise and crowds contribute to patient (and operator) stress.

- Those patients requiring immediate management upon arrival at the clinic should be moved on a stretcher or a trolley; avoid letting them walk to avoid collapse. **Do not** place a leash around the neck of patients with head, ocular, neck or respiratory injuries or problems. As you approach the patient, prior to moving them, observe the **ventilatory pattern** (normal, tachypneic, dyspneic, hyperpneic, orthopneic), and note whether there is an upper (i.e., stridorous with obstruction) or lower airway component (i.e., small excursions with pneumothorax). Note **mentation.** Be cautious when proceeding with examination to **avoid injury to you and your staff.** Use appropriate restraint where needed. Chemical rather than manual (brutacaine!) restraint is less stressful to both patient and caregiver when dealing with uncooperative animals. Place them on a fleece or pad on the table to avoid heat loss (unless hyperthermic). If possible, assign someone to document any procedures performed and the results of diagnostic tests.

- While the primary survey is being conducted, simultaneous **life-saving procedures** can be performed (*see MANAGEMENT p. 6*). Unless obvious problems require immediate attention, (Class I and II), commence examination.

- **Head and neck,** while **protecting the cervical spine** look for blood from nose, mouth ears, eye injuries, check mucous membrane colour and capillary refill time (CRT). Gently palpate face and skull for fractures. Palpate the trachea and neck for crepitus or wounds. Note hydration status.
- **Thorax,** auscultate lung sounds; if absent (dorsal-air or ventral-fluid *see Respiratory Emergencies p. 555*); heart sounds, if absent and lung sounds audible, pericardial effusion likely present (s*ee Pericardial Effusion p. 145*). Otherwise, note heart and respiratory rates. Palpate for crepitus or wounds.
- **Circulation.** Palpate **femoral and dorsal pedal pulses** for rate, rhythm and strength. Recheck **mucous membrane colour and CRT.** Evaluate these parameters **q2–5min** initially.
- **A rapid examination of the abdomen, flank, spine, limbs, anus, vulva or penis** should be performed prior to continuing to the secondary survey. Remember if a diagnostic test or procedure is *imperative for diagnosis and essential treatment,* chemical restraint (*see Chemical Restraint for Specific Emergencies p. 100*) rather than manual restraint should be used as this may be less stressful to the patient, and you!
- Apply **ECG leads** and note rate and rhythm (dependent on priority).
- Apply **blood pressure** cuff (dependent on number of personnel and priority).
- **Incidental findings** such as evidence as to what might have occurred (scraped nails, road dirt, oil, etc).

Laboratory Evaluation/Diagnostic Imaging

Stat

When frequency, type, and degree of illness or injury is not known then a minimum data base should be obtained for baseline and screening. An expanded laboratory data base should be performed based on history, physical findings and results of the minimum data bases (stat tests).

- **Blood pressure** if not yet obtained.
- **IV** catheter to obtain:
  - **PCV** to identify blood loss, anemia or polycythemia. PCV maybe normal even with blood loss due to splenic contraction. Anemia may be present due to immune-mediated disease.
  - **TS** must always be performed to assess blood loss. If PCV is within normal limits, and the TS is below normal, hemorrhage must still be considered. TS is usually normal with immune-mediated anemia.
  - **Stick BUN, creatinine, or urea** to establish if renal dysfunction is present as a cause or effect of other problems.
  - **Glucose** may be decreased for several reasons (*see Hypoglycemia p. 280*).
  - **Blood gases or total CO_2** to assess perfusion and metabolic status. Arterial gases to assess oxygenation (respiratory system); venous blood may be of value in assessing respiratory system ($PvCO_2$) also. (*see Respiratory Emergencies p. 555*).
  - **Electrolytes** are essential in ruling out life-threatening abnormalities (potassium 3.0 <6.0 mEq/L, *see Hypo/Hyperkalemia p. 394,* sodium 130 <168 mEq/L *see Hypo/hypernatremia p. 381*).
  - **ACT** (**and platelet** count if indicated) to assess for coagulopathy or as a baseline.
  - Also obtain blood for **extended laboratory data base**. Individual tests should be performed immediately based on the presenting complaint and physical findings.
- **Urine specific gravity** (culture and sediment where appropriate) should be measured to confirm potential renal dysfunction, assess hydration and volume status, and as a baseline.
- **Diagnostic imaging** following physical examination to evaluate area in question, once patient stabilized adequately.

Extended Laboratory Data Base

- **A CBC and biochemical profile** is always advised for the Class I-III, and IV if warranted. Individual further testing is performed based on history, physical findings, and response to emergency therapy.

While individual procedures and treatments are listed, it will be necessary to perform more than one at a time, i.e., IV access should be obtained while oxygen is being administered or hemorrhage is controlled.

A. Always administer oxygen. Suction **airway** and intubate if necessary.

B. Thoracocentesis if severely dyspneic with **reduced/absent lung sounds** (dorsal for air, ventral for fluid – blood, pus, transudate *see Respiratory Emergencies p. 555*).

C. Apply external pressure to **active bleeding** from vessels or fracture sites. For non-compressible sites (e.g., abdomen, nose, vulva *see Hemorrhage p. 619*).

D. Cover **open wounds** with sterile (clean!), saline (tap water!) moistened towels.

E. **Seizures:** if possible place IV catheter, rather than hypodermic needle, for injection but only if time taken to perform either is the same. Administer **diazepam 0.5 – 1.0 mg/kg once.** For dogs only: repeat in 5 minutes if necessary. (*see Seizures in Dogs p. 460,* and *Seizures in Cats p. 456*).

F. **Head injury** *see Head Trauma p. 691* for detailed management while continuing with Primary and Secondary Survey.

G. **Catheter placement** (cephalic, jugular, intraosseous) depending on the circumstances; catheter size will vary with the size of the patient, ease of access and rapidity of fluid delivery 22 – 20 gauge for cats and 20 – 14 for dogs. If semi-conscious or unconscious (not head injury) due to blood loss, place a catheter into the jugular vein (2", 5 cm, 18 gauge for a cat and 16 – 10 gauge or bigger for a dog). Do not use long catheters unless >5 Fr. If unable to obtain access percutaneously, infiltrate skin, SC tissue over venipuncture site with lidocaine if patient is conscious (this procedure is not needed if the patient is unconscious), and cut down onto the vein (*see Rapid Access Techniques p. 609*).

H. If not yet collected, **obtain blood**, via the catheter, for above laboratory tests.

I. **Start fluids,** *see Fluid Therapy p. 347* for general approach. Type and rate will depend on underlying problem (*see specific problem i.e., Hemorrhage p. 619, Congestive Heart Failure p. 149, Oliguric/Anuric Renal Failure p. 709, Urethral Obstruction p. 745*). Attach to pressure bag if shock dose fluids are required. Run desired volume of fluids into a burette if patient <5 kg.

J. **Temperature** maybe normothormic, hypothermic with shock or CVS disease, or hyperthermic if heat stressed (*see Heat Stress p. 297*), or fever if septic (*see Sepsis p. 588*).

K. **Blood pressure** (Dynamap or doppler). Hypotension occurs in many pathophysiological states such as: hemorrhage, distributive (anaphylaxis, sepsis, drug-induced), third space losses (e.g., peritonitis, pleural effusion, cellulitis/fasciitis), and cardiovascular system problems.

L. **ECG** to monitor heart rate and rhythm. Various abnormalities may be noted as either primary or secondary pathology (*see Bradycardia p. 164, Supraventricular Tachycardia p. 170, Ventricular Tachycardia p. 179*).

SECONDARY SURVEY

Once the primary survey is complete and life-threatening problems have been (are being) dealt with, the secondary survey should begin. This is an organized evaluation of the patient to identify all problems and continue with an in-depth assessment and treatment while prioritising the most life-threatening. This is essential in order to anticipate further life-threatening problems, and possibly to avoid spending a lot of money on resuscitation with blood products etc., only to find the patient has a fractured spine with severe irreversible neurological deficits necessitating euthanasia. The use of the acronym **A CRASH PLAN** is helpful with examination to ensure no system is missed.

A – AIRWAY, BREATHING, BLEEDING
C – CIRCULATION, CARDIOVASCULAR
R – RESPIRATION
A – ABDOMEN, (ANALGESICS)
S – SPINE, SKIN, SCROTUM
H – HEAD, ([mentation: depressed, semi-coma, coma] ears, eyes), HYDRATION, HYPO-, HYPERTHERMIA
P – PELVIS, PERINEUM (vulva, scrotum, anus, rectal exam), PENIS, PROSTATE, PAIN
L – LIMBS (wounds, fractures, swelling, pain)
A – ARTERIES/VEINS
N – NERVES/NEUROLOGIC, NECK, NUTRITIONAL status

A. Airway, Breathing: (Respiratory Emergencies) 100% oxygen delivery via mask, hood, nasal canula or prongs, tracheal insufflation or tracheostomy. Respiratory compromise can result from **bleeding** causing tachypnea due to low circulating volume; dyspnea due to hemorrhage into the airway or parenchyma; or dyspnea and decreased lung sounds due to bleeding into the pleural space.

C. Circulation, Cardiovascular: If pulse quality and blood pressure are poor identify cause:
- Low circulating volume; blood or fluid loss (*Hemorrhage p. 619, Acute Diarrhea and Vomiting p. 32/74*, third space losses in abdomen, chest, fracture, massive inflammation e.g., a limb).
- Vasoconstriction (*sympathetic stimulation with or without shock p. 603*). Weak to absent peripheral (dorsal pedal) pulses.
- Hypothermia, hyperthermia. Weak to absent or bounding pulses.
- Myocardial injury or, *Supraventricular Arrhythmias p. 170, Bradyarrhythmias p. 164, Ventricular Arrhythmias p. 179*. Pulse deficits may or may not be detectable.
- Toxicities (to include medications recently administered) *p. 630*.
- *Sepsis p. 588*. Pulse quality may be bounding.
- *Head Trauma p. 691*.
- *Cardiac tamponade p. 145*. Lung sounds normal but heart sounds absent or muffled.

R. Respiratory Emergencies: These include:
- **upper airway** obstruction (foreign body, laryngeal paralysis,blood), and tracheal injuries.
- **lower airway pathology** due to pulmonary contusions, hemorrhage, parenchymal disease (pneumonia, pneumonitis, lung neoplasm, non-cardiogenic pulmonary edema, asthma), diaphragmatic hernia, pleural space problems (pneumothorax, hemorrhage and effusion).
- **thoracic wall injury,** such as penetrating wound, or fractured ribs with or without flail chest.

A. Abdomen. Consider Acute Abdomen (*p. 21*). Identify cause by history, physical examination (deep and superficial palpation of skin, abdominal wall and intraabdominal organs), radiographic imaging ± contrast study (*urological injury, p. 727*), ± abdominocentesis (peritoneal effusion of: urine, bile, amylase, blood, plant and fecal material, transudate fluid, air), ± peritoneal lavage (after radiographic imaging). Continue with resuscitative measures of fluid, plasma and blood, pressor agents if necessary, and appropriate therapy for electrolyte and acid-base disorders. Most causes of acute abdomen require exploratory laparotomy, therefore, the patient should receive adequate resuscitative therapy while preparing for surgery.

Analgesics (*p. 81*). Most traumatized patients are painful. After, or during, the primary survey consider giving butorphanol 0.1 – 0.4 mg/kg IV, IM (cat and dog) for mild to moderate pain. Oxymorphone or hydromorphone 0.02 – 0.1 mg/kg IV, IM (cat and dog), or more to effect, in extremely painful cases.

S. Spinal injuries (*p. 478*) can occur with any type of trauma. Palpate cervical, thoracic and lumbar spine as soon as possible to identify injuries and avoid further injury or costs if euthanasia is inevitable. Place the patient on a board and avoid movement, especially with physical and radiographic examination.

Skin. Assess injuries (farm, road, *see Wounds p. 702*), type of contamination (chemical *see Toxicities p. 630*), burns (*see Burns p. 682*), dermatologic causes for emergent presentation (*see Dermatologic Emergencies p. 216*). **Assess hydration,** if dehydrated >7% (*see Fluid Therapy p. 347*) while investigating cause.

H. Head trauma, seizures, altered sensorium, stupor, coma. Consider perfusion status, toxicities and other possible causes (*see Head Trauma p. 691, see Stupor/Coma p. 478*).

Hydration status must be assessed for dehydration >7% (*see Fluid Therapy p. 347*) while investigating cause. Hydration status must be considered in addition to perfusion status.

Hypo-, hyperthermia may be the basis of presenting problem (*see Hypothermia p. 291, Hyperthermia p. 297*).

P. Pelvic fractures can result in shock due to urethral and colonic tears (*see Acute Abdomen p. 21*), or significant blood loss into the **retroperitoneal** space and **perineum**. Urethral tears may result in urine leakage into the fascial planes of the perineum, legs or dorsum. This results in swelling and bruising of the area (*see Uroabdomen/perineum/dorsum p. 727*). Blood and urine may be retained in the retroperitoneal space and perineum and will not be detected on abdominocentesis initially. Diagnostic peritoneal lavage may detect small amounts of translocated blood, urine or fecal material. **ALWAYS** perform a rectal examination to detect bone fragments piercing into the rectum. Monitor urine output, perineum for swelling and patient straining. If retroperitonel hemorrhage is suspected·then vital signs, PCV, TS and repeat radiographs/ultrasonograhic examination are required to monitor progress and determine if surgical exploration is warranted.

Perineum. Examination of the perineum should include:
- All the perineal area. May need to shave the area to assess injuries and monitor bruising.
- **anus and vulva** to note bleeding, or other discharge, wounds, maggots, etc.
- **scrotum** should be examined for swelling, hemorrhage, pain, inflammation, testicular torsion, presence or absence of testicles (*see Male Urogenital Emergencies p. 736*). If no testicles present, confirm that two were present at time of castration. Should the dog not be castrated with only one testicle present, or only one testicle was present at the time of castration, a torsion of a cryptorchid testicle may be a cause of acute abdomen.

Penis is examined for bleeding or other discharge, wounds or obstruction, phimosis or paraphimosis (*Male Urogenital Emergencies p. 736*).

L. Limbs should be examined for fractures, hemorrhage, lacerations, heat and swelling (i.e., fasciitis, myositis due to *streptococcal infection see Sepsis/Shock p. 588*), necrosis, crepitus (i.e., *clostridial* sp infection, open fracture).

A. Small **arteries and veins** with continued blood loss (large arterial bleeding should be managed during primary survey). Counterpressure is the preferred treatment. Tourniquets should be avoided unless limb amputation is necessary (*see Hemorrhage p. 619*).

N. Nerves and Neurological assessment. Exposed **Nerves** are managed as other traumatised tissue (*see Wound Management p. 702*). **Neurological** assessment of the **peripheral** (*see Spinal injuries p. 473, Weakness p. 491*), and **central, nervous system** (*see Head Trauma p. 691, Spinal Injury p. 473*) should be performed as soon as possible for management and prognosis.

After completion of the Primary and Secondary Surveys, a problem list should be formulated with diagnostic and therapeutic plans for each problem. Patients should be monitored frequently, even if they appear stable for 24 hours and possibly longer (*see Monitoring p. 12*).

SUGGESTED READING

1. Crowe DT Jr. Triage and Trauma Management In: Murtaugh RJ, Kaplan PM (ed). Veterinary Emergency and Critical Care Medicine, Toronto, Mosby, 1992:77-121.
2. Davenport DJ, Martin RA. Acute Abdomen. In: Murtaugh RJ, Kaplan PM (ed) Veterinary Emergency and Critical Care Medicine, Toronto, Mosby, 1992:153-162.
3. Fossum TW. Various traumatic injuries by system. Small Animal Surgery. St. Louis, MO, Mosby, 2002.
4. Stamp GL, Crowe DT. Triage and resuscitation of the catastrophic trauma patient. In: Kirk RW, Bonagura JD (ed). Kirk's Current Veterinary Therapy XI, Toronto, Saunders, 1992:75-82.
4. Various traumatic injuries by system In: Slatter D. Textbook of Small Animal Surgery, 3rd ed, Philadelphia, WB Saunders, 2003.

INTRODUCTION

It is essential to have all emergency medications and supplies in one area that is readily accessible when working with the patient. These items are listed here. The emergency drug cart may be one specifically designed for this, or an excellent alternative is the floor-sized mechanics toolbox (e.g., Snap-On® Tools). In addition to the main emergency drug cart, a small 'carry' toolbox with essential items is also recommended which can be placed at the cageside. This is especially useful if the patient is a large dog and only one person is available. In addition, the emergency area should have an oxygen supply and suction unit. An accessible assortment of supplies on shelves should also be available.

ITEM	QUANTITY

ORGANIZED ON TOP OF THE EMERGENCY CART

Defibrillator with ECG paper	2 rolls
Defibrillator gel	2 tubes
ECG monitor (if separate from defibrillator) and paper	2 rolls
Pulse Oximeter	
Heparinized saline filled (1U/mL) syringes	10
Penlights	2

ORGANIZED AT SIDE OF EMERGENCY CART

Chlorhexidine scrub	
Isopropyl Alcohol	
Tincture of chlorhexidine	
Gauze squares	
Band-Aids to cover IV entry site	
Bandage material for IV catheter placement	
Injection port adaptors for IV catheters (PRN adaptors)	10

DRUG DRAWERS OR BINS

First drawer

Those drugs being used during more common emergencies should be placed in the top drawer as this is usually left open during the emergency situation and the drugs are continuously accessible.

Epinephrine – 1:1000 (1 mg/mL) 50 mL bottle	1
Lidocaine – 2% 50 mL bottle	1
Sodium Bicarbonate – 50 mL bottle	1
Ampule breakers	2
Atropine – 0.5 or 0.6 mg/mL in 1 mL ampule	10
Glycopyrolate – 0.2 mg/mL 20 mL bottle	1
Diazepam – 5 mg/mL in 2 mL ampule	5
Furosemide – 50 mg/mL 50 mL bottle	1
Calcium gluconate – 10% 100 mg/mL (9.3 mg/mL elemental calcium) 10 mL	2
Esmolol – 10 mg/mL 10 mL bottle	1
Propanolol – 1 mg/mL 1 mL ampule	2
Dopamine – 40 mg/mL 5 mL bottle	1
Norepinephrine – 1 mg/mL 4 mL	2
Isoproterenol – 0.2 mg/mL 1 mL ampule	5
Dobutamine – 12.5 mg/mL 20 mL bottle	1
Dopram – 20 mg/mL 20 mL bottle	1
Ready syringes with 20 G needles attached	5 – 1 cc
	5 – 3 cc
	5 – 6 cc
	2 – 12 cc
Extra syringes of 1, 3, 6 & 12 mL	4 each
25, 20, 18 G needles	10 of each
IV Catheters	
25, 20, 18 & 16 G	6 each
14 G	3
Sterile lubricant	4
Eye lubricant	2

Second drawer

Laryngoscopes	2
Laryngoscope Blades small, medium & large	1 of each
Lidocaine 2% spray	2
Endotracheal tubes sizes 3 to – 14	1 of each size
Endotracheal tube stylets	2
Mouth gags, small, medium & large	1 of each
Endotracheal tube cuff inflating syringes	2

Third drawer

Sterile endotracheal tubes, variety of sizes	
8 FR feeding tubes	5
3-way Stopcocks	5
3-way Stopcocks with extension tubing	5
Butterfly catheters 21 G	2
19 G	2
Catheter Introducers (little yellow hockey sticks)	4
Urinary catheters (6, 8 & 10 Fr) and adaptors	2 of each

Fourth drawer

Non-latex gloves (size 6, 7 & 8)	2 of each
Sterile gauze	4 pkg
Sterile gloves	2 of each size
Oxygen analyzer	
Flashlights	2
Balfour retractor	1

Emergency Cutdown kit   1

1 Sponge forcep with 3X3 sponge clipped on	1 Needle driver
1 Rochester Pean – large curved	1 Rochester Pean – small curved
1 Hemostate curved	2 Mosquitoes, 1 straight
2 Bachhaus towel forceps 3"	1 Mayo scissor
1 Metzenbaum scissor 1 Sharp/sharp scissor	1 Tissue forceps 1 Adson tissue forceps
1 Scalpel handle #3	
1 Umbilical tape 1/8"X18"	2 Black silk #0X21"
1 2/0 Vetafil with MS 431 – 2" needle threaded	12 sponges

Wound closure kit   1

1 Needle driver	1 Straight sharp-blunt scissor
1 Metzenbaum scissor	1 Straight mosquito forcep
1 Adson tissue forceps 1 X 2 teeth	1 Scalpel handle # 3
6 Sponges	

Bottom shelf

Oxygen Masks, small, medium and large size	2 of each
Ambubags, Small & Large	1 of each
Tensor bandage wide rolls	4
Defibrillator gel	2
Emergency checklist log	

Suction Area adjacent to the crash cart

Suction unit	
Suction catheters – 8 F(blue tip)	10
– 14 F(green/clear tip)	10

SUPPLIES ADJACENT TO THE EMERGENCY ROOM TABLE

Small boxes, within a larger container on wheels, containing assorted sizes of IV catheters, hypodermic needles and syringes.
EDTA, Serum, ACT & PT/PTT vacutainers.
IV pole with fluid bag and IV delivery set ready for use, and pressure bag for rapid delivery of fluids.

PORTABLE CRASH KIT

Epinephrine	1
Lidocaine	1
Atropine	5
Layrngoscope	1
Laryngoscope Blades small & large	1 of each
Gauze roll	
Endotracheal tube cuff inflating syringe	1
Endotracheal tube Size 4, 5.5, 6.5, 8.0 & 9.0	1 of each
Ready syringes with 20 G needle attached	2 – 1 cc
2 – 3cc	
2 – 6cc	
Needles 25, 23, 20, 18 G	4 of each
16 & 14 G	2 of each
Syringes	2 – 1 cc
	2 – 3 cc
	2 – 6 cc

ACCESSIBLE SUPPLIES

Assorted IV fluids: 0.9% & 0.45% sodium chloride, lactated Ringer's, Normasol® R or Plasma-Lyte® A or 148, synthetic colloid, hypertonic saline, 5% dextrose in water.
IV delivery sets
Burrettes
Thoracotomy tubes sizes 12 to 22
Thoracotomy extension tubing and adapters
3-way stopcocks with extension tubing
Butterfly catheters: 19-21G

The following are at hand to add to IV fluids

Magnesium sulphate 200 mg/mL	
(0.8 mmol/mL, 1.6 mEq/mL) 10 mL	1
Potassium phosphate	
(K$^+$ 4.4 mmol/mL, Phosphate 3 mmol/mL) 10 mL	1
Potassium Chloride 2 mEq/mL 10 mL	2

NOTES

INTRODUCTION

The importance of monitoring or 'trending' the ill or injured patient cannot be emphasized enough. These animals cannot communicate their concerns so as caregivers we must observe mentation, behaviour and physiological parameters in order to determine response to therapy, their current state of health and level of pain. Patient deterioration can occur very slowly, with only subtle signs indicating this, or, there may be a dramatic change from moment-to-moment. It is advisable to utilize a flow sheet when monitoring patients (see attached). This enables accurate record keeping at the cage side, facilitating trending, as well as alerts the attending staff as to when various parameters should be observed and medications administered. The frequency and level of monitoring is dependent on the case at hand. Patients in shock, for example, require moment-to-moment monitoring until stabilized; the monitoring can then be reduced to every 30 minutes, then 60 minutes and so on until consistently stable. There are many electronic devices available to the veterinary practitioner which measure various physiological parameters. However, nothing can replace a good physical examination and patient observation. In addition, specific laboratory tests are required to fully evaluate the ill or injured patient. While monitoring tends to be emphasized for the 'critical' patient, it is important to keep in mind that monitoring is also important in a potentially critical patient; hopefully this will prevent them from becoming a critically ill case.

A 'PATIENT MONITORING TO-DO LIST' (a glance at this list frequently acts as a prompt)

WEIGHT	crystalloids
mentation	blood/plasma
temperature	colloids
heart rate, rhythm	drugs/dose/metabolism
mucous membranes	antibiotics
pulse quality	analgesics
blood pressure/pulse quality	ulcer prophylaxis
airway	blood gases
ventilation	electrolytes
oxygenation	serum titres
pancreas	albumin
liver function	CPK
renal function	coagulopathy, platelets, Activated Clotting Time
GI motility	PCV/TS
bowel movements	WBC/CBC
nutrition	wound care
glucose	bandage/dressing
nursing care	tender loving care
catheter care (U,A,V)	

I. VITAL SIGNS

The basic **A**ttitude, **R**espiration, **P**ulse and **T**emperature, in that order, should always be included in the monitoring regimen. Approach the patient quietly and assess their behaviour before contact; measure respiratory rate and observe pattern (before opening the cage door), follow with palpation of a peripheral (preferably dorsal pedal) pulse before doing anything else, then gently interact to complete assessment of attitude. Many procedures, especially taking the temperature, will increase respiratory and pulse rate and therefore, should be left to the end of the cursory exam. Also, this flows with the **A**irway, **B**reathing, **C**irculation of triage. The extent and depth of monitoring will vary with the severity of illness and availability of monitoring equipment.

A. State of consciousness (attitude)

- Important to note; problems associated with the CNS may be the first clue to unsuspected problems and can reflect systemic disorders as well as problems associated with post-anesthetic and surgical procedures.
- Disorders of consciousness include lethargy, aggression, coma and seizures (maybe confused with delerium and blindness, and severe apprehension or excitability) caused by prolonged anesthesia, hypoxia, embolism,

intracranial hemorrhage, thrombosis, alterations in cerebral metabolism, hypoglycemia, hypocalcemia, liver disease or drug reaction. If a high level of suspicion exists of any of these disorders, based on patient history and clinical assessment, **expand the data base by doing appropriate tests and specialty consultation.**

- *Refer to Neurological Examination in Head Trauma p. 691.*

B. Respiratory status

- Airway, Breathing, Ventilation, Oxygenation. ALL contribute to oxygen delivery to the tissues. Trending the respiratory rate and effort is very important, noting that even the slightest alteration from normal (dogs: 12 – 40 b/min, cats: 20 – 40 b/min) may signal problems.
- **Respiratory insufficiency** is detected by abnormal rate, rhythm and depth of ventilation.
    - **Apnea** may be caused by airway obstruction, drugs, muscle paralysis, hyperventilation.
    - **Dyspnea** may be due to anxiety or pain, obstruction to air flow, chest wall problems, cardiac disease, pulmonary parenchymal disease, pulmonary thromboemboli or cardiac tamponade. Note whether dyspnea is inspiratory OR expiratory.
    - **Paradoxical.** Upper airway obstruction results in a bilateral inward thoracic motion, whereas fractured ribs may cause segmental or hemithoracic (flail) inward motion.
    - **Tachypnea** is due to pain, anxiety, hyperthermia, respiratory acidosis, respiratory insufficiency, drugs (opioids), pleural space disease, hypovolemia.
    - **Bradypnea** may be normal as in sleep, or caused by opioids and other analgesics and tranquilizers, which may not be of concern, whereas respiratory decompensation or CNS disease is of concern.
    - **Hyperpnea** – pain, hypoxia, acidosis (hypercarbia – Kussmahl).
    - Various named abnormal respiratory rhythms are associated with CNS abnormalities (*see Head Trauma p. 691*).
- **Etiologies of respiratory insufficiency.** Consider cardiac insufficiency, pulmonary congestion, oversedation, unstable-injured chest wall, laryngotracheal/pulmonary edema, lung collapse, space occupying lesion in the thorax, obesity, pneumothorax, coughing/bronchospasm, parenchymal disease, pain and splinting, tight bandage etc., CNS abnormalities.

C. Cardiovascular status

1. **Pulse** should be monitored every 15 – 60 minutes as indicated. Assessment should be made with regard to rate, rhythm and **strength** (an indicator of arterial blood pressure). *See Fuid Therapy p. 347 for physical assessment.*
    a. **Rate**
        i. **Normal heart rate.** Cat 120 – 240 bpm (mean 187); Dog 70 – 160 bpm for adult dogs, 60 – 140 bpm for giant breeds, up to 180 bpm for toy breeds, and up to 220 bpm for puppies.
        ii. **Bradycardia** can be due to hypothermia, hyperkalemia, drugs, hypothyroid and terminal stages of shock or respiratory diseases, or CNS abnormalities.
        iii. **Tachycardia** can be due to pain, apprehension, hyperthermia, hypoventilation, hypotension (with or without blood loss) – any cause of endogenous epinephrine or corticosteroid release, fever, sepsis/bacteremia or CNS abnormalities, anemia, hypoxia, or hypercarbia.
    b. **Rhythm**
        i. **Rhythm** can be altered for many reasons. When an abnormal rhythm (arrhythmia) is detected, ECG assessment should be performed.
        ii. **Arrhythmias** may increase with surgical procedures longer than 3 hours. Most common arrhythmias associated with anesthesia in dogs are wandering sinus pacemaker, sinus bradycardia and sinus arrhythmia. Sinus bradycardia may also occur in patients with respiratory disease. Atrial and ventricular arrhythmias are associated with extubation, primary cardiac disease or systemic, electrolyte, organ and acid-base abnormalities, hypoxia, drug interactions, increased catecholamines, traumatic myocarditis and splenic disorders, to name a few (*see cardiac arrhythmias in 3 below p. 14*).
    c. **Strength (blood pressure [BP])** Normal systemic BP: 120 – 150/80, MAP 100 (*see Fluid Therapy p. 347 for assessment*)
        i. **Hypotension** results from hypovolemia, cardiac depression, adrenal insufficiency, various drugs and shock (hypovolemic, septic, cardiogenic, distributive, obstructive).
        ii. **Hypertension** is seen as a patient awakens from anesthesia due to anxiety or pain, with overuse of colloids, the use of hypertensive drugs, and many other conditions (*see Hypertension p. 205*) .

2. **Mucous membranes**
        i. **Capillary refill time** can be used for assessment of peripheral perfusion. Normal refill time is 0.5 to <2 seconds. Prolonged refill time may indicate, hypotension, hypovolemia or hypothermia. A shortened time may indicate early sepsis.

ii. **Mucous membrane colour** can also be used to assess peripheral perfusion, however anemia is a confounding factor as anemic patients may have pale mucous membranes yet perfusion may be normal. **Pale** mucous membranes may be due to vasoconstriction (endogenous epinephrine in response to blood loss, hypothermia, pain). **Red** (injected) mucous membranes may indicate, fever, bacteremia/sepsis, hyperthermia, polycythemia. **Blue/purple (cyanosis)** is an unreliable and late warning of low oxygen tension and may be central or peripheral. Confirmation of respiratory abnormalities is based on blood gas measures with low PaO_2 or pulse oximetry (*see Respiratory Emergencies p. 555*). *Cyanosis* may indicate right-to-left shunting of blood, decreased cardiac output with peripheral stagnation, hypothermia, local vasoconstriction or respiratory insufficiency. Cyanosis can only be visualized with a hemoglobin >50 g/L [5g/dL] (PCV > 15%). **Yellow or orange (icterus)** (*p. 70*) may result from pre-, intra- or post- hepatic causes and include hemolysis (autoimmune-disease or post-transfusion), pre-existing liver disease, liver hypoxia, drug or anesthetic toxicity, sepsis, hepatic lipidosis and hepatitis. **Brown** suggests methemoglobinemia (acetaminophen toxicity *p. 651*).

3. Complete **cardiovascular assessment** should be carried out when abnormalities are detected.
   i. **Thoracic auscultation** should be performed to directly assess heart sounds, rate and rhythm in conjunction with palpation of the peripheral pulse. Lung sounds should also be assessed.
   ii. **Electrocardiographic** assessment should also be made.
   Cardiac arrhythmias
   - Ventricular arrhythmias are the most common in the ill or injured animal. This may be due to metabolic acidosis which is frequently corrected with fluid therapy, pain, electrolyte disturbances, splenic pathology or associated with trauma. *Refer to Ventricular Arrhythmias p. 179.*
   - Supraventricular arrhythmias may also be secondary to conditions similar to those for ventricular arrhythmias. *Refer to Supraventricular Arrhythmias p. 170.*
   - Bradyarrhythmia may be physiological or secondary to electrolyte or metabolic disturbances, or opioid administration. *Refer to Bradyarrhythmias p. 164.*
   iii. **Adjunct tests.** Chest radiographs, central venous pressure measurement and assessment *p. 370/15*, blood gas measurements (*Acid-Base Assessment p. 406, and Respiratory Emergencies p. 555*), or pulse oximetry (*p. 580*) may also be required.

D. **Temperature** must be monitored. Continuous reading thermometers are recommended in critically ill patients, otherwise record every 5 – 60 minutes as indicated. The ambient temperature should be 21 – 24° C (68 – 72°F). The patient should be kept clean of blood, urine and feces. Normal body temperature for dogs and cats is 38.5 – 39.5°C (101.5 – 102.5°F).

   - Hypothermia is best controlled with circulating water heating pads, warmed cage and blankets (*see Accidental Hypothermia p. 291*). Warm the IV fluid line under a warm water bottle or 'oat bag'. Warm water bottles should not be warmer than that tolerated by the palmar surface of a human wrist with a towel or blanket placed between it and the patient. Cage fans must be hospital approved otherwise they may be a fire hazard. Never leave a heating fan running when there is no attendant close by. Only warm the patient to 37.5°C, 100°F. Re-check temperature in 30 minutes. Pediatric incubators are useful for small animals but care should be taken that overheating does not occur.
   - Underlying causes for hypothermia:
     Heat loss during surgery and anesthesia
     Shock   Cardiovascular insufficiency
     Hypothyroidism   Poor perfusion
     Hypovolemia   Problems with thermometer
   - Hyperthermia may develop with infection, CNS disease, seizures, increased work-of-breathing, overzealous re-warming or high ambient temperatures. Continuous, or at least q5–10min, temperature monitoring is required where a rapid increase in temperature may occur. Cool to 39.5°C, 102.5°F (*Refer to Hyperthermia p. 297 for management*).

E. **Pain is considered the fifth vital sign.** Medical as well as surgical and traumatic problems cause pain. Pain assessment must be included in the monitoring orders (*see Pain Assessment & Management p. 117*).

II. CARDIOVASCULAR MONITORING TECHNIQUES

A. **Central venous pressure** (CVP) is a measure of the hydrostatic pressure within the intrathoracic vena cavae with a normal range $1 - 5$ cm H_2O. The CVP is slightly higher than the right atrial pressure (RAP), and RAP is quantitatively similar to right ventricular pressure at end diastole or preload. However, CVP does not reliably predict right ventricular end-diastolic volume. Accurate placement of the catheter and consistency in positioning of the animal is extremely important in interpretation of results and determination of trends. Central venous pressure measurements may be obtained from the caudal vena cava in cats. Keeping in mind potential pitfalls discussed below, measurement of the CVP during a fluid challenge, such as would be administered in hypovolemia or acute renal failure, can be valuable in assessing the effect of therapy. In the hypovolemic patient, for example, if no appreciable increase in CVP is observed after a fluid bolus, additional fluid or colloid should be administered. *Refer to Fluid Therapy p. 347* for technique and interpretation of findings. The CVP does not reliably predict whether administration of a fluid bolus will or will not significantly increase cardiac output under all conditions. Factors other than intravascular volume that influence CVP measurements include cardiac function (e.g., systolic or diastolic dysfunction), pulmonary hypertension (e.g., pulmonary thromboembolic disease), venous compliance (e.g., increased systemic vascular resistance), and intrathoracic pressure (e.g., pleural effusion, pneumothorax, pericardial effusion, mechanical ventilation). Although mechanical ventilation affects CVP, threshold values of CVP in ventilated patients still may be of value to predict hemodynamic instability when assessed in response to increasing airway pressure induced by positive end-expiratory pressure (PEEP). Human patients with CVP <10 mmHg usually had decreased cardiac output when challenged with increasing PEEP whereas those with CVP >10 mmHg had increased, decreased or unchanged cardiac output.

B. **Arterial blood pressure.** Although systemic blood pressure is not an absolute measure of volume, it is of value to measure during periods of bolus fluid administration when managing shock. When extensive monitoring is required, direct arterial pressure measurements should be obtained. However, on presentation, it may not be possible to successfully perform arterial catheterization and pressures may be obtained with oscillometric or Doppler monitors. When the limbs are poorly perfused or the patient is cold, the oscillometric and Doppler methods are insensitive, and accurate measurements are difficult to obtain, especially in small animals. In the author's experience, the coccygeal artery, with the cuff postioned as far proximal as possible, tends to be more reliable in this instance (disinfect the cuff after). The mean arterial pressure (MAP) is dependent on cardiac output (CO) and systemic vascular resistance (SVR)(MAP $=$ CO $\times$ SVR). Therefore, adequate MAP does not necessarily indicate adequate CO if SVR is increased as may occur in a compenstory sympathetic response. During acute blood loss, especially in otherwise healthy animals, the compensatory response can be quite dramatic and result in nearly normal MAP. If resuscitation is based on normal MAP or SBP alone, inadequate resuscitation with continued poor perfusion likely will occur until the patient decompensates. If however normal MAP or SBP is accompanied by a physical examination that indicates the presence of a sympathetic response, the clinician will be aware of the requirement for additional resuscitation or analgesics. In this setting, it is difficult to know how much blood has been lost and the contribution of pain and anxiety. Pain, anxiety and hypothermia also contribute to the sympathetic response, and the findings observed may be more a result of these factors than of fluid and blood loss. In this setting, intravascular volume loss may be over-estimated resulting in excessive fluid administration. Fluid requirements and monitoring progress should therefore be assessed based on several factors in addition to pressure measurements. These considerations include a relatively pain-free patient and an improvement in physical findings (*see Fluid Therapy p. 347*).

C. **Cardiac output measurements.** Several techniques are available to measure CO but most are technically challenging. Recently lithium dilution cardiac output (LiDCO, London, UK) and PulseCO™ have been investigated for use in humans[3] as well as in large[11] and small animals. Briefly, isotonic lithium chloride is injected as a bolus via a central or peripheral vein and a concentration-time curve generated by an arterial ion-selective electrode attached to an arterial manometer system. The CO is calculated from the lithium dose and the area under the concentration time curve before recirculation. The PulseCO™ Hemodynamic Monitor was developed to be used in conjunction with the LiDCO™ to give a beat-by-beat estimate of CO which is derived from analysis of the arterial trace. Although these systems have limitations, their use in veterinary research indicates potential value in clinical practice in anesthetized animals or non-moving critically ill animals. Movement, flexion and extension of the catheterized limb contributes to erroneous results (personal observations). A great advantage of this system is that a central catheter is not required and continuous CO can be measured. Measuring CO during fluid resuscitation has definite advantages over determination of SABP because the former is a more accurate measure of volume. Pre-determined goals for CO, stroke volume and oxygen delivery can be set and monitored with this system.

III. OXYGENATION AND VENTILATION MEASUREMENT TECHNIQUES

(*see Assessment of Oxygenation and Ventilation in Respiratory Emergencies p. 580*)

A. Pulse oximetry

Pulse oximetry is a non-invasive method of measuring the percentage of oxygen bound to hemoglobin (hemoglobin saturation) in arterial blood ($SpaO_2$) and can be performed in any animal.

B. Arterial blood gases

Measurements of arterial blood gases is the gold standard for assessing oxygenation and ventilation.

C. Venous blood gases

The measurement of base deficit (negative base excess), which is calculated from the directly measured pH and $PvCO_2$ included in all blood gas measurements, provides the clinician with a nonspecific marker of lactate production and therefore, anaerobic metabolism and oxygen debt. A $PvCO_2$ measurement can be used for assessing ventilation with normal range of $PvCO_2$ being ~ 5 mmHg higher than $PaCO_2$ values. While PvO_2 measurements are not valid in assessing oxygenation, jugular venous PvO_2 may be used to assess adequacy of oxygen delivery and oxygen extraction.

D. Blood lactate levels

Blood lactate levels also reflect oxygen utilization and aerobic metabolism. Where perfusion is inadequate anaerobic metabolism occurs resulting in increased lactate production and metabolic acidosis. (*see Lactate p. 406*).

E. End Tidal Capnography

For intubated patients, continuous capnographic display of end tidal CO_2 ($ETCO_2$), is very useful in monitoring mechanically ventilated patients. *Refer to Assessment & Measurement of Oxygenation & Ventilation p. 580.*

IV. FLUIDS: ADMINISTRATION AND LOSSES

The administration of any fluid has to be monitored closely.

A. CVP monitoring (*p. 15*) is advised if cardiac, pulmonary or renal disease is present.

B. Signs associated with overhydration/hypervolemia (*p. 358*), can be used to guide fluid therapy.

C. Urine volume and renal parameters must be included in ongoing management of the critically ill patient to assess efficacy of therapy, to prevent, identify, and treat, any abnormalities should they arise (*see Acute Renal Failure p. 709*).

1. measure creatinine, urea or BUN daily initially.
2. urine volume measurement every 1 – 4 (8) hours plus urine specific gravity. Measure urine via
   a. free catch
   b. urinary catheter
   c. weighing a diaper initially and weighing after voiding, the difference = urine volume 1 g =1 mL
3. urine sediment (every 48 hours if acute tubular injury may occur with drug therapy).
4. Refer to Acute Renal Failure for detailed management of 'Ins and Outs'.

D. Vomitus volume should be assessed or measured. If possible place a diaper under the patient and weigh as IV.C. 1c above.

E. Serum electrolytes measurement, specifically potassium or sodium (every 4 – 24 hours with hypo- or hyperkalemia, or hypo- or hypernatremia) is recommended.

F. Weight should be obtained every 8 – 24 hours to assess fluid loss/gain. Assume a weight loss of 0.1 – 0.3 kg BW/1000 kcal energy requirement per day in an anorexic animal. Assess third space losses as weight loss will not be evident here. After urine flow has been established, regardless of the underlying problem, ongoing fluid requirements are based on sensible and insensible losses (*see Fluid Therapy p. 347 and Acute Renal Failure p. 709*).

V. HEMATOLOGY AND TOTAL SOLIDS

A. **Packed cell volume (PCV) and total solids (TS)** are easily performed at the cage-side and allows the clinician to monitor dilution due to fluid therapy, or losses due to visible or occult blood loss. (*see Hemorrhage p. 619 and Fluid Therapy p. 347*).

B. **Activated clotting time (ACT)** is a very useful cage-side test of the coagulation status of the patient and DIC (*see Disseminated Intravascular Coagulation p. 417*). In addition to coagulation status, this author finds the prolonged ACT a valuable test to identify a potential inflammatory focus, and to monitor patient's improvement (reduced time) or deterioration (prolonged time). When using grey top tubes containing diatomaceous earth, the normal ACT at the Ontario Veterinary College obtained via axilla or heating block is 70 – 120 sec in dogs and 60 – 90 sec in cats.

C. Platelet count in combination with the ACT is a useful cage-side method of monitoring DIC, progression or deterioration of illness.

D. Complete blood count is often required in the acutely ill patient. *See Neutropenia p. 435, Thrombocytopenia p. 451, Sepsis/Septic Shock p. 588, Hemorrhage p. 619 and Disseminated Intravascular Coagulation p. 417 for details.*

VI. ACID-BASE ASSESSMENT

Assessment of acid-base status is extremely important in guiding therapy in the critically ill patient. A reflection of perfusion status, and a guide for fluid selection and electrolyte therapy (*see Acid-Base Assessment p. 406*).

VII. GASTROINTESTINAL SYSTEM

A. Potential immediate post-operative (any) problems are vomiting with possible aspiration, and gastric dilation with possible volvulus.

B. Constipation following pelvic injury or prolonged recumbency may occur. Add a stool softner to diet (*see Constipation/Obstipation p. 51*).

C. Diarrhea may be a primary problem or occur whilst in hospital. Caution is required when dealing with patients with diarrhea as this may be infectious (*see Acute Diarrhea p. 32, Nosocomial Infection p. 600*).

D. Ileus may be associated with opioid administration, illness and surgical procedures.

E. Other problems would be associated with the patient's primary problem or surgical procedure. Specific orders should be given for these cases.

F. Gastrointestinal hemorrhage may occur following hypovolemia, corticosteroid therapy, non-steroidal anti-inflammatory analgesics and 'stress' of various medical, surgical and traumatic conditions (*see Gastrointestinal Hemorrhage p. 67*).

SUGGESTED READINGS

See the various chapters referred to.

NOTES

HOSPITAL NAME

Date _____

Clinician _____

Phone _____ Pager _____

Student _____ Phone _____

Problem List
(updates daily)

1.
2.
3.

cath J C S date _____
R or L

4.
5.
6.

	FREQ.	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6
WEIGHT (DAILY)																									
ATTITUDE																									
T ≤																									
P ≤																									
R ≤																									
mm/CRT																									
PCV																									
TS																									
CVP or PULSE OX																									
ARTERIAL S/D																									
MAP																									

FLUIDS		FREQ.	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6
TYPE _____	ml																									
	cum																									
TYPE _____	ml																									
	cum																									
BLOOD/PLASMA/PRBC's	ml																									
	cum																									
URINE OUTPUT	ml																									
	cum																									
BM/V																										

18

FOOD	FREQ.	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6
WATER																									

MEDICATION AND MISCELLANEOUS	FREQ.	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6

CLINICAL PATHOLOGY	TIME	LAB	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6
		GLUCOSE																								
CBC ☐		Na																								
PROFILE ☐		K																								
PT/PTT ☐		CL																								
		PH																								
ACT-ISTIM	PRE ☐	$PaCO_2$																								
	POST ☐	Pa_2																								
		HCO_3																								
	☐	ABE																								
	☐	SAT.%																								
	☐	EKG																								
	☐																									

OBSERVATIONS: INDICATE TIME (24 HR. CLOCK) OF OBSERVATION AND SIGN EACH OBSERVATION.

SPECIAL ORDER: NUMBER EACH ORDER. REFER TO SPECIAL ORDERS ON FRONT PAGE BY CIRCLED NUMBER.

20

INTRODUCTION

A syndrome characterized by sudden onset of acute abdominal pain with possible vomiting, diarrhea, fever, dyspnea, anorexia, depression, shock, coma and death. Prompt diagnosis is essential to avoid irreversible progression, to identify neccesary surgery quickly, but to avoid unnecessary surgery. However, if in doubt as to whether surgical intervention may be beneficial, it is prudent to err on the side of surgical exploration rather than wait and the patient succumb to a surgical disease. If gastric dilation/volvulus is suspected refer to *Gastric Dilation-Volvulus p. 59.*

Abdominal Pain Mechanisms: Hollow organs react painfully to tension (e.g., distension, dilation, volvulus), forceful contractions (hypersegmentation) or traction (adhesions). Pain in solid organs (e.g., liver, spleen, kidney) is generated by capsular stretch. Capsular stretch also occurs in the inflammed pancrease and is very painful. Damage to adventitia of blood vessels also induces pain. Abdominal nerve endings are stimulated by proteinases and vasoactive substances released by inflammation, and/or ischemia within the abdomen.

Specific Abdominal Pains: Bowel obstruction causes pain by distension, which leads to reflux fluid secretion, further distension, hypersegmentation and increased pain. Pyloric stenosis pain occurs with contraction against a closed sphincter. Intussusception may be painful acutely but non-painful in the chronic case. Disease processes (e.g., salmonella, parvovirus, heavy metal poisonings, gastrointestinal ulceration), with acute invasion or denuding of bowel mucosa, causes severe abdominal pain. Loss of blood supply to small areas of infarcted bowel is often non-painful but severe vascular occlusion (volvulus or torsion) is painful. Septic, chemical or bile peritonitis causes severe pain.

Until proven otherwise, assume that acute abdominal pain is a disorder that can be corrected **surgically.**

DIAGNOSIS

History/Signalment

The patient with an 'acute abdomen' is frequently presented with obvious signs of deterioration; however, on occasion this may not seem obvious. Therefore, a thorough history as to recent history and duration of illness is essential. **See Patient Evaluation Figure 1.** Examine the patient while obtaining the history.

Clinical Signs/Physical Examination

- Follow the principles of Triage (*p. 4*).
- Evaluate for shock (*p. 603*).
  - Hypovolemic shock: pale mucous membranes, prolonged capillary refill time, cold appendages, weak, depressed, rapid heart rate, weak and thready peripheral pulses.
  - Early septic shock: flushed, hyperemic mucous membranes, brick red or muddy in colour. **Administer oxygen and fluid therapy (A & B below) and continue with examination.**
  - Addisonian crisis may present in a similar manner, including abdominal pain (*p. 274*).

Abdominal Examination

- Observe shape, altered contours, distension or obvious masses, skin discolouration (bruising or abdominal hemorrhage), lacerations or punctures. Clip hair if necessary.
- Palpate thoroughly using gentle persistent digital pressure. Locate all normal structures, before searching for abnormality. Elevate front limbs for anterior abdominal examination. Note organ displacement, enlargement, masses, fluid distension of bowel, presence of pain and location.
- Alteration in abdominal contour occurs with hollow organ dilation, hemoperitoneum, hydroperitoneum (ascites), pneumoperitoneum or enlargement of an abdominal organ (e.g., splenomegaly, gastric dilation/volvulus).
- Evaluate for retroperitoneal enlargement indicative of the presence of blood or urine (*see p. 69*).
  - If unable to palpate urinary bladder or if it is distended, catheterize and note if obstructed (*p. 745*), presence of blood, or leakage (*see Urine Leakage p. 727*).

FIGURE 1. Patient History and Potential Etiologies

```
┌─────────────────────────────────────┐
│ Question the owner during examination │
└─────────────────────────────────────┘
                │
                ▼
┌─────────────────────────┐         ──→ peracute
│ Duration of Abdominal Pain? │ ═════──→ acute
└─────────────────────────┘         ──→ chronic
                │                    ──→ recurrent
                ▼
```

┌─────────────────────────────┐   ┌──────────────────────────────┐
│ History of Abdominal Surgery? │ ──────→ <2 weeks ──────→ │ Possibilties are internal   │
└─────────────────────────────┘   │ iatrogenic trauma (including │
                │   │ biliary tree), leakage from   │
                │   │ hollow viscus, abdominal   │
                │   │ contamination, foreign material│
                │   │ in abdominal cavity (surgical │
                │   │ sponge) or devascularisation of│
                │   │ vital structure.   │
                │   └──────────────────────────────┘

                                       ──────→ >2 weeks ──────→ ┌──────────────────────────────┐
                                                                │ Consider adhesion or stricture│
                                                                │ formation.   │
                                                                │ Similar conditions may be   │
                                                                │ found after abdominal injury │
                                                                │ secondary to trauma.   │
                                                                │ Foreign body from surgery.   │
                                                                └──────────────────────────────┘

┌─────────────────────────────────┐   ┌───┐
│ Prior medical or surgical conditions? │ ──────────→ │ e.g., Pancreatitis, cholelithiasis, urinary calculi, neoplasia │
└─────────────────────────────────┘   └───┘

                                  ──→ ┌──────────┐   ┌────────────────────────┐   ┌──────────────────┐
                                      │ Castrated │ ──→ │ 2 testicles within scrotum │ ──→ │ Testicular torsion │
┌────────────────────┐   └──────────┘   │ prior to castration   │   └──────────────────┘
│ No testicles present? │ ──   └────────────────────────┘
└────────────────────┘   ──→ ┌────────────┐
                             │ Cryptorchid │
                             └────────────┘

┌───┐   ┌─────┐
│ Is animal lethargic, still eating or drinking, has it diarrhea (how often, how much, appearance), │ ──→ │ R/O │
│ is it retching or vomiting (how often, how much), is there excessive swallowing or drooling?   │   └─────┘
└───┘

┌───┐   ┌─────┐
│ How painful? Does animal assume praying position (position of relief)? This is often seen with │ ──→ │ R/O │
│ abdominal pain.   │   └─────┘
└───┘

┌───┐   ┌─────┐
│ Are there factors which aggravate or alleviate the pain such as eating, drinking, vomiting,   │ ──→ │ R/O │
│ defecating, medication, time of day, exercise or posture? Many dogs and cats show no obvious   │   └─────┘
│ signs of abdominal pain.   │
└───┘

┌───┐   ┌─────┐
│ Has there been exposure to drugs (steroids, NSAIDS), chemicals (e.g., antifreeze), heavy metals │ ──→ │ R/O │
│ (e.g., lead), excessive eating or ingestion of inappropriate foods (fats, garbage, bones), trauma│   └─────┘
│ (fall, dog fight, hit by motor vehicle), penetrating wounds (gun shot, sharp implement, stick) or│
│ contact with infectious animals?   │
└───┘

- Note if abdominal pain is present. Animal cries out, tries to escape or bite, tenses abdominal muscles or shifts side to side. With severe depression or generalized peritonitis, pain may not be evident.
  CAUTION: Animals with pleuritis or pneumonia may exhibit pain upon palpation of the abdomen. Where no abnormalities are detected on abdominal examination, radiograph the chest to rule out a pleural space lesion or pneumonia.
- Location of pain can be diagnostic.
  - Upper right quadrant: pancreatitis or a duodenal or pyloric disorder.
  - Cranial abdomen: acute liver disease, cholecystitis, gastric or duodenal ulcer perforation.
  - Caudal abdomen: prostatic disease, pyometra, uterine torsion, cryptorchid testicular torsion (scrotal torsion can present as acute abdominal pain also) or urethral obstruction.
  - Localized pain is suggestive of a localized peritonitis, whereas a diffuse pain response could indicate that a significant portion of small and/or large bowel is involved.
- At least 5+ minutes of auscultation is required to determine presence/absence of bowel sounds, however, these paramaters are not always reliable.
  - **Increased bowel sounds (hypermotility):** acute enteritis, bowel obstruction, fluid accumulation and reaction to toxins or toxic compounds.
  - **Decreased gut sounds (hypomotility):** chronic distension, peritonitis, chronic enteritis with increased intestinal fluid.
- Percussion may elicit a fluid wave or tympany if there is dilatation of a hollow organ.
- Rectal examination combined with abdominal palpation. Note enlargement, asymmetry or pain in prostate gland. Check for rectal tear with pelvic fractures and note presence of melena or frank blood.
- Clinical signs that correlate with involved organ or system.
  - Vomiting can indicate gastric problems, upper intestinal disease, cholecystitis or pancreatitis.
  - Projectile vomiting is suggestive of pyloric or intestinal obstruction.
  - Hematemesis occurs with gastrointestinal ulcers, neoplasia, severe gastroenteritis and coagulopathy.
- Constipation or loose/semisolid/mucoid diarrhea with normal to increased volume and increased frequency/+ tenesmus, is suggestive of lower bowel; when combined with vomiting indicates extensive gastrointestinal involvement.
- Hematuria, anuria or polyuria indicates a primary or secondary urinary system problem.
- Altered gait may indicate abdominal adhesions, prostatic disease, muscular problems, skeletal injury, spinal injuries, or rarely intracranial disease or multiple myeloma. Note if pain present on palpation of spine or pelvis.
- Altered posture can occur with spinal injury, muscle or rib injury, or to afford pain relief ("praying position" in gastric or duodenal pain).
- If the animal is pregnant, in estrus or has had a recent heat period, examine the reproductive system closely.
- Monitor vital signs frequently during examination and response to emergency therapy.

Laboratory Evaluation/Diagnostic Imaging

'The Diagnostic/Treatment Dilemma'

Diagnostic and treatment plans are dictated by acuteness and severity of patient's condition. Recurrent abdominal pain requires deliberate diagnostic plans, while a life-threatening condition requires prompt supportive action based on a tentative diagnosis and exploratory surgery. **If diagnostic results are equivocal – favour a surgical approach.**

Initially, attempt to classify the acute abdomen into one of four broad categories:

1. Inflammatory
2. Hemorrhagic } Neoplasia may be included in all 3
3. Obstructive
4. Traumatic

Other than hemorrhage, it usually takes from 3 – 6 hours minimum to identify peritoneal contamination after injury.

EMERGENCY MINIMUM DATA BASE

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV** may be increased relative to the **TS** if there is capillary leak or third-spacing of fluid; TS will be low in these settings, occasionally very low 20 g/L (2.0 g/dL) especially in the later stages of sepsis in both cats and dogs. PCV may be low if anemia is due to infection (especially in cats), or if hemorrhage is present.
- **Stick BUN, urea or creatinine** as an estimate of renal function or presence of pre-renal azotemia.
- Glucose may be normal or low. Cats tend to exhibit a transient hyperglycemia when stressed but hypoglycemia frequently occurs if septic.
- **ACT** using grey top (silica) tube is usually increased in DIC, and sepsis from our observations (normal 70 – 120 sec in dogs, 60 – 90 sec in cats using deep axilla (under the 'white coat' or heating block). The ACT is very useful for trending during therapy. ACT may be used instead of PT/PTT.
- **PT/PTT** in addition to ACT, or instead of but for the same reasons. Normal values are generated for each laboratory.
- **Urine** as a baseline for urinalysis and concentrating ability, or collected by cystocentesis for culture and sensitivity if suspect sepsis involving the urinary tract.
- **Serum electrolytes** may be altered in hypovolemic and abnormal metabolic states. Assessment of acid-base status also requires this information (*p. 406*). Correction of abnormalities is necessary. Hypokalemia is not uncommon in sepsis and may be associated with cardiac arrhythmias. Decreased ionized calcium has been documented in septic cats. *See chapters on the specific electrolyte abnormality p. 347.*
- **Venous blood gases (or total CO$_2$)** is necessary for assessment of the metabolic status of the patient (*see Acid-Base Assessment p. 406*). Sepsis and hypovolemia frequently results in a significant base deficit, the value of which may reflect the perfusion deficit. Trending of these values is important in management.
- **Systemic blood pressure** may be normal in compensated shock, or low (SBP <90 mmHg) in septic shock. SBP is important to document as it will identify the severity of the patient's condition and direct therapy. Trending is essential during therapy.
- **ECG** findings may be normal or identify an abnormality such as ventricular (*p. 179*) or supraventricular (*p. 170*) tachycardia.
- **Biochemical profile** is necessry to assess the patient's general condition and identify organs affected i.e., abnormalities in amylase and lipase in pancreatitis; bilirubin, ALT or ALP with primary or secondary liver involvement. As any, or a combination of organs may be affected, refer to appropriate chapters when abnormalities are identified.
- **CBC** to identify SIRS or sepsis, DIC, anemia.
- **Lactate** is extremely useful in assessing perfusion status and for trending. Normal is <2.5 mmol/L in dogs and <1.5 mmol/L in cats. (*see Acid-Base Assessment p. 406*).
- **Diagnostic imaging** is essential to diagnose the primary problem in most animals with an acute abdomen. Radiograph under sedation if necessary, right and left lateral and ventrodorsal abdomen. For evaluation of air/fluid level in bowel or free air in abdomen take a standing lateral. Use contrast materials to outline gastrointestinal or urinary tract as warranted. **Interpretation see Fig. 2** *p. 26*.
- **Abdominal ultrasonographic** examination to evaluate subtle changes in organ size, metastatic disease, vascular occlusion, pancreatitis, and identify abnormalities of the liver and biliary tree, spleen, reproductive tract, urinary system, gastrointestinal tract and associated lymph nodes.
- **Abdominocentesis** (after diagnostic imaging to avoid introduction of air into the abdomen) using a two quadrant centesis or a four quadrant centesis for biochemical and cytological analysis. ***See Appendix 1 below p. 28 for interpretation.*** **Gram stain and cytology of effusions** will assist with diagnosis and selection of antibiotics (Table 1).

Extended Laboratory and Imaging Data Base

Although the following may be considered in an extended data base, they are frequently necessary for diagnosis and therefore should be performed where indicated.

- **Contrast radiography** (barium series) *p. 27* is indicated where an obstruction is suspected but cannot be visualized on survey radiographs. *Refer to Table 1 for gastrointestinal emptying times.*
- Submit **samples** of aspirates from **abdominal effusion** and submit for Gram stain, culture and antibiotic sensitivity and cytology. *See Table 2 for interpretation p. 30.*
- **Blood culture and sensitivity.** Blood should be collected from two separate veins consecutively, after surgical preparation of the skin. It is not necessary to wait an hour as previously recommended.
- **Diagnostic Peritoneal Lavage** (*DPL – see Appendix 2 below p. 29 for technique*) is indicated when a surgical approach is equivocal, palpable, radiographic or ultrasonographic evidence of abdominal fluid of questionable etiology, loss of abdominal detail on radiography, history of blunt abdominal trauma with negative abdominocentesis (*see Table 2 for Evaluation of Peritoneal Lavage Fluid p. 30*).

Contraindications for DPL

- pregnancy
- organomegaly
- previous abdominal surgery and high suspicion of adhesions
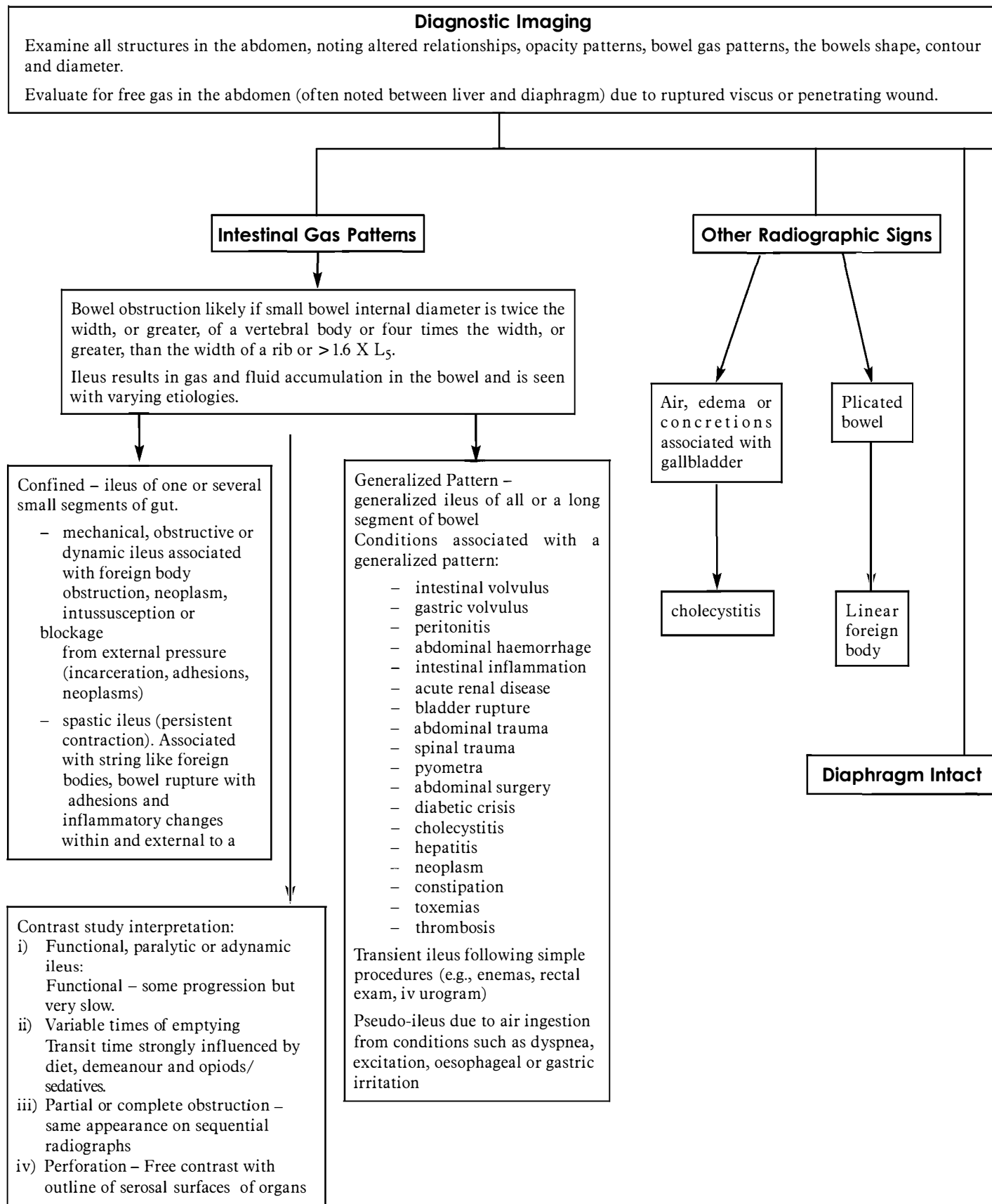
TREATMENT

Use Supportive treatment until a definitive diagnosis is made and correction of the underlying cause performed. Order and intensity of therapy is dependent upon the physical and metabolic status of the animal. (*see appropriate chapters: Septic Shock p. 588, Pancreatitis p. 45, Acute Diarrhea p. 32, Urinay Leakage p. 727* and *Gastric Dilation-Volvulus p. 59*).
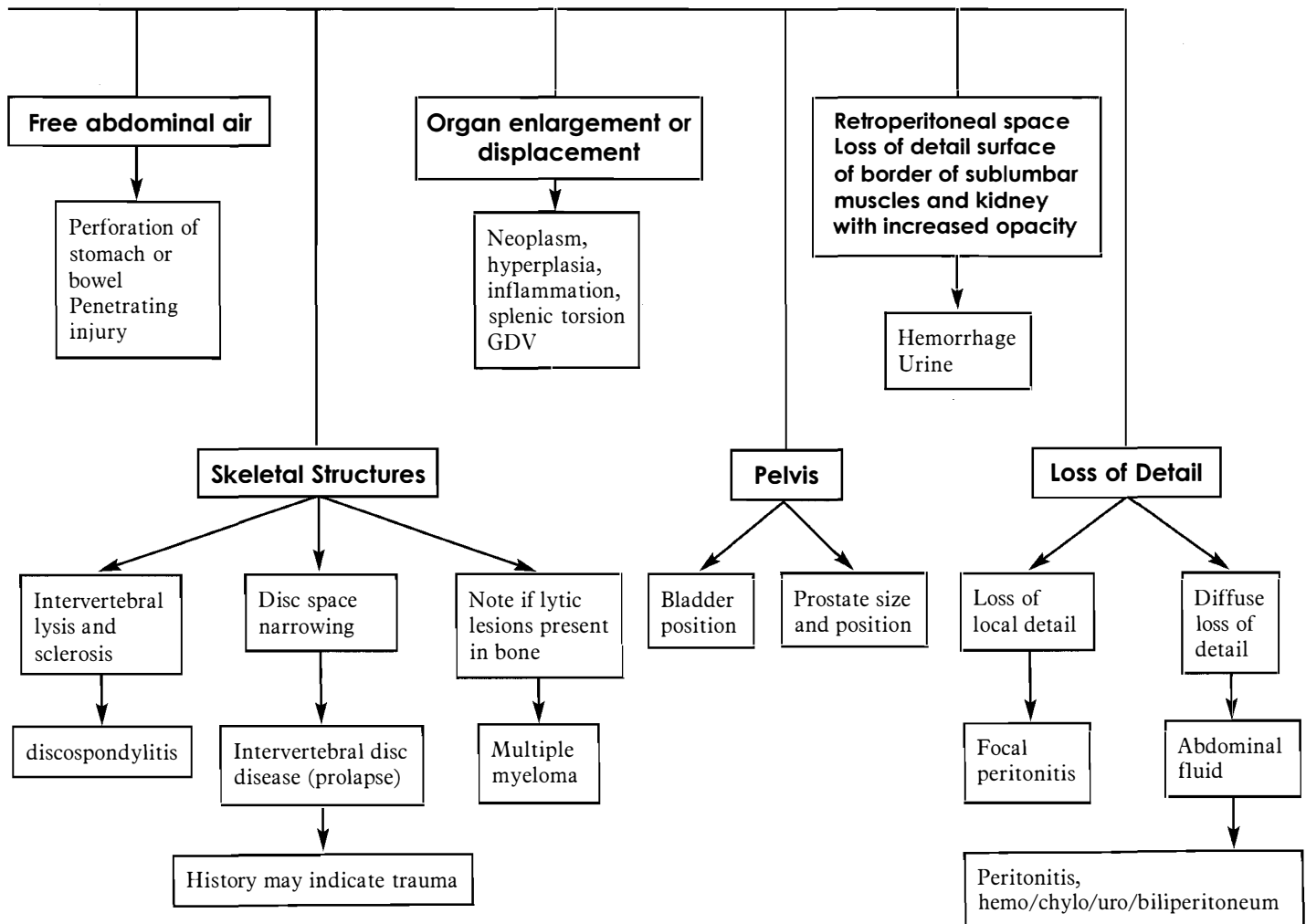
A. **Oxygen supplementation** if warranted (face mask, hood, nasal oxygen or intubation and ventilation in extreme cases).

B. **Establish IV** access and commence a balanced, isotonic crystalloid solution (Plasma-Lyte® 148 or Normasol® R or lactated Ringer's). Volume expand the patient. As many patients are in shock, or septic (*see Shock p. 603 and Septic Shock p. 588 for complete supportive therapy*).

C. **Broad Spectrum Antibiotics,** must be effective against both gram positive and gram negative bacteria as well as anaerobic bacteria. Use a combination of antibiotics (*see Septic Shock p. 588*).

D. Cases of uroperitoneum (*p. 727*) and bile peritonitis may benefit from 24 hours of aggressive fluid therapy and abdominal lavage (*see Appendix 2 below p. 29*).

E. **Exploratory Surgery** is diagnostic and allows treatment. Failure to determine cause for acute abdomen at laparotomy is still a useful result. If no abnormality is found, rule out intracranial diesease i.e., meningoencephalitis, neoplasia, and the potential for intra-thoracic pathology.

INDICATIONS FOR EXPLORATORY LAPAROTOMY

- Penetrating abdominal wound (*see Wounds and Open Fractures p. 702*)
- Gastric dilation-volvulus (*see Gastric Dilation-Volvulus p. 59*)
- Abdominal mass and the presence of vomiting
- Signs of small bowel obstruction
    - See Radiographic Interpretation Fig. 2 p. 26
- Gas pattern suggesting mesenteric torsion
- Gallbladder distension with concretions, edema or gas
- Gross hollow organ distension
- Free air in the abdomen
- Traumatic hemoperitoneum nonresponsive to medical management (*see Hemorrhage p. 619*)
    - Hemopoperiteoneum secondary to liver, splenic, renal or gastrointestinal neoplasia
- Continuing peritoneal irritation despite medical therapy
- Ongoing melena, hematemesis, hematochezia or melena non-responsive to medical management
- Abdominal hernia
- Bacteria (especially intracellular) on abdominocentesis or peritoneal lavage
- > 2000 wbc/uL on peritoneal lavage
- > 500 wbc/uL if toxic neutrophils on peritoneal lavage
- Vegetable fibres on abdominocentesis or lavage
- Abdominal effusion (*see Diagnostic Abdominocentesis Appendix 1 below p. 28*)
- Bilirubin on abdominocentesis or in lavage fluid
    - Uroabdomen
    - Septic peritonitis
- Any case which is equivocal (exploratory laparotomy is a diagnostic tool)

F. **Postoperative** – continue to monitor and respond to changing status. The patient may require nasogastic intubation for stomach decompression and fluid removal, use of gut protectants and the maintenance of urinary and feeding tubes (e.g., esophageal, gastrostomy, jejunostomy – *see Nutrition p. 499*). DIC is a potential problem (*p. 417*). Constant monitoring is required (*see Monitoring p. 12*)

G. **Specific therapy** is dependent on the specific disease process diagnosed/corrected at surgery, or determined during case workup.

FIGURE 2. Etiology of Acute Abdomen

Diagnostic Imaging

Examine all structures in the abdomen, noting altered relationships, opacity patterns, bowel gas patterns, the bowels shape, contour and diameter.

Evaluate for free gas in the abdomen (often noted between liver and diaphragm) due to ruptured viscus or penetrating wound.

Intestinal Gas Patterns

Bowel obstruction likely if small bowel internal diameter is twice the width, or greater, of a vertebral body or four times the width, or greater, than the width of a rib or $>1.6 \times L_5$.

Ileus results in gas and fluid accumulation in the bowel and is seen with varying etiologies.

Confined – ileus of one or several small segments of gut.

- mechanical, obstructive or dynamic ileus associated with foreign body obstruction, neoplasm, intussusception or blockage
  from external pressure (incarceration, adhesions, neoplasms)
- spastic ileus (persistent contraction). Associated with string like foreign bodies, bowel rupture with adhesions and inflammatory changes within and external to a

Contrast study interpretation:
i)   Functional, paralytic or adynamic ileus:
     Functional – some progression but very slow.
ii) Variable times of emptying
     Transit time strongly influenced by diet, demeanour and opiods/ sedatives.
iii) Partial or complete obstruction – same appearance on sequential radiographs
iv) Perforation – Free contrast with outline of serosal surfaces of organs

Generalized Pattern – generalized ileus of all or a long segment of bowel
Conditions associated with a generalized pattern:

- intestinal volvulus
- gastric volvulus
- peritonitis
- abdominal haemorrhage
- intestinal inflammation
- acute renal disease
- bladder rupture
- abdominal trauma
- spinal trauma
- pyometra
- abdominal surgery
- diabetic crisis
- cholecystitis
- hepatitis
- neoplasm
- constipation
- toxemias
- thrombosis

Transient ileus following simple procedures (e.g., enemas, rectal exam, iv urogram)

Pseudo-ileus due to air ingestion from conditions such as dyspnea, excitation, oesophageal or gastric irritation

Other Radiographic Signs

Air, edema or concretions associated with gallbladder

cholecystitis

Plicated bowel

Linear foreign body

Diaphragm Intact

```
Free abdominal air          Organ enlargement or        Retroperitoneal space
                            displacement                Loss of detail surface
                                                        of border of sublumbar
                                                        muscles and kidney
                                                        with increased opacity

Perforation of              Neoplasm,
stomach or                  hyperplasia,
bowel                       inflammation,
Penetrating                 splenic torsion                    Hemorrhage
injury                      GDV                                Urine
```

Skeletal Structures

- Intervertebral lysis and sclerosis → discospondylitis
- Disc space narrowing → Intervertebral disc disease (prolapse) → History may indicate trauma
- Note if lytic lesions present in bone → Multiple myeloma

Pelvis

- Bladder position
- Prostate size and position

Loss of Detail

- Loss of local detail → Focal peritonitis
- Diffuse loss of detail → Abdominal fluid → Peritonitis, hemo/chylo/uro/biliperitoneum

Contrast Radiography

- Barium sulphate is the media of choice however, controversy exists as to whether barium is contraindicated where gastric or intestinal perforation is suspected or surgery is contemplated. Should you be adverse to using barium sulphate in these circumstances, then iodine based contrast media (ionic media Hypaque®, Gastrografin®) is suggested. However quality of study is reduced. The ionic media is absorbed systemically and visualized in the urinary system.
- Dosage (barium 60% w/w)
  - Small dog and cat 10 – 12 mL/kg body weight
  - Large dog 5 – 10 mL/kg body weight
- Iodine (diluted 1:3) dog and cat 10 mL/kg

Do not use less than this as there will be an inadequate bowel filling and a non-diagnostic study.
NOTE: The ionic media (i.e., Hypaque®, Gastrografin®) cause severe pulmonary edema even when a small amount is aspirated. Barium can be tolerated if aspirated unless large amounts obstruct the airways.
Analgesia and sedation may affect emptying times.
Radiographic time intervals – 0 (pre-), 1 min, 15 min, 30 minutes, 1, 3 (6 and 24 hours if necessary).
See Table 2 for normal emptying times *p. 28.*

TABLE 1. Normal Emptying Times using Barium or Iodine-based Contrast Agents, or Food

		DOG	**CAT**
Gastric emptying begins	Barium	15 – 30 min	Immediate
	Iodine	0 – 15 min	Immediate
Gastric emptying time	Barium	1 – 4 h often <2 h	15 – 60 min
	Iodine	30 – 120 min	10 – 30 min
Small intestinal transit time (initial intestinal emptying time)	Barium	73 min 1 – 3 h	30 – 90 min
	Iodine	60 – 90 min	10 – 20 min
Gastric emptying with kibble	Intact	Solid phase emptying should occur within 1 h Duration 7 – 15 h	
	Ground	Solid and liquid phase occur together so onset is almost immediate Duration 7 – 15 h	11 hours

TECHNIQUES

DIAGNOSTIC ABDOMINOCENTESIS (APPENDIX 1)

Indications
1. Aspiration of abdominal fluid for diagnostic purposes.

Materials
- 20 gauge hypodermic needle, 1 1/2" 18 gauge spinal needle or 18 gauge over-the-needle catheter.
- EDTA and serum tube for samples.

Technique
- It may be necessary to express a large urinary bladder.
- Best performed with animal standing but may not be possible.
- Aseptic preparation 1" – 2" caudal to, and right and left of, the umbilicus on the midline.
- Insert 20 gauge hypodermic needle immediately posterior to the umbilicus. Collect free flowing fluid into sterile red-top and EDTA tubes. If no fluid is obtained on free flow, gently aspirate with a syringe. In a large dog, if no fluid is collected try again with an 18 guage spinal needle or 18 gauge over-the-needle catheter. If negative perform,
- Aseptic preparation for a **two quandrant centesis** 1' – 2" caudal to the umbilicus each side of the rectus muscle, OR
- Aseptic preparation for a **four quandrant centesis** where the abdomen is divided into four quandrants and centesis is performed in the centre of each quandrant (cranial right and left, caudal right and left) after surgical preparation of these areas.
- Infiltrate each centesis area with 1/2 mL lidocaine prior centesis, even if the animal is depressed.
- 5 – 6 mL of fluid/kg body weight within the abdominal cavity is required to obtain fluid by centesis.

Interpretation
- positive results:
  - >0.5 mL of unclotted blood aspirated indicates hemoperitoneum.
  - >0.5 mL of opaque fluid aspirate (any fluid aspirated should undergo cytological examination and submit for urea/creatinine, bilirubin, amylase/lipase and comparisons made with serum. If fluid levels >serum then urinary, biliary or pancreatic disease respectively, should be suspected; however, occasionally some results are equivocal.

- Uroabdomen: Compare [effusion creatinine]:[serum creatinine]; effusion:serum creatinine ratio >2:1 indicates urine (85% dogs).
- Compare [effusion creatinine]:[serum potassium]; effusion:serum potassium >1.4:1 indicates urine (100% dogs).
- Septic peritonitis: Blood to fluid glucose difference >20 mg/dL (1.1 mmol/L) with lower glucose in the abdominal fluid.
- Septic peritonitis: Lactate concentration on abdominal effusions (prior to dextrose administration) >2.5 mmol/L is 100% sensitive and 91% specific for septic peritonitis in dogs; in cats, 67% specific. In one study all dogs with septic peritoneal effusions had effusion lactate concentrations >2.5 mmol/L; this may also indicate a pyogranulomatous pancreatitis in dogs. In cats, in addition to sepsis lactate concentrations >2.5 mmol/L may also be associated with intestinal neoplasia, pancreatitis. Rare cases of septic effusion in cats may have <2.5 mmol/L lactate concentration. A value of -1.5 mmol/L difference with subtraction of effusion lactate from venous lactate in dogs, had an accuracy of 90% for diagnosing septic peritonitis; in cats a difference of -0.5 mmol/L was 78% accurate.
- A positive centesis is repeatable.
- If **no fluid is aspirated** and there is a high level of suspicion of intra-abdominal pathology (i.e., perforated viscous) proceed to diagnostic peritoneal lavage or surgery.

PERITONEAL LAVAGE (APPENDIX 2)

Indications

1. **Diagnostic** when unable to obtain fluid on abdominocentesis where a high level of suspicion exists of intra-abdominal pathology.
2. **Therapeutic** when stabilization of the patient with bile or chemical (urine, pancreatic) peritonitis is necessary prior to exploratory laparotomy.

Materials

- 11F peritoneal dialysis catheter or 16-gauge over-the-needle catheter with extra holes (stagger the holes so as not to weaken the catheter)
- sterile, unopened bag of 0.9% sodium chloride
- EDTA and serum tubes
- Sterile collecting system (therapeutic lavage)

Technique

- place the animal in lateral or dorsal recumbency
- empty urinary bladder and prepare abdomen aseptically
- infiltrate local anesthetic into abdomen on midline 2 cm caudal to the umbilicus
- **Perform a "Minilap"**
  - Make a 1 cm skin and subcutaneous incision using meticulous hemostasis to avoid false positive results.
  - Grasp linea alba with forceps, carefully place two stay sutures 1cm apart, elevate the linea alba (or ask an assitant to elevate the linea alba with two forceps) and incise 0.5 cm length through the peritoneum.
  - Insert the dialysis catheter.
  - If the dog exceeds 25 kg the catheter with stylet may be 'forced' through the peritoneum without prior incision.
  - Remove the stylet and advance the catheter into dependent parts of abdominal cavity in a caudal direction (gutters of the posterior abdomen) where any fluid present will pool.
  - Gently aspirate with a syringe or apply gentle abdominal pressure and collect any returning fluid.
        2 mL blood/5 kg body wt = intra-abdominal injury/hemorrhage
  - If little or no fluid is obtained, warm 20 mL/kg body wt 0.9% sodium chloride to 37°C (96.8°F) and instil rapidly through the catheter while observing for increased respiratory rate or other signs of discomfort. Stop should this occur. (see Peritoneal Dialysis p. 723 for ongoing instructions).
  - Gently roll patient side to side, then lower infusion bag or bottle to the floor and allow gravity drainage of abdomen.
  - Gentle abdominal pressure and minor catheter adjustment will keep fluid flowing. If no fluid appears, place animal in sternal recumbancy or standing position.
  - Observe returning fluid and collect 20 mL sample for laboratory analysis.
  - If returning fluid pink or light reddish in colour or animal has been injured within the previous 3 hours; the catheter should be sutured in place and a sterile dressing applied.

TABLE 2. Evaluation of the DPL Fluid

PARAMETER/FINDING	INTERPRETATION
Gross examination – clear	no injury or generalized peritoneal disease
– opaque & bloody	intra-abdominal hemorrhage
– darker on repeat examination	continuing intra-abdominal hemorrhage
– turbid or cloudy	peritonitis (perform cytology)
– bluish tinge	bile leakage or upper GI tract leakage
Packed Cell Volume 2%	mild intra-abdominal haemorrhage
3 – 10%	moderate intra-abdominal hemorrhage
>10%	significant intra-abdominal hemorrhage
RBC Count >0.2 x 10^{12}/L	significant intra-abdominal hemorrhage
White Cell Count >1000 x 10^9/L	mild to moderate peritoneal irritation
>2000 x 10^9/L	marked peritoneal irritation, significant peritonitis
Amylase Activity > serum	pancreatitis, trauma to small pancreas or small bowel leakage
Alkaline Phosphatase > than serum	significant intestinal trauma, ischemia or leakage
Bilirubin sticks – positive	leakage from biliary system or proximal bowel (not accurate in icteric patient)
Creatinine > than serum. CAUTION: BUN sticks frequently give false positive results. Always confirm a positive BUN stick with creatinine measurments. Occasionally, creatinine concentration in abdominal fluid may be the same as serum and a leak still may be present. Contrast studies of the urinary system are advised in this situation (*see Urinary Leakage p. 727*).	significant urine leakage (uroabdomen)
Bacteria (intracellular)	bacterial peritonitis
Neutrophilia (toxic neutrophils)	suppurative peritonitis
Plant Fibres (vegetable matter)	gastrointestinal leakage
Neoplastic Cells	intra-abdominal neoplasm

– further samples are taken to assess ongoing haemorrhage, biliary, urinary or gastrointestinal leakage.
– where bile or urine peritonitis is diagnosed and the patient is not able to go to surgery due to unavailability of a surgeon or the critical condition of the patient, the catheter should remain in place for drainage and intermittent lavage (*see Peritoneal Dialysis p. 723 for ongoing instructions*).

Diagnostic Accuracy in DetectingAbdominal Injury in Small Animals

- needle centesis – 47.3%
- peritoneal catheter – 82.9%
- peritoneal catheter + lavage – 94.6%
- the use of a peritoneal dialysis catheter allows detection of abdominal fluid as low as 1 mL/kg body wt

Interpretation of the DPL Fluid (Table 2)

- if you **can read dark print** under the tubing containing returning fluid regardless of the fluids colour, there is a lack of serious abdominal injury.
- if you **cannot read the print** (opaque fluid) then serious hemorrhage, peritonitis or leakage of gastrointestinal contents has occurred.
- a false positive is due to faulty technique or overzealous interpretation of results.
- a false negative is usually associated with retroperitoneal injuries or failure to repeat sampling in very acute injuries.

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NOTES

INTRODUCTION

Acute diarrhea has many etiologies and can occur in cats and dogs of all ages. Infectious causes, toxicities, mechanical/functional obstruction, acute enteritis of unknown cause (e.g., hemorrhagic gastroenteritis), acute pancreatitis, hepatitis, renal disease and hypoadrenocorticism can all be potentially life threatening. Dietary indiscretion, parasites, maldigestive and malabsorptive intestinal disease, neoplasia and acute colitis tend not to be as serious. Clinical signs, physical examination, history and laboratory data should assist with the final diagnosis. This protocol is designed for dogs or cats with a high suspicion of **infectious diarrhea.** The causative agents to consider most commonly are canine parvovirus, canine coronavirus, feline parvovirus (panleukopenia), feline coronavirus, feline leukemia and immunodeficiency virus-associated diarrhea, giardiasis, campylobacteriosis, salmonellosis, E.coli and clostridial diseases. **Hemorrhagic gastroenteritis,** likely associated with bacterial infection, is also included. Various portions of therapy can be omitted according to the etiology and severity of the patient's condition. Assume all patients with diarrhea are infectious until proven otherwise. It is important to establish an infectious/contagious protocol for your practice and to follow it upon admission of any patient where there is a suspicion of contagion. This chapter will focus on acute, severe, small intestinal diarrhea.

The degree of associated illness is dependent upon the underlying cause of diarrhea, age of the animal and severity of fluid loss. Consequences requiring immediate therapy and ongoing monitoring are: poor perfusion, dehydration, third space losses, hypokalemia, hyponatremia, hypoglycemia, hypoproteinemia, aspiration pneumonia if vomiting is also occurring, sepsis/septic shock, intussusception, hyperthermia, hypothermia. These animals frequently require massive fluid replacement, plasma transfusion, colloid transfusion, nutritional support and analgesics.

DIAGNOSIS

History and Signalment

Specific breeds such as Rottweilers, Pit Bull Terriers and Doberman Pinschers tend to be susceptible to infectious diarrhea (Parvo virus), while Schnauzers, Beagles, Shihtzus, Yorkshire Terriers and Maltese Terriers appear to be more susceptible to hemorrhagic gastroenteritis. Obtain a thorough history as to:

- Age.
- When and where acquired (especially puppies and kittens).
- Vaccination history.
- Recent hospitalization (clostridial infection), boarding, or other possible infectious contacts.
- Access to garbage/compost/farm manure/foreign bodies.
- Medications receiving or may have access to.
- Diet change, including rawhide 'toys'.
- Other medical problems or signs of other illness.
- Duration and character of feces prior to the presenting event.
- Frequently, hemorrhagic gastroenteritis is peracute in onset without premonitary signs.

Clinical Signs/Physical Examination

- Typically animals with infectious diarrhea are presented with a short duration of soft to watery stool with or without blood. Mucus is usually a feature of colitis.
- They are frequently depressed, febrile, anorectic and dehydrated.
- Vomiting may be mild or severe.
- Severely affected animals may present in septic shock where the temperature may be normal or sub-normal.
- Abdominal pain may be present causing the animal to moan or cry, or having difficulty finding a comfortable position to lie down.
- Depending on the severity, oral mucous membranes may be tacky (not if vomiting or nauseated), pale with a slow capillary refill time (due to poor perfusion or blood loss), or hyperemic if septic or dehydrated with an increase in PCV (e.g., hemorrhagic gastroenteritis).
- Heart rate may be increased and peripheral pulses weak or absent if hypovolemic or septic shock is present. In the early stages of septic shock, the peripheral pulses are easily palpated and often bounding.
- Abdominal palpation may identify fluid or gas filled loops of bowel which may elicit pain when touched.

- Assess fullness of bladder to determine if urine is produced with respect to hydration status/renal function.
- Rule out other causes of diarrhea such as foreign body, intussusception, neoplasia, etc., (e.g., to identify thickened and/or dilated portions of bowel or a mass) (*see Acute Abdomen p. 21*).

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV/TS** to assess hydration i.e., increased PCV and TS, especially in viral infectious diarrhea; or hypoproteinemia and increased PCV (>55%) with hemorrhagic gastroenteritis; anemia with severe blood loss (parasites or neoplasia).
- **CBC** to assess sepsis with potential increased white count, or leukopenia (neutropenia) associated with parvovirus and panleukopenia infections, and severe, acute sepsis.
- **Blood or serum electrolytes,** as these may be abnormal with losses associated with diarrhea, especially sodium, calcium and potassium.
- **Blood/serum glucose** may be low in young anorectic animals and sepsis, but may be increased in a stressed cat.
- **Stick BUN, serum urea or creatinine** to assess renal function, which may be abnormal due to pre-renal causes (diarrhea, vomiting).
- **Blood gases** to assess acid base status, which may be severely altered with vomiting and diarrhea. Sodium and bicarbonate losses may be severe (*see Acid Base p. 406*).
- **Fecal sample** for gross examination and serology (ELISA for Parvovirus and *Giardia*).
- **Radiographic examination** of the abdomen if indicated (initiate treatment first if in shock).

Extended Laboratory/Imaging Data Base

- **CBC** if not already performed (*see above*).
- **Serum biochemistry profile** should be performed to obtain baseline overall assessment and to note any specific co-morbid conditions.
- **Urinalysis,** or at least a urine specific gravity prior to fluid therapy if possible. If specific gravity is <1.025 (dogs), 1.035 (cats) in the face of dehydration and increased urea or BUN, renal compromise is present. Should the urine specific gravity be >1.030 (dogs), >1.050 (cats), even if urea or BUN is increased, this is appropriate for dehydration and renal function is normal.
- **Fecal flotation, smear, cytology and culture** for pathogens, such as multi-drug resistant *E. coli*, *Campylobacter*, *Salmonella*, *Clostridium* and *Yersinia spp.*
- **Abdominal radiographs** are essential if a non-infectious or parasitic cause is suspected to rule out intussusception or other intestinal accident (*see Acute Abdomen p. 21*).

MANAGEMENT

A. **Oxygen** by mask, hood, nasal cannula or prongs if poor perfusion.

B. **Venous access,** jugular or cephalic (avoid saphenous if possible due to soiling).
  1. Obtain blood for above laboratory evaluation if not already obtained.
  2. Peripheral 2" catheter into a jugular vein frequently works well in puppies and kittens.
  3. Place an intraosseous catheter into puppies or kittens if unable to establish IV access.

C. **Fluid therapy.**
  1. Administer isotonic fluids (**Plasma-Lyte® 148 or A, lactated Ringer's or Normosol® R**) IV at a rate based on hydration and perfusion status (*see Fluid Therapy p. 347*) which could be up to, or much greater than, 90 mL/kg/h (dogs), 50 mL/kg/h (cats) initially if the patient is in shock and total solids (protein) are >45 g/L.
  2. If protein is <45 g/L, and the patient is in shock give **pentastarch or hetastarch** in 2.5 mL (cat), 5.0 mL/kg boluses to effect to a max of 20 mL/kg (dog), 10 mL/kg (cat) no faster than over 15 minutes (to treat shock). Most patients are resuscitated with less than the maximum dose. The remainder of the maximum volume may be given as a CRI for the remainder of the 24 hours. The crystalloid volume may be reduced by 40% with co-administration of a colloid. Colloids will dilute the plasma proteins requiring administration of species specific plasma (ideally FFP) and/or 25% human serum albumin (*see Hypoalbuminemia p. 431*) depending on the total protein, the amount of fluid required for resuscitation, and the severity of illness with potential DIC (*p. 417*).
  3. If poorly perfused but not in shock, give fluids as calculated based on hydration status (*see Fluid Therapy p. 347*). You may need up to 40 mL/kg/h initially.

4. After initial fluid resuscitation (emergency phase), an hourly fluid rate is based on deficits due to dehydration (replacement phase), ongoing losses (vomiting and diarrhea) and maintenance requirements (*see Fluid Therapy p. 347*). In addition, 10% maintenance rate should be added for each degree celcius above 39.5°C (slightly less for each degree fahrenheit above 102.5°). The hourly rate could be as high as 5 – 10 mL/kg/h.

5. Weigh twice daily to assist with assessment of ongoing losses and hydration status. The weigh scale should be disinfected before and after its use.

6. REMEMBER THIS IS A POTENTIALLY CONTAGIOUS DISEASE, THEREFORE TAKE APPROPRIATE PRECAUTIONS WHEN MOVING THE ANIMAL.

7. This initial phase of fluid therapy will depend on the individual patient. Frequent examination and re-assessment should be made. A set volume of fluid/plasma cannot be given as each patient has different fluid and protein losses. What is important is fluid resuscitation to achieve and maintain normovolemia. Monitor body weight q12h; PCV, TS, blood gases, electrolytes, glucose q6–12h initially; perfusion parameters (CRT, pulses, heart rate), temperature and respiration q2–4h; character and quantity of vomitus and stool, measure or estimate urine output q2–4h and calculate ins and outs q2–4h (*see Monitoring p. 12*).

D. Antibiotics.
   1. Cefoxitin 20 mg/kg IV q6h or cefotetan 20 mg/kg q6h (dogs, q8h (cats).
   2. In severe cases with normal renal function
      a. gentamicin 9 – 14 mg/kg (adult dogs), 5 – 8 mg/kg (cats), IV, IM, SC q24h OR
      b. amikacin 15 – 30 mg/kg (dogs), 10 – 14mg/kg (cats) IV, IM, SC q24h combined with
      c. cefazolin 20 mg/kg IV q6h (dogs), q8h (cats) OR
      d. ampicillin 20 mg/kg IV q6h (dogs), q8h (cats), has been recommended as long as the WBC is low, usually 3 – 5 day.
   3. Alternatively, **enrofloxacin 5 mg/kg IV slowly q24h (cats & dogs),** [not in dogs <8 mos (small breeds), <18 mos (large breeds) **exceptions see 4c below**] for gram negative aerobes **in combination** with
      a. **metronidazole 10 mg/kg IV** as a CRI over one hour q8h, **OR**
      b. **ampicillin 20 mg/kg IV q6h (dogs), q8h (cats), OR**
      c. **clindamycin 10 mg/kg IV q12h** for anaerobes.
   4. Pediatrics < 10 weeks of age with severe parvo diarrhea and sepsis.
      a. **cefoxitin 20 mg/kg IV OR cefotetan 20 mg/kg q6h (dogs), q8h (cats)**
      b. **aminoglycosides after re-hydration** and with **normal renal function,** for 3 – 5 days
         i. **gentamicin 7 mg/kg (dogs), 5 mg/kg (cats) IV, IM, SC q24h OR**
         ii. **amikacin 30 mg/kg (dogs), 14 mg/kg (cats) IV, SC, IM q24h combined with**
         iii. **ampicillin 20 mg/kg q6 (dogs) 8h (cats) OR**
         iv. **cefazolin 20 mg/kg q6 (dogs) q8h (cats)**

         NOTE: Ideally the use of an aminoglycoside should be monitored daily:
            1) examining urine for casts
            2) serum pharmacokinetic studies
      c. **fluoroquinolones** – (enrofloxacin **5 mg/kg IV q24h,** over 20 min (dogs), IM (dogs and cats) for 3 – 5 days if severe illness where aminoglycosides are contraindicated. Monitor for joint swelling several times/day in dogs; stop the fluoroquinolones should this occur. Swelling occurs prior to actual joint injury.
   5. In mild cases, antibiotics should be avoided.

E. **Antiviral agents. Oseltamivir (Tamiflu®** Hoffman La-Roche **available** as 75 mg capsule and a 12 mg/mL oral suspension). **2 mg/kg PO q12h for 5 days** has proved to be of great value in managing puppies with gastroenteritis, severe leukopenia, hypovolemia, increased or decreased body temperature and positively diagnosed with parvoviral infection. The response to oseltamivir was considered a return to normal white cell count within 24 – 48 hours and cessation of vomiting within 24 hours. Adverse effects felt to be associated with oseltamivir noted in a few puppies after 3 days of therapy, were recurrence of lethargy, abdominal pain and diarrhea, restlessness, and gastric dilation. These signs ceased when oseltamivir was discontinued. No dogs receiving oseltamivir died (personal communication Dr. N. Paixao, Lisbon, Portugal).

F. **Serum/Plasma Products**
   1. **Antiserum against LPS endotoxin** (present in severe parvovirus infection) (Polyvalent equine origin antiserum-SEPTI-serum, Immvac Inc., Colombia MO 75201) may prevent acute septic shock. 4.4 mL/kg diluted 1:1 with IV crystalloid fluids, administer over 30 – 60 min prior to antibiotic therapy as LPS

concentrations increase after institution of antibiotics. Immunologic reactions may occur if repeat dosing after 5 – 7 days. The authors have no experience with this product.

2. **Fresh frozen plasma 10 – 20 mL/kg IV** may provide passive immunity in addition to replacing some serum albumin.
3. **Serum from recovered dogs 2 – 4 mL/kg IV, SC** may reduce morbidity and mortality
4. **Passive immunity** for ill kittens, especially if deprived of colostrum, using plasma or serum from healthy vaccinated cats. 15 mL (~25 – 30 mL collection of whole blood) adult cat serum contains similar amount of IgG obtained by nursing kittens. Can be frozen for up to 1 year.

G.   Electrolytes.
1. Maintenance fluids should contain **potassium at 30 – 40 mEq/L** depending on the serum potassium. Monitor potassium levels closely. Supplementation should not exceed 0.5 mEq/kg/h unless serum concentration is less than 3.0 mEq/L, then administer up to 1.0 mEq/kg/h for 4 hours. Potassium levels can change quickly with pH changes (i.e., if acidemic or alkalemic prior to fluid resuscitation). Monitor potassium q3–4h at high infusion rate (*see Hyper/Hypokalemia p. 394*).
2. Maintain serum sodium and chloride within normal range (*see Hyper/Hyponatremia p. 381, Acid Base p. 406*).

H.   Hypoglycemia (<3.6 mmol/L) frequently occurs and maintenance fluids should contain glucose (2.5% – 5%).

I.   Add multiple B vitamins, 1 mL/250 mL fluids. If the fluid bag is to be hung >24 hours, it should be protected from light at the outset as vitamin B is light sensitive.

J.   Temperature.
1. **Hypothermia.**
   a. Administer warm fluids.
   b. Further warming of the patient can be achieved using a circulating hot water blanket if needed.
2. **Hyperthermia** measured after fluid resuscitation and **due to pyrogens,** not heat stress (*see Heat Stress p. 297*). Reduce temperature if
   a. **41.5 – 42.0°C (106.5°F – 107.5°F)**
      Non-steroidal anti-inflammatory analgesic (NSAIA) may be used **once** for antipyretic activity, rarely would this be repeated in 24 hours.
      i.   **meloxicam 0.05 – 0.1 mg/kg IV** dogs and cats, **OR**
      ii. **carprofen 1 – 2 mg/kg IV** in dogs or SC in cats (no repeat), **OR**
      iii. **tolfenamic acid 2 mg/kg IV** dogs and cats, **OR**
      iv. **dipyrone 10 – 15 mg/kg IV, OR**
      v.   **acetaminophen (elixir preferable) 10 mg/kg** in dogs may be repeated in 8 hours. **Do not use in cats.**
   b. **Temperature > 42°C (107.5°F)** and rising rapidly, administer NSAIA as in 1. above and cool the patient only until the temperature starts to drop. Never go below 40.5°C (103°F) with cooling.
      i.   **administer cool fluids**
      ii. **apply wet towels and a fan**
      iii. **room temperature saline urinary bladder lavage via urinary catheter**
      iv. **crushed ice packed in towels and placed next to the patient**
   c. Continuous monitoring of temperature is mandatory as rapid temperature changes can occur.

K.   Antiemetics (*see Vomiting p. 74*).
1. Should be administered when
   • vomiting is frequent
   • the patient is exhausted
   • dyspneic
   • nauseated
   • mentally depressed
   • has impaired gag reflex
   • bradycardic with nausea or vomiting.
2. **Metoclopramide 1.0 – 2.0 mg/kg/day IV CRI** (*see chart for doses*) or **0.2 – 0.4 mg/kg SC q8h** (metoclopramide should not be used when a mechanical obstruction may be suspected or with excessive intestinal hypermotility, **OR**
3. **Ondansetran 0.1 – 0.5 mg/kg IV or SC q6–8h.**
4. Palpate abdomen q2–4h to detect pain or intussusception as cause of vomiting. Auscultate for bowel sounds.

L. **Withhold food.**
1. Nothing per os until well hydrated and vomiting is controlled.
2. Consider parenteral nutrition *p. 499*.
3. The volume of ongoing losses must be replaced with crystalloid solutions. The PPN volume administered equals maintenance fluid requirements.
4. **Early enteral micronutrition solution (such as Gastrolyte® or intravenous solutions with dextrose added) at 0.5 mL/kg/h CRI via nasoesophageal tube,** should begin within 12 hours, if vomiting is controlled, with a glucose-electrolyte.
5. Alternatively, if vomiting is not controlled, but animal is alert, give **glucose-electrolyte solution 1 – 2 mL/kg via syringe q2–4h.** Stop if induces vomiting. Do not persist if the animal struggles as aspiration may occur.

M. **Intestinal protectants.**
1. **Bismuth subsalicylate (Pepto-Bismol®) 2 mL/kg PO q6–8h for 1 – 2 days (caution in cats** due to salicylate) may benefit some patients.
2. Do not administer to a patient that is vomiting.

N. **Analgesics.**
Some animals are extremely painful requiring analgesics.
1. **butorphanol 0.1 – 0.4 mg/kg q2h** for mild pain (*see Butorphanol Infusion Chart for CRI dosing p. 229*), **OR**
2. **fentanyl low dose 2 – 6 μg/kg/h** for moderate to severe pain (*see Fentanyl Infusion Chart for CRI dosing p. 237*), **OR**
3. **NSAIA** see H2 above, once or twice

O. **NSAIAs meloxicam 0.1 mg/kg (dogs and cats) or carprofen 2 mg/kg (dogs only)** for one or two days may be useful in reducing the secretory response of the enteric nervous system triggered by products of inflammatory cells. The use of cyclooxygenase inhibitors is a relatively new theoretical concept in the management of inflammation-induced hypersecretion associated with cryptosporidiosis, *clostridium difficile* and rotavirus infections. There is however, potential concerns for mucosal healing if used for more than a short period. Ensure optimal hydration and gastroprotectants (proton pump inhibitor i.e., omeprazole). Avoid salicylates **L above.**

P. **Nursing care.** Keep the animals clean and dry. Wrap the tail with Vetrap®, bathe frequently as needed. Apply petroleum jelly (Vaseline®) around the anus and perineum to prevent scalding.

Q. **Monitoring** (*see Monitoring p. 12*).
These patients can deteriorate rapidly. Frequent or constant monitoring/observation is required. Ongoing concerns in these patients are sepsis, pyrexia, further/ongoing dehydration, development of intussusception or other intestinal accident.

PHARMACOLOGY

1) **Metoclopramide** is a centrally (chemoreceptor trigger zone) acting antiemetic. It also has promotility activity.
2) **Ondansetran** is a selective antagonist of the serotonin receptor, sub-type 5-HT3, on neurons located in either the peripheral or central (or both) nervous systems.
3) **Bismuth subsalicylate** is an effective agent for treatment of acute non-specific diarrhea. It has antienterotoxin, antisecretory and anti-inflammatory actions possibly mediated by antiprostaglandin activity. Caution in cats due to the salicylate.

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HEPATIC ENCEPHALOPATHY, PORTO-SYSTEMIC SHUNT/MICROVASCULAR DYSPLASIA, COAGULOPATHY, HEPATIC LIPIDOSIS, COPPER STORAGE DISEASE

INTRODUCTION

The liver plays a central role in body homeostasis. Drug metabolism, production of blood coagulation factors, energy storage, and metabolism are some of the many functions performed by the liver. As a result of these many different functions, clinical manifestations of acute hepatic failure differ in their presentation depending on which of these elements is most affected. With liver failure, gut derived toxins and bacteria transported in portal blood bypass the liver and thus bypass immunologic surveillance resulting in systemic infection. Animals with severe liver dysfunction may present with hepatic encephalopathy (HE). Failure of clearance of ammonia (NH_3), formed during protein degradation by intestinal bacteria and normally converted to urea in the liver, diffuses across the gut wall, enters the blood, and crosses the blood brain barrier. Other toxins potentially implicated in causing neurologic signs are short chain fatty acids, mercaptans, γ-aminobutyric acid, false neurotransmitters and benzodiazepines. For acute liver failure (ALF) to occur it is estimated that 70 – 80% of hepatic function has to be compromised.

There are many etiologies of liver failure which can occur in all ages of cats and dogs (Table 1). In addition to those listed, animals with portosystemic shunts (PSS) may present with clinical signs of liver failure. Here too cats and dogs of varying ages may be affected. A single extrahepatic shunt is most often found in small-breed dogs and cats, while a single intrahepatic shunt is most common in large-breed dogs. Acquired shunts are formed secondary to sustained portal hypertension caused by chronic liver disease, fibrosis, or cirrhosis. These shunts are multiple, and extra hepatic in their location. Ascites is a common clinical sign in these patients. Ascites can also be the result of decreased oncotic pressure as albumin production is decreased in liver failure. Prognosis for this etiology of ascites formation is poor. Microvascular dysplasia is a congenital disorder in dogs with similar vascular and cellular abnormalities associated with PSS; it may occur alone or in conjunction with a congenital PSS. In middle-aged cats, hepatic lipidosis is a fairly common cause of liver dysfunction. It is secondary to the accumulation of fat into the liver as a response to inadequate energy and/or protein intake, frequently associated with another disease processe that induces anorexia. The presence of hepatic lipidosis in cats has been associated with concurrent pancreatitis and inflammatory bowel disease. Copper storage is another presentation of liver dysfunction or failure, which can be primary (e.g., Bedlington terrier) or secondary (most often the result of chronic hepatic disease).

TABLE 1. Potential Etiologies of Acute Liver Failure

Category	Items	Category	Items
Anesthetics	Halothane Methoxyflurane	**Medications**	Acetaminophen — Megesterol acetate Azathioprine — Methimazole Carprofen — Phenobarbital Diazepam — Phenylbutazone Griseofulvin — Salicylates Ketoconazole — Thiacetarsamide L-asparaginase — Tetracycline Mebendazole — Trimethoprim Sulfa
Biological Toxins	Aflatoxin *Amanita* mushroom poisoning Blue green alga toxins		
Chemical Exposure	Arsenic Heavy metals Iron or Copper overload Selenium	**Metabolic**	Acute copper associated liver disease in: • Bedlington Terriers • West Highland White Terriers • Skye Terriers • Doberman Pinchers Lobular dissecting hepatitis
Infectious Agents	Blastomycosis Clostridia Dirofilaria Immitis (post caval syndrome) Feline infectious peritonitis Histoplasmosis Infectious canine hepatitis Leptospirosis Salmonellosis Toxoplasmosis	**Neoplastic**	Lymphoma Other neoplasia
		Systemic Disease	Acute pancreatitis Heat stroke Hypoxia (IMHA, cardiovascular) Sepsis Shock

History

- Questions pertaining to the etiologies in Table 1 will help detect exposure to toxins, drugs, or manifestations of systemic disease.
- Questions related to the environment may identify potential exposure to water, soil or airborne pathogens.

Clinical Signs/Physical Examination

- No single specific clinical sign is associated with ALF.
- Most often reported are anorexia, vomiting, diarrhea, lethargy, polyuria/polydipsia and abdominal pain especially on palpation.
- Depression.
- Drooling, especially in cats.
- Hepatomegaly and ascites.
- Coagulopathy (petechia, blood loss from orifices, hematomas).
- More specific clinical signs related to the liver:
    - Icterus (*see Icterus p. 70*)
    - Hepatic encephalopathy
        - waxing and waning of clinical signs.
        - acute onset of hepatic encephalopathy causes dramatic onset of clinical signs i.e., agitation, continuous whining and (uncommon) seizures.
        - chronic hepatic encephalopathy more commonly presents with depression, stupor, walking endlessly in (semi) circles, head pressing, blindness, and eventually coma.

Laboratory Evaluation/Diagnostic Imaging

Stat

Use a peripheral vein to collect blood. Should a coagulation disorder be present a venipuncture may result in ongoing bleeding requiring a pressure bandage.

- **Serum bile acids** will provide an insight into liver function. While, ideally, pre- and post-prandial (2 hours post fatty meal) serum bile acids are obtained, often the post-prandial test cannot be obtained, due to the condition of the patient (i.e., vomiting, anorexia). A single serum bile acid is still informative as an increased level indicates decreased liver function. However the converse is not true. A normal pre-prandial serum bile acid concentration does not rule out liver dysfunction.
- **Blood ammonia** measurements above normal, are compatible with impaired liver function (*see hepatic encephalopathy p. 40*). A single, normal blood ammonia value does not rule out hepatic encephalopathy. This test must be performed immediately after blood collection.
- **ACT** is variable depending on the severity and duration of liver failure. The ACT can be increased in DIC or with a coagulation factor deficiency, independent of liver failure.

Extended Laboratory Data Base

Obtain as soon as possible:

- **CBC** may show a mild to moderate anemia and microcytosis (i.e., blood loss, liver disease, hepatic encephalopathy, or anemia of chronic disease). Target cells and thrombocytopenia may indicate DIC.
- **Serum biochemical profile,** for systemic evaluation of the patient.
- **Alanine Aminotransferase (ALT)** is elevated with hepatocellular necrosis or damage to liver parenchyma secondary to biliary stasis. Unfortunately ALT is not liver specific and can also be elevated in patients with severe skeletal muscle damage.
- **Alkaline Phosphatase (ALP)** is increased in cholestatic liver diseases, or may be drug induced in mature animals.
    - In dogs (not cats) the most common drug induced elevations in ALP are related to the use of anticonvulsants and corticosteroids.
    - In immature animals, or patients with severe bone disease, an increased ALP may not be related to liver involvement.
    - In cats the half-life of ALP is short (6 hours) and therefore even mild elevations of the ALP may indicate significant cholestatic disease.
- **Gamma glutamyl transferase (GGT)** is elevated with cholestatic disease. It behaves like ALP in dogs. In cats GGT tends to increase more rapidly than ALP and seems to be a more sensitive indicator of cholestatic disease.
- **Bilirubinemia** (s*ee Icterus p. 70*) may or may not be increased in liver failure.

- **Albumin** levels are reduced when functional liver mass is reduced by 70 – 80%. Other causes of low albumin are protein losing nephropathy, protein losing enteropathy, malnutrition etc.
- **Blood Urea Nitrogen (BUN) or urea** is reduced when the liver is unable to convert ammonia to urea. However, in patients with severe anorexia, feeding a low protein diet, or severe PU/PD causing medullary washout, the BUN or urea may be low and unrelated to liver failure. BUN or urea may be normal in liver failure with gastrointestinal hemorrhage.
- **Blood glucose** may be low due to impaired hepatic gluconeogenesis, hepatic glycogen stores, and hepatic insulin degradation. Liver disease severe enough to cause hypoglycemia (*p. 280*) requires a reduced functional liver mass of 70 – 80% and indicates a poor prognosis.
- **Serum electrolytes** may reveal hyponatremia (*ADH effect p. 381*), hypernatremia (*free-water loss p. 381*), hypokalemia (*p. 394*), and hypophosphatemia (*p. 390*) which are common findings in patients with ALF. Both hypernatremia and hyponatremia may be indicators of poor prognosis when associated with ALF and a small liver.
- **Urinalysis** may reveal bilirubinuria, iso- or hyposthenuria in liver failure. Urine culture and sensitivity panel are recommended, as urinary tract infections are common in patients with ALF. The antibiogramme on isolates determines the choice of antibiotic. The most common bacteria isolated are several species of gram negative organisms, and gram positives such as *Staphylococcus* sp, *Steptococcus* sp.
- **PT and PTT** frequently increased in severe liver disease but this may also be a feature of DIC. Spontaneous bleeding in patients with ALF due to lack of coagulation factors (not Vit. K deficiency) indicates a very poor prognosis with very short survival times (days).
- **Abdominal radiographs** should be obtained in the patient with acute hepatic disease. Hepatomegaly frequently indicates acute disease, but may also be chronic secondary to infiltrative disease (i.e., neoplasia). Microhepatica is usually present in patients with congenital portosystemic shunts and patients with chronic hepatic disease resulting in fibrosis/cirrhosis. Abdominal fluid may also be detected.
- **Abdominocentesis** for cytological evaluation and bacterial culture of abdominal fluid must be performed carefully due to coagulopathy.
- **Ultrasonographic examination** is very useful in identifying diffuse and localized lesions of the liver, the presence of free abdominal fluid, intra- and extra-hepatic portosystemic shunts, and hepatic fibrosis and lipidosis.
- **Biopsy** of the liver is required for definitive diagnosis for ALF (i.e., hepatic necrosis, neoplasia). The patient must be stabilized and fresh, or fresh frozen plasma administered peri-biopsy to prevent unrelenting hemorrhage.
- **Blood cultures** bacteremia has been reported. The antibiogramme on isolates determines the choice of antibiotic. Most common bacteria isolated are several species of gram negative organisms, gram positives like *Staphylococcus* sp, *Steptococcus* sp, and fungi e.g., *Candida* and *Aspergillus* sp.

MANAGEMENT

A. Remove the causative agent where identified; or administer specific antidote.

B. Carefully place a **peripheral IV catheter**; bleeding from the venipuncture site may be difficult to stop.

C. **Fluid therapy** (*see Fluid Therapy p. 347*) to correct dehydration, acid-base and electrolyte disturbances.
1. Avoid lactate containing fluids (i.e., Lactated Ringers solution), because this requires adequate liver function to metabolize the lactate. Poor perfusion, hypotension, and lactate accumulation contribute to the development of acidosis in patients with ALF.
2. Alkalinizing fluids (Plasma-Lyte• or Normasol• products) should be avoided if the patient is alkalemic; 0.9% sodium chloride with potassium supplementation is recommended.
3. Hyponatremia (*see p. 381*), hypokalemia (*see p. 394*), and hypophosphatemia (*see p. 390*) are common findings in patients with ALF, and should be corrected with appropriate fluid therapy and electrolyte supplementation.

D. **Hypoglycemia** (*see p. 280*). Hypoglycemia may develop rapidly.
1. Monitor blood glucose q2–4h (0.1 mL blood). Use 25 gauge needle to avoid bleeding (compress site). If hypoglycemia is discovered, bolus with 10% dextrose IV. The clinical signs associated with hypoglycemia, i.e., seizures, collapse, weakness, unrest, and other abnormal behavior, should decrease and stop within 5 minutes. To maintain euglycemia a constant rate infusion (CRI) with 2.5 or 5% dextrose solution IV may be required. Refractory hypoglycemia carries a poor prognosis. Hypoglycemia must be ruled out as imposter for hepatic encephalopathy.

E. **Hepatic encephalopathy** secondary to liver failure regardless of etiology. Treatment is directed towards a decrease in NH3 production and conversion of NH_3 to NH_4^+.

1. **Fluid support** should include correction of hypokalemia and metabolic alkalosis (these two abnormalities exacerbate clinical signs of hepatic encephalopathy), because they increase NH_3 production.
2. **Lactulose 0.5 mL/kg q8h–q12h**
   a. as a retention enema (administer per rectum using a feeding tube and retain by digitally closing the anal sphincter for 5 – 10 minutes) in the acute phase patient with altered mentation where vomiting or aspiration are concerns **OR**
   b. PO where the patient is alert. Continue therapy until the stool is soft.
3. **Neomycin 10 – 20 mg/kg PO q6–12h** is not systemically absorbed and kills NH_3 producing bacteria in the colon.
4. **Note: Metronidazole 7.5 mg/kg PO q12h** warrants close observation to detect signs of toxicity in the treatment of patients with hepatic encephalopathy as this drug requires hepatic metabolism for elimination. Toxicity is neurologic in its clinical presentation and may be confused with the signs of hepatic encephalopathy.
5. **Avoid the use** of barbiturates and benzodiazepines as they act via neural inhibition in an already impaired brain.

F. **Portosystemic shunts**

1. Initially, medical management as HE in E as indicated above.
2. Surgical correction should be considered for congenital (intra- or extra-hepatic) shunts.
3. Treat the underlying cause of acquired shunts where possible.

G. **Microvascular dysplasia:** medical management as HE (E above.)

H. **Nutritional support.** High protein diets should be avoided initially as these exacerbate hepatic encephalopathy. Protein restriction (low protein, high quality availability i.e., K/D diet, L/D diet) decreases substrate availability for intestinal NH_3 production. Once the acute hepatic failure episode is resolved, dietary protein requirements can be re-evaluated.

I. **Coagulopathies**

1. Avoid any drugs that promote bleeding i.e., non-steroidal anti-inflammatory analgesics.
2. Special attention should be given to blood coagulation parameters prior to any invasive procedure.
3. Gastrointestinal bleeding occurs frequently and may lead to clinical manifestation of HE.
4. Vitamin K deficiency may be present and impair the function of factors II, VII, IX, X. **Vitamin K_1 0.5 – 2.5 mg/kg SC, IM q12h,** preferably 3 doses before a liver biopsy is obtained, is recommended.
5. **Ulcer treatment/prophylaxis is important.**
   a. **Sucralfate 0.5 – 1 g PO q8–12h** (dogs) OR **0.25 g PO q8–12h** (cats).
   b. **Famotidine 0.5 mg/kg PO, IV, SC q12h.**
6. If a **blood transfusion** is indicated, avoid blood transfusion with blood stored longer than 2 weeks. NH_3 production increases over time.

J. **Antibiotic therapy, Ampicillin Sodium 10 – 20 mg/kg IV q6–8h** in combination with **enrofloxacin 5 mg/kg IV q24h** is recommended while results of bacterial cultures are pending. Endotoxemia, the result of infection with gram negative organisms may be present and contributes to hypotension.

K. **Cerebral edema** may be manifested by rapid deterioration of mental status; mydriasis with delayed pupillary light reflex and an abnormal breathing pattern (*see Head Trauma – Neurological Examination p. 691*).

1. **Mannitol 0.25 – 2 g/kg of 15% – 25% solutions** IV over 10 – 15 min, IV (repeat in 6h if necessary).
2. **Furosemide 2.0 – 6.0 mg/kg IV q8–12h** if mannitol is not available. **Furosemide can cause alkalosis which may precipitate worsening of clinical signs.** 0.9% sodium chloride fluid support with monitoring of acid-base status is recommended.
3. **Lidocaine 1.0 mg/kg IV** may reduce intra-cranial pressure enough to avoid tentorial herniation.
4. **Lidocaine** as in 3 above, prior to intubation and hyperventilation will help to decrease intracranial pressure during the emergent period, until mannitol or furosemide is effective. Fluid balance must be monitored to avoid hypotension and dehydration (*see Head Trauma p. 691*). Overall, the development of cerebral edema in a patient with ALF is considered a poor prognostic sign.

L.   **Renal failure.** Unexplained oliguric renal failure in a patient with ALF (and at times formation of ascites) suggests the development of the hepto-renal syndrome. This syndrome carries a poor prognosis. Acute tubular necrosis is another cause of acute renal failure in patients with ALF. Treatment is geared towards maintenance of systemic blood pressure by judicious fluid loading; monitoring urine output and the treatment of ARF (*see Acute Renal Failure p. 709*).

M.   **Copper accumulation.** There is no quick fix for Copper toxicosis; removal is a slow lifelong process. **Trientine 10 – 15 mg/kg PO q12h** is suggested and supplementing with **Zinc gluconate 1.5 – 2.5 mg/kg PO q8h** to eliminate copper from the body.

N.   Ascites

1. Abdominocentesis with removal of a volume of fluid to relieve tamponade and improve ventilation. Avoid removing large volumes of ascitic fluid as vascular collapse and hypotension may occur.
2. **Diuretics such as furosemide 2 – 4 mg/kg PO q6–q12h combined with Spironolactone 1 – 2 mg/kg PO q12h** may be required to control ascites formation. Caution: furosemide may result in alkalosis which may precipitate or worsen HE.

O.   Hepatic Lipidosis

1. Fluid and electrolyte support.
2. May require esophagostomy or gastrotomy tube placement to meet caloric requirements.
3. Feeding low content, high-quality protein, high-energy, balanced cat food, 70 – 80 Kcal/kg (based on ideal body weight)/day. Recommended is a low content but high quality protein source protein (i.e., kidney diet) in the acute patient to avoid clinical manifestations or worsening of the HE. Long term nutritional support requires a gradual change over to feeding of high-protein, high-energy, balanced cat food.
4. Avoid appetite stimulants, such as the benzodiazepines in patients with liver failure. These drugs require hepatic metabolism, coma may develop.
5. Owners must be prepared to tube feed for up to six months as it may take this long before the cat's appetite and voluntary feeding is restored.

P.   **S-adenosyl methionine** (SAMe, Denosyl SD4®) may be of benefit in reducing the oxidative damage done to the liver. Dosing recommendations.

Body Weight	Dose SW-adenosylmethionine
<5.5 kg	One 90 mg table q24h PO
5.5 – 11	Two 90 mg tablets q24h PO
11 – 15	One 225 mg tablet q24h PO
16 – 30	Two 225 mg tablet q24h PO
31 – 41	Three 225 mg tablet q24h PO
>42	Four 225 mg tablet q24h PO

Q.   **Milk thistle** (silymarin marianum) at a dose of 100 mg/day for a 10 kg (22 lbs) animal has reportedly been effective as a free radical scavenger in patients with liver disease and may be used as a less expensive alternative to SAMe. This product is not registered as a drug but considered a food supplement.

PHARMACOOGY

1) **Lactulose** is a nonabsorbable disaccharide which is metabolized in the colon by the microflora. In the colon, hydrogen is formed, and binds with NH3 to form NH4$^+$. Lactulose alters the make up of colonic bacterial flora, and thus decreases the production of NH3. Lactulose acts as cathartic and decreases the contact time of the food in the colon, thereby additionally decreasing the time available for NH3 production and absorption.

2) **Trientine (Syprine®)** is a chelating agent used to chelate copper. May be less effective than penicillamine in the removal of copper from the patient, but side effects have not been reported with the use of this drug.

3) **Furosemide (Lasix®)** is a potent loop diuretic. It blocks the chloride on the Na-K-2Cl transporter, and, thus, sodium and water re-absorption. Furosemide can cause SEVERE alkalosis, which may precipitate worsening of clinical signs in patients with HE.

4) **S-adenosyl methionine** (SAMe, Denosyl SD4®) might be beneficial in reduction of the oxidative damage done to the liver. It helps to increase hepatic glutathion levels in cats and dogs. Glutathione, an antioxidant, acts as hepatic cytoprotectant Note: This product is not registered as a drug but considered a food supplement.

SUGGESTED READING

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2. Johnson SE, Diseases of the liver and biliary tract. In: Saunders manual of small animal practice, 2nd edition. Birchard SJ, Sherding RG (eds). WB Saunders, Philadelphia. 2000:824-873.
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NOTES

Introduction

Rectal prolapse involves the protrusion of rectal mucosa from the anus.

DIAGNOSIS

History

- Recent straining, defecation, or perineal or anal surgery.

Clinical Signs/Physical Examination

- Protrusion of rectal mucosa from the anus. This usually appears as a cylindrical mass. Depending on the duration and degree of prolapse, the mucosa may be edematous, erythematous, ulcerated, or devitalized.
- Rectal prolapse will have a blind end when gently probed at the junction of the anus and rectal mucosa. (Note: prolapse of an intestinal intussusception will have a potential space when probed between the anus and prolapsed mucosa).
- Prostatomegaly/prostatic mass, if cause of tenesmus.
- Mass in pelvic canal, if cause of tenesmus.
- Perineal hernia, if cause of tenesmus (assess for urinary bladder within perineal hernia).

Laboratory Evaluation to Assess Cause of Tenesmus

- **CBC.** Left shift if septicemic or devitalized mucosa; eosinophilia if endoparasites.
- **Biochemical Profile.** Azotemia and/or hyperkalemia if perineal hernia with retroflexed and obstructed urinary bladder.
- **Urinalysis.** Proteinuria, bacteria, and/or active sediment if bacterial prostatitis; transitional cells if neoplasia.
- **Abdominal Ultrasound.** Prostatomegaly may be present if underlying cause; pelvic mass may be present if underlying cause.
- **Fecal floatation and Analysis.** Endoparasites, especially in an immature animal.

MANAGEMENT

Treatment of rectal prolapse depends on the cause, chronicity and severity of the prolapse. It should be performed as soon as possible, to prevent dessication or further trauma to the everted tissues. In some cases, self-mutilation may be an additional source of trauma. If the mucosa is grossly edematous, erythematous, or hemorrhagic, attempt manual reduction. If the viability of the mucosa is compromised, surgical resection of the affected region is indicated.

A. MANUAL REDUCTION
1. Manual reduction should be attempted under epidural or general anaesthesia.
2. To remove gross debris, the affected mucosa should be lavaged with warm saline prior to reduction.
3. **Treatment of edema:** topical administration of hypertonic saline or 50% dextrose may be used to reduce the edema and facilitate tissue reduction.
4. Reduction may be digitally performed using a water-soluble lubricant (e.g., KY Jelly) and gentle pressure on the protruding tissues.
5. Following reduction, a purse-string suture (3-0 nonabsorbable monofilament) should be placed at the anorectal mucocutaneous junction to attenuate the anal orifice and maintain reduction of the prolapse, while still allowing soft feces to pass.
6. Sutures should remain in place for 3 – 5 days.
7. To prevent recurrence, it is ALWAYS indicated to identify and treat the underlying cause.
8. **Stool softners** should be prescribed and the patient must maintain normal hydration.
9. Recurrence following suture removal warrants further diagnostic work-up to identify the underlying cause, and surgical resection or colopexy considered.

B. SURGICAL EXCISION

1. Nonreducible, nonviable or severely traumatized rectal prolapses require surgical resection of the affected region and anastomosis of the margins. This condition is considered a surgical emergency, as devitalized rectal wall may result in bacterial translocation, septicemia, and free radical tissue damage.

2. As this surgery may present technical challenges and be associated with major complications, we recommend referral of these cases to an experienced surgeon.

3. Pre-operative management of cases requiring amputation of devitalized rectum involves:

   a. Identifying the underlying cause
   b. Intravenous fluid therapy
   c. Intravenous broad-spectrum antimicrobials (e.g., Cefazolin or Cefoxitin 20 mg/kg IV q6–8h) should be initiated.
   d. The prolapsed tissues should be covered with saline-soaked laparotomy sponges and protected from further trauma.
   e. Placement of an Elizabethan collar on the patient may prevent self-mutilation.

SUGGESTED READING

1. Aronson L. Rectum and Anus. In: Slatter D. Textbook of Small Animal Surgery (3rd ed), Philadelphia, WB Saunders, 2003:682-708.
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NOTES

INTRODUCTION

Acute pancreatitis is a common occurrence in both cats and dogs. Most cases are mild and easily managed, while a few progress to moderate to severe pancreatitis with an unpredictable outcome. Acute necrotising pancreatitis tends to be a devastating disease. The mortality rates of **severe** pancreatitis in dogs and cats ranges from 27 – 42%. Proteolytic enzymes within the pancreatic acinar cells are activated causing injury to the gland with subsequent release of activated proteolytic enzymes into the systemic circulation. Endogenous antiproteases, alpha-macroglobulins and alpha-antiptrypsins, found in plasma bind and facilitate clearing of these enzymes. However, the antiproteases soon become depleted with progression to an acute, systemic inflammatory response syndrome (SIRS) with mediator/cytokine release similar to that of sepsis. In fact, acute pancreatitis can evolve into the sepsis syndrome if not managed appropriately in the early stages. Vasculitis from pancreatic enzymatic inflammation, and cytokine-mediated capillary leak is a major problem in these patients resulting in protein and fluid loss from the intravascular space. Peritonitis may be severe with further intravascular losses. Fluid therapy is a challenge in these patients requiring careful selection, volume titration and monitoring. Surgical management is often required where pancreatic masses, massive necrotizing pancreatitis, or bile duct/gallbladder pathology are identified. Early, aggressive treatment is required to improve outcome.

Optimal medical and post-surgical management of these patients is necessary to enhance recovery and reduce morbidity. Nutritional support is an important aspect of management. A combination of partial parenteral (PPN) and enteral (jejunostomy tube) nutrition, or PPN alone, is used depending on the severity of illness and requirement for surgical management. While hyperglycemia, technical problems and catheter-related sepsis have been reported as potential complications of parenteral nutrition (more specifically total parenteral nutrition), this author has not observed these problems with PPN. Occasional phlebitis is noted if a peripheral vein is used in smaller (<20 kg) patients. Reported complications associated with jejunostomy feeding range from mild to severe in up to 34% of patients. *See Nutritional Support p. 499* for further details.

Many studies investigating various therapies have been conducted in human patients with pancreatitis. However, the etiology of pancreatitis in humans is different from those in veterinary patients as is the anatomical location of the pancreas. Therefore, direct extrapolation from the human patient to the veterinary patient may not be appropriate in every aspect of management. No published prospective clinical trials to verify specific guidelines in the treatment of severe pancreatitis are available in veterinary medicine. The protocol presented here is a combination of recommendations for treating ACUTE pancreatitis based on a recent review (*Suggested Reading 1 below*) and the author's practice.

DIAGNOSIS

History/Signalment

Diagnosis is based on a history of vomiting and/or anorexia, diarrhea and depression.
- As the etiology of both feline and canine pancreatitis is frequently unknown, a careful history with regard to dietary indiscretion, including high fat consumption, and medication (azathioprine, trimethoprim-sulphonomides, furosemide, chemotherapy etc.) should be obtained. Corticosteroids are currently not considered to predispose to pancreatitis, although very high dosages may.
- Other causes to consider are duct obstruction, duodenal reflux, ischemia, trauma, hypertriglyceridemia (especially Schnauzers), hypothermia, acute spinal injury (including intervertebral disc herniation), insect venoms, recent abdominal surgery, hypotension, severe pain. Occasionally, there is nothing to report.
- As many of these patients are geriatric, question the owner with regard to underlying cardiac, or any other, disease.
- Obese animals may be pre-disposed.
- As hypercalcemia (*p. 373*) may also predispose to pancreatitis investigate this as a potential cause.

Clinical Signs/Physical Examination

- Presentation is from mild to moderate depression to moribund depending on the severity of the disease.
- Palpation of the anterior abdomen frequently elicits pain but this is not consistent. An abdominal mass (abscess), or abdominal fluid may be noted.
- Dehydration and fever are frequently present.
- Icterus may be present.
- Dyspnea may be marked as these patients may have non-cardiogenic pulmonary edema or pleural effusion due to vasculitis/capillary leak, acute respiratory distress syndrome (ARDS), or aspiration pneumonia due to vomiting.
- There may be pulse deficits if a cardiac arrhythmia is present.
- The patient may be hypovolemic (prolonged capillary refill time, poor peripheral pulses, tachycardic) or in shock due to fluid loss into the abdomen or interstitial spaces.
- Cats may appear as above, or relatively normal on physical examination. Some cats will only present as "not doing well."

Laboratory/Diagnostic Imaging Data Base

Stat

- **PCV** may be increased initially due to dehydration and later with SIRS, pleural effusion and peritonitis, but PCV may be normal or decreased with hemorrhagic, necrotising pancreatitis.
- **TS** may be increased initially due to dehydration but decreased later with SIRS and pleural effusion and peritonitis. It is important to note the colour of the plasma, icteric if biliary involvement and various degrees of lipemia may be noted. Lipemia will increase the TS reading dramatically, therefore, assessment of albumin is required to obtain a true picture of hypoalbuminemia.
- **Stick BUN** is almost always increased due to reduced GFR in the presence of dehydration and hypovolemia.
- **Blood glucose** may be normal, high, or low the latter often associated with sepsis.
- **ACT** is often increased, ≥125 secs (dogs), ≥90 secs in cats.
- **Urinalysis.** Specific gravity is often increased with dehydration and hypovolemia. Oliguria/anuria may be present due to hypovolemia.
- **Electrolytes** are generally altered according to severity of illness. Normal or hypo/hypernatremia, hypokalemia, or hyperkalemia if renal function is reduced. Chloride may be normal or low.
- **Venous blood gases** frequently reflect a high anion gap, non-respiratory acidosis and low bicarbonate.
- **Arterial blood gas** or **pulse oximetry** to assess oxygenation and requirement for oxygen if dyspneic.
- **ECG.** VPCs and ventricular tachycardia may be present.
- **Systemic blood pressure** must be obtained as this may be low in hypovolemic states and will guide volume of fluids to be administered.

Extended Laboratory Data Base

- **CBC.** The red blood cell count and hematocrit reflect PCV above. Leukocytosis >24 x 10^9/L, >10% Band neutrophil count. Leukopenia with increased band neutrophils may be seen in acute severe pancreatitis.
- **Biochemical profile** frequently shows hypoalbuminemia, with ALT, ALP increased >3 times normal. However, frequently ALP alone, and/or lipemic serum, may be the only laboratory evidence, of pancreatitis. Amylase and lipase are increased in only 50% of dogs with pancreatitis, therefore normal or low values do not rule out pancreatitis. Urea and creatinine are usually increased for reasons stated for stick BUN above. Serum glucose is frequently >13 mmol/L (260 mg/dL). Hypocalcemia (if unable to measure ionized calcium refer to formula *Hypocalcemia p. 377*) may be real or associated with hypoalbuminemia or saponification.
- **Pancreatic lipase immunoreactivity (PLI)** values >200 μg/L is highly specific for canine pancreatitis. In cats the normal fPLI range is 2 – 6.8 μg/L with a cutoff value of 12 μg/L for a diagnosis of pancreatitis.
- **Fasting serum triglycerides** are frequently increased, especially in Schnauzers.
- **Beta-hydroxybutyrate** is often >1 mmol/L.
- **Radiographs** of the abdomen and (if indicated) thorax.
- **Urinalysis** for base line.
- **Abdominal ultrasound examination** may confirm pancreatitis and its severity (necrotising or not), and identify abscess/tumour, free fluid.
- **Abdominocentesis** should be performed to assess appearance of the fluid. Serosanguinous or wine coloured fluid on abdominocentesis may be found with acute, hemorrhagic pancreatitis. Cytological examination may show increased numbers of neutrophils, frequently degenerate. Amylase level of the fluid is often greater than serum of patients with severe necrotizing pancreatitis.
- **Central venous pressure** is recommended where cautious delivery of fluids is required.
- **C-reactive protein measurements** are increased in patients with pancreatitis and may be useful as a measure of inflammation.

MANAGEMENT

A. Oxygen. If respiratory rate is increased or if dyspneic or depressed, administer oxygen by mask.

B. Place an **IV catheter,** preferrably in the jugular vein as CVP can be measured and blood sampling is easier and more comfortable for the patient. Patients with pancreatitis are more prone to the development of thromboemboli, therefore, use violon catheters (Becton Dickinson), as they are less thrombogenic than Teflon catheters. Violon peripheral catheters are also available and recommended. Obtain blood for Laboratory Data Base. Establish a central line to measure CVP if patient is geriatric or has underlying cardiac disease or is dyspneic.

C. Fluid therapy.

1. A balanced, isotonic, alkalinizing, crystalloid solution is preferred (Plasma-Lyte® 148, Normosol® R or lactated Ringer's solution). If blood products are used they should be delivered through a separate line to lactated Ringer's; this is not necessary with Plasma-Lyte® 148 or Normosol® R.

2. Calculate **fluid volume** replacement (*see Fluid Therapy p. 347*) and administer over 1 – 24 h depending on the presentation of the patient and presence of cardiac disease. If chronic fluid loss, dehydration should take 24 hours to correct. Fluid volumes 2 – 3 times the calculated dose may be required initially due to previous, and continued losses through peritonitis, vomiting, diarrhea. A cautious approach is required due to capillary leak. Fluid therapy should be tailored to the patient's needs rather than a fixed amount as continuing losses vary with the severity of the disease and associated problems

3. These patients are almost always **acidemic** due to poor perfusion and duodenal vomiting. Fluid resuscitation using an alkalinizing solution commonly improves the acidosis.

4. If in **shock** *see Fluid Therapy – Emergency Phase (p. 351)*. Combination fluid and plasma will be required. *See 7 below*. Maintain a CVP 5 – 10 cm H_2O. Monitor response to therapy q5–10min.

5. **Synthetic Colloids (pentastarch or hetastarch).** Colloids are indicated in low oncotic states where large volumes of crystalloids are required to raise and maintain systemic blood pressure to an adequate level. With severe pancreatitis, it has been this author's experience that pulmonary edema has worsened with recommended (20 mL/kg/day) volumes of these solutions in dogs. Personal preference is to administer fresh frozen plasma (*see 7 below*) and, if needed to manage hypotension with moderate to severe, hypoalbuminemia and moderate to severe capillary leak, with 25% human serum albumin (25% HSA) *see 8 below*. For cats and dogs requiring oncotic support, a minimal amount of synthetic colloid is administered as a CRI. The progress of the individual patient will dictate which, and how much, fluid should be administered. A suggestion for administration of synthetic colloids to raise blood pressure is to administer 2.5 mL/kg boluses (maximum of 10 mL/kg in the dog, 5 mL/kg in the cat) with delivery of the remaining 5 – 10 mL/kg as a CRI over 24 hours, reducing the volume of crystalloid by approximately one-quarter to one-half. Pentastarch may be added to 0.9% saline, Plasma-Lyte® 148 or Normosol• R. Due to the presence of calcium in lactated Ringer's the mixing compatibility is unknown. The key to preventing capillary leak is to avoid an increased hydrostatic pressure by administering an excess of crystalloids.

6. Measure blood pressure, assess bladder size (or preferrably, measure urine output), dorsal pedal and femoral pulses for improvement in rate and strength, capillary refill time and mucous membrane colour for perfusion status. Monitor respiratory rate and pattern.

7. **Fresh/fresh-frozen plasma (FFP).** Currently, there are no prospective clinical trials in veterinary medicine to support the use of FFP in severe pancreatitis, however, this author feels benefit may exist in this patient population. Administer 10 mL/kg over 1 – 2 hours and an additional 10 – 20 mL/kg at some time during the remaining 22 – 23 hours if needed. Initially, it is necessary to give it more rapidly to attain adequate plasma levels of antithrombin, alpha-macroglobulins, and alpha-1 protease inhibitors which bind to and inactivate the pancreatic enzymes which have leaked, and continue to leak, into the intravascular space.

8. **25% Human Serum Albumin** may show benefit in hypoalbuminemic (albumin <15 g/L [1.5 mg/dL]) patients with capillary leak/vasculitis. In hypotensive states, following a test dose of 0.25 mL/kg/h for 15 minutes (if time permits) to identify potential acute reactions, administer **2 mL/kg IV** given slowly in aliquots of one-quarter the volume. Monitor blood pressure after each aliquot. As pressures normalize, reduce the administration to 0.025 – 0.5 mL/kg/h and reduce the volume of crystalloids (*see Hypoalbuminemia p. 431*).

D. If **PCV** is higher than 45%, red cells may stick to the injured endothelium in the capillary bed resulting in microthrombosis and poor tissue oxygenation.

1. With fluid therapy maintain PCV between 30 – 45%, however, don't dehydrate to achieve a normal PCV.
2. If PCV is between 25 – 30%, check that the patient is not over-hydrated (*see Fluid Therapy p. 347, Monitoring p. 12*) due to excessive fluids/colloids. This must be avoided as pulmonary edema may occur. Monitor q15–30min during rapid fluid resuscitation.
3. If PCV <25% rule out dilutional change; if it is, slow down the infusion and it should correct within a few hours. If not dilutional, ascertain source (*intra-abdominal hemorrhage p. 619, Gastric Hemorrhage p. 67*).
4. If blood loss is diagnosed, administer blood (fresh blood if fresh plasma required), or packed cells (use cells <12 days old to avoid abnormal deformability) if plasma transfusion is underway. You must calculate the amount of blood required for transfusion to avoid polycythemia and microthrombosis. Aim for a PCV 27 – 30% (*see Blood/Plasma Transfusion p. 671*).

E. **Total solids** or total protein should be >40 g/L. Where possible, albumin should be measured daily and a combination of 25% HSA, and synthetic colloid may be required if <15 g/L (1.5 mg/dL) and the patient is deteriorating. Further plasma administration may be required depending on the severity of the case.

F. Treat any concurrent disease that may have precipitated, or is contributing to, the pancreatitis.

G. **Peritoneal lavage** has not proven to be beneficial and may increase risk for infection. If elected in severe cases, *see Peritoneal Dialysis p. 723* for technical direction. Normal saline at 20 mL/kg at 37° – 38°C, is used for lavage. Strict aseptic technique is necessary. This may be very painful.

H. **Surgical** debridement of an extensive area of necrosis or abscess is advised, especially if not responding to conservative therapy. Biliary obstruction must be corrected. A jejunostomy tube should be placed if laparotomy is performed.

I. **Acid-base status and electrolytes** (include calcium) should be re-assessed after fluid resuscitation. Potassium supplementation (*see Hypokalemia/Hyperkalemia p. 394*) may be necessary. If alkalemic, change fluids to 0.9% saline.

J. **Glucose.** If blood glucose <3.6 mmol/L add 50 mL (2.5%) to 100 mL (5%) of 50% dextrose per litre of fluids (*see Hypoglycemia p. 280*).

K. **Pain control is very important.**

1. **Butorphanol 0.2 – 0.4 mg/kg q2h** continued as a CRI of 0.1 mg/kg/h or to effect, is only suitable for mild-moderate pancreatitis. Stop the CRI for 30 – 60 minutes if appears overdosed and reinstitute at one-half the previous dose.
2. **Oxymorphone or hydromorphone at 0.05 – 0.1 mg/kg q3–4h,** or as a CRI (*see p. 255 and p. 243*), or more to effect,
3. **Morphine or methadone at 0.2 – 0.5 mg/kg very slow IV,** continued as a CRI (*p. 251*), OR
4. **Fentanyl 3 – 6 µg/kg/h** (*see CRI p. 237*).
5. It may be necessary to increase the dose of pure mu opioid if butorphanol has already been administered due to its antagonistic effect.
6. **Epidural analgesia** (*p. 112*) should be considered if surgical intervention is performed.
7. **Pain** activates the sympathetic nervous system which causes vasoconstriction and therefore poor splanchnic (especially pancreatic) perfusion. This, in itself, can cause pancreatitis.

L. **Monitor blood pressure.** Attempt to achieve normal blood pressure (MAP >80 mmHg and systolic pressure 120 mmHg). This facilitates perfusion of the pancreas and kidneys. Fluid rate can be adjusted down once an improvement in overall patient status is noted. If normal blood pressure cannot be achieved with fluid and colloid therapy, consider **dopamine at 4 – 10 µg/kg/min.** (*see Dopamine Infusion Chart p. 233*) or **norepinephrine 0.1 – 0.5 µg/kg/min** (*see Norepinephrine Infusion Chart p. 253*).

M. **Urine output.** A urinary catheter should be placed in recumbent animals (*see guidelines for steriile technique p. 720*). Urine output should be 1 – 2 mL/kg/h. Measure volume and specific gravity hourly initially and adjust fluid rate accordingly. If urine output is inadequate following fluid resuscitation, refer to *Acute Renal Failure p. 709*.

N. **Activated clotting time** should be measured once or twice daily to alert for possible disseminated intravascular coagulation (DIC). Normal range for ACT (Ontario Veterinary College) using grey top tube with silica is 70 – 120 secs (dog) 60 – 90 secs (cat). If ACT is prolonged, do a platelet count to rule out prolongation potentially due to thrombocytopenia (<50 x 10^9/L) and coagulogram (PT, PTT, fibrinogen, fibrin degradation products) to confirm DIC. Thrombocytopenia is associated with DIC. If ACT is less than normal, continue to monitor as this may indicate a procoagulable state. If pancreatitis is severe, this author treats for DIC with fresh or fresh-frozen plasma prior to receiving results of the coagulogram.

O. **DIC/Pulmonary thrombosis.** The endothelial injury and activation of the coagulation cascade caused by systemic proteases, predispose patients with pancreatitis to thromboembolic disease (*p. 194*) and DIC (*p. 417*). Pulmonary thromboemboli must be considered in all patients developing acute tachypnea or dyspnea (*see Thromboembolic Disease p. 194*). **Heparin 10 – 12 U/kg/h CRI** (preferred by the author) or **100 U/kg SC q8h** to an increase of 1.5 – 2 x high normal ACT (180 – 250 sec in dogs and 120 – 180 sec for cats), or high normal PTT. Perform ACT prior to next SC heparin dose or q8–12h with CRI. Adjust dosage accordingly.

P. **Antibiotic coverage.** Antibiotics are not routinely prescribed for mild to moderate pancreatitis without evidence of infection. However, in protracted cases that are unresponsive to supportive measures, obtain blood cultures, or aspirate abdominal fluid or pancreatic tissue to identify potential bacterial involvement. Empirical antibiotic therapy should then commence as these may be beneficial in the meantime.

  1. Where evidence of systemic infection exists and may be due to translocation of intestinal flora **Cefoxitin 20 mg/kg IV q6h** (dog), q8h (cat), has good gram negative and anaerobic coverage; it also achieves high levels in the biliary system which is frequently involved in these patients.
  2. Reported therapeutic levels in pancreatic tissue are reached with
     a. **Clindamycin 10 mg/kg q12h (dogs and cats)**
     b. **Ciprofloxacin 10 mg/kg IV, SC q24h (dogs and cats)**
  3. If other infections are identified, culture the appropriate fluids/catheters etc. and treat based on susceptibility.

Q. **Antiemetic therapy.** Vomiting is common in these patients.

  1. **Metoclopramide 1 – 2 mg/kg/24h CRI** is frequently used. However, as increased gastric emptying occurs, this may increase the delivery of gastric secretions to the duodenum and stimulate further pancreatic secretions.
  2. **Ondansetran 0.1 – 0.2 mg/kg IV q6–8h** (dogs and cats) is preferred.
  3. An alternative is to give **chlorpromazine 0.05 – 0.1 mg/kg** slowly IV q4h or **prochlorperazine 0.13 mg/kg** IM (hurts!) or SC q6h. These two drugs can cause hypotension therefore should only be given in the normotensive re-hydrated patient.
  4. A **nasogastric tube** should be inserted for intermittent aspiration of gastric fluid in the patient with refractory, or large volume vomiting.

R. **Ulcer prophylaxis/treatment.** If vomitus contains blood or the patient is ulcer prone (i.e., history of high dose corticosteroid treatment), commence

  1. **Famotidine 0.5 – 1.0 mg/kg IV (dogs), SC (dogs and cats) q12h OR**
  2. **Omeprazole 0.7 mg/kg PO q24h** if oral medication possible as the patient improves.
  3. **Pantoprazole 1 mg/kg, max 30 mg IV** over 20 mins q24h.
  4. **Sucralfate 0.5 – 1.0 g PO** should only be given if significant gastric bleeding is present (*see Gastrointestinal Hemorrhage p. 67*).

S. **General nursing care.** Very important. Many of these patients are middle aged to elderly, well house-trained dogs. They get very upset when soiled. Keep them clean and comfortable. Turn q6h, keep the bandages clean and dry. Check the IV catheter site carefully, daily and remove the catheter and culture if appears contaminated (infected site).

T. Patients with pancreatitis require continual monitoring. Fluid, electrolyte and acid-base status, total solids and PCV, urine output, blood pressure, temperature and pulse rate need to be assessed at regular and initially frequent intervals. Adjustments in therapy should be made where appropriate.

U. Nutrition. No published prospective clinical trials to verify specific guidelines are available in veterinary medicine. The following is the author's practice in patients with **severe** pancreatitis.

1. NPO for at least three days, longer in patients with necrotising pancreatitis.
2. Start partial parenteral nutrition (*see Parenteral Nutrition p. 511*) with a mixture of 3.5% amino acid and a maintenance IV solution such as Plasma-Lyte® 56 OR Normosol® M, given at maintenance fluid rate once re-hydrated and within 24 hours if possible.
3. Parenteral lipid solutions. It is the author's preference not to use these solutions in lipemic animals, those with increased triglyceride levels, and in patients with severe or necrotising pancreatitis; the observation has been an association with jugular vein thrombosis and worsening of the patient's condition. For these reasons lipid solutions are not recommended in the first few days.
4. If a jejunostomy tube is placed, the author prefers to withhold 'feeding' for the first few days to ensure total rest of the pancreas as occasionally, there may be retrograde flow causing vomiting. However, in addition to parenteral nutrition, immediate institution of a CRI at 0.1 mL/kg/h for 12 hours via the jejunostomy tube with 5% dextrose plus electrolyte solution (e.g., Plasma-Lyte® 56, Normosol® M, or add 100 mL 50% dextrose to IV electrolyte solution) is advised. If tolerated, the CRI is increased to 0.5 mL/kg/h for 12 hours. If well tolerated, add Clinicare® 0.3 mL/kg to 0.6 mL/kg Plasma-Lyte® or Normosol® M/h. If well tolerated, increase the ratio of Clinicare® to Plasma-Lyte® q12h until 100% Clinicare® is administered. Increase the volume to illness energy requirement (*see Nutritional Support p. 499*) by the 3rd day if tolerated. While Clinicare is isosmolar, this author has experienced 'cramping' when used undiluted initially.
5. If a jejunostomy tube is not in place, it is the author's practice to keep the patient NPO for a minimum of three days, or until the serum lipase is decreased to normal, or almost normal range. Experience has shown that vomiting frequently recurs if food is introduced earlier. Lipase may also be increased with corticosteroid use.
6. As pancreatic secretions can be stimulated by the cephalic phase of eating, move the patient away from any odour of food, even that given to the patient in the next cage.

PHARMACOLOGY

1) **Metoclopromide** is an antiemetic and promotility drug. In this protocol it is used for its centrally acting antiemetic effects. It may cause drowsiness and lower the seizure threshold in susceptible individuals. Use with caution when administering with epileptogenic drugs. Metoclopromide is a dopinergic antagonist.

2) **Chlorpromazine** is a phenothiazine derivative used in this protocol for its centrally acting antiemetic effects. It may cause hypotension and frequently produces sedation.

3) **Prochlorperazine** is similar to 2) above but less sedating.

4) **Ondansotron** is a selective antagonist of the serotonin receptor subtype, 5-HT3, located centrally and peripherally. This is the preferred antiemetic.

5) **Famotidine** is an H2 blocker, reducing the secretion of gastric acid.

6) **Sucralfate** is the most effective medication for treating actively bleeding ulcers. It binds to gastric erosions or ulcers, prevents backflow of acid and enhances healing.

7) **Omeprazole** is a proton pump inhibitor reducing gastric acid secretion.

8) **Pantoprazole** is a proton pump inhibitor reducing gastric acid secretion.

SUGGESTED READING

1. Freeman LM, Labato MA, Rush JE. Et al. Nutritional support in pancreatitis: a retrospective study. J Vet emerg Crit Care. 1995;5(1):32-41.
2. Holm JL., Chan DL, Rozanski EA. Acute pancretitis in dogs. J Vet Emerg Crit Care 2003;13(4):201-213.
3. Holm JL, Rozanski EA, Freeman LM, Webster CRL. C-reactive protein concentrations in canine acute pancreatitis. J Vet Emerg Crit Care 2004;14(3):183-186.

NOTES

INTRODUCTION

Constipation is a common clinical sign of many diseases in the dog and cat. Disorders that cause prolonged fecal transit time allow for increased absorption of fluid and produce a dry, firm fecal mass. Fecal concretions cause mucosal irritation that increase secretion from the colonic mucosa leading to fluid, protein and electrolyte loss. In severe cases, bacteria and toxins can be absorbed across the colonic mucosa causing bacteremia and toxemia. Obstipation is a severe form of constipation in which defecation cannot occur due to fecal impaction. Recurrent constipation and obstipation can lead to chronic distention of the colon, degeneration of colonic smooth muscle and a hypomotile, flaccid colon.

CONDITIONS PREDISPOSING TO CONSTIPATION
Ingestion of hair, bones, plastic or excessive fiber
Painful defecation (inflammatory/neoplastic anorectal diseases, pelvic or rear limb fractures/orthopedic abnormalities)
Inability to posture
Mechanical obstruction (narrowed pelvic canal, intraluminal or intramural mass/stenosis)
Neuromuscular diseases (dysautonomia, lumbosacral disease)
Drug-induced (anticholinergics, opioids, phosphate binders, sucralfate, barium)
Colonic weakness due to metabolic conditions (hypercalcemia, hypothyroidism, hypokalemia)

Megacolon is usually an idiopathic condition seen in cats (primarily). Irreversible colonic dilation occurs, while decreased colonic motility leads to severe impaction of feces. In addition, severe dehydration predisposes to constipation by causing excessive fluid absorption from the feces and hypomotility (cats especially). Simple constipation in a well patient (hydration normal, no vomiting or anorexia) can be easily treated. This protocol is designed for treatment of constipation in the sick patient.

DIAGNOSIS

History/Signalment

- Attempts to determine an underlying disease must be made.
- Confirmation of a history of previous trauma, weakness, use of medications (see above), or access to garbage or bones can help to determine the cause of constipation.
- Question the owner as to whether they have observed defecation or attempts to defecate and the appearance and shape of the stool passed (blood or mucus, foreign material, thin or large diameter may indicate obstruction or enlarged colon).

Clinical Signs/Physical Examination

- Tenesmus and frequent, often painful, attempts to defecate with scant feces produced. Feces that are produced may be firm and dry, may have blood or mucus, or may be liquid diarrhea.
- Systemic signs of illness may include weight loss, depression, weakness, anorexia, diarrhea and vomiting.
- Physical findings may be nonspecific, other than a firm, enlarged colon on abdominal palpation, or may reflect an underlying disease process. Palpation of the colon may be painful.
- Severe hypokalemia may cause ventroflexion of the neck and weakness in the cat, and may be the etiology of constipation.
- Orthopedic abnormalities of the pelvis, limbs or spine may be palpable.
- Dehydration frequently predisposes to constipation in cats.
- Neurological abnormalities may be present with lumbosacral/pelvic disease or dysautonomia.
- A complete neurological and rectal examination must be performed.
- Inflammatory anorectal conditions such as perianal fistulas, abscessed anal glands or ulcerated masses/polyps may be observed during rectal palpation.
- Assess fullness of the bladder. Inability to void may be associated with dysautonomia or pelvic injury.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, total solids, BUN stick, glucose, urine specific gravity and body weight** as baseline information, to assess hydration, renal concentrating ability, and a screen for potential emergent conditions.
- **Electrolytes** to identify hypokalemia.
- **Venous blood gas or total CO_2** to assess for acidosis if dehydrated, or if poor perfusion is detected on physical exam.
- **Radiographs of the abdomen** to assess the size of the colon/prostate, identify orthopedic abnormalities of the pelvis or narrowed pelvic inlet, foreign material in the feces, identify an intraluminal/intramural or extramural mass/stenosis. Extreme dilation of the colon is characteristic of megacolon.
- **Radiographs of the spine and lumbosacral area** to identify fractures or other orthopedic abnormalities.
- **Ultrasonographic examination** to assess colon wall thickness, when colonic pathology is suspected.
- **A barium enema or endoscopy** (after all feces are removed following appropriate cleansing protocol) to identify and allow biopsy of strictures or masses.

Extended Laboratory Data Base

- **CBC** to assess ongoing illness predisposing to dehydration and constipation, or as a result of constipation; leukocytosis, leukopenia ± left shift or degenerate left shift, toxicity may be a result of severe constipation with absorption of toxins and bacteria.
- **Serum biochemical profile** to assess organ function and underlying illness, pre-renal azotemia due to severe dehydration, hyperbilirubinemia due to sepsis, hypercalcemia (*see Hypercalcemia p. 373*), hyperparathyroidism (*See Hypothyroidism p. 285*) and other potential causes, and to rule out metabolic disorders.
- **Total T4 and free T4** by equilibrium dialysis if hypothyroidism (*see Hypothyroidism p. 285*) is suspected (dogs primarily).
- **Urinalysis** to assess renal function.

MANAGEMENT

Treatment is dictated by the severity of the disease.

A. Place an IV catheter.

B. Fluid therapy. Administer balanced electrolyte solution fluids (e.g., Plasma-lyte• 148, Normasol•R, Lactated Ringers) after calculating fluid volume replacement, based upon hydration status and ongoing losses (*see Fluid Therapy p. 347*). Replace deficit over 8 – 24 hours, depending on the clinical condition of the patient. Fluid therapy will help to soften impacted feces. Metabolic acidosis will likely be corrected with fluid therapy.

C. Electrolytes. Potassium supplementation 20 – 40 mEq/L may be indicated depending upon the serum potassium. Potassium should be closely monitored (especially dehydrated cats). Sodium and chloride should be maintained within normal range.

D. Antibiotics are indicated with severe obstipation/constipation, evidence of infection (pyrexia, neutrophilia with a left shift, toxic neutrophils), or bloody feces/diarrhea. **A second generation cephalosporin (cefoxitin 20 mg/kg IV q6h) is preferred, OR enrofloxacin (5 mg/kg IV q24h, NOT in young dogs <18 mos or cats, here ampicillin alone may be used) COMBINED with ampicillin 20 mg/kg IV q8h** may be used due to the mixed bacterial flora (primarily gram negatives and anaerobes) present in the large intestine.

E. Removal of feces. The patient must be rehydrated and metabolically stable prior to attempts to remove the impacted feces. Sedation/anesthesia (*see F below p. 53*) are usually necessary. **Enemas** of warm water or warm normal saline (5 mL/kg) may be instilled using a well-lubricated, soft, red rubber catheter and a large syringe. Enemas must be infused slowly to allow for retention (to soften feces) and to prevent vomiting caused by rapid colonic distention. Simultaneous infusion of lubricants (mineral oil or sterile lubricant jelly 50:50) or laxatives (docusate sodium 5 – 10 mL or mild soap such as povidone iodine 1 mL/10 mL enema) may be beneficial. Suppositories such as biscodyl or docusate (pediatric) are useful in mild cases only. **In cats, DO NOT use sodium-phosphate (Fleet) enemas OR soaps with hexachlorophene. DO NOT use mineral oil with ducosate in any species (causes mineral oil to be absorbed). After feces are softened, they may be normally defecated or may require manual removal.** In the awake, sedated or anesthetized animal, the feces can be gently compressed and milked into the rectum using abdominal palpation and then gentle digital manipulation can be used to remove the feces. Depending on the amount of feces, several procedures performed on consecutive days (over 2 – 4 days), may be necessary. It is important to be **extremely gentle** to prevent mucosal trauma, tearing and perforation.

F. Sedation. It is common to require restraint to remove stool from cats with severe constipation or obstipation. The procedure can take a long time to accomplish, sometimes up to 2 hours. In cats with good renal function, chemical restraint (rather than inhalant or general anesthesia) using diazepam (5 mg/mL), ketamine (100 mg/mL) [combine 1 mL of each and administer at 0.02 mL/kg IV or more] to a level of heavy sedation. The patient is able to assist in evacuating the feces as it is broken up. Be cautious to titrate low doses of ketamine/diazepam to achieve, and then maintain, a state of restraint that retains full laryngeal and swallowing reflexes. These reflexes may not be maintained sufficiently to avoid aspiration if anesthesia is approached with this combination. If general anesthesia is more desirable due to concerns for vomiting, or renal/liver function is a concern, an appropriate anesthetic protocol based on serum biochemical findings can be chosen. This protocol must include intubation due to the possibility of vomiting and aspiration.

G. Chronic management. Depending upon the underlying disease, chronic therapy using oral laxatives (*see Pharmacology below*) and dietary modification (canned food, appropriate fiber supplementation – *see Pharamcology*) is usually indicated. Dehydration must be avoided. Close monitoring should ensure that soft feces are passed by the pet on a daily basis.

H. Cisapride. Dogs: 0.7 mg/kg PO q8–12h. **Cats:** <5 kg 2.5 mg, >5kg 5 mg PO q8–12h. **The stool must be soft or normal in consistency, and obstruction cannot be present if a promotility agent is to be administered** (cisapride is only available through pharmacy compounding facilities).

I. Subtotal colectomy is indicated for recurrent obstipation or megacolon that fails medical management.

PHARMACOLOGY

1) **Docusate sodium (Colace) and docusate calcium (Surfak)** are emollient laxatives that help to soften feces and stimulate colonic secretions. Docusate promotes absorption of mineral oil and can cause lymphadenitis. Therefore, these products should not be used concurrently.

2) **Petroleum products** and mineral oil are lubricant laxatives that can be given orally or rectally. Because mineral oil is easily aspirated, it is not recommended as an oral medication. Lubricants act to coat the fecal mass and soften the feces (by decreasing fluid reabsorption) thus, allowing for easier passage. Oral lubricants should be given between meals to prevent decreased fat-soluble vitamin absorption.

3) **Lactulose (Duphalac syrup)** is a nondigestable solution of carbohydrates that acts an oral osmotic laxative. The osmotic action of lactulose retains water in the bowel, keeps the feces moist and stimulates motility. As lactulose is metabolized by colonic bacteria, low molecular weight acids are formed and the pH of the colonic contents is lowered. This stimulates colonic motility and also acts to draw water into the bowel. Lactulose 0.5 mL/kg q 8-12h can cause severe, watery diarrhea and the dose should be adjusted to produce a soft stool.

4) **Bisacodyl (Dulcolax)** is a stimulant laxative that acts to increase motility in the large and small intestine and to decrease fluid reabsorption. This type of laxative can cause discomfort and is not recommended. The enema formulation (Fleet) should not be used in cats or small dogs, as severe toxicity may result.

5) **Bulk forming laxatives** such as canned pumpkin (1-2 tsp/meal) or psyllium (Metamucil, 1-2 tsp/meal) act to increase fecal bulk, and therefore stimulate the defecation reflex. In addition, as the fiber source is metabolized by colonic bacteria, fatty acids are released which act to increase colonic secretions and motility and promote epithelial health. High-fiber diets are also commercially available and act in a similar manner. Excessive fiber is contraindicated in cases with decreased colonic motility.

6) **Cisapride** increases acetylcholine release in the gut to promote motility and can be used in combination with stool softeners to treat chronic constipation and idiopathic megacolon. Adverse effects include diarrhea and abdominal pain. Do not use in cases where increased gastrointestinal motility is contraindicated. Use only after fecal impaction is removed. This drug is no longer available.

SUGGESTED READING

1. Handbook of Small Animal Gastroenterology, 2nd edition, Tams TR, Saunders, St. Louis, MO, 2003:274-281.
2. Veterinary Internal Medicine, 5th edition, Ettinger and Feldman, (eds). WB Saunders, Philadelphia, PA. 2003:129-132.

INTRODUCTION

Esophageal foreign bodies (FB) are a common occurrence in veterinary medicine and require emergency treatment due to the potential for serious complications if not removed. At the Ontario Veterinary College, the most common objects lodged in the esophagus include bones, rawhide (including both rawhide strips and bone shaped rawhide), and fish hooks. Other foreign objects encountered are large pieces of hard fruit or vegetables, impacted meat and small bones secondary to eating raw food diets, needles, fabric, stones, chew toys, and hairballs (cats). Serious complications that may be encountered are esophageal perforation and concurrent mediastinitis, pleuritis, pyothorax and pneumonia. Regurgitation can lead to aspiration pneumonia. These complications may lead to sepsis. Additional complications include stricture, diverticulum, bronchoesophageal fistula formation and, in rare cases, hemothorax or pericarditis. Bronchoesophageal fistula formation is an unusual complication associated with chronic esophageal foreign bodies.

DIAGNOSIS

History/Signalment

- Most common in young, small breed dogs but can be seen in any age, breed or sex: rare in cats. Although the following refers primarily to dogs, it is also applicable to cats; exceptions will be noted.
- Recent history of bone or other FB ingestion followed by: drooling, dysphagia, repeated attempts to swallow or, conversely, reluctance to swallow, gagging (note the owner may interpret aggressive gagging as coughing), extending the neck, pawing at the face if the FB is lodged in an extreme proximal location and, commonly, regurgitation.
- The dog may have the ability to drink but not to ingest solid food.
- Anorexia may be noted secondary to pain or systemic illness. At times, the dog may seem interested in food but either avoids eating or immediately regurgitates.
- The owner may notice halitosis.
- After an extended period of time since ingestion (i.e., 3 days or more), the clinical history may reveal more evidence of systemic illness related to sepsis in the likelihood of esophageal perforation and/or aspiration pneumonia.
- Historical findings at this time may include mild to severe lethargy, depression, anorexia, and cough. Rarely, the reason for presentation is dyspnea (secondary to tracheal compression) if the FB ingestion is acute and may or may not have been witnessed.

Clinical Signs/Physical Examination

- **Respiration** is normal to increased. If increased, consider pain and anxiety, or secondary aspiration pneumonia especially if a fever is present. Extremely large FBs may cause respiratory distress if they concurrently compress the trachea.
- **Pulse rate and quality** is normal to elevated. An increased heart rate may be secondary to pain, dehydration and subsequent hypovolemia or sepsis in the most severe case. Poor pulse quality may be present in cases of sepsis.
- **Temperature** is normal to elevated. If a fever is noted, consider the possibility of an esophageal perforation and secondary mediastinitis and pleuritis. The second possibility is aspiration pneumonia or bronchoesophageal fistula if the obstruction has been longstanding. In extremely rare cases bronchoesophageal fistulation may occur earlier if the object is large enough to puncture both the esophagus and airways.
- **Mucus membranes** are normal, dry secondary to dehydration, or moist due to drooling secondary to pain and/or nausea (therefore, unreliable in assessment of hydration status – see following).
- **Hydration.** History with regards to duration of obstruction, drooling, inability to drink and regurgitation should be considered in addition to skin tent and absence of moist mucous membranes and cardiovascular status.
- **Sclera.** Petechiation may be present if there has been any concurrent choking-like episodes or extreme retching. The platelet number should be normal in this setting; however if thrombocytopenic, consider sepsis.

Oral Examination

- Halitosis – impacted foreign bodies associated with meat become putrid and cause severe halitosis.
- Be thorough on examination, especially under the tongue in both dogs and cats as fish hooks, needles etc. in the esophagus may have string attached which could lodge anywhere in the mouth. This may be the case if the foreign body is not in the typical location in the esophagus as the fixed string prevents passage.

Cervical palpation

- Cautious palpation of the neck may reveal a swelling consistent with a FB.
- An area of pain, associated with esophagitis where the foreign body may have been lodged for a period of time before becoming lodged distally.
- A cough may be elicited on palpation due to presence of FB, inflammation, aspiration pneumonia or a bronchoesophageal fistula.

Thoracic auscultation

- Normal with no associated pathology, pneumomediastinum, or mediastinitis.
- Decreased lung sounds if pneumothorax or pleural effusion is present; areas of consolidated lung and pneumonia.
- Increased lung sounds with increased respiratory rate – pain, pneumonia.

Abdominal palpation

- Generally within normal limits.
- Abdominal pain may be noted if there is a concurrent gastritis, pancreatitis secondary to "dietary indiscretion", or in the unlikely event of an intestinal obstruction from the same type of foreign material.

Digital rectal examination

- Melena may be noted if considerable esophageal hemorrhage is swallowed, however this is extremely rare.

Laboratory Evaluation/Diagnostic Imaging

Stat
Depending on the age of the patient and physical examination findings, the following may be the minimum required data base prior to anesthesia, or serve as a guideline for initial emergency care and stabilization in those cases that are systemically ill, and not suitable candidates for anesthesia immediately upon presentation.

- **PCV** is expected to be normal or elevated secondary to dehydration. Severe anemia may be present in the case where hemorrhage may have occurred secondary to laceration by a sharp object (rare).
- **TS** is normal, or elevated if patient is dehydrated. Low in the rare instance of hemorrhage.
- **Stick BUN** is normal, or increased if dehydrated or blood present in gastrointestinal tract.
- **Blood glucose** may be low in sepsis or neonatal/pediatric animals due to anorexia.
- **Systemic Blood Pressure** is normal, or increased if painful and anxious. Low in cases of severe dehydration, hypovolemia or sepsis.

Extended Laboratory Data Base

Perform if the patient is systemically ill
- **CBC** is indicated if a fever is present on initial presentation, if there is an obvious esophageal tear, marked inflammation and necrosis on endoscopic examination, or if mediastinal, pleural space or pulmonary pathology is noted on radiographs. **WBCs** are normal to increased depending on the severity of the esophagitis, presence of concurrent esophageal tear or full thickness necrosis. A degenerative left shift would be consistent with a significant esophageal tear/rupture and thoracic infection or severe aspiration pneumonia. **Platelets** are typically normal, if low consider DIC secondary to severe sepsis. **RBCs** are consistent with PCV as mentioned above.
- **Chemistry Panel** is not necessary unless severe infection, severe dehydration, systemic clinical signs noted on physical examination or abnormal findings on minimum data base.
- **Urinalysis.** Measure urine specific gravity and assess in conjunction with hydration status and where renal function is questionable.

Thorax
- Must perform lateral and dorsoventral thoracic and cervical radiographs.
- The entire esophagus should be evaluated.
- The most common locations for obstruction are the thoracic inlet, the base of the heart and the diaphragmatic hiatus.
- Radiopaque FB are easily visualized. Sharp objects such as needles or fish hooks should be evaluated for location, inside or outside the esophageal lumen. If not visualized but suspect, perform abdominal radiographs.

- If FB is not visualized, note if food or fluid has accumulated cranial to obstruction.
- If FB is not visualized, take a contralateral view before performing a contrast study.
- Assess for presence of pneumomediastinum, pneumothorax, pleural effusion, or widened medistinum on the dorsoventral view which could indicate the presence of fluid and esophageal perforation.
- **Note:** the lack of the previously mentioned radiographic changes does not rule out a FB.
- **Esophageal perforation generally requires emergency thoracotomy. If a contrast study is required to confirm site of perforation, a water soluble, ionated agent should be used. Never use barium to outline a FB or identify a potential perforation. Barium is contraindicated prior to endoscopy and is harmful if it leaks into the thoracic cavity. If perforation isn't suspected then barium is the contrast of choice to identify a FB.**
- **Note:** the false negative rate for identifying a perforation with contrast esophagram is 15%, especially if the FB is still present covering a tear.

Abdomen

- Determine whether the FB has moved into the stomach.
- Identify additional FBs that are either causing an obstruction, or are anticipated to cause an obstruction, and warrant surgery upon presentation.
- **Note:** most bones will be digested by the stomach acid in 7 – 10 days and pass into the feces and therefore may not cause an obstruction despite initial appearance.
- If a linear object is found on oral examination, the abdomen should be evaluated for a linear FB obstruction, which warrants surgical exploration.

MANAGEMENT

All esophageal foreign bodies need to be removed immediately to prevent perforation and potential esophageal stricture.

A. ACUTE EMERGENCY THERAPY

1. **IV access should** be established.
2. **IV fluids** based on physical findings and laboratory data (*see Fluid Therapy p. 347*).
3. **Pain management** and/or anti-anxiety therapy must be considered. If not critical, pre-medication, induction and maintenance according to the animal's health and age is indicated. Acepromazine 0.02 – 0.05 mg/kg IV **(before)** or 0.01 – 0.05 mg/kg **(during anesthesia)** will facilitate a smooth recovery. Butorphanol 0.1 – 0.2 mg/kg IM, IV or oxymorphone 0.02 – 0.5+mg/kg IM, IV can be used should analgesia be required. Pre-medication can often be eliminated for a more rapid induction when emergent.
4. **Induction and maintenance of anesthesia.** Since these cases are usually healthy outpatients, induction with **propofol** 4 mg/kg to effect, **or diazepam/ketamine** (2.5 mg/50 mg/mL of mixture @ 0.05 mL/kg increments to effect intubation, the dose will depend on the status of the patient) + maintenance **isoflurane.**
5. **Antibiotics.** In those instances where specimens can be collected (thoracotomy, transtracheal wash, bronchioalveolar lavage) empirical antibiotic therapy with ampicillin 20 mg/kg should be initiated after specimen collection and appropriate therapy can be instituted based on culture and sensitivity of submitted specimens. If sepsis suspected but unable to obtain specimens ampicillin should be instituted. See Pharmacology – Antibiotics for guidelines.
6. If perforation is suspected *see Part E Surgery p. 57*.

B. ENDOSCOPY

On occasion, small or minimally lodged objects can be retrieved using the flexible biopsy channel FB retrieval instruments. The majority of cases require a long rigid alligator forceps to be passed alongside the flexible endoscope to facilitate FB removal. If a fish hook is being removed, a flexible stomach tube should be placed into the esophagus and the endoscope passed through the stomach tube. The fish hook is brought into the stomach tube during retrieval preventing further damage to the esophagus. If the fish hook is fairly proximal, a rigid endoscope is utilized to protect the esophagus during removal. The fish hook usually penetrates the mucosa and sometimes the submucosa. Rigid equipment will have to be used to force the barb/tip of the hook out of the mucosa. A flexible stomach tube can be used to facilitate removal of other sharp objects or by slightly

dilating the esophagus to dislodge the object. Do not push a FB into the stomach unless it moves easily and the surface (not sharp or jagged) that is moving aborally will not cause further damage as it is pushed into the stomach. This is extremely important as the distal esophageal deviation at the gastroesophageal junction causes resistance to the passage of a FB.

C. Perform transtracheal wash (TTW) or broncho-alveolar lavage (BAL) where aspiration pneumonia is present to facilitate appropriate antibiotic therapy.

D. Radiographs +/- contrast should be taken post retrieval to evaluate for possible rupture during retrieval and to ensure that the FB was not acting as a plug over a site of perforation (resulting in negative findings prior to removal).

E. Surgery – Perform thoracotomy or laparotomy if the FB cannot be retrieved without excessive force. If the esophagus is perforated or lacerated before or during retrieval, surgical therapy MUST be considered. Small holes, tears or ulceration of the mucosa may heal with medical management.

F. Gastrostomy tube placement

Controversy exists as to whether food should be withheld, giving the esophagus a significant rest period, or whether to allow the passage of food of the largest diameter possible, to prevent stricture formation. At this time there are no studies to suggest one method is better than the other. At the Ontario Veterinary College (OVC) we allow the esophagus to rest. This period of rest is based on endoscopic examination. Dogs which present for acute ingestion and rapid removal of the FB can often eat within 12 hours. A recent unpublished study at the OVC indicates that gastric pH frequently remains greater than 4 in the non-fed state suggesting that fasting may not contribute to chemical esophagitis.

A gastrostomy tube may be placed percutaneously utilizing an endoscope (*see Nutritional Support p. 499*) or via left flank approach or laparotomy, at the time of FB removal. A gastrostomy tube is usually placed when: upon initial or follow up endoscopic examination, a prolonged recovery time is expected due to moderate to severe esophageal necrosis; a stricture is likely to develop; significant pain on swallowing is expected; and to allow for the administration of enteral medications while bypassing the esophagus. There is a risk for oral medications to exacerbate underlying esophagitis if their transit stops in the esophagus, leading to dissolution of the tablet at that site. If the lower esophageal sphincter is injured and unable to close, full distention of the stomach to facilitate safe PEG tube placement may not be possible, and a left flank approach is recommended.

G. Post-FB Removal Management
   1. **Oral Feeding.** Depending on the severity of the lesion, several small meals are gradually introduced. A slurry or soft meatballs are offered initially.
   2. **Gastroprotectants**
      a. **Famotidine** 0.5 mg/kg SC, PO q12h dogs/cats (*see Pharmacology p. 58*) OR omeprazole – approximately 1 mg/kg q12h in dogs (20 mg/dog if >20 kg, 10 mg if dog is >5 kg and <20 kg or 5 mg if <5 mg). Cats: 0.7 mg/kg PO q24h (*see Pharmacology p. 58*) OR pantoprazole 1 mg/kg to maximum 40 mg q12h.
      b. **Sucralfate Suspension** 1 g/10 mL – don't use tablets. **Dogs – 0.5 – 1 g q8h. Loading dose of 3 – 6 g** if severe concurrent gastrointestinal ulcer noted. **Cats – 0.25 – 0.5 g q8h.** Administer on an empty stomach 2 hours apart from other medication to avoid interference with absorption (*see Pharmacology p. 58*).
   3. **Prokinetics (increase lower esopohageal sphincter tone)**
      Metoclopramide: Dogs and Cats – 0.2 – 0.4 mg/kg PO or SC q6–8h or as a continuous intravenous infusion at 1 – 2 mg/kg/day. Cisapride may be used in addition to metoclopramide if required.
   4. **Antibiotics**
      a. **Aspiration pneumonia.** Ideally, antibiotics should be based on culture and sensitivity results from a TTW through a sterile endotracheal tube or BAL.

      Appropriate first line antibiotics would include combinations of:
         i. **Ampicillin** 20 – 40 mg/kg IV q6h (Dog & Cat) OR cephalexin 30 mg/kg IV q8h (Dog & Cat).
         ii. In severely ill or septic patients, ampicillin 20 – 40 (50 in neonates) mg/kg IV q6h + enrofloxacin 5 – 10 mg/kg IM, IV q24h. Do not exceed a 5 mg/kg q24h in cats. Do not use enrofloxacin in animals less than 8 – 10 months of age in large breeds; **aminoglycosides – gentamicin 6 mg/kg IV/SC q24h OR amikacin 20 mg/kg IV, SC q24h (Dog & Cat)** are appropriate alternatives

providing renal function is normal and normal hydration is maintained OR **clindamycin 10 mg/kg IV q12h (Dog & Cat) + enrofloxacin 5 – 10 mg/kg IV q24h (not to exceed 5 mg/kg/day in the cat).**

Extend therapy 2 weeks past resolution of radiographic evidence of pneumonia; aminoglycosides, however should be discontinued at or before 5 days.

   b. **Severe esophagitis. Ampicillin 20 – 40 mg/kg IV q6h (Dog & Cat)** if parenteral administration OR **amoxicillin 20 mg/kg PO q12h (Dog & Cat)** OR **amoxicillin-clavulanate Dogs 14 mg/kg PO q12h Cats 62.5 mg/kg PO q12h. Addition of clindamycin 10 mg/kg PO q12h (Dog & Cat)** may be required if slow to no improvement noted.

PHARMACOLOGY

1) **Famotidine (Pepcid®):** H2 receptor antagonist will help decrease the acidity within the stomach thus preventing acid reflux from further damaging the esophagus. Recent work at the OVC indicates that ranitidine may not be effective in raising gastric pH, therefore, famotidine is recommended.

2) **Omeprazole (Losec®)** is proton pump inhibitor which acts to decrease gastric acid secretion. Omeprazole is superior to the H2-receptor antagonists in the blockade of acid production and is the therapy of choice at OVC for esophagitis. The expense of this medication is outweighed by its effectiveness especially in the long term.

3) **Sucralfate (Sulcrate®)** is a aluminum complex of sucrose sulfate that in an acidic environment binds to the injured mucosal surface acting as a barrier against ongoing acidic injury. Sucralfate is also considered a cytoprotective agent. Conflicting evidence for the use of sucralfate for esophagitis exists. In theory, refluxed gastric sucralfate, activated by the acid in the stomach coats and protects the ulcerated lower esophageal mucosa. Human studies have shown that sucralfate is beneficial for reflux esophagitis. Note If interferes with dosing of more important medications such as antibiotics or prokinetics (below), rely on proton pump inhibitors or H2 blocking agents.

4) **Metoclopramide (Reglan®)** is a dopaminergic antagonist. It is advocated to tighten the lower esophageal sphincter and prevent gastroesophageal reflux.

5) **Cisapride** increases the release of acetylcholine at the myenteric plexus to stimulate gut motility. Superior to metoclopramide with respect to tightening the lower esophageal sphincter and enhancing gastric emptying. Parenteral formulations are not available and oral medication has to be obtained from a compounding pharmacy.

6) **Antibiotics:** Ampicillin, amoxicillin and amoxicillin-clavulanate have gram positive, gram negative and anaerobic coverage of common community acquired organisms; first generation cephalosporins cover both gram positive and negative organisms, none are effective against pseudomonas. Clindamycin covers gram positive and anaerobic organisms while the fluoroquinolones have primarily gram negative coverage including pseudomonas. Note: Clindamycin and Fluoroquinolones have been shown to reach substantially high levels within bronchial mucus in humans. The fluoroquinolones are not effective against streptococcal species including enterococcus.

SUGGESTED READING

1. Guilford WG, Strombeck DR: Diseases of Swallowing. In Guilford WG et al: Strombeck's Small Animal Gastroenterology 3rd ed. Philadelphia, WB Saunders, 1996:226-227.
2. Gualteiri M. Esophagoscopy. Vet. Clin. N Am 2001;31(4):605-630.

NOTES

INTRODUCTION

Gastric dilatation-volvulus (GDV) is a complex medical and surgical emergency. The frequency of occurrence has been reported at 2.4 to 7.6 per 1,000 canine hospital admissions. The etiology of GDV has not been fully elucidated. Delayed gastric emptying, pyloric obstruction, aerophagia and engorgement contribute to gastric dilatation (GD) with volvulus possibly occurring secondarily. Gastric volvulus can occur without prior dilatation. Splenic torsion has also been causally implicated as malposition of the spleen frequently occurs with GDV, however GDV can occur in splenectomized dogs. Cereal diets have been suggested as a cause for GD, yet studies have not been able to confirm this finding.

Recent studies in patients with GDV and surgical intervention, reported mortality rates as low as 15% to 18%. Of the non-survivors, postoperative mortality associated with gastric resection was 28% to 35%, splenectomy 32% to 38%, and cardiac arrhythmias present upon admission 38%. Cardiac arrhythmias developing postoperatively do not influence outcome. Blood lactate levels may be used in determining prognosis (*see Laboratory Evaluation below p. 60*).

Local and systemic effects of GDV occur to varying degrees. The sequelae of these events are hypotension, hypovolemia (blood loss, plasma loss, increased production and sequestration of gastric secretions), hypoxemia, acid-base and electrolyte abnormalities, sepsis, myocardial dysfunction and disseminated intravascular coagulation (DIC). A thorough examination is therefore required to identify the severity of illness. All patients with GDV require surgical correction as soon as possible, as medical management alone results in a 75% recurrence rate. This discussion will focus on the initial and postoperative treatment of the animal with GDV.

DIAGNOSIS

History/Signalment

The clinical signs vary with the extent of GD or GDV and may not parallel the degree of gastric or splenic injury.
- GDV typically occurs in large and giant-breeds of dogs, but rarely occurs in cats and smaller breeds of dogs. In smaller breeds, the Dachshund is over represented. Deep chested conformation may increase the susceptibility to GDV.
- The prevalence of GDV increases with increasing age with the greatest occurrence between seven to ten years of age.
- Question the owner regarding exercise after consuming a large meal.
- Is the dog receiving medications that may inhibit gastric motility?
- Is there a history of blunt abdominal trauma, or spinal cord injury?
- Stress such as boarding or hospitalization may be a predisposing cause.
- While in hospital, prolonged surgical procedures or prolonged recumbency may predispose dogs to GD.
- Rotating the patient for various procedures (e.g., radiographs) may also predispose to GDV.

Clinical Signs/Physical Examination

- Owners aware of the clinical signs associated with GDV may seek veterinary assistance at the onset of GD where the dog may be bright and alert, whereas dogs with more advanced disease may present moribund.
- Typically, dogs with GD or GDV have varying degrees of distension and tympani of the cranial abdomen. Early GD may not be detected on physical examination as the dilated stomach is contained within the ribcage.
- Hypersalivation and unproductive retching are common.
- These animals are restless, dyspneic or tachypneic.
- In the early stages of GD, tachycardia with strong pulses, normal capillary refill time (CRT) and mucous membrane (MM) colour may be noted.
- In animals with advanced GDV, weak, rapid pulses, possibly associated with pulse deficits are present; mucous membranes may be pale pink, pale to grey with prolonged CRT and petechiae may be present.
- Splenomegaly may be detected.
- Free abdominal fluid may be present as gastric ischemia progresses to necrosis with possible perforation and peritonitis. Avulsion of the short gastric and right gastroepiploic vessels cause intra-abdominal hemorrhage.

- With gastrointestinal mucosal injury and subsequent translocation of bacteria and endotoxins, the patient is predisposed to sepsis and septic shock (*p. 588*) and associated physical findings may be variable.
- Body temperature may be increased if sepsis is present, or below normal if the condition has progressed to hypovolemic shock .

Laboratory Evaluation/Diagnostic Imaging

Stat

- **Radiographic** examination is only necessary if the diagnosis is **equivocal,** or if after decompression surgical management may not be an option (differentiation of dilatation from volvulus will direct further management). The ability to pass an orogastric tube does not rule out the presence of volvulus. Fluid resuscitation should always be instituted prior to radiographic examination. A **single abdominal radiograph** with the animal in *right* **lateral recumbency** is usually diagnostic. When **volvulus** is present, the pylorus is visualized as a gas filled structure, dorsal and cranial to the gastric fundus ('double-bubble' or 'Popeye-Sign'). A compartmentalization line is frequently observed between the pylorus and fundus. This line represents the pyloric antral wall folding back and contacting the fundic wall. **Dilation alone** reveals a very large, round air-filled structure that may occupy most of the abdomen. **Free air** within the abdomen, usually visualized between the liver and diaphragm indicates gastric rupture or air leakage after gastrocentesis.
- **PCV and TS** are required to assess potential blood loss which may occur with avulsion of short gastric vessels.
- **ACT** will give a rapid evaluation of potential coagulopathy such as DIC.
- **Platelet count** is advised where the ACT is prolonged, where DIC is suspected (including sepsis).
- **Stick BUN, serum creatinine or urea** are frequently increased due to hypovolemia/hypotension.
- **Blood glucose** may be increased due to stress but decreased in sepsis.
- **Venous blood gases or total serum CO_2** should be obtained to assist with evaluation and fluid selection. The most common acid-base abnormality in animals with GDV is non-respiratory (metabolic) acidosis. In the early stages, patients are frequently alkalemic but eventually become acidemic as the disease advances and perfusion is compromised (mixed metabolic disturbance) (*see Acid-Base Assessment p. 406*).
- **Lactate** is frequently increased (>2.5mmol/L) in the advanced stages where perfusion is compromised. Plasma lactate concentrations are a useful indicator of gastric necrosis. In one study, 71% of dogs with lactate values ≥6.0 mmol/L had gastric necrosis compared to only 21% with values <6 mmol/L that had gastric necrosis. In this study a lactate value of <5 mmol/L had a 96% survival rate. Values >5 mmol/L had a 71% survival rate. Gastric necrosis is an indicator of duration of torsion and subsequently reduced perfusion.
- **Serum electrolytes** are frequently abnormal, especially potassium, which tends to be low. Sodium and chloride are variable depending on the volume of gastric secretion, peritonitis and dehydration.
- **ECG** monitoring is essential. Ventricular arrhythmias are the most common arrhythmia caused by reduced perfusion of the myocardium, release of myocardial depressant factor due to compromised gastrointestinal tract, pancreas, and/or splenic pathology (thrombosed vessels/infarcts).
- **Systemic arterial blood pressure** (SBP) measurement is essential as compression of the caudal vena cava and portal vein result in decreased venous return to the heart with subsequent reduction in cardiac output and hypotension.

Extended Laboratory Data Base

- **CBC** is suggested (usually post-op) as a baseline. Red cells are reduced if hemorrhage has occurred. The white blood cell count may be increased or decreased reflecting the severity of illness (determined during surgery). **Thrombocytopenia** occurs secondary to consumption if **hemorrhage** has occurred, or with **DIC** (*p. 417*) splenic pathology (infarcts), ischemia/necrosis of the stomach or intestine, or both.
- **Biochemical profile** is required as a baseline and to identify organ dysfunction (pancreas, liver, kidney) and electrolyte disturbances. Abnormalities may reflect changes associated with GDV, shock or pre-existing disease.

MANAGEMENT

I. INITIAL TREATMENT

Based on clinical signs and the consequences of the known pathophysiologic events. The primary objectives are to: (1) prevent or reverse circulatory collapse (fluid and colloid resuscitation), (2) prevent or reduce the local and systemic events associated with GD or GDV by removing the inciting cause (gastric decompression and lavage), (3) treat associated complications (electrolyte and acid-base abnormalities, pain, cardiac arrhythmias, sepsis) and, (4) prepare the animal for surgical treatment.

A. For the rare case that is presented with **dilation alone and without evidence of circulatory compromise** (vital signs within normal range), orogastric decompression is the initial treatment (*see O below p. 63*). These animals are bright and alert and the stomach is usually within the ribcage.

B. The **typical patient with GDV,** circulatory compromise or collapse is present and reversal of the shock state should be addressed **prior** to gastric decompression.

C. Gastrocentesis (*see Gastric Decompression O below p. 63*) **should be performed immediately in patients with severe gastric distension and incipient cardiopulmonary arrest.** Gastrocentesis is recommended in these situations to avoid the stress, and difficulty, of orogastric intubation. Decompress to improve ventilation. Complete decompression **must be avoided** until rapid fluid resuscitation is well underway.

D. **Oxygen** by flow-by for respiratory compromised patients.

E. Place a 14 or 16 gauge, 2" to 4" catheter into the jugular or cephalic vein(s); **not** saphenous. The saphenous vein may be used temporarily while a cutdown (*p. 609*) onto the jugular or cephalic vein is performed.

F. **Fluid therapy.** Caution is used when delivering fluids rapidly to **geriatric patients and those with cardiac disease** (not arrhythmias unless severe).

   1. In **dehydrated patients** with MAP <60 mmHg or systolic pressure <90 mmHg, commence fluids at 20 mL/kg bolus crystalloid (Plasma-Lyte® 148, or A, Normosol®, or lactated Ringer's), under pressure and assess in 5 min. Repeat. If no clinical improvement, add colloid (pentastarch, hetastarch, or Dextran-70) in boluses of 5 mL/kg in dogs and 2.5 mL/kg in cats to a maximum of 20 mL/kg (dogs) and 10 mL/kg (cats). Otherwise, continue crystalloid at 1.5 mL/kg/min (90 mL/kg/h dog), 1.0 mL/kg/min (60 mL/kg/h cat) with subsequent adjustment to effect. Continue to monitor q5min. The total volume of synthetic colloid should not be given in less that 15 min as rapid administration may induce vomiting. Reduce rate of infusion by 25% as pressures rise. If pressures continue to rise, reduce by a further 25%. If pressures continue to be inadequate *see H below p. 62* and if PVC/TS are inadequate *see I below p. 62*.

   2. If **not dehydrated** and MAP <60 mmHg or systolic pressure <90 mm Hg, bolus with 20 mL/kg crystalloid (Plasma-Lyte® 148, or A, Normosol®, or lactated Ringer's), under pressure , then assess q5min. If **"dying before your eyes"**, give **hypertonic saline** at **1 mL/kg/min: 5%** (dogs: 6 – 10 mL/kg) or **7.5%** (dogs: 4 – 8 mL/kg), one-quarter the dose for **cats.** Do not administer more rapidly as respiratory arrest and/ or vagoreflex bradycardia may occur (which can be treated with 0.02 mg/kg atropine). Follow with an IV bolus of pentastarch, hetastarch or Dextran-70, **5 mL/kg in dogs and 2.5 mL/kg in cats,** repeat as required to a maximum of 20 mL/kg (dogs) and 10 mL/kg (cats). Alternatively, a hemoglobin-based oxygen carrying solution (HBOCS) may be administered. This product will also increase SBP (*see Hemorrhage p. 619 for guidelines*). Continue with crystalloids, with adjustment to effect, to complete the resuscitation. Blood pressure, vital signs and mentation should be assessed q5min. Reduce infusion by 25% as pressures rise; if pressures continue to rise decrease by a further 25% and *see H below p. 62*. Measure PCV/TS (*see I below p. 62*). If pressures are inadequate, *see H below p. 62*.

   3. If **alkalemic,** administer 0.9% sodium chloride at a rate appropriate for the clinical findings. These patients are usually relatively stable.

   4. If **PCV <25%,** transfusion of packed red blood cells OR whole blood is required. If **PCV <25% and TS <40 g/L,** whole blood transfusion is required (*see Transfusion Therapy p. 671*). Alternatively, a HBOCS may be administered (*see Hemorrhage p. 619 for guidelines*). If **TS <40 g/L** prior to fluid resuscitation, plasma may be required as TS will drop significantly after resuscitation.

G. Potassium-supplemented fluids should be delivered through an IV line separate from the rapid infusion of crystalloids. The former should be administered at 30 – 80 mEq/L, delivered at a maintenance fluid rate when serum potassium concentrations are 3.5 mEq/L to <2.0 mEq/L, respectively. If the animal is acidemic, the serum potassium concentration may decrease during resuscitation with alkalinizing solutions. This possibility should be anticipated, assessed, and addressed by an increase in the rate of potassium infusion. Potassium infusions can be delivered at a maximal rate of between 0.5 – 1.0 mEq/kg/h when: serum potassium levels are <3.0 mEq/L, ventricular arrhythmias are present, and continuous/serial ECG and serum potassium monitoring q2h are possible.

H. If hypotension persists after adequate fluid resuscitation (*review as in Fluid Therapy p. 347*), try the following:

1. **Dopamine 5 μg/kg/min (cats and dogs)** and increase by 1 μg/kg/min every 2 – 3 min (max 15 μg/kg/min) until target blood pressure (MAP 80 – 100 or systolic 100 – 120 mmHg) is reached. (*see Dopamine Infusion Chart p. 233*). Stop if tachycardia develops and then re-introduce at a lower rate. If vasopressor effects are inadequate, try
2. **Norepinephrine 0.1 – 0.5 μg/kg/min** (*see Norepinephrine Infusion chart p. 253*).

I. PCV and TS must be monitored q15 min with high volume, high rate crystalloids and synthetic colloid administration if hemorrhage is suspected. If TS <50 g/L prior to fluid resuscitation, plasma will be required as TS will drop significantly after resuscitation. If **TS <40 g/L** at any time, plasma transfusion will be required. If PCV <25%, transfusion of packed red blood cells OR whole blood is required. If **PCV <25% and TS <40 g/L**, whole blood transfusion is required (*see Transfusion Therapy p. 671*).

J. Analgesics should be administered as soon as possible in the alert patient, and as the patient responds to resuscitation in the hypotensive depressed patient.

1. **Hydromorphone 0.025 – 0.1 mg/kg IV** titrate to effect to reduce nausea with overdose
2. **Fentanyl 4 – 6 mg/kg IV q30 min** or CRI
3. **Morphine 0.2 – 0.3 mg/kg IV (over 3 – 5 min)** to avoid hypotension
4. **Methadone 0.2 – 0.3 mg/kg IV** titrate to effect
5. **Butorphanol 0.2 – 0.4 mg/g IV** for mild discomfort or sedation

K. Antibiotic therapy is directed towards potential pathogens associated with inadequate splanchnic perfusion. This author administers **cefoxitin or cefotetan 30 mg/kg IV** (**ampicillin** using the same regimen is an alternative) assuming bacterial translocation may have occurred, or will during reperfusion and surgical correction. Continue at 20 mg/kg q6h IV (dogs), q8h (cats).

L. Ventricular arrhythmias (*p. 179*) may improve after circulatory resuscitation and gastric decompression. Prior to and during surgery, treatment is advised if the arrhythmia is sustained, paroxysmal or polymorphic at an instantaneous rate ≥130/min, when pre-existing cardiac disease is present, with R on T phenomenon or when Torsades de Pointe is observed on ECG (see reduction in rate to 120/min and a reduction in abnormal complex morphology).

1. **Lidocaine 2 mg/kg IV bolus.** If the initial bolus is not effective within 2 – 3 minutes, repeat.
2. **Lidocaine 30 – 80 μg/kg/min CRI** if the arrhythmia is lidocaine-responsive. Failure of the rhythm to improve with lidocaine administration requires re-assessment of the ECG diagnosis and overall status of the patient (e.g., electrolyte, acid-base, pain) with consideration of alternative antiarrhythmic therapy. Do not expect to totally abolish the arrhythmia (*see Ventricular Arryhthmias p. 179*).
3. **Procainamide 6 – 10 mg/kg (rarely up to 20 mg/kg) IV by 2 mg/kg increments every 5 minutes** (to avoid hypotension) should be administered if there is uncertainty as to whether the arrhythmia is ventricular or supraventricular in origin, or the ventricular arrhythmia is not lidocaine-responsive. Continue with
4. **Procainamide 6 – 15 mg/kg IM q 6 h or IV CRI 25 – 40 μg/kg/min** if (3 above) is effective.
5. **20% magnesium sulfate solution 0.15 – 0.3 mEq/kg (30 – 40) CRI over 2 – 4 hour q8h,** may enhance the treatment response of patients with ventricular arrhythmias OR **for life-threatening arrhythmia,** administer over 15 – 20 min. Reduce in patients with renal insufficiency.

M. Sinus tachycardia frequently resolves with resuscitative treatment and analgesic support. If sinus tachycardia persists, consider: hypotension, hypovolemia (i.e. if not hypotensive the patient may be compensating, thereby requiring continuation of resuscitative treatment), hypoxemia, anemia, hypercarbia, inadequate control of pain, gastric perforation, splenic infarction or other major organ complication requiring immediate exploratory laparotomy.

N. **Other medication.** Corticosteroids are not recommended. Non-steroidal anti-inflammatory analgesics are not recommended. **Deferoxamine** (Desferal, Ciba-Geigy Pharmaceutical Inc.) 50 mg/kg slowly IV, administered 10 minutes before gastric decompression, has shown promise in prevention of reperfusion injury when administered to dogs with experimentally-induced GDV, however, hypotension may result.

O. **Gastric decompression.** After resuscitative fluid administration, gastric decompression is initiated. Administer an analgesic (*Initial Treatment* [J] *p. 62 above*). The addition of **diazepam 0.2 – 0.5 mg/kg IV** can be used concomitantly if needed, in non-compliant dogs, prior to decompression. If surgical correction is planned, a pure mu agonist (J *1 – 4 above p.* 62), is preferred as the inhalant anesthetic requirements are reduced, there is a greater analgesic and sedative effect that facilitates pre-operative tracheal intubation.

   1. **Tube decompression:** Place the dog in sternal or lateral recumbency or in an upright sitting position. A large bore tube is pre-measured from the chin to the xiphoid and the distance is marked on the tube with tape. The tube is lubricated with water soluble jelly and passed through an oral speculum (or 2" roll of tape), carefully through the esophagus and into the stomach (the mark on the tube is at the level of the incisor teeth). Rupture of compromised areas of the lower esophagus or stomach can occur if excessive force is used in orogastric entubation. If resistance to passage of the orogastric tube is experienced, gently rotate the tube while re-attempting passage or change the position of the dog to facilitate passage.

   2. **Gastrocentesis** should be performed in patients where attempts at orogastric intubation have been unsuccessful and delay in partial decompression with further repositioning will be detrimental to the patient. A 10 x 10 cm area is aseptically prepared caudal to the *right* **costal arch.** The area is percussed to identify the tympanic stomach and to avoid needle puncture of the spleen (non-tympanic sound). An 18 gauge needle or needle-styleted catheter is placed through the abdominal wall into the lumen of the stomach to allow gas to escape. Slight upward pressure from the 'down' (left) side will press the stomach towards the left abdominal wall maintaining the needle in the lumen of the stomach. Orogastric decompression should be repeated after gastrocentesis as release of pressure on the cardia usually facilitates passage of the tube.

   3. **Lavage** the stomach with warm tap water to remove residual food. The absence of blood or coffee ground material in the lavage fluid does not rule out the presence of gastric necrosis. The tube should be 'kinked' prior to and during removal.

P. **If surgical correction cannot be performed immediately,** decompression may be maintained by placement of a weighted nasogastric tube with stylet (EN-tube, Entech Inc. Lebanon, NJ), or temporary gastrostomy. Intermittent orogastric intubation is not recommended as this procedure is stressful and iatrogenic gastric rupture is a potential concern with repeated orogastric tube placement. The indications for maintaining temporary gastric decompression in these patients include: 1) maintenance of gastric decompression for patient transportation to a referral facility and, 2) unavailability of immediate surgical intervention at the site.

Q. **Temporary gastrostomy.** Preparation for placement of a temporary gastrostomy is as described for gastrocentesis. A pure mu agaonist (*see Initial Treatment p. 62* **J** *above*) is administered. Anesthesia of the area to be incised can be obtained by infiltration of 4 – 6 mL 1% lidocaine, through the skin, subcutaneous and muscle layers including the peritoneum, in an inverted 'L' pattern. A 6 cm incision is made through the skin and the approach to the peritoneum is made through muscle separation. The peritoneum is incised with caution as the stomach is adjacent to it. A circumferential, simple continuous suture pattern is placed through the skin, abdominal wall, serosa and muscularis of the stomach. The stomach is then incised. Gastric emptying and lavage is then performed. Any temporary gastrostomy is closed and locally irrigated during the subsequent surgical approach for definitive surgical correction.

II. SURGICAL TREATMENT

In general, the recommendation would be for definitive surgical correction for GDV within 1 – 2 hours after presentation in the majority of cases. Early intervention, after an initial period of circulatory resuscitation, has been shown to reduce post-operative fatality rates. The disadvantages of postponing surgical intervention are:

   i. the increased prevalence of cardiac arrhythmias at 12 – 72 hours,
   ii. an increased risk of splenic and gastric infarction due to continuing malposition, and
   iii. the increasing risk with time of gastric perforation, with consequent peritonitis.

Various **techniques** are described in readings 4 and 5 below. The permanent incisional gastropexy technique is fast and not technically challenging. An incision is made into the peritoneum and internal fascia of the rectus abdominus or

transverse abdominal muscles located in the right ventrolateral abdominal wall. An incision is then made into the serosal and muscularis layers of the pyloric antrum. The edges of the gastric incision are sutured to the abdominal incision using a simple continuous suture pattern. The deeper (dorsocranial incisional) margins are sutured first followed by the more superficial margin. If there is a concern that pancreatitis or any other potential cause for extended (>36 hours) restriction of oral food intake is anticipated, a jejunostomy tube should be placed for nutritional support.

III. POSTOPERATIVE MANAGEMENT

Complications to be anticipated in patients after surgical correction of GDV include: cardiac arrhythmias, fluid overload, gastroparesis and ileus, vomiting, pancreatitis, DIC, gastric and incisional dehiscence, gastric ulceration, ischemic necrosis of stomach, spleen or gallbladder with peritonitis; incarceration of small bowel dorsal to the gastropexy site or the development of acute renal failure. The intensity of postoperative care will vary depending on the severity of illness and surgical intervention.

A. **During the first 24 hours** postoperatively, monitoring orders on the flow sheet in all patients until stable, should ideally include:

1. intermittent or continuous ECG (*see C below*)
2. hemodynamic monitoring (goal – MAP >70 mmHg, systolic pressure >110 mmHg, CVP 3 – 5 cm H_2O) q1– 4h (*see E below p. 65*)
3. mucous membrane colour (pink) and CRT (1 – 2 sec)
4. pain assessment and hydromorphone 0.05 – 0.2 mg /kg q4h, OR CRI fentanyl 3 – 5 μg/kg/h or morphine 0.2 – 3 mg/kg/h [*see Morphine Infusion chart p. 251*] all titrated to effect
5. measurement of urine output (1 – 2 mL/kg/h) q1–2h
6. assessment of serum electrolytes (normal limits, with K^+ to 5.5 mmol/L) (*see B below*)
7. venous blood gases for acid-base assessment (venous pH 7.3 – 7.4, [HCO_3^-] 18 – 24 mmol/L, base excess ±4) q4–6h (*see Acid-Base Assessment p. 406*)
8. venous blood lactate (*see Lactate p. 400*)
9. PCV q4–12h depending on previous result
10. ACT q12h (*see F below p. 65*)
11. blood glucose q6–12h depending on previous result (*see Hypoglycemia p. 280*)
12. daily assessment of serum magnesium (*see B below*) creatinine and albumin (*see D3 below p. 65*)
13. daily CBC, where patient is not improving or deteriorating

B. **Serum electrolytes.** The major electrolyte disturbance is hypokalemia. Hypokalemia potentiates cardiac arrhythmias and hypokalemia is potentiated by hypomagnesemia. Hypokalemia also exacerbates ileus.

1. In severely hypokalemic patients, **potassium supplementation** in intravenous fluids may exceed **80 mEq/L** even though crystalloids are being delivered at twice to three times the normal requirement for maintenance (*see Hypokalemia p. 394* for guidelines).
2. **Magnesium sulfate 20% 0.25 mEq/kg (30 mg/kg) IV, CRI divided over 4 hours** repeated for three times in 24h, or 1.0 mEq/kg/day (125 mg/kg/day) IV, CRI (*see Magnesium p. 403*).
3. Serum potassium levels require frequent monitoring during potassium and magnesium infusions. Magnesium is excreted via the kidney, therefore a reduced dosing is recommended in renal insufficiency.

C. **Cardiac arrhythmias/dysrhythmia**

1. **Sinus tachycardia** should not be present postoperatively. Sinus tachycardia in these patients often represents a physiologic response to heart failure, hypovolemia, pain, hypoxia, anemia, hypotension, sepsis and other potential problems previously mentioned in the section on Initial Treatment. These primary abnormalities should be identified and treated.
2. If **supraventricular tachyarrhythmia** has been identified, appropriate antiarrhythmic therapy is administered based on the specific rhythm problem (*see Supraventricular Tachycardia p. 170*).
3. **Ventricular tachyarrhythmias** are the most common and may be due to conditions in (1) above, or will continue for up to 72 hours after the initial event (GDV, GD). Treat as described Initial Treatment (L) *p. 62* or refer to *Ventricular Tachycardia p. 179* for further guidelines.
4. **Pain** will contribute to arrhythmias. Analgesics must be administered (*see Initial Treatment J above p. 62*), until the patient is pain-free (*see Assessment of Pain p. 117*), usually 48 – 72 hours for uncomplicated cases.

D. **Isotonic crystalloid fluids and synthetic colloids.** Administer:

1. **Crystalloids** at a rate to maintain normal hydration, acid-base status and urine output (*see Fluid Therapy p. 347 for guidelines*).
2. **Synthetic colloids 20 mL/kg/day** CRI, should be administered when large volume crystalloids (~>4 mL/kg/h) are required to maintain MAP >70 mm Hg, systolic arterial BP >110 mm Hg and urine output >1 mL/kg/h, or to prevent the development of interstitial or pulmonary edema in patients with decreased TS or oncotic pressure.
3. **A natural colloid, such as fresh frozen plasma,** is recommended for patients with TS<45 g/L (4.5 g/dL). **25% Human Serum Albumin (Plasbumin®, Bayer)** may benefit patients with albumin <15 g/L (1.5 g/dL) or capillary leak and hypotension.

E. If **hypotension persists** after adequate fluid resuscitation (*review as in Fluid Therapy p. 347*), try the following:

1. **Dopamine 5 μg/kg/min (cats and dogs)** and increase by 1 μg/kg/min every 2 – 3 min (max 15 μg/kg/min) until target blood pressure (MAP 80 – 100 or systolic 100 – 120 mmHg) is reached. (*see Dopamine Infusion Chart p. 233*). Stop if tachycardia develops and then re-introduce at a lower rate. If vasopressor effects are inadequate, try
2. **Norepinephrine 0.1 – 0.5 μg/kg/min** (*see Norepinephrine Infusion Chart p. 253*)

F. **DIC** should be assumed to be present where gastric or splenic necrosis are apparent at surgical correction. Gastric necrosis has been associated with abnormal hemostatic profiles.

1. **The continued "bedside" assessment** (normal in brackets) of these cases beyond 24 hours includes serial assessment of :
   a. **ACT** (heat block or axilla method [*see DIC p. 417*] for guidelines) (70 – 120 seconds)
   b. **PCV** (25% – 45%), **TS** (45 – 70 g/L)
   c. **platelet count** (>100 x 10⁹/L)
   d. **physical examination** (incisional oozing, petecchial hemorrhages, mucous membrane colour, and deterioration in attitude).
2. **Management**
   a. **surgical treatment** should be considered if abnormalities in 1 – 4 above persist as progression of splenic or gastric necrosis (± rupture), or other lesion may exist.
   b. **fresh frozen plasma** (*see Transfusion Therapy p. 667*) 20 mL/kg, repeated if needed.
   c. **heparin** therapy is not routinely recommended, however if thrombosis is a concern the current suggestions are **100 – 150 units/kg SC q8h OR** a CRI of **12 – 15 U/kg/h** although a dosing regimen is not established. The CRI is recommended when jugular catheters are in use. Monitor PTT or ACT before each SC heparin dose, or twice daily with the CRI. The goal of heparin therapy is to achieve a PTT or ACT of 1.5 – 2 times normal prior to the next dose. At OVC, normal ACT (human axillary incubation) is 75 – 120 sec and the target value with heparin therapy is 150 – 180 sec.

G. **Antibiotic therapy,**
   a. as recommended in Initial Treatment (K), should be continued intravenously for 72 hours in patients requiring gastric resection or when gastric mucosal injury is highly suspect.
   b. should deterioration occur, discontinue the cefoxitin and change to
      i. clindamycin 10 mg/kg IV q12h plus enrofloxacin 5 mg/kg IV q24h, OR
      ii. imipenem 5 – 10 mg/kg q8h IV 1 – h infusion, OR
      iii. meropenem 20 mg/kg IV q12h, or 8 mg/kg SC q12h.
   c. patients with simple GD or GDV without notable mucosal injury **do not** require continuation of antibiotic therapy beyond the immediate postoperative period.

H. **Gastric atony and ileus** is frequently present postoperatively, which predisposes to recurrence of GD and vomiting. Ensure the patient is normokalemic to within the high end of the normal range.
   a. Maintenance of **gastric decompression** may require placement of a nasogastric tube if a gastrostomy tube is not in place,
   b. **Metoclopromide 0.2 – 0.5 mg/kg q8h SC, OR 1 – 2 mg/kg/day** IV, CRI is recommended as a promotility drug to enhance gastric emptying and as an antiemetic.
   c. To enhance **gastric mucosal healing,** reduce the possibility of gastric ulceration with hemorrhage, and to prevent esophageal stricture secondary to reflux esophagitis, the following are recommended:

      i. famotidine 0.5 mg/kg IV q12h OR

      ii. omeprazole 0.7 mg/kg PO q24h OR

      iii. pantoprazole 1 mg/kg max 30 mg total over 15 min q24h, IV AND

      iv. sucralfate suspension 5 mL/dog PO q8h.

      v. **Ranitidine 0.5 mg/kg IV q12h is ineffective** in raising gastric pH in dogs, however it may enhance gastrointestinal motility.

    d. antiemetics for refractory vomiting (*see Vomiting p. 79 for recommendations*).

I. Nutrition.

  1. In most patients with uncomplicated surgical correction of GDV or GD, water should be offered at 12 hours, postoperatively and a low-fat, good quality protein canned dog food slurry should be offered after if the patient is alert and not vomiting. Oral feeding to those patients with gastric resection should be started at the discretion of the surgeon based on the extent of, or surgical complications associated with, the resection and the presence or absence of a jejunostomy feeding tube.

  2. If a jejunostomy feeding tube is in place, a CRI of an electrolyte solution with 5% dextrose (Plasma-Lyte® 56 with 5% dextrose, Baxter) delivered at 0.5 mL/kg via the tube for the initial 12 hours postoperatively. If this is tolerated by the patient, the addition of a prepared liquid diet (Canine Clinicare®, PetAg) at one-half the daily, non-protein, caloric requirements (*see Nutrition p. 499*) diluted 50:50 with the aforementioned crystalloid solution is delivered at 1 mL/kg/h for the subsequent 24 hours. If no signs of discomfort or nausea are noted after this 24 hour infusion, the infusion should be increased to meet full nutritional requirements. Peripheral intravenous fluid therapy should be reduced by the appropriate amount once oral intake occurs or enteral nutritional support is instituted. The duration of jejunostomy feeding is individualized to each patient.

  3. Parenteral nutritional support is recommended for those patients unable to eat or drink, or receive enteral nutrition for >36 hours, postoperatively. Partial peripheral parenteral nutrition (amino acids + lipids *see Nutritional Support p. 499* for guidelines) is frequently administered to these patients in our hospital. The hourly rate of administration for crystalloid fluid support should be reduced by an amount equal to that delivered via PPN to avoid overhydration.

J. The length of hospital stay will depend on the severity of illness but is expected to be 2 – 7 days.

K. Advice to owners

  **1. **All dogs recovered from GDV or GD should be fed a good quality canned dog food, in small amounts (based on their normal daily nutritional requirements *p. 499*) 4 or 5 times daily initially, and no less than 3 times daily in the future, to avoid engorgement.

  **2. **Exercise after eating should be avoided.

  **3. **Owners should be made aware that gastropexy is not a guarantee against future episodes of GD or GDV in the patient.

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INTRODUCTION

There are several causes of gastrointestinal (GI) hemorrhage. Gastroduodenal erosions and ulceration are major causes of hemorrhage. 'Stress' ulcers/erosions are associated with the triad of trauma, hypovolemia and surgery, with non-steroidal antiinflammatory analgesics (NSAIAs) administration, and with high doses of corticosteroids, especially dexamethasone. Other less common causes of ulceration/erosion are mast cell tumours, neurological injury (head and spinal injuries, intervertebral disc disease), as well as renal and hepatic disease, *Helicobacter*-associated gastric disease and gastrinoma. Hemorrhage may also be due to an adenocarcinoma, lymphoma and coagulopathies. This chapter will deal primarily with acute gastric hemorrhage, and ulcer therapy and prophylaxis for acute situations. Dogs with hemorrhagic gastroenteritis may appear to have significant blood loss through the feces; however, these animals tend to be hypoproteinemic and potentially polycythemic.

DIAGNOSIS

History/Signalment

- Dogs are more prone to GI ulceration/erosion than cats.
- Owners should be questioned regarding NSAIA or glucocorticoid administration and other pertinent information associated with the above causes of GI ulceration.
- Patients recovering from recent trauma and/or surgery (within 48 – 96h post-operatively) in the hospital are prime candidates for 'stress' GI erosion and ulceration.
- Question the owner regarding stool colour and potential rodenticide toxicity.
- Inappetance and weight loss over time might indicate neoplasia.

Clinical Signs/Physical Examination

- There can be a range of clinical signs and physical findings, such as, peracute collapse, hematemesis, poor pulse pressure, pale mucous membranes, prolonged capillary refill time, tachycardia and tachypnea, altered mentation (hemorrhagic shock) to intermittent vomiting and melenic stool.
- The vomitus may or may not contain 'coffee ground' material or blood.
- Cachexia or some weight loss and edema, due to inappetance and hypoproteinemia, respectively, may be evident in chronic disease.
- Pain and nausea may be induced upon palpation of the cranial abdomen.
- Peritonitis secondary to perforation of a gastroduodenal ulcer may be localized or generalized with physical findings ranging from minor pain to abdominal effusion and septic shock.
- Petechial hemorrhages may be noted in a patient with thrombocytopenia/thrombopathia.
- Hemorrhage elsewhere might suggest a coagulopathy.
- Cutaneous or subcutaneous nodules/masses (mast cell tumours) may be an indication of associated GI ulceration.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV** & **TS** to assess degree of blood loss.
- **Stick BUN**, urea or creatinine to assess pre-renal azotemia or primary renal disease if ulceration associated with NSAIA use. The BUN will be increased with intestinal bleeding, therefore the BUN will not discriminate this from renal failure/insufficiency; however it is a quick screening test if negative. Assess urine specific gravity.
- **ACT** to assess presence of coagulopathy, which is prolonged in rodenticide toxicity and DIC.
- **Platelet count** to rule out thrombocytopenia as a cause for hemorrhage (e.g., immune-mediated thrombocytopenia or DIC).
- **Serum electrolytes** and **blood lactate** to assess status and guide fluid therapy.
- **Venous blood gases** to assess perfusion status (acidemia), or if alkalemic may indicate gastrinoma or mast cell tumour.
- **Blood pressure** to evaluate severity of hemorrhage and as a guide for volume replacement therapy.
- **ECG** monitoring to rule out arrhythmias potentially associated with hypovolemia and inadequate myocardial perfusion.
- **Abdominocentesis** (cytology, culture and sensitivity) if abdominal fluid is detected.
- **Abdominal radiographs** and/or ultrasonographic examination where indicated from physical examination and history.
- **Fine needle aspiration** and **cytology** of cutaneous masses may reveal mast cell tumour.

Extended Data Base

- **CBC** to rule out thrombocytopenia, leukocytosis or leukopenia (sepsis), and assess severity of anemia and whether anemia is regenerative responsive (indication of duration of hemorrhage as ~5 days required for a regenerative response).
- **Serum biochemical profile** as a baseline and to identify associated co-morbid conditions or potential cause of hemorrhage (Renal Failure [*p. 709*] or Hepatic Failure [*p. 37*]).
- Relevant tests, based on stat laboratory data and physical findings, to definitively diagnose any of the above etiologies for hemorrhage.
- **Endoscopy** may be necessary with massive hemorrhage as arterial bleeding may require surgical correction. Diffuse 'oozing' is managed medically.

MANAGEMENT

A. For shock (hemorrhagic or septic, *see Shock p. 603*). Place a large bore IV catheter, and obtain blood samples for above tests.

    1. **Commence IV fluids** (Plasma-Lyte® 148, Normosol® M, lactated Ringer's) at 90 – 120 mL/kg/h = 1.5 – 2 mL/kg/min (dog); 45 – 60 mL/kg/h = 0.75 – 1.0 mL/kg/min (cat), reassess q5min. [For blood loss *see B below*].

    2. Synthetic colloid 5 mL/kg IV push (dog); 2.5 mL/kg over 5 min (cat) if poorly responsive to crystalloids. [For blood loss *see B below*]. Reasses and repeat if necessary.

B. **If shock** due to acute gastric or duodenal hemorrhage (severe hemorrhage with history of NSAIA, corticosteroid use or trauma, hypovolemia, surgery, PCV< 25):

    1. Whole blood transfusion is necessary. While administering crystalloids, commence blood transfusion at a rate up to 20 mL/kg over 30 – 60 min to raise blood pressure to mean of 60 – 70 mmHg, or systolic 90 – 100 mmHg. Then reduce the transfusion until PCV of 25 achieved. Do not raise pressures above those recommended as further hemorrhage will occur (*see Hemorrhage p. 619* for severe, moderate and mild hemorrhage). Reasses as hemorrhage may continue.

    2. Note signs of reaction (facial swelling, nausea, shivering, increase or decrease in temperature [*see Transfusion Therapy p. 667*]) and slow down the infusion.

    3. **Hemorrhaging ulcer** (without perforation) therapy. Administer **sucralfate 1 – 2 g** (1 or 2 tablets pulverized with water or preferably, **5 – 10 mL suspension**)/dog; **0.5 g** (5 mL suspension) **per cat** PO as soon as possible. Repeat at half the dose q1h for 3 treatments, tapering off to q4h then q8h for 7 days. There are NO concerns for overdose. Sucralfate may cause constipation and in rare occasions, hypophosphatemia.

C. Administer **famotidine 0.5 mg/kg IV (slowly and diluted) q12h** initially (cat & dog), or **pantoprazole 1 mg/kg (max 30 mg) over 30 min q12h.** If able to take oral medication, **omeprazole 0.7 mg/kg q12h** dog and cat is another alternative. However with sucralfate treatment other oral medication should not be administered within 2h of sucralfate administration, conversely, sucralfate should not be administered within at least 1 hour (2 preferred) of other oral medications.

D. **Monitor blood pressure,** pulses, heart rate, respiratory rate, CRT and mucous membrane colour q 5 min. Note return or improvement in peripheral pulses, an improvement in CRT and mucous membrane colour, an increased level of consciousness or improved response to the caregiver. Heart rate may decrease. The fluid rate should be reduced to one-half of that being administered at this point (for hemorrhage) and reduced by one-quarter in septic cases depending on tolerance of fluid rate and volume and blood pressures achieved. Continue to monitor and adjust fluid/colloid administration to maintain patient stability.

E. **Monitor PCV and TS q15–30min.** Consider packed cells or whole blood when PCV decreases to <25% or plasma or whole blood if TS <35 g/L.

F. **If septic, cefoxitin 20 mg/kg IV q6h** for antimicrobial therapy. An alternative is **ampicillin 20 mg/kg IV q6h** combined with **enrofloxacin 5 mg/kg IV q24h** in septic shock. Collect samples for culture and sensitivity prior to administration. Definitive antibiotic therapy should be used based on final assessment of laboratory and physical findings. Antibiotics are not recommended for gastric hemorrhage without sepsis.

G. **Discontinue all ulcer-causing medication** in all patients presenting with GI signs. For those with mild signs (stable, normal laboratory evaluation with or without small amount of 'coffee ground' material or flecks of blood in the vomitus and mild evidence of melena, go to (I) below.

H. **Emergency laparotomy** may be required for correction of gastric hemorrhage should an arterial bleed be located at endoscopy, or perforation be diagnosed.

I. **Prophylactic/treatment for ulcer therapy** is advised when NSAIAs are being administered after trauma and surgery in any dog, geriatric and other ulcer prone individuals (*see Non-steroidal anti-inflammatory analgesics in Analgesics & Sedatives p. 88*). **Sucralfate 0.5 – 1.0 g q8h,** for duration of NSAIA treatment in the hospital is recommended if **there is evidence** of erosions or ulceration ('coffee grounds' present in vomitus or regurgitated fluid). Although misoprostol 2 – 5 μg/kg q12h is recommended with NSAIA use, it will not necessarily prevent ulceration in all cases. **Omeprazole 0.7 mg/kg q12h** confers greater GI protection with NSAIA use.

PHARMACOLOGY

1) **Sucralfate** is a complex salt of sucrose sulfate and aluminum hydroxide. It is available as tablets (1g) or a suspension, (1 g/5 mL). It binds to mucosal defects and provides a protective barrier against entry to gastric acid. It accelerates healing of ulcers and erosions directly, as well as indirectly, by stimulation of production of local prostaglandins. Sucralfate suspension is effective for the control of major and minor gastric ulcer hemorrhage and is preferred in this situation to tablets. Constipation is the only reported side effect. Sucralfate should be administered on an empty stomach 1 h before meals. Other prescribed oral medication should be given at least 1 h before or 2 h after sucralfate administration to avoid decreased absorption. Although not recommended for ulcer prophylaxis, in the author's experience, sucralfate appears to be effective in preventing clinically significant ulcer formation (vomiting blood or coffee ground material and melena) when short term NSAIAs are used in perioperative patients. Sucralfate should be stocked by all veterinary practices as owner administration of NSAIAs is common, and gastritis, with or without ulceration, has been reported with aspirin, ibuprofen, naprosyn, ketorolac, etc.

2) **Misoprostol** is a synthetic prostaglandin E_1 analogue. It is available in 100 and 200 μg tablets. Misoprostol is recommended for concurrent use with some NSAIAs to enhance the natural mucosal defense mechanisms. Misoprostol has been demonstrated to prevent NASAI-induced ulcers in dogs. It can be prescribed with sucralfate, however, it should be administered a minimum of 1h before or 2 h after sulcralfate. It is potentially epileptogenic in humans and therefore its use in epileptic patients may be contraindicated, unless the benefit outweighs the risk of increasing seizure activity. Misoprostol is a synthetic prostaglandin E_1 analog that inhibits gastric acid secretion and stimulates gastric mucosal defense mechanisms. Its primary therapeutic indication tends to be as prophylaxis against gastric mucosal injury caused by NSAIDs. The drug is generally well tolerated, however, it can cause GI cramps and secretory diarrhea. Due to its ability to increase uterine contractility, abortion may be induced and should therefore not be used in pregnant animals. When prescribing misoprostol, this information must be given to the client to avoid a potential risk of accidental administration to the pet owner, by the pet owner!

3) **Famotidine** is an H2 receptor blocker. It is available as a solution for injection 10 mg/mL; tablets 20 mg and 40 mg. It is more effective than other H2 blockers and is recommended based on efficacy.

4) **Omeprazole** is a proton pump inhibitor and prevents gastric acid secretion by any mechanism. It is available as 20-mg capsules. It is the most effective medicament at raising the gastric pH as it blocks all three receptors responsible for HCl production. Its use is indicated for treatment and prophylaxis in highly susceptible ulcer-prone individuals (gastric erosions, and esophageal injuries prone to stricture).

5) **Pantoprazole** is an injectable proton pump inhibitor with actions similar to omeprazole.

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INTRODUCTION

Icterus may be due to several etiologies and these are grouped into three main categories, pre- hepatic, hepatic and post-hepatic. Pre-hepatic refers to the increase in red cell destruction (*see Immune-mediated Hemolytic Anemia p. 411, Sepsis/Septic Shock p. 588*), hepatic causes are primary liver disease (*see Acute Liver Failure/Dysfunction p. 37*), and post-hepatic relates to the biliary system (*see Acute Abdomen p. 21*). History and laboratory/diagnostic imaging are required to reach a definitive diagnosis (see Fig. 1). Icterus is not a common presentation. When pre-hepatic (i.e., IMHA) is ruled out hepatic and post-hepatic causes to consider are shown in Fig. 2 with their relative frequency of occurrence.

DIAGNOSIS

History

Presenting complaint is frequently yellow discoloration of the mucous membranes, sclera, and skin of the pinna. The owner may notice dark yellow urine, especially in the snow. "Weight gain" in the face of anorexia may be reported; this actually relates to abdominal distension due to bile peritonitis should biliary rupture be present either as a spontaneous event, or due to a history of trauma 1 – 7 days prior to presentation. Acute depression, tachypnea and anorexia may be present when hemolytic anemia (IMHA) is present or where gallbladder disease is the cause of icterus. Where chronic IMHA is present, a protracted, slowly progressive, exercise intolerance and loss of appetite is reported. The owner may report discomfort or pain when the animal is picked up and pressure applied to the abdomen, which may be associated with pancreatitis or gallbladder disease. Vomiting and inappetence is also present when associated with pancreatitis or gallbladder disease. Patients with hepatic lipidosis tend to be depressed. Severe icterus usually is associated with depression.

Clinical Signs/Physical Examination

Depression and weakness, anorexia, vomiting, abdominal pain, and pale or yellow mucous membranes are commonly present. Abdominal masses or abdominal fluid may be palpable.

Laboratory Evaluation

Stat
- **PCV.** Pre hepatic: Minimum database screen for anemia PCV <20. If PCV not <20 then acute anemia ruled out as cause for icterus unless acute history of trauma which may have caused blood loss and biliary tract injury.
- **TS** is reduced in hemorrhage and bile peritonitis and chronic liver failure but normal in IMHA.
- **ACT.** A prolonged ACT could indicate clotting factor deficiency as seen with severe hepatic necrosis or lipidosis, sepsis or neoplasia. Prior to obtaining liver biopsies blood coagulation should be assessed to minimize the risk of bleeding after the procedure.

Extended Laboratory Data Base
CBC
- May show anemia of chronic disease (non regenerative mild anemia).
- Elevated WBC's may indicate a primary infectious cause or secondary to liver failure.
- Microcytosis may be found in patients with portosystemic shunts (*see Acute Liver Failure/Dysfunction p. 37*).

Serum Biochemical Profile
- Elevated **ALT** and **ALP** are noted in moderate to severe liver disease. Elevated ALP (severe) and γ-GT are consistent with occlusion of the common pancreatic duct in cats (i.e., pancreatitis, or extra hepatic tumors). Secondary involvement of the liver parenchyma will be responsible for elevated ALT values as disease persists. Therefore, hepatic and post hepatic icterus cannot reliably be distinguished based on values or ratios of ALT and ALKP.
- **BUN** and **urea** may be decreased due to impaired hepatic function.
- **Cholesterol** may be increased in liver disease and in hypothyroidism.
- **Amylase** and **lipase** may be elevated in dogs with pancreatitis. This is not a consistent finding in cats.
- **Bile acids** and **bilirubin** require the same transport mechanisms. If clinical icterus is detected no additional information can be obtained by performing bile acid measurements. In non-icteric patients bile acid measurements provide an insight into function of the liver (*see Acute Liver Failure/Dysfunction p. 37*).

Abdominal Radiographs and Ultrasound
- Hepato-splenomegaly may indicate extra vascular hemolysis or primary neoplasia. Free abdominal fluid should be collected for cytology. If blood, urine, bile or bacteria are present then pursue etiologies for acute abdomen (*see Acute Abdomen p. 21*).
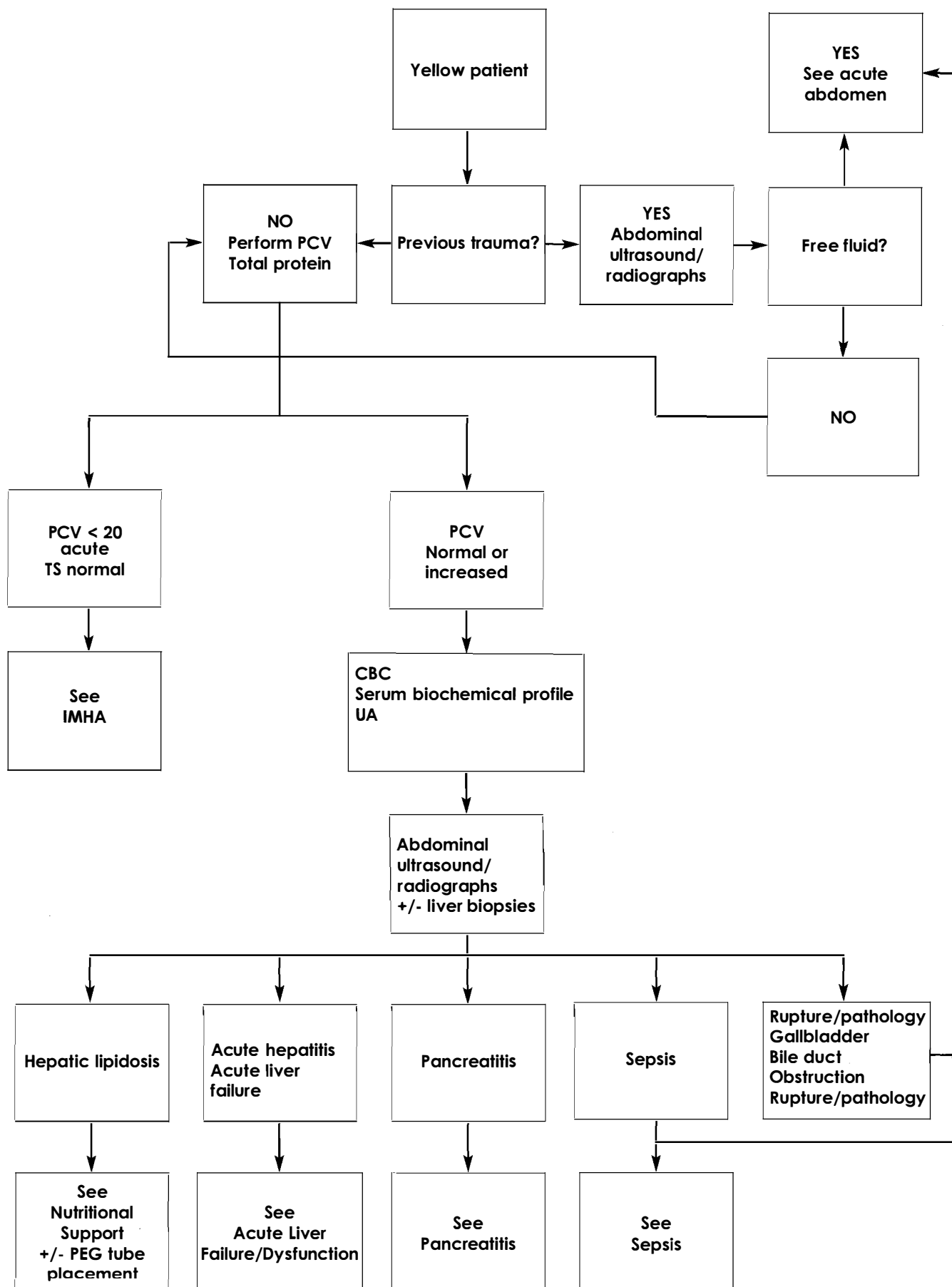
FIGURE 1. History and laboratory/diagnostic imaging.
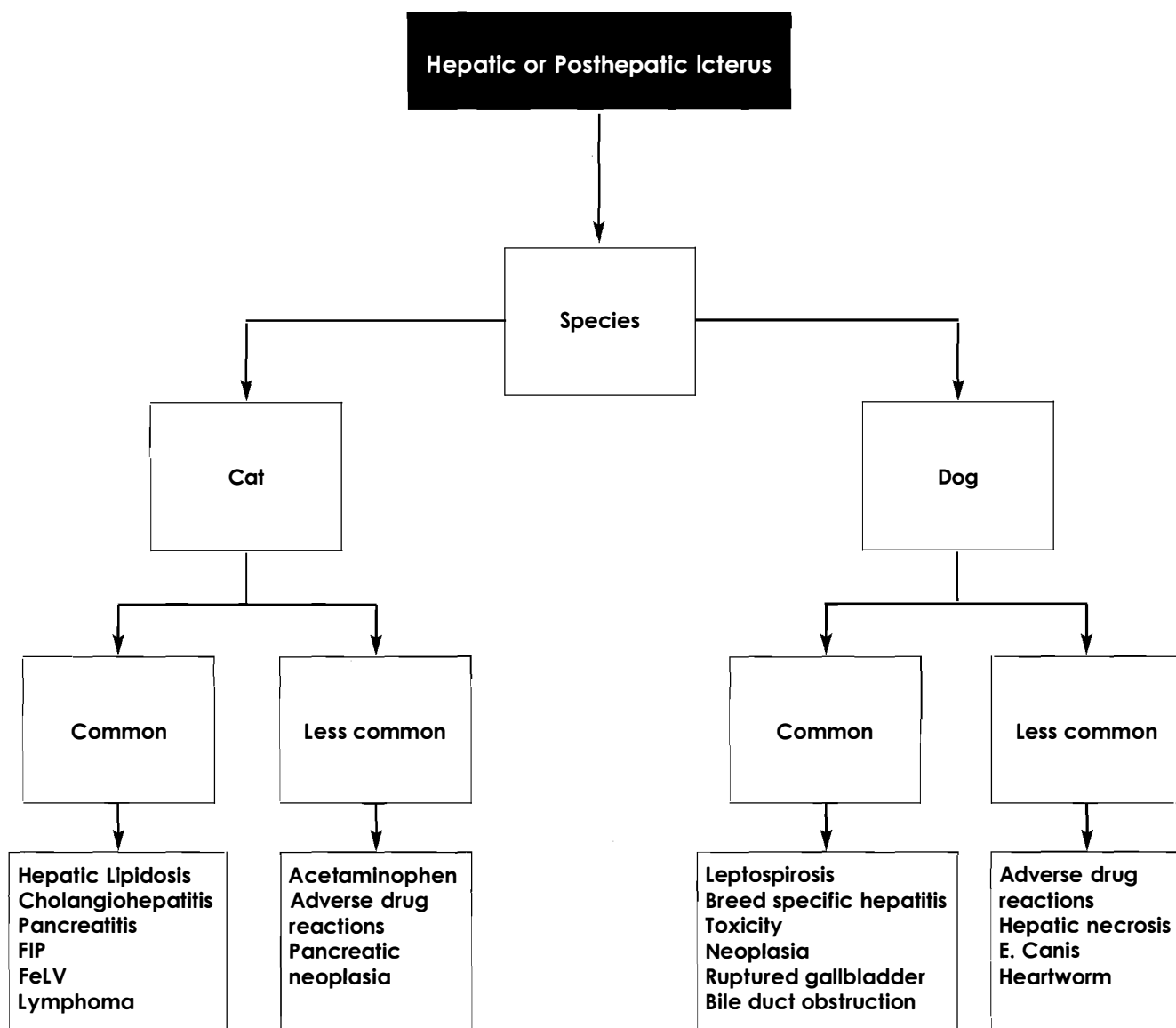
FIGURE 2. Hepatic or post hepatic icterus.

MANAGEMENT

A. Prehepatic icterus
1. See management IMHA.

B. Hepatic Icterus (*see Acute Liver Failure/Dysfunction p. 37*)

1. Employ fluid therapy to correct dehydration due to loss of appetite (*see Fluid Therapy p. 347*). Fluid solutions which contain lactate should be avoided as this requires conversion by the liver.
2. Institute cage rest.
3. Discontinue any potentially hepatotoxic drugs.
4. Determine underlying disease process. Ultrasound guided liver biopsy is frequently required for definitive diagnosis. Assess coagulation status prior to biopsy.
5. Handle urine carefully to avoid exposure to potential pathogens (e.g., Leptospirosis in dogs).

C. Post Hepatic Icterus

1. **Surgical exploration** is **necessary** where biliary obstruction, rupture or other evidence of serious pathology of the gallbladder (i.e., emphysema, mucocoele) is noted as sepsis and peritonitis frequently develop.
2. Treatment of **cholangiohepatitis, if bile sludge** can be seen without obstruction of the bile duct:
   a. **Ursodeoxycholic acid 10 – 15 mg/kg PO q24h, in combination with**
   b. **Amoxicillin 22 mg/kg PO q12h.**
   c. Ampicillin 20 mg/kg IV q6h (dogs) q8h (cats) can be substituted for amoxicillin in patients unable to take oral medications.
3. **S-adenosyl methionine** (SAMe, Denosyl SD4®) may be of benefit in reducing the oxidative damage done to the liver. Dosing recommendations.

Body Weight	Dose S-adenosylmethionine
<5.5 kg	One 90 mg tablet q24h PO
5.5–11	Two 90 mg tablets q24h PO
11–15	One 225 mg tablet q24h PO
16–30	Two 225 mg tablets q24h PO
31–41	Three 225 mg tablets q24h PO
>42	Four 225 mg tablets q24h PO

4. **Milk thistle** (silymarin marianum) at a dose of 100 mg/day for a 10 kg (22 lbs) animal has reportedly been effective as free radical scavenger in patients with liver disease and may be used as a less expensive alternative to SAMe. This product is not registered as a drug but considered a food supplement.
5. If evidence for pancreatitis (*see Pancreatitis p. 45*).

PHARMACOLOGY

1) **Ursodiol** (Urosodeoxycholic acid, Ursofalk®, Actigall®). Hydrophilic bile acid which increases bile flow. Used to replace more hydrophobic bile acids.

2) **S-adenosyl methionine** (SAMe, Denosyl SD4®) might be beneficial in reduction of the oxidative damage done to the liver. It helps to increase hepatic glutathion levels in cats and dogs. Glutathione, an antioxidant, acts as hepatic cytoprotectant Note: This product is not registered as a drug but considered a food supplement.

SUGGESTED READING

1. Center SA.Diagnostic procedures for evaluation of hepatic disease. In: Small Animal Gastroenterology, 3rd edition. Eds. Guilford WG, Center SA, Strombeck D, Williams D, Meyers D. WB Saunders, Philadelphia. 1994:30-188.
2. Messonnier, S. Milk thistle. Veterinary Forum. 2002:15:36-37.

NOTES

INTRODUCTION

Vomiting is a common clinical problem resulting from a variety of disorders (Fig. 1). Vomiting is a *clinical sign* and does not constitute a diagnosis in itself. Although vomiting is important in protecting the animal from ingested noxious substances, vomiting can result in serious consequences, such as esophagitis, aspiration pneumonia, fluid and electrolyte deficits and malnutrition.

The act of vomiting consists of three components: nausea, retching and vomiting. It occurs as gastric contents are forcefully expelled out of the mouth. The driving force is contraction of the abdominal muscles and diaphragm causing intrathoracic pressure changes, from negative during retching, to positive during vomiting. Activation of the vomiting centre occurs either through a humoral pathway initiated by blood-borne substances, or via various neural pathways. Neural stimulation of the vomiting centre arises from afferent vagal, sympathetic, vestibular and cerebrocortical pathways. Peripheral receptors stimulating these neural pathways are found throughout all abdominal organs, the peritoneum, and the heart.

Vomiting must be differentiated from regurgitation. Vomiting is active as described above, whereas regurgiation is a passive movement of esophageal contents into the pharyngeal or oral cavity and does not have a prodromal phase. Regurgitation may be congenital or acquired. Differential diagnosis may include; *Weakness p. 491, Gastric Dilation-Volvulus p. 59, Hypoandrenocorticism p. 274, Toxicities (lead) p. 642,* and *Esophageal Foreign Body p. 54.* Aspiration pneumonia is a potential emergent presentation (*see Respiratory Emergencies p. 555*).

FIGURE 1. Causes of Vomiting

Adverse Reactions to Food

1. Dietary indiscretion (ingestion of foreign material)
2. Sudden diet change
3. Eating too rapidly
4. Intolerance to specific foods
5. Food allergy

Gastrointestinal Inflammatory Disorders

1. Pharyngitis
2. Gastritis
   a. superficial
   b. atrophic
   c. hypertrophic
   d. eosinophilic
   e. others
3. Inflammatory bowel disease of the small & large intestine
4. Infectious
   a. viral
      • canine parvovirus
      • canine coronavirus
      • canine distemper
      • infectious canine hepatitis
      • feline panleukopenia
   b. bacterial or rickettsial
      • leptospirosis
      • salmonellosis
      • *Helicobacter* spp.
      • salmon poisoining (*Neorickettsia helminthoeca*)
      • *Ehrlichia* spp.
      • Rocky Mountain Spotted Fever
   c. fungal or protozoal
      • giardia
      • leishmania
5. Hemorrhagic gastroenteritis
6. Gastrointestinal neoplasia
   a. lymphoma
   b. adenocarcinoma
   c. leiomyosarcoma and leiomyoma
   d. mastocytosis
7. Gastric polyps
8. Gastroduodenal ulcers
   a. non-steroidal anti-inflammatory (NSAIDs) drugs
   b. mastocytosis
   c. glucocorticoids
   d. stress
9. Lymphangiectasia

Gastrointestinal Obstruction and Ischemic Disorders

1. Foreign bodies
2. Pyloric hypertrophy/stenosis
3. Mural thickening
   a. neoplasia
   b. granulomas
   c. strictures
   d. gastric polyps
4. Extraluminal compression
   a. neoplasia
   b. adhesions
5. Delayed gastric emptying
6. Ileus
7. Gastric-dilation (eating too much, such as in puppies)
8. Gastric-dilation volvulus (GDV)
9. Intussusception
10. Intestinal and/or mesenteric volvulus
11. Infarction
12. Other organ torsions (e.g. spleen)
13. Constipation/obstipation
14. Trichobezoars (hairballs)

Parasitism

1. Intestinal nematodes
2. *Physaloptera rana* (dogs and cats)
3. *Ollulanus tricuspis* (cats)
4. Heartworm disease (cats)

Disorders of Other Abdominal Organs

1. Hepatic
   a. hepatobiliary inflammation hepatitis cholangitis/cholangiohepatitis
   b. hepatic neoplasia
   c. bile duct obstruction
   d. choleliathiasis
   e. portosystemic shunts
2. Pancreas
   a. pancreatitis
   b. pancreatic adenocarcinoma
   c. gastrinoma (Zöllinger-Ellison syndrome)
3. Renal disease
   a. renal failure (uremia)
   b. pyelonephritis
4. Peritonitis
5. Steatitis
6. Prostatitis
7. Pyometra
8. Metritis
9. Urinary obstruction
10. Hernia
    a. diaphragmatic
    b. hiatal

Metabolic/Endocrine Diseases

1. Hepatic failure/hepatic encephalopathy
2. Uremia
3. Sepsis
4. Heatstroke
5. Acidosis
6. Neoplasia
   a. metastatic
   b. tumour lysis syndrome
7. Electrolyte imbalance(s)
   a. hypokalemia
   b. hyperkalemia
   c. hypocalcemia
   d. hypercalcemia
   e. hypomagnesemia
8. Diabetic ketoacidosis
9. Hyperthyroidism
10. Hypoadrenocorticism
11. Congestive heart failure
12. Post-renal obstruction
13. Hypoparathyroidism
14. Hyperparathyroidism

Neurologic Disorders

1. Psychogenic
   a. pain
   b. fear
   c. excitement
2. Vestibular disturbances
   a. old dog vestibular disease
   b. motion sickness (rotation or unequal input from the labyrinths)
3. Elevated intracranial pressure
   a. head trauma
   b. brain tumours
   c. hydrocephalus
4. Meningitis
5. Encephalitis
6. Dysautonomia

Drugs

1. Intolerance
   a. anti-neoplastic agents
   b. cardiac glycosides
   c. potassium bromide
   d. antimicrobial drugs
   e. arsenical compounds
   f. narcotics
   g. xylazine
2. Blockage of prostaglandin biosynthesis (NSAIDs)
3. Accidental overdosage

Toxins

1. Lead
2. Zinc
3. Copper sulfate
4. Ethylene glycol
5. Insecticides
6. Mycotoxins
   a. *Fusarium* spp
   b. "vomitoxin" on moldy wheat
7. Household plants
8. Strychnine

Miscellaneous

1. Bilious vomiting syndrome (enterogastric reflux syndrome)
2. Irritable bowel syndrome
3. Transfusion-induced complication

History/Signalment

- A complete review of the history of the animal, with emphasis on all body systems, is essential in determining an initial work-up and treatment protocol.
- When questioning the owner, it is extremely important to differentiate regurgitation from vomiting if it is still unclear whether regurgitation is present, even after the history.
- Survey thoracic radiographs should be performed to evaluate for the presence of megaesophagus.
- Occasionally, contrast studies are required to identify the presence of esophageal dilation.

The following historical features are often useful in assessing and diagnosing the disorders that cause vomiting:

- Duration of the clinical signs
- The contents of the vomitus
- The time relation to eating and drinking
- The nature of vomiting (type and frequency)
- Dietary and environmental history

See Fig. 2 for a detailed list of questions asked to the owner to obtain pertinent information in the investigation of vomiting.

FIGURE 2. Questions

Duration and Frequency of Vomiting

1. Acute
   a. dietary indiscretion
      - foreign body
      - garbage ingestion
   b. improper feeding habits
      - consumption of a high fat meal
      - overfeeding
      - abrupt change of diet
   c. administration of drugs
   d. exposure to infectious organisms (e.g., parvovirus)
   e. investigation for environmental intoxicants (e.g., ethylene glycol)
   f. presence of associated clinical signs may help guide you in the work-up, (e.g., diarrhea, lethargy, pyrexia, abdominal discomfort, anorexia or CNS signs).
2. Chronic (greater than 7 – 10 days), or vomiting that has not responded to symptomatic therapy requires further investigation.

Exposure to Infectious Organisms

Administration of Drugs

Dietary History

1. Dietary indiscretion
2. Improper feeding habits

Description of Vomitus

1. Amount
2. Colour
3. Consistency
4. Odour (vomitus having a fecal odour suggests a low intestinal obstruction or small intestinal bacterial overgrowth, or necrotic foreign body or neoplasm)
5. Presence of bile suggests that there is no pyloric outflow obstruction
6. Presence of blood in the vomitus, either fresh or digested ("coffee grounds"), indicates gastrointestinal erosion or ulceration, or coagulopathy. Hematemesis with metabolic-related ulcers, such as hypoadrenocorticism, uremia, drug-induced ulceration, gastritis and gastric neoplasia are possible etiologies.

Time Relation of Vomiting to Eating and Drinking

1. Immediately post-prandial or within 30 minutes after eating may suggest an adverse reaction to food or simply overeating (gluttony).
2. Vomiting undigested or partially digested meal more than 8 – 10 hours after eating suggests a gastric outflow obstruction (e.g., foreign bodies, mucosal hypertrophy, tumours or polyps) or a primary gastric hypomotility disorder.
3. Vomiting of bile-tinged fluid, especially in the morning, is often due to bilious vomiting syndrome (enterogastric reflux syndrome).
4. Digested vomitus containing bile suggests an intestinal origin.

Clinical Signs/Physical Examination

A thorough physical examination is imperative in the evaluation of a vomiting patient. A systematic approach will prevent unnecessary diagnostic tests and inappropriate treatment.

- Assess the patient's overall attitude, posture and energy level (is the dog active in the exam room or lethargic?).
- A thorough examination of the mucous membranes and oral cavity may reveal pale or icteric membranes, uremic breath, ulceration and dehydration. Tumours of the oral cavity and pharynx may result in regurgitation or licking of the lips but where the owner describes vomiting. Sweet smelling breath is suggestive of diabetic ketoacidosis. Salivation suggests the presence of nausea. A foreign body lodged in the hard palate or a linear foreign body located around the tongue at the frenulum may be observed. The free end of the string subsequently advances along the intestinal lumen as a result of progressive peristalsis. Intestinal plication and potential peritonitis may result.
- The presence of a fever suggests an infection or inflammatory process or neoplasia.
- Vomiting cats should be assessed for the presence of an enlarged thyroid nodule(s) (*see Hyperthyroidism p. 288*).
- Cardiac auscultation may reveal rate and rhythm disturbances that may result from metabolic disorders. For example, hypoadrenocorticism (*p. 274*) may be associated with bradycardia. Tachycardia and weak pulses may be present with infectious enteritis (*see Acute Diarrhea p. 32* and *Septic Shock p. 588*). A dog with GDV (*p. 59*) may have tachycardia, weak pulses and pulse deficits.
- The abdomen should be palpated for:

  - distention and tympany
    - a. GDV
  - effusion
    - a. hepatic disease
    - b. peritonitis
  - presence of a mass
    - a. foreign body
    - b. intussusception
    - c. neoplasia
    - d. lymphadenopathy
  - presence of organomegaly
  - pain
    - a. pancreatitis
    - b. peritonitis
    - c. intestinal obstruction or volvulus (intestinal or splenic)
    - d. pyelonephritis
    - e. hepatic disease
    - f. neoplasia

- Auscultation of the abdomen may reveal decreased bowel sounds, which can occur with peritonitis or ileus, while increased sounds may be present in acute inflammatory disorders. An increased pitch suggests distention of the intestinal loops.
- Rectal palpation may provide information regarding the colonic mucosa and feces. Melena suggests upper gastrointestinal bleeding. The presence of foreign material supports a foreign body etiology. Animals with colitis or obstipation often vomit due to the gastro-colic reflex.
- A neurological examination may reveal signs of vestibular disease (*see Head Tilt p. 465*). Dogs with intervertebral disk disease (*p. 473*) may occasionally vomit due to pain and/or secondary intestinal ileus.

Laboratory Evaluation/Diagnostic Imaging

Based upon the history and physical examination, the animal should be classified as having **acute or chronic** vomiting.

- If the vomiting episodes are acute and of short duration, they may be self-limiting and are frequently treated with symptomatic therapy.
- A **routine fecal examination** for parasites should be performed to eliminate the possibility of intestinal parasites.
- The minimum database should consist of a **complete blood count (CBC), serum biochemical profile,** including amylase and lipase enzyme activities, and **urinalysis.** Cats should have an FeLV/FIV test and T4 concentration assessed.
- Young, unvaccinated dogs should have a **parvovirus test** performed.
- **Survey radiographs** should be performed if the history or physical examination indicates this, or if regurgitation due to esophageal lesion must be ruled out. Abdominal radiographs will reveal radioopaque foreign bodies, pyometra, abdominal masses, GI obstructive gas patterns, signs of peritonitis (e.g., lack of contrast) and abdominal fluid accumulation may be revealed (*see Acute Abdomen p. 26 for interpretation*).
- **Abdominocentesis and cytology** may be required to rule out peritonitis, hemoabdomen, etc.
- **Contrast radiography** may be useful for identification of a gastric or intestinal foreign body, gastric hypomotility, gastric outflow obstruction, and intestinal obstruction (see *Acute Abdomen p. 26 for protocol and interpretation*). A barium series, the use of barium impregnated polyethylene spheres (BIPs), or iodinated contrast materials are available. In addition, fluoroscopy may aid in the diagnosis of motility disorders and hiatal hernias, however, the latter is usually only available at referral institutions.
- An **ACTH stimulation test** may be required to confirm a diagnosis of hypoadrenocorticism (*p. 274*) in a patient with an abnormal sodium to potassium (Na:K) ratio, and/or suggestive CBC changes (non-regenerative anemia,

absence of a stress leukogram). Do not rule out hypoadrenocorticism based on normal electrolytes. Ten to 20% of dogs do NOT present with electrolyte abnormalities.

- The **trypsin-like immunoreactivity** (cTLI and fTLI) test and the **canine and feline pancreatic lipase immunoreactivity** (cPLI and fPLI) may be used for the diagnosis of pancreatitis (*p. 45*). The latter assay specifically measures the concentration of lipase originating from the exocrine pancreas. The TLI assay may be increased in infiltrative and inflammatory disease, as well as renal failure. The assay for cPLI and fPLI uses species-specific antibodies directed against pancreatic lipase and therefore directly measures pancreatic lipase. The test is both very sensitive and specific in diagnosing pancreatic inflammation. The test is available at the GI Laboratory at Texas A&M University in College Station, Texas.
- **Serum bile acids assay** is used to assess for hepatic dysfunction (*p. 37*).
- **Thoracic radiographs** may identify metastatic disease if neoplasia is suspected. Where appropriate, thoracic radiographs should be performed in middle-aged and older dogs with GDV, as anecdotal evidence suggests that neoplasia may predispose to GDV.
- **Abdominal ultrasonography** can be useful in diagnosing disorders of the liver, gallbladder and bile ducts, as well as intestinal foreign bodies, intussusception, intestinal and gastric wall thickening, GI masses, pancreatitis, pancreatic neoplasia, and renal disease. Fine needle aspirations and/or biopsies may be performed under ultrasound guidance.
- **Endoscopy** allows for direct gastric and duodenal evaluation (erosion and ulceration), mucosal biopsies (inflammatory, *Helicobacter* spp and neoplastic disorders), and gastric foreign body retrieval. Vomiting due to *Physaloptera* is best diagnosed via direct visualization with endoscopy.
- Chronic vomiting in cats may be due to *Ollulanus tricuspis*. Young, free-roaming cats are most often affected. Diagnosis is made by evaluation of gastric contents via the **Baermann technique** or by microscopically examining the filtered vomitus.
- Vomiting is a frequent (and sometimes only) presenting clinical sign in cats with heartworm disease. A feline **heartworm antibody test** should be done if the disease is endemic to the area of your practice.
- **Serum gastrin** concentrations may be performed if a gastrinoma is suspected.
- **Exploratory laparotomy** is indicated for foreign body removal, intussusception, gastric mucosal hypertrophy syndromes, biopsy samples of different organs and resection of neoplasms. The author cannot stress enough the importance of obtaining biopsies of the liver, GI tract, lymph nodes and pancreas (judiciously) EVEN IF NO GROSS ABNORMALITIES ARE OBSERVED.
- **All cutaneous and subcutaneous masses should be aspirated** to rule out a mast cell tumour.

MANAGEMENT

Treatment depends on the suspected cause and the reader is directed to the specific chapters of this manual, i.e.: Acute Abdomen *p. 21*, Gastric Dilation-Volvulus (GDV) *p. 59*, Diabetic Ketoacidosis *p. 263*, Oncologic Emergencies *p. 443* and Acute Pancreatitis *p. 45*.

Treatment of acute vomiting, which is not complicated by shock or excessive abdominal pain, is most often treated symptomatically.

A. Fluid, electrolyte and acid-base therapy must be addressed (*see Fluid Therapy acid-base assessment p. 406 and appropriate electrolyte chapters*).

B. Withholding food and water for 12 – 24 hours depending upon the severity of the episode(s).

C. Do not administer medication per os.

D. Pharmacologic control of vomiting (Table 1) should be considered if:

1. obstructive disease has been ruled out
2. the patient is uncomfortable (e.g., the patient cannot adequately rest due to persistent vomiting)
3. there is excessive loss of fluids and electrolytes

Anticholinergic drugs (e.g., atropine) are NOT recommended, as they do not inhibit the vomiting reflex, nor reduce gastric acidity.

TABLE 1. Anti-emetic Drugs (dogs and cats unless stated otherwise)

*Prochlorperazine	0.1 – 0.5 mg/kg IM, SC, IV (slowly) every 6–8h 1 mg/kg PO q12h
*Chlorpromazine	0.2 – 0.5 mg/kg IM, SC q6–8h 0.05 mg/kg IV (slowly) q4h 1 mg/kg rectally q8h (dog)
+*Metoclopramide	0.2 – 0.5 mg/kg SC q8h 1 – 2 mg/kg/day IV as a constant rate infusion (CRI)
Ondansetron	0.5 – 1.0 mg/kg IV slowly q8–12–24h 0.5 – 1.0 mg/kg PO q8-12h
Dolasetron	0.5 mg/kg IV, SC, PO q24h
Butorphanol	0.2 mg/kg SC, IM, IV q4–6h 0.1 mg/kg IV as a CRI
Cisapride	0.1 – 1.0 mg/kg PO q8h
Cyproheptadine	1 – 2 mg per CAT PO q8–12h
Ranitidine	0.5 mg/kg IV (slowly), SC, PO q12h

*may precipitate seizures in animals with a history of seizure activity
+do not use if obstruction is suspected

E. Systemic antibiotics should be considered when disruption of the GI mucosal wall is suspected in order to decrease the risk of bacterial translocation. Antibiotics chosen should be broad-spectrum and treat both aerobic and anaerobic enteric bacteria (*see Acute Diarrhea p. 32, Shock p. 603 , Septic Shock p. 588*).

F. Histamine (H_2) antagonists and proton pump inhibitors reduce gastric acidity and irritation (i.e., acute or chronic gastritis, pancreatitis, uremia). Drugs available include:

   1. famotidine: 0.5 mg – 1.0 mg/kg IV, PO q12h
   2. nizatidine: 5 mg/kg PO q24h
   3. omeprazole: 0.7 mg/kg PO q24h
   4. pantoprazole: 1 mg/kg IV (max 30 mg) slow infusion over 30 minutes q24h
   5. ranitidine: 0.5 mg/kg IV, PO q12h may also be useful as a prokinetic, but not as useful as an acid lowering drug

G. Other medications that may be useful if gastrointestinal hemorrhage is evident:

   1. sucralfate: dogs: 0.5 – 1 g PO q8–12h
                 cats: 0.25 – 0.5 g/cat PO q8–12h

H. Locally acting medication containing bismuth subsalicylate (Pepto-Bismol) at 0.25 mg/kg PO q4h may be helpful in reducing gastric irritation associated with prostaglandin release. However, these products are reserved for dogs with mild signs. Caution should be used when treating cats with such products.

I. Once vomiting has ceased, small quantities of crushed ice, ice cubes or water may be introduced, followed by (small quantities of) a bland diet, such as 1% cottage cheese and rice, boiled hamburger meat, chicken or turkey breast and rice, or commercial diets (Medi-Cal Gastro, Eukanuba Low Residue, Hill's i/d, Purina EN). The author usually waits 24 – 48 hours from the last vomiting episode before attempting to feed the patient (depending upon the initial severity of the vomiting).

PHARMACOLOGY

1) **Prochlorperazine** and **chlorpromazine** are histaminergic and adrenergic antagonists that act upon the emetic centre and chemoreceptor trigger zone (CRTZ).

2) **Metoclopramide** is a dopaminergic and weak serotonergic antagonist that acts at the level of the chemoreceptor trigger zone (CRTZ), as well as the GI smooth muscle (acting as a prokinetic agent).

3) **Ondansetron** and **dolasetron** are serotonergic ($5HT_3$) receptor antagonists, which act upon the CRTZ and vagal afferent neurons. They are extremely effective, but costly. Ondansetron also exists as a "pill form" which dissolves when placed on the gingiva.

4) **Butorphanol** is a narcotic (opioid), which likely exerts its anti-emetic effect on the CRTZ.

5) **Cisapride** is a mild serotonergic (5HT4) antagonist and prokinetic drug, which acts upon the myenteric neurons.

6) **Cyproheptadine** is a histaminergic and a mild serotonergic antagonist. It can cause sedation, and should be used with caution in cats with cardiac disease.

7) **Ranitidine's** apparent anti-emetic effect is likely due to its prokinetic effect.

8) **Famotidine, ranitidine** and **nizatidine** are histamine (H_2) receptor antagonists. Ranitidine and nizatidine have been shown to have prokinetic effects. Cimetidine is not recommended.

9) **Omeprazole** and **pantoprazole** are proton pump inhibitors. The final step in acid secretion involves the exchange of cellular H^+ for luminal K^+ by the proton pump on the apical border of the oxyntic cell. Inhibition of the proton pump (H^+/ K^+ ATPase) prevents gastric acid secretion by any secretagogue. It also has cytoprotective qualities by enhancing mucosal cell prostaglandin production. Pantoprazole is available for IV use. It is reconstituted using 4 mL of sterile water and must be discarded within six hours of reconstitution; this, unfortunately, makes the use of the product quite expensive.

10) **Sucralfate** is a complex salt of sucrose sulfate and aluminum hydroxide. It promotes ulcer healing by binding to the surface of the ulcer and providing a physical barrier between luminal contents and the mucosal surface. This in turn impairs the diffusion of acid and pepsin. It also stimulates mucosal defense, reparative mechanisms and anti-peptic effects via both prostaglandin-dependent and independent pathways. Although sucralfate requires the presence of acid to bind to the ulcer bed, it has been shown to be effective at a neutral pH as well. Only small amounts of sucralfate are absorbed systemically due to its poor solubility. Sucralfate can affect the absorption of other drugs from the GI tract. It is therefore recommended that it be administered at a staggered interval from other drugs and food. Constipation and hypophosphatemia may also occur.

11) **Bismuth subsalicylate** inhibits the synthesis of protaglandins responsible for GI hypermotility and inflammation. The drug may also have antibacterial and anti-secretory properties. It relieves indigestion by forming insoluble complexes with offending noxious agents and by forming a protective coating. Cats may be more sensitive to the salicylate content, especially in the presence of an inflamed bowel. More than 7 mL/kg of Pepto-Bismal contains enough aspirin to cause toxicity. Constipation may occur with high doses. It is also radioopaque and may therefore interfere with radiographic GI studies. The tablet form of the chewable triangular product Pepto-Bismal is often swallowed "whole" by the animal, and may be misinterpreted as a GI foreign body. Therefore, question the owner if any medication has been administered prior to presentation.

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NOTES

INTRODUCTION

This section is not intended to be a comprehensive pharmacology or anesthesia textbook. The material included should assist in decision-making, as most of the key applied information on the drugs and their use is included. Please refer to more in-depth resources as needed.

OPIOID ANALGESICS

Oxymorphone

Acts as an agonist at opioid receptors resulting in analgesia and a degree of sedation, which is more profound in older or depressed patients. Schedule N: Records must be kept (U.S. Schedule II).

A. Indications: Sedation, analgesia (3 – 4 h effect) for moderate to severe pain. Duration of action is inversely related to the degree of pain. An antitussive effect is present at analgesic doses.

B. Adverse Effects: Vomiting (rare), panting and bradycardia may occur if used in animals without moderate to severe pain (e.g., for diagnostic procedures or premedication). However, these effects are rarely a concern with moderate to severe pain and should not limit the use of this agent.

    1. Bradycardia may occur more frequently in larger dogs (>25 kg) than smaller ones when oxymorphone is administered for restraint or as a pre-med rather than for analgesia. Bradycardia should only be treated if the heart rate is less than 45 – 50 beats/minute (bpm) and peripheral pulses are poor. In larger dogs, heart rates are normally low when resting quietly and pain free. However in anesthetized animals it is beneficial to treat low heart rates to improve perfusion (<60 – 80 bpm in dogs and <120 bpm in cats) Atropine (0.01 – 0.04 mg/kg) or glycopyrrolate (0.005 – 0.015 mg/kg) will be effective (dose required varies with intensity of vagal tone and is inversely proportional to size).

    2. Respiratory depression rarely occurs in awake animals (if present, it is obvious due to the associated significant CNS depression), but may be present during general anesthesia (easily addressed by positive pressure ventilation if a concern).

        a. Reversal of adverse effects in the awake or recovering animal can be achieved with naloxone without reversing analgesia (*see Naloxone p. 85*).

        b. Butorphanol (0.1 – 0.4 mg/kg) will also help reverse adverse effects while maintaining some analgesia. This can be titrated to effect as well by giving increments of 0.1 mg/kg every 2 – 5 min until the desired effect is achieved. However, if the condition is not improving or worsening, discontinue and titrate naloxone (below).

    3. Dysphoria and excessive panting is a potential problem in animals with less than a moderate degree of pain, or when an effective overdose has been given. Use cautiously if history of narcotic excitement is present. *See Naloxone p. 85, for reversal.* Butorphanol reversal may not always be effective for excessive panting, rarely it may make dysphoria and panting worse. Reduced gastric emptying and constipation can occur. Not recommended in endoscopy due to increased sphincter tone that could make scope passage into the duodenum more difficult.

C. Contraindications: Caution must be used when oxymorphone is administered to patients with head trauma and/or significant CNS depression. Careful monitoring of the depressant and respiratory effects while titrating to the desired level of analgesia, together with calming the patient, should allow the safe use of oxymorphone (*see Head Trauma p. 694*). The ability to reverse untoward effects provides safety (*see Naloxone p. 85*).

D. Comments: One of the best analgesics as it is effective for severe pain and is relatively long acting and reversible. It may be more predictable in its responses and duration than other mu agonists.

E. Dose: Dosing depends on the degree of pain or need for restraint. Generally, the **0.05 mg/kg** dose is effective when supplemental techniques have been used (epidural, local blocks, etc.) or the pain is moderate or less; however **0.1 mg/kg** is recommended in small dogs and cats (<10 kg) with severe pain and without supplemental analgesic techniques (*see Oxymorphone Infusion Chart p. 255 for CRI dosing*).

1. **Dog:** 0.02 mg/kg to 0.2 mg/kg IM, SC, IV (higher doses for restraint). A total dose of 3.0 mg may be suggested as a starting dose in very large dogs (>60 kg) although they may require higher amounts, especially if significant pain is present.
2. **Cat:** 0.05 – 0.1 mg/kg IM, SC, IV. The higher dose is common in these smaller patients due to the influence of surface area on dosing.
3. **Epidural** use – see section on Epidural Analgesia *p. 113.*

Hydromorphone

Acts as described for oxymorphone. Schedule N: Records must be kept (US Schedule II).

A. Indications: See oxymorphone. Duration of effect may be slightly longer.

B. Adverse effects: See oxymorphone for major effects. Reversal is possible (as above), if needed.

1. Vomiting is more common than with oxymorphone.
2. Cats can become **hyperthermic** if high doses are used (0.1 mg/kg dose should not be repeated before 6 h unless evidence of pain exists). Lower doses may not last as long and are less likely to cause hyperthermia.

C. Contraindications: Same as noted for oxymorphone, with the addition of GI obstruction (stimulates vomiting).

D. Comments: Duration of effect is less predictable than oxymorphone and may be longer in some animals. Cheaper alternative to oxymorphone.

E. Dose: Dosing depends on the degree of pain or need for restraint. Generally, the **0.05 mg/kg** dose is effective when supplemental techniques have been used (epidural, local blocks, etc.) or the pain is moderate or less; however **0.1 mg/kg** is recommended in small dogs and cats (<10 kg) with severe pain and without supplemental analgesic techniques (*see Hydromorphone Infusion Chart p. 241 for CRI dosing*).

1. **Dog:** 0.02 mg/kg to 0.2 mg/kg IM, SC, IV (higher doses for restraint). A total dose of 3.0 mg may be suggested as a starting dose in very large dogs (>60 kg) although they may require higher amounts, especially if significant pain is present.
2. **Cat:** 0.05 – 0.1 mg/kg IM, SC, IV. The higher dose is common in these smaller patients due to the influence of surface area on dosing.
3. Epidural use (*see section on Epidural Analgesia p. 113*).

Morphine

Acts as described for oxymorphone. Schedule N: Records must be kept. (US Schedule II)

A. Indications: See oxymorphone (may have a slightly shorter duration of effect).

B. Adverse effects: See oxymorphone for major effects. Reversal is possible (as above), if needed.

1. IV administration will cause hypotension due to histamine release if given as a rapid bolus.
2. Dysphoria and excitement. Refer to that noted for oxymorphone. Cats are more sensitive to the excitatory effects of this agent and therefore lower doses are recommended.
3. Gastrointestinal segmental hyperactivity is profound when given initially, but ileus and constipation occur if long term use (*see oxymorphone p. 81*). Vomiting is common at high doses.

C. Contraindications: Same as noted for oxymorphone, with the addition of GI obstruction (stimulates vomiting and defecation).

D. Comments: Duration of effect is less predictable than oxymorphone and often shorter. Disadvantage in inability to give IV rapidly in a rescue situation. Cheap alternative to oxymorphone if the differences are kept in mind.

E. Dose: Select a dose appropriate for the size of the animal and degree of pain.

1. **Dog:** 0.3 – 0.5 mg/kg IM, subcutaneous.
2. **Cat:** 0.1 – 0.2 mg/kg IM, subcutaneous. Although MAC reduction has been shown with morphine, analgesia produced in cats is not very good, compared to oxymorphone or hydromorphone. This dose will likely be ineffective in cats with severe pain. The doses quoted are related to the concern for excitement, rather than effectiveness.

3. **Morphine Infusion** – Selected for pain that is more difficult to manage. Monitor for respiratory depression. If some agitation results, consider acepromazine to calm the animal allowing an enhanced analgesic effect.

    a. Loading dose: **0.3 – 0.5 mg/kg** IM (another mu agonist can also be used for loading dose).

    b. Infusion drip: **0.1 – 0.2 – 0.4 mg/kg/h** IV (can be added to the hourly fluids) for mild-moderate-severe pain (*see Morphine Infusion Chart p. 251 for CRI dosing*).

4. **Epidural** use (*see section on Epidural Analgesia p. 113*).

Fentanyl

Acts as noted for oxymorphone. The analgesia is short in duration (20 – 30 min) and therefore it is best given as an infusion or provided as a slow release product in commercially available patches. Schedule N: Records must be kept (U.S. Schedule II).

A. Indications: Infusions are generally reserved for use during anesthetic management or severe postoperative pain. Patches are used alone or with supplemental analgesia, if required and provide a 3 – 5 day duration of effect.

B. Adverse Effects: See oxymorphone. Reversal as noted under oxymorphone is effective. Minor problems associated with patch use will reverse fairly quickly with patch removal.

    1. Mild contact dermatitis may occur in around 50% of patients with a patch and resolves in 24 h after patch removal.

    2. Avoid laying the patch on a warm area (e.g., heating pad) as there is increased absorption and overdose.

C. Contraindications: The patch should not be sent home when concerns exist for client abuse, if there are children in the home or the animal is likely to remove it.

D. Comments: The patches are costly but will last several days. If patients are sent home with the patch in place, it may be advisable to require the owner to return the patch for disposal.

E. **Dose:**

    1. **5 µg/kg** is often selected for premedication or an initial loading dose.

    2. An infusion can be used at **30 – 50 µg/kg/h** for significant MAC reduction during anesthesia. Start at 4 µg/kg/h (range 3 – 6 µg/kg/h *see Fentanyl Infusion Chart p. 237 for CRI dosing*) to start for analgesia in awake animals.

    3. Patches in **25, 50, 75 and 100 µg/h dosage.** Therapeutic blood levels are achieved with 75 and 100 µg/h in dogs around 20 kg and require 12 – 24 h to reach therapeutic levels (great variability has been noted). Cats appear to achieve analgesia in 6 – 12 h. Smaller animals require the smaller size patch (25 µg/h patch resulting in approximately 4 µg/kg/h). If a low dose is required only part of the seal is removed and exposed to the skin. DO NOT CUT. The patch can be removed at any time adverse effects are noted and the reversal is generally fairly rapid (2 – 3 h). Should immediate reversal be required, naloxone as described below, can be titrated to effect. The skin requires shaving but not cleaned unless seborrhea noted, then clean with warm water and allow to dry prior to patch application. No other solutions should be used or skin damaged in any way as enhanced absorption will occur.

Meperidine

Meperidine acts as an agonist at opioid receptors and produces sedation and relief from mild pain for short duration (30 – 60 min); duration inversely proportional to severity of pain. An antitussive effect is present at less than analgesic doses. Schedule N: Records must be kept (US Schedule II).

A. **Indications:** Good, short term analgesic for geriatrics, brachycephalics and the mildly depressed with mild pain (minor surgical procedures, e.g., small lump removal). Premedication prior to general anesthesia for non-painful procedures or to avoid panting or vomiting that may occur with other opioids.

B. **Adverse Effects:** Histamine release resulting in hypotension if given IV. Less likely than other mu agonists to produce vomiting, panting, respiratory depression, bradycardia or dysphoria.

C. Contraindications: No significant ones if appropriate doses used. Due to lesser adverse effects than other mu agonists, the concern for use when CNS depression or head trauma exists is less. Reversal with naloxone is easily achieved if any problems arise.

D. Comments: Good choice to start with when fear of opioid effects exists, but must recognize the limited and short analgesia achieved. The advantage of its use is that a more profound mu agonist can be added on top, if needed.

E. Dose: Never IV.

 1. **Dog: 3.0 – 5.0 mg/kg** IM, subcutaneous (>200 mg rarely needed).
 2. **Cat: 5.0 – 10.0 mg/kg** IM, subcutaneous.

Tramadol

50 mg tablets, also in combination with acetaminophen. May be compounded into an injectable form and an oral solution. Tramadol is an opiate but is not controlled by Drug Enforcement Agencies. It is not approved for veterinary use. Both the parent drug and active metabolite bind the mu receptors (with weak activity there). The metabolite has a much higher affinity for the mu receptors than the parent compound in humans. Inhibition of noradrenaline and seratonin reuptake (similar to antidepressants) or some alpha-2 effects may be responsible for part of the analgesia. Time to peak effect in humans is 2 hours for the parent compound and 3 hours for the metabolite. It is metabolized in the liver via N- and O-demethylation and glucuronidation or sulfation with only 30% excreted unchanged in the urine.

A. Indications: Moderate to severe pain, associated with osteoarthritis, cancer and surgery. May be comparable to morphine following ovariohysterectomy in dogs.

B. Adverse Effects: In humans dizziness, nausea, vomiting, constipation, diarrhea, headache, somnolence, pruritus, CNS stimulation, asthenia, dyspepsia, dry mouth have been reported.

C. Contraindications: Due to mode of metabolism, tramadol is not recommended for cats. Tramadol should not be co-administered with opiates, centrally-acting analgesics, psychoactive drugs or hypnotics.

D. Comments: Naloxone only reverses some of the adverse effects of overdose, but its use may precipitate seizures. Tramadol is inexpensive, easily obtainable and effective. Tramadol should not be discontinued abruptly but slowly weaned off as withdrawal may be experienced due to acquired dependence.

E. Dose: **1 – 4 mg/kg PO q6h** is suggested for management of cancer pain.
1 – 2 mg/kg PO q12h is suggested for osteoarthritis.

Codeine

Metabolized to morphine and thus acts similar. Schedule N: Records must be kept (US Schedule II).

A. Indications: Moderate pain, post-operative orthopedic, soft-tissue or dental surgery for 24 – 48h then step down dose. Good antitussive at low doses.

B. Adverse Effects: As other opioids, although may be less profound (more like meperidine).

C. Comments: Oral medication. Be careful of combinations of codeine with acetaminophen or aspirin, since an overdose of these drugs will occur when the medication is dosed based on codeine levels.

D. Dose: 1 – 2 mg/kg (dog); **0.5 – 1 mg/kg** (cat); PO.

Butorphanol

Acts as an agonist – antagonist at opioid receptors resulting in analgesia and a degree of sedation that is more profound in older or depressed patients. In the presence of an agonist, at the same receptor, a degree of reversal will occur (noted above). In our experience, the duration of action is approximately 2 h, occasionally 4 h, and rarely longer. However, duration is inversely related to the degree of pain. An antitussive effect is present at very low doses. Schedule G: Less concern for drug abuse (although has been reported) and therefore less strict record keeping is required although recommended (US Schedule IV).

A.   **Indications:** Analgesia for mild to moderate pain, sedation, antitussive action, partial reversal of other opiates.

B.   **Adverse effects:** Less profound than noted with profound mu agonists. Panting may occur in patients with minimal to no pain. Bradycardia is possible.

C.   **Contraindications:** Use with other pure opiates unless attempting reversal.

D.   **Comments:** Good choice to start with when fear of opioid effects exist, but must recognize the limited and short analgesia achieved, as well as the antagonist effect if it is determined that a more profound mu agonist is required.

E.   **Dose:** Selection based on degree of pain or restraint needed (low doses selected for very minor procedures) and adjusted for the size of the animal (*see Butorphanol Infusion Chart p. 229 for CRI dosing*).
   1. **Dog: 0.1 – 0.4 mg/kg** IM, SC, IV
   2. **Cat: 0.2 – 0.6 mg/kg** IM, SC, IV (0.8 mg/kg has been recommended in cats after declaw and moderate somatic surgical pain, although mu agonists and local blocks are better choices.)

OPIOID ANTAGONIST

Naloxone HCl

It is effective at reversal of both opioid agonists and agonist/antagonist drugs by competitive inhibition at opioid receptors. Full or partial reversal is possible. Analgesia can persist when low doses are used to reduce CNS depression (including respiratory depression), excessive panting or dysphoria.

A.   **Indications:** Reversal of adverse affects associated with opioid analgesics. Dilute naloxone (0.1 – 0.25 mL of 0.4 mg/mL naloxone) in 5 – 10 mL of saline and slowly titrate to effect by volumes of 0.5 – 1.0 mL each minute. As soon as respiratory depression, excessive sedation, panting or dysphoric behaviour begins to subside discontinue administration. This may have to be repeated should signs re-appear as the duration of action of opiates is greater than that of naloxone. The duration of effect is as short as 15 min, although it is uncommon to require repeated doses.

B.   **Adverse Effects:** No analgesic activity or adverse effects occur when this drug is used alone as directed above; however, if excessive doses are used and analgesia is abruptly withdrawn, tachycardia, vasoconstriction, hypertension and even pulmonary edema may occur (humans). In dogs where an assumed dose is given rather than titration, abrupt withdrawal of analgesia with excitement and difficult to control behaviour does occur. Pain will occur if full reversal is carried out in a painful animal that has no other effective analgesia present.

Other Antagonists

Nalorphine and diprenorphine have mild opioid agonistic activity, but in the presence of other opioid agonists, an antagonistic effect is apparent. Their effect is considerably longer than naloxone (up to 8 h).

Nonsteroidal Anti-inflammatory Analgesics

As the indications, adverse effects and contraindications are very similar for all NSAIAs, these are presented collectively rather than individually followed by unique differences related to each drug.

A.   **Indications**

The non-steroidal anti-inflammatory analgesics (NSAIAs) are effective in controlling most acute and chronic painful conditions. In veterinary practice some of these analgesics may be superior to opioids in that the duration of action is much longer, with equal efficacy in many instances. The NSAIAs act synergistically in combination with other modalities of pain management including all opioids, local anesthetics and various sedatives. NSAIAs usually take 30 – 60 minutes for an analgesic effect to be recognized when administered by the oral and IV routes, and much longer when given subcutaneously. In the post-operative setting an opioid should be administered concurrently to ensure adequate analgesia until the NSAIA becomes effective. Generally, the combination of an opioid with a NSAIA confers excellent analgesia in patients with moderate to severe pain. As these two groups of analgesics modulate nociceptive input through different mechanisms, their combination likely has a synergistic effect. This combination given after surgery facilitates sleep and profound analgesia.

The indications for NSAIA use proposed here assumes there are no contraindications to their use. Contraindications are discussed further in this chapter.

1. **Post-operative pain.** Orthopedic and selected soft tissue surgical procedures, especially where extensive inflammation or soft tissue trauma is present. Opioid administration is preferred immediately after any surgical procedure, due to the sedative/analgesic effects and to ensure a smooth recovery. However, the injectable NSAIAs, (carprofen, ketoprofen, meloxicam, tolfenamic acid or ketorolac[see description below]) can be co-administered with an opioid initially and subsequently used alone as the repeat analgesic following orthopedic and selected soft tissue surgery. The initial dose of NSAIAs depends on the expected severity of pain. Assuming a difficult fracture repair would require the recommended loading dose, then a laparotomy without complications, may be successfully treated with half this dose. When combination opioid and NSAIA are used, it is wise to reduce any repeat opioid dose to avoid potential dysphoria or panting that might occur due to a 'relative' opioid overdose in patients with mild to moderate pain. This very rarely occurs for a short period of time when therapeutic blood levels of both analgesics exist and the degree of pain does not warrant this level of analgesia.

2. **Inflammatory conditions.** For pain due to meningitis, bone tumors (especially after biopsy), soft tissue swelling (mastitis), polyarthritis, cystitis, otitis, severe inflammatory dermatologic diseases or injury (e.g., degloving, animal bites), combination opioids and low dose NSAIAs are also effective. As a cautionary note, where a combination of a fluroquinolone and an NSAIA were administered to dogs with *streptococcal* fasciits, there appeared to be an increased morbidity and mortality.

3. **Miscellaneous conditions.** Other indications for the use of NSAIAs are panosteitis, hypertrophic osteodystrophy (HOD), cancer pain, (especially of bone) and dental pain. COX-1 selective NSAIAs may cause hemorrhage when used with dental extractions, while thromboxane activity may be unaltered with COX-2 preferential NSAIA administration (see individual NSAIA below). For severe panosteitis and HOD the loading dose of a NSAIA is required to see an effect. The HOD of Weimaraners is poorly responsive to NSAIA therapy and is better treated with high dose, short term, corticosteroids provided infectious disease has been ruled out and clinical signs are consistent with HOD alone (*see corticosteroids p. 93*). Irish Setters and Great Danes are also prone to refractory HOD and have responded well to corticosteroids.

4. **Osteoarthritis.** Few long-term studies of the adverse effects of NSAIAs have been completed. However in the majority of cases the adverse effects appear minimal, predominantly associated with the gastrointestinal tract. As many patients with osteoarthritis are geriatric a rapid reduction of the dose to affect a comfortable state is advised to reduce potential toxicity. As some geriatric patients may have renal insufficiency and yet be in a great deal of pain, the consideration of the 'risk vs benefit' of therapy with an NSAIA for these dogs may be appropriate. Anecdotal reports of dogs and cats with renal insufficiency have improved quality of life, without alteration from baseline of creatinine, after administration of meloxicam or carprofen (personal communications with practicing veterinarians). If an individual patient requires a persistent high dose of a particular NSAIA to manage it's pain, prescribing a different NSAIA may be more effective due to individual variation in response to the different analgesics. Where the adverse effects of an NSAIA is a concern, reducing the dose and adding an opioid may be equally as effective for chronic severe pain. Other adjunctive modalities should also be considered.

   During NSAIA therapy all patients should be monitored for inappetance, hematochezia or melena, vomiting, increased water consumption and a non-specific change in demeanour. If this occurs, the owner should be instructed to stop the medication and consult their veterinarian. Intermittent monitoring of creatinine and alanine aminotransferase (ALT) is recommended when NSAIAs are prescribed chronically to identify potential toxicity. With the use of any NSAIA the drug should be decreased to the lowest possible dose that will confer a comfortable state. This may reduce the potential for toxicity, especially with long-term use.

5. **Pyrexia.** Most NSAIA have anti-pyretic activity and can be used for this purpose. The antipyretic activity of ketoprofen and meloxicam has been studied in cats. In the author's experience, half, and sometimes less, of the analgesic dose of meloxicam, ketoprofen, ketorolac (or if no other NSAIA is available, flunixin meglumine) is adequate for this effect. Aspirin or acetaminophen frequently requires the recommended dose for the anti-pyretic effect in dogs only. Dipyrone is an excellent antipyretic and is available as tablets and solution for injection. Dipyrone should be given intravenously to avoid the irritation when given intramuscularly. The analgesia produced is not adequate for moderate to severe postoperative pain. Gastric ulceration or nephrotoxicity with dipyrone is not a concern in the short term even in critically ill patients.

B. Adverse Effects

Due to their mechanism of action of the NSAIAs, there is a potential for perturbation of several homeostatic functions mediated by prostaglandins. Depending on the NSAIA selected, primary plug formation of platelets, modulation of vascular tone of the kidney and gastric mucosa, cytoprotective functions on the gastric mucosa,

smooth muscle contraction, and regulation of body temperature will all be affected. However, in this regard not all NSAIAs are created equal, as the COX-1, COX-2 and COX-3 isoenzymes variably control these functions, therefore, careful patient and NSAIA selection, with appropriate monitoring is advised. Unlike opioids, where there are no 'contraindications' for use just 'cautions', there are definite and relative contraindications for the use of NSAIAs. The general health of the patient greatly influences the decision to use NSAIAs. Cats and dogs are more susceptible than people to the adverse effects of NSAIAs therefore, the reported safety of any one analgesic in the human patient should not be assumed to be so in the veterinary patient. When given per os, NSAIAs must be given with food to protect the gastric mucosa. If food is not present in the stomach the contact area of the tablet on the mucosa results in a high localized concentration of the drug increasing the potential for localized ulcer formation. Potential for generalized gastric ulceration exists with all NSAIAs regardless of the route of administration.

C. Contraindications

1. **Relative contraindications for the use of nonsteroidal anti-inflammatory analgesics.** The use of NSAIAs should be used with caution in geriatric patients in that normal renal and hepatic function should be established prior to administration of these drugs unless there is no other alternative for management of chronic pain (*see management of osteoarthritis p. 86*). If the use of NSAIAs is being considered after a traumatic incident, the patient (see absolute contraindications for NSAIA use) should be stable with no evidence of hemorrhage (it may take several hours to determine this) and maintained on IV crystalloid therapy until adequate fluid intake has been guaranteed. Opioids may be required in the interim.

2. **Absolute contraindications for the use of NSAIAs.** Nonsteroidal anti-inflammatory analgesics should not be administered to patients in renal or hepatic failure, dehydration, hypotension, conditions associated with low "effective circulating volume" (e.g., congestive heart failure, ascites, diuretics in the acute setting), coagulopathies (e.g., thrombocytopenia, von Willebrand's disease, factor deficiencies), concurrent use of other NSAIAs (i.e., all human or veterinary NSAIAs, homeopathic compounds including willow bark) or corticosteroids, evidence of gastric ulceration (vomiting with or without the presence of 'coffee ground material', melena,) or gastrointestinal disorder of any kind. As intervertebral disc disease can be considered a 'spinal injury' NSAIAs are contraindicated due to potential hemorrhage after acute herniation (with subsequent worsening of neurologic function), and prior to laminectomy as bleeding may be increased in this difficult to compress area. The COX-2 preferential NSAIAs may not cause, or worsen, hemorrhage in spinal injury, however at this time it is not known whether this may be a problem. If these patients receive corticosteroids for medical management, NSAIAs would be contraindicated. NSAIAs should never be administered to patients in shock, trauma cases upon presentation or where hemorrhage is evident (e.g, epistaxis, hemangiosarcoma, head trauma). Animals with severe or poorly controlled asthma, or other moderate to severe pulmonary disease, may deteriorate with NSAIA use due to potential for antagonism of prostaglandin-mediated smooth muscle relaxation. COX-2 selective or preferential NSAIAs may be suitable in these conditions. The NSAIA may also have effects on the reproductive tract and fetus, it is advised that NSAIAs should not be administered during pregnancy. As COX-2 induction is necessary for ovulation and subsequent implantation of the embryo, NSAIAs should be avoided in breeding females during this stage of the reproductive cycle. The canine kidney is not fully mature until 3 weeks after birth; continual administration of a NSAIA to the bitch during this time (as the drug may pass into the milk), or prior to birth, may cause a permanent nephropathy.

D. Comments and Other Considerations

The NSAIAs are highly protein bound. While this may not be of significance in most instances (since increases in free drug that result from protein binding interactions are offset rapidly by increased clearance of the extra free drug), concommitent drug interactions may occur and should be considered. Caution here would apply to patients with even mild or potential organ dysfunction, hypoalbuminemia, and in those receiving medication which are also highly protein bound, and those with a narrow therapeutic index.

Due to the effects of the NSAIAs on dilatory PGs, co-administration with angiontensin-converting enzyme inhibitors (ACEI), and beta-blockers may reduce the efficacy of these drugs. Combination ACEI and tepoxilin in normal dogs had no adverse effects on renal function. The NSAIAs do not appear to affect the efficacy of calcium channel blockers such as amlodipine. As this has not yet been reported in cats and dogs, careful monitoring is necessary on an individual basis.

Some NSAIAs may induce the syndrome of inappropriate secretion of antidiuretic hormone and enhance sodium reabsorption and water. Clinically, both mechanisms may result in a low urine output with high specific gravity, and a dilutional hyponatremia. Urine volume may be decreased through this mechanism but without renal injury.

Acute NSAIA-induced renal insufficiency is usually temporary and reversible with drug withdrawal and administration of IV fluids. Accidental ingestion of NSAIAs should be managed with gastric lavage followed by administration of activated charcoal and gastric protectants (*see Toxicological Emergencies p. 634*). If evidence of gastric ulcers (*p. 69*) exist, aggressive sucralfate therapy is necessary. Intravenous fluid therapy should continue for a minimum of 24 hours. Therapy beyond this period will depend on the renal and gastric status of the individual patient.

VETERINARY APPROVED NSAIAs

Carprofen (Rimadyl®, Pfizer)

Tablet and parenteral formulation. Studies indicate that carprofen is a COX-2 preferential NSAID although other mechanisms of action may exist. Carprofen is approved for peri-operative and chronic pain management in dogs in Australasia, Europe and North America. Carprofen is approved for a single dose, peri-operative use in cats in Europe. Based on the European literature, potential adverse effects of NSAIAs, such as nephrotoxicity, hepatotoxicity, gastrointestinal bleeding, or hemostatic deficiencies, have not been reported with carprofen use. In North America, acute hepatotoxicity and death after carprofen administration has been reported in dogs (Labrador retrievers highly represented) with previously reported normal liver function.

Surgical pain	Dogs ≤4.0 mg/kg IV, SC	Once upon induction
	≤2.2 mg/kg PO	Repeat q12h–24h PRN
	Cats ≤4.0 mg/kg SC lean weight	Once upon induction
Chronic pain	Dogs ≤2.2 mg/kg PO	q12h–24h

Dosage:

Deracoxib (Deramax®, Novartis)

Tablet formulation. Deracoxib is a COX-2 specific inhibitor. Deracoxib is approved for control of postoperative pain and inflammation associated with orthopedic surgery in dogs. The incidence of vomiting and diarrhea were similar to dogs receiving placebo in a perioperative field trial, however, overall the drug was well tolerated and effective. This group of NSAIAs appeared to be gastroprotective in human patients when compared to the less COX-2 specific NSAIAs, when used for eight days to three months. However, more recent studies in humans indicate these NSAIAs cannot guarantee gastroprotection in chronic use. Anecdotal reports indicate this may also be the case in dogs. It has been recommended that deracoxib should not be administered for a period of 7 days after discontinuing a previously administered NSAIA, other NSAIAs should not be administered within 7 days of deracoxib administration. The reason for this is that the COX-2 isoenzyme is required for gastrointestinal healing. Should erosions or ulcers be present, the down-regulation of COX-2 in this area will prolong healing and potentially predispose to deeper ulcer/perforation.

Dosage: Perioperative: Dogs: 3 – 4 mg/kg PO q24h. Reduce after 1 – 2 days, to 1 – 2 mg/kg q24h.

Etodolac (Etogesic®, Fort Dodge)

Tablet formulation. Etodolac selectively inhibits COX-2 and is approved in the United States for use in dogs for the management of pain and inflammation associated with osteoarthritis. The adverse effects appear to be rare and primarily associated with the gastrointestinal tract; however etodolac has been associated with excessive bleeding in dogs during experimental surgery (Etogesic label, Wyeth Animal Health).

Dosage: Dogs: ≤10 – 15 mg/kg q24h.

Firocoxib Previcox Merial

Tablet formulation. Firocoxib selectively inhibits COX-2 and is approved in the United States for use in dogs for the management of pain and inflammation associated with osteoarthritis. The adverse effects appear to be rare and primarily associated with the gastrointestinal tract. At the time of publication, this NSAIA is a new release onto the veterinary market and full assessment of potential adverse effects are not known beyond the controlled published studies.

Dosage: 5.0 mg/kg (2.27 mg/lb) q24h for dogs >3.5 kg (7 lbs). Due to the tablet formulation, accurate dosing in smaller dogs is not possible and therefore, not recommended.

Flunixin meglumine (Flunixin®, Schering-Plough)

Parenteral formulation. Flunixin meglumine is a COX-1 and COX-2 inhibitor and is approved for use in dogs in Europe but not North America. In dogs, it is reported to be an effective analgesic for surgical pain, however, the potential for side effects such as increased ALT, nephrotoxicity, and gastric ulceration is of major concern. Flunixin meglumine is also used as an antiinflammatory in selected ophthalmological surgical procedures; however safer NSAIAs appear to be as effective.

Dosage:

Surgical pain	Dogs ≤1.0 mg/kg IV, SC, IM	Once
	Cats 0.25 mg/kg SC	q12–24h PRN for 1 or 2 treatments
Pyrexia	Dogs and Cats 0.25 mg/kg	q12–24h PRN for 1 or 2 treatments
Ophthalmological procedures	Dogs 0.25 – 1.0 mg/kg	q12–24h PRN for 1 or 2 treatments

Ketoprofen (Anafen®, Merial)

Tablet and parenteral formulations. Ketoprofen is approved for postoperative and chronic pain in both dogs and cats in Europe and Canada. As ketoprofen is an inhibitor of both COX-1 and COX-2 adverse effects are a potential problem requiring careful patient selection. Although several laboratory studies using ketoprofen pre-operatively indicate its effectiveness in controlling post-operative pain, it is the authors' opinion that ketoprofen should be reserved for post-operative use to reduce the potential for hemorrhage. Ketoprofen should not be administered to patients where hemorrhage is a potential problem. Ketoprofen may be administered to animals immediately after orthopedic procedures (e.g., fracture repair, cruciate repair, onychectomy); however, it is advised to restrict administration after laparotomy or thoracotomy until such time that hemorrhage is not a concern and when intra-cavitary 'tubes' have been removed.

Ketoprofen should be avoided following dental procedures until the primary clot is formed due to the potential for hemorrhage.

Dosage:

Surgical pain	Dogs ≤2.0 mg/kg IV, SC, IM, PO	Once
	Cats ≤2.0 mg/kg SC	Postoperative
	Dogs and Cats ≤1.0 mg/kg	Repeat q24h
Chronic pain	Dogs and Cats ≤2.0 mg/kg PO	Once
	≤1.0 mg/kg	Repeat q24h

Meloxicam (Metacam®, Boehringer-Ingelheim)

Oral liquid and parenteral formulation. Meloxicam is a COX-2 preferential NSAID approved for peri-operative and chronic pain management in dogs in Australasia, Europe and North America. The parenteral formulation is approved for cats in Australasia and the USA. Its use in cats in Canada is under investigation with completed studies indicating safety and efficacy. Studies indicate no renal or hepatic abnormalities with acute administration and minimal to no anti-thromboxane activity suggesting hemostasis in normal animals may not be a problem. Adverse reactions with chronic administration are primarily gastrointestinal. It is the author's opinion that the recommended dose of 0.3 mg/kg for cats is too high (and should not be administered).

Surgical pain	Dogs ≤0.2 mg/kg IV, SC	Once
	≤0.1 mg/kg IV, SC, PO	Repeat q24h
Chronic pain	Dogs ≤0.2 mg/kg PO	Once
	≤0.1 mg/kg PO	Repeat q24h
Surgical pain	Cats ≤0.2 mg/kg SC, PO, IV slowly	Once
	≤0.1 mg/kg SC, PO, IV slowly lean weight	Daily x 2 – 3 days
Chronic pain	Cats ≤0.2 mg/kg SC, PO, IV slowly	Once
	≤0.1 mg/kg PO, IV slowly lean weight	2 – 3 days
	0.025 mg/kg PO, IV slowly (0.1 mg/CAT max) lean weight	Alternate days

Dosage:
Tepoxalin (Zubrin®, Schering-Plough)

Dissolvable waifer. Tepoxalin is, to varying degrees, a COX-1, COX-2 and lipoxygenase inhibitor with efficacy comparable to meloxicam or carprofen and safety comparable to placebo. Tepoxalin, has recently been approved for management of osteoarthritic pain in dogs. The safety profile of tepoxalin showed no difference from placebo with respect to surgical hemorrage when administered prior to a 30 minute anesthesia period and a minor surgical procedure in dogs. In addition to osteoarthritis, tepoxalin may be also be suitable for managing dermatological discomfort and pain.

Dosage: Dogs: 10 mg/kg PO q24h.

Tolfenamic Acid (Tolfedine®, Vetoquinol)

Tablet and parenteral formulation. Tolfenamic acid preferentially inhibits COX-2 and is approved for use in cats and dogs in Europe and Canada for controlling acute post-operative and chronic pain. The dosing schedule is 3 days on and 4 days off which must be strictly adhered to. Reported adverse effects are diarrhea and occasional vomiting. Tolfenamic acid is reported to have significant anti-inflammatory and anti-thromboxane activity, therefore, post-traumatic and surgical hemostasis may be compromised during active bleeding after administration of this NSAIA.

Dosage: Surgical and chronic pain. Cats/Dogs: ≤4 mg/kg SC, PO. Once daily for 3 days. 4 days off. Repeat the cycle.

Vedaprofen (Quadrisol-5®, Intervet)

Paste in a tube. Approved for management of chronic pain in dogs in Europe and Canada. Vedaprofen preferentially inhibits COX-2. Caution is advised with prescribing (especially for small dogs) as the current dosing guidelines from the tube may be difficult for some clients to manage.

Dosage: Chronic pain. 0.5 mg/kg q24h using a small volume of paste proportional to weight according to a syringe guide provided. Caution here is essential when dispensing to small dogs as it may be dificult to retrieve an accurate dose with this syringe dispenser.

NSAIAs NOT SPECIFICALLY APPROVED FOR USE IN VETERINARY PATIENTS (OFF LABEL USE)

Acetaminophen

Tablet and oral suspension formulations. Generic or Tylenol®. Acetaminophen is a COX-3 inhibitor with minimal COX-1 and COX-2 inhibition. It should not be administered to cats due to deficient glucuronidation of acetaminophen in this species. Acetaminophen may be administered to dogs as an antipyretic, and analgesic for mild pain and can be used in combination with opioids for a synergistic analgesic effect or opioid-sparing effect. Acetaminophen can be prescribed as an individual drug (which the author [KM] prefers as this allows more flexibility in dosing of the opioid) in addition to any opioid, or in a combined formulation with an opioid, (e.g., codeine plus acetaminophen, or oxycodone plus acetaminophen). Acetaminophen is an effective antipyretic agent.

Dosage: Dogs only 15 mg/kg q8h.

Aspirin

Tablet formulation. Aspirin is primarily a COX-1 inhibitor. It is most commonly used as an analgesic for osteoarthritic pain in dogs. It is formulated in combination with opioids, aspirin plus codeine or aspirin plus oxycodone, for a synergistic effect for the treatment of moderate pain, or can be administered for an opioid-sparing effect. It is also used as an antipyretic and anticoagulant.

Dosage: Dogs only 10 mg/kg q12h.

Dipyrone (Vetoquinol)

Tablet and parenteral formulations. Dipyrone is a COX-3 inhibitor and is approved for use in cats and dogs in Europe and Canada. Dipyrone should be given intravenously to avoid the irritation experienced when given intramuscularly. In the author's (KM) experience, the analgesia produced is not adequate for moderate to severe postoperative pain, and dipyrone is reserved for use as an antipyretic in cases where other NSAIAs are contraindicated. Nephrotoxicity or gastric ulceration is not a major concern in the short term even in critically ill patients. Dipyrone induces blood dyscrasias in humans, this has not been reported in animals.

Ketorolac (Toradol®, Hoffman-LaRoche)

Parenteral and oral formulations. Ketorolac is a COX-1 and COX-2 inhibitor and is included for the benefit of those working in the research setting associated with human hospitals where the availability of ketorolac is more likely than other NSAIAs. Ketorolac is comparable to oxymorphone in efficacy and to ketoprofen in duration and efficacy in managing post-laparotomy and orthopedic pain in dogs. Only 1 – 2 doses should be administered to dogs or cats post-operatively. Ketorolac has been used successfully for treatment of severe panosteitis in dogs where all other therapies had failed. Ketorolac given with food for two to three days eliminated clinical signs in approximately 99% of these dogs; in the other 1%, signs recurred within a few days to months (KM unpublished observations). Gastroprotection should be co-administered.

Dosage:

Surgical pain	Dogs 0.3 – 0.5 mg/kg IV, IM	q8–12h for 1 – 2 treatments
	Cats 0.2 mg/kg IM	q12h for 1 – 2 treatments
Panosteitis	Dogs: 10 mg/**DOG** ≥30 kg, PO	Once daily for 2 – 3 days
	5 mg/**DOG** >20 kg<30 kg, PO	

Piroxicam

Capsule formulation. Generic or Feldene·. Piroxicam is valuable for its anti-inflammatory effects on the lower urinary tract in dogs with transitional cell carcinoma or cystitis and urethritis. It is also used as an analgesic in dogs. Gastroprotectants are recommended.

Dosage: Dogs 0.3 mg/kg PO q24h for 2 treatments, then q48h.

ADJUVANT ANALGESICS

Adjuvant analgesic drugs such as lidocaine, N-methyl-D-aspartate (NMDA) receptor antagonists (ketamine, amantidine), gabapentin and tricyclic antidepressants are not primary or first choice analgesics. Adjuvant analgesics are typically used in combination with other known analgesic drugs in acute pain states to manage severe pain, where they appear to enhance their analgesic action, or reduce the dose of the primary analgesic. In certain chronic pain states where pain appears to be refractory to the commonly used classes of analgesics (i.e., opioids, NSAIAs) the adjuvant analgesic may be used successfully alone. Indications and adverse effects are discussed for specific conditions throughout this manual.

Lidocaine

In addition to the local anesthetic effects, lidocaine has been shown to alleviate neuropathic pain and hyperalgesia and to reduce opioid requirements following surgery when administered as a CRI. A CRI can be used intra-operatively to reduce the inhalant requirements or post-operatively in combination with opioids and ketamine for the severely painful patient. While not necessarily used as an adjunctive analgesic, lidocaine may be useful in managing head trauma patients during periods of increasing intracranial pressure (ICP) such as occurs during vomiting or 'gagging'. Lidocaine has been reported to lower intracranial pressure during endotracheal intubation. This author has used lidocaine 1 mg/kg bolus, to treat impending tentorial herniation and suggest a 2 mg/kg/h CRI, in some cases, to reduce the opioid requirement in this acute setting for the ensuing 24 hours only. Lidocaine overdose may predispose to seizure activity (higher doses have been used and will provide greater MAC reduction intraoperatively).

Dosage:

Dogs: 1 – 4 mg/kg IV bolus, followed by 1 – 3 mg/kg/h CRI.
Cats: 0.25 – 1 mg/kg IV bolus, followed by 10 – 40 μg/kg/h CRI (the author has not used this in cats).
Dogs: 40 – 80 μg/kg/min, CRI, Intra-operative + inhalant ± opioids.

Ketamine

Ketamine is an *N*-methyl-D-aspartate (NMDA) antagonist, blocking the NMDA receptor wind-up and subsequent sensitization of dorsal horn neurons. Ketamine may also abolish established central sensitization. Ketamine should not be used alone for pain management. Ketamine, via constant rate infusion, is used as an adjunctive analgesic in severe pain states in combination with an opioid to enhance analgesia or reduce opioid requirements. The infusion should be tapered down to prevent potential hyperalgesia. The hourly dosage varies considerably and is dependent on the pain experienced. The dosages below are those recommended, however, the author has used as high as 4 mg/kg/hour in dogs, in addition to high dosages of opioid (fentanyl or morphine), to achieve a level of comfort facilitating sleep in patients with severe to excruciating pain. At the lower dosages required to relieve pain, the patient is alert and comfortable. **Ketamine is excreted via the kidney in cats and metabolized by the liver in dogs. It is essential that these organs are functioning normally prior to administration of ketamine. U.S. Schedule III.**

Dosage: Dogs/Cats: 0.2 – 4.0 mg/kg IV bolus for control, followed by, 0.2 – 4.0 mg/kg/h CRI depending on severity of pain.

TRICYCLIC ANTIDEPRESSANTS

Tricyclic antidepressants may be effective adjunctive analgesics for a range of chronic painful conditions in animals such as cancer pain, neuropathic pain or, used alone in such conditions as inflammatory bowel disease and feline interstitial cystitis, to name a few. In humans, the analgesic effects of these drugs appear to occur at lower than the anti-depressant doses. When all other traditional treatments of pain with appropriate analgesics have failed, imipramine or amitriptyline may prove successful in managing the refractory, chronic pain experienced. These two drugs do produce analgesia in humans. These products may be distasteful and may require some creative method of administration. The time it takes to achieve maximal effectiveness with these drugs in some animals may be 2 – 4 weeks.

Amitriptyline
Dosage:

> **Dogs:** 1 – 2, PO q12–24h.
> **Cats:** 2.5 – 12.5 mg/cat PO q24h.

Imipramine
Dosage:

> **Dogs:** 0.5 – 1, PO q8h.
> **Cats:** 2.5 – 5 mg/cat PO q12h.

Gabapentin

Gabapentin is used in human patients for management of neuropathic pain associated with diabetes, cancer or primary nerve compression. One of the classic features of this type of pain is the presence of abnormal pain induced by a non-noxious stimulus (allodynia). Frequently conventional analgesics such as opioids and NSAIAs show limited value in treating this type of pain. In dogs and cats suffering from neuropathic pain secondary to cervical or thoracolumbar intervertebral disc disease or pelvic trauma, gabapentin has reduced the pain in these severe pain states. Initially, gabapentin is administered in combination with an opioid and an NSAIA but gradually these drugs can be tapered off and gabapentin may remain the sole method of analgesia. There is an extremely wide dose range for gabapentin and it should be given to effect. The dose limiting affect generally observed is sedation. Frequently, some animals need several weeks to months for resolution, if ever, of their pain. This author has found gabapentin useful in treating animals following cardiopulmonary arrest, or seizures, that are extremely restless, disoriented, vocalizing and/or manic. Again, dosing to effect and resolution of these signs is the goal. Sedation in this instance is appropriate! Careful lowering of the drug is recommended. Gabapentin is an antiepileptic agent. It has been reported that gabapentin binds with the high affinity αδ subunits of voltage dependent calcium channels, blocking calcium currents in isolated cortical neurons and blocking maintenance of spinal cord central sensitization. Gabapentin is excreted by the kidneys; animals with renal insufficiency may require less frequent dosing due to slower elimination. As dosing to effect is the method by which the appropriate dose is selected, once this effect is reached, twice a day rather than three times daily treatment may suffice. Tapering the dose down is important, as stopping the drug abruptly may lead to rebound pain which may be severe.

Dosage:

> **Dogs:** 5 – 25 mg/kg, usually starting at 10 mg/kg PO q8–12h. Dose to effect.
> **Cats:** 5.0 – 25 mg/kg 10 mg to start, taper up or down to effect, PO q8h for pain.
> up to 12 mg/kg PO q6h for post-seizure or post-CPR vocalization and thrashing. Wean off slowly.

Amantadine

Amantadine is an NMDA receptor antagonist and may be useful as an adjunct to a non-steroidal anti-inflammatory analgesic for chronic pain management. Results may not be appreciated for 5 – 7 days. Potential adverse affects are agitation and diarrhea during the initial use of the drug. As with any other drug, its use should be discontinued, or the dose lowered, should adverse effects persist more than one day.

Dosage: Dogs/Cats: 3 mg/kg PO q24h.

CORTICOSTEROIDS

Among other actions, corticosteroids inhibit COX–2 gene expression, which is upregulated in inflammatory states, reduces aberrant firing originating from nerve injury and reduces inflammation at the site of injury. However, corticosteroids should not be used as analgesics but should be used to treat the underlying problem where appropriate such as in immune-mediated disease or as part of the regimen for the treatment of certain neoplastic diseases. Corticosteroids should not be administered with NSAIAs. Ascertain no infection present prior to starting a course of corticosteroid therapy. Hypertrophic osteodystrophy has been managed successfully using the following dosing regimen:

a. Prednisone 0.75 mg/kg PO q12h for 4 – 5 days, extending to no more than 7 days if signs are persisting.
b. Gradually wean off over a 4 – 5 week period, reducing the total daily dose by one-half each week, then administer 5 mg of Prednisone every other day for an additional 1 – 2 weeks.
c. In all cases, also administer 3V Caps (or Derm Caps•) and either Glyco-Flex or Multi-source Glucosamine.
d. Supportive care should be provided as needed.
e. Oral antibiotics, usually Clavamox, Amoxicillin or Clindamycin for 3 – 4 weeks are co-administered.
f. Antacids (famotidine or ranitidine) are also co-administered.
g. Dogs should not be exposed to possible contagious disease, and owners should be advised not to take their dogs to dog shows, dogs parks, etc.

SEDATIVES

Acepromazine

Phenothiazine derivative acts by depression of the reticular activating system of the brain. The effect produced is mild sedation. Schedule F2: No records are required.

A. **Indications:** Mild restraint, calming, sedation. Commonly used in combination to reduce dose needed and improve effect of other drug (i.e., with ketamine or an opioid).

B. **Adverse Effects:** Induces hypotension via vasodilation (hypothermia also occurs). Rare potential for unexpected aggression when used alone.

C. **Contraindications:** Animal is in shock, weak, dehydrated or severely debilitated. Advanced kidney, liver, or cardiovascular disease. Trauma (especially to head or chest). History of epilepsy, or seizures (somewhat controversial, but the patient should be observed if administered), or actively displaying signs of seizure disorder. Should be avoided if possible in animals undergoing diagnostic myelograms. May unmask underlying cardiac problems in Boxer dogs (anecdotal descriptions of arrhythmias, hypotension), but is still indicated in an otherwise young, healthy dog.

D. **Comments:** Can be mixed with most drugs (not diazepam). Always assess heart rate and peripheral pulses when effect appears more profound than expected in order to identify hypotension or other problems.

E. **Dose: 0.01 mg/kg – 0.1 mg/kg** IM, SC. Use the lower end of the dose for quiet, depressed patients, geriatrics, if cardiac or renal concerns exist or at anesthetic recovery. Combinations allow reduced dose selection. Young and healthy dogs are often given 0.1 mg/kg if used alone or 0.05 mg/kg when used with opioids. Cats can receive up to 0.2 mg/kg alone and 0.05 – 0.15 mg/kg with opioids, depending on health and desired restraint.

Diazepam

Benzodiazepines act at GABA receptors to produce tranquilization and muscle relaxation. Schedule F1: This is now a targeted drug, so increased record keeping is recommended (US Schedule IV).

A. Indications: Produces mild to moderate sedation (dependent on patient condition and opioid chosen) when combined with opioids in animals with a known history of epilepsy, undergoing CSF taps or myelographic studies, neurological disorders requiring surgery, head injuries, cardiovascular disease or geriatric animals. Produces good muscle relaxation especially when combined with ketamine. Diazepam is the best treatment for seizures. It has been used in combination with barbiturates and propofol for induction, prolonging their effect slightly and reducing the dose required, often smoothes intubation and transfer to inhalant.

B. Adverse Effects: It is rarely effective as a sedative on its own except in the severely depressed animal. Some animals will show excitement if adequate depression is not present. **Reversal with flumazenil** 0.01 mg/kg IV to effect prn in dogs and cats.

C. Contraindications: History of excitement with previous administration or use alone in the healthy animal. Significant liver disease.

D. Comments: Should be given intravenously as it is painful if given IM. However, if combined with ketamine, it is not likely more painful than ketamine alone. The IM route has a more variable effect due to the drug depot of the vehicle (not water soluble). Precipitates when mixed with most drugs (except ketamine). No precipitation if added to a large volume of saline for infusion. High concentrations for infusion (i.e., less than hourly maintenance requirements) will precipitate. Light sensitive if infusion is longer than 2 hours, therefore wrap infusion tubing with foil wrap.

E. Dose: Usually **0.2 mg/kg** IV (max 10 mg), although up to 0.5 mg/kg can be used in smaller patients. (*See Seizures Cat p. 458 and Seizures Dog p. 462 for further recommendations*).

Midazolam

Identical to diazepam, except formulated as a water soluble solution eliminating concerns for precipitation, pain on injection or depot accumulation with unpredictable results. Schedule F1: This is now a targeted drug, so increased record keeping is recommended (US Schedule IV).

A. Indications: See diazepam.

B. Contraindications: See diazepam.

C. Comments: More expensive, so usually reserved when IM injections used or drug mixing an advantage.

D. Dose: Usually **0.2 mg/kg** IV (max 10 mg), although up to 0.5 mg/kg can be used in smaller patients.

Medetomidine

Xylazine-like drug (alpha-2 agonist) provides mild sedation to profound chemical restraint in healthy animals, analgesia and muscle relaxation. Schedule F2: No records are required.

A. Indications: Analgesia can be significant, but should not be assumed complete without assessment. Restraint is excellent. Adds muscle relaxation when needed.

B. Adverse effects: It is not recommended in other than the young, healthy patient due to the depression in cardiac function.

1. Severe cardiac output depression, bradycardia and vasoconstriction occur, and impair perfusion. The impact of this is not clear on organ function. Arrhythmias have occurred in dogs with myocardial disease.
   Do not treat the bradycardia noted (35 – 55 bpm commonly) with an anticholinergic unless other vasodilating drugs (like isoflurane) are also in use, due to the increased workload on the heart. If concerned about the bradycardia in a sedated (non-anesthetized) animal, reverse the medetomidine.
   a. **Reversal: Yohimbine (0.125 mg/kg IM or IV),** or the more specific antagonist, **atipamezole (same volume** as medetomidine used; administer, IM, subcutaneous or very slow titration IV to effect when medetomidine wearing off or partial reversal desirable) are capable of fully reversing the effects. Animals that are not reversed appear to recover totally in 2 – 2½ h and eat and act normally at this time, although analgesia effect is much shorter (approximately 1 h).

  b. Animals that appear to be very depressed, have become vicious if suddenly approached. Approach the patient carefully and assess the 'sedation' to make sure it is real.

  c. Intermittent spastic jaw tone, muscle twitching and tail wagging can make some procedures more difficult.

  d. Veins and arteries may be more difficult to access in some animals due to the perfusion effects. Monitoring with pulse oximetry and blood pressure equipment may also be difficult due to the vasoconstriction.

  e. Grey mucus membranes are often produced due to vasoconstriction and venous desaturation secondary to low cardiac output. Oxygen supplementation is advised.

  f. Vomiting can occur following administration.

C. **Dose:** The dose recommendations on the bottle are based on surface area, while doses here are noted in mg/kg with the suggestion that the higher doses are for small animals and lower for large. It can be given IM or IV and requires 15 min for the drug to reach the peak effect (leave the animal undisturbed). The drug produces a more consistent effect when it is administered IV and/or with an opioid (standard doses of any of them), or with ketamine in cats (*see below*).

  1. **Dogs:** 2 – 10 μg/kg (lowest dose is more commonly effective in animals recovering from anesthesia to calm them and add mild analgesia)

  2. **Cats:** 10 – 20 μg/kg. As with most drugs, cats require a higher dose/kg.

  3. **CRI:** 1 – 3 μg/kg/h combined with an opioid in stable but difficult to physically manage painful animals

Ketamine

This dissociative anesthetic agent can be used in low doses to provide sedation and restraint and is very effective in cats. In combination, it produces smoother, more relaxed sedation to anesthesia (and thus is recommended in combination if possible), and can be suitable for dogs, too. More information is provided about ketamine in the section on Induction and Maintenance of General Anesthesia (US Schedule III).

A. **Indications:** The bad cat, that can't be handled to administer other means of restraint, can be given ketamine by spraying onto the mucous membranes of the mouth. There is little reason otherwise to use it alone. Ketamine is also used as an adjunctive analgesic when pain is difficult to manage with an opioid alone. Can be used in conjunction with opioids, lidocaine and NSAIAs for severe pain.

B. **Adverse Effects:** Muscle rigidity, salivation, rough recovery if sedatives are not added after restraint has been achieved. Must be combined with an opioid when used as an analgesic.

C. **Contraindications:** Suspicion of renal failure (cats), hyperthyroidism or hypertrophic cardiomyopathy. In dogs, adequate liver function is required for elimination.

D. **Dose:** 5.0 – 10.0 mg/kg PO (since we often miss with some of it, the higher dose is usually chosen). Heavily sedated animals may be restrained further by administering 2 mg/kg ketamine to effect, although ketamine/diazepam is more frequently selected due to familiarity. In aggressive dogs, 5.0 mg/kg may be added to other premedication drugs to enhance the effect. The analgesic dose has a wide range. Load with 0.2 – 1.0 mg/kg and continue as an infusion at this dose/h (*see Ketamin Infusion Chart p. 245 for CRI dosing*). Titrate to effect.

Propofol

This general anesthetic can be administered in low doses to achieve sedation and restraint. IV access is necessary. The desired effect can be achieved by titration of incremental IV doses **(0.5 – 1 mg/kg).** This is most commonly done when other restraint was not effective for a procedure to be carried out, but is also useful to move an aggressive animal or a painful animal out of a cage. More information is provided about propofol in the section on Induction and Maintenance of General Anesthesia. Propofol may also be used as a constant rate infusion (see CRI chart for dosing) when combined with an opioid or ketamine for maintenance on mechanical ventilation (*see Chemical Restraint for respiratory compromise p. 101*) and in combination with diazepam, or alone, when controlling status epilepticus (*see Seizures Cat p. 458, Seizures Dog p. 463*).

Pentobarbital

This short acting oxybarbiturate is rarely used in small animals for anesthesia, but is suitable as a preanesthetic medication or mild sedative **(5.0 mg/kg IM)** in dogs that may be sensitive to acepromazine seizure activity. It is also used as a CRI in combination with midazolam or opioid for restraint during longterm mechanical ventilation (US Schedule II).

COMBINATION THERAPY

Opioid Combinations

Chemical restraint with a significant analgesic effect can be expected from these combinations. It is recommended that animals are left undisturbed for 15 min after administration to reach the full extent of sedation. IV administration is usually more effective than IM. In dogs, opioids alone may provide adequate restraint in the older or more depressed animal. Cats rarely demonstrate more than moderate sedation even when combinations are used.

A. **Oxymorphone or hydromorphone 0.05 – 0.2 mg/kg** dogs and cats IV, IM; **morphine 0.3 – 0.5 mg/kg** dog IM; 0.1 mg/kg (cat) IM; or **butorphanol 0.1 – 0.4 mg/kg** dogs and cats IV, IM in combination with

    1. **Acepromazine 0.01 – 0.05 mg/kg.** The lower doses are more effective in older and depressed patients.
    2. **Diazepam 0.2 – 0.5 mg/kg,** or **midazolam 0.2 – 0.5 mg/kg.** Diazepam or midazolam replace acepromazine in the typical combination when less cardiovascular depression is desirable or the patient already has a degree of CNS depression associated with the disease.

Medetomidine Combinations

See above under Medetomidine. Also can be used with ketamine in cats (*see below*).

Ketamine Combinations

In combination, it produces smoother, more relaxed sedation to anesthesia, and can be suitable for dogs, too. Refer to Ketamine above.

A. **Acepromazine/ketamine** – IM in cats with or without an opioid (any of the opioids in standard doses) to produce sedation (lower ketamine dose) to general anesthesia. (higher ketamine dose) – *see General Anesthesia section p. 114.*

    a. **Doses: Acepromazine 0.05 – 0.2 mg/kg** can be mixed with **ketamine 5.0 – 20.0 mg/kg** and a suitable opioid in the same syringe – *see Acepromazine and Opioids above.*

B. **Diazepam/ketamine** – IV titration preferred, although IM will work. If IV, a 1:1 (by volume – 5 mg/mL:100 mg/mL, respectively) mixture can be titrated using **0.02 – 0.03 mL/kg** to the desired effect. If IM restraint is needed, **0.06 – 0.1 mL/kg** is given (dose based on health of patient). Midazolam can replace diazepam and is preferred for IM injection – *see Diazepam or Midazolam above.*

C. **Medetomidine/Ketamine** – IM administration to produce restraint can be achieved with **10 μg/kg medetomidine** and **5 mg/kg ketamine** in healthy, 'bad cats'. Refer to concerns related to medetomidine use.

SUGGESTED READING

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4. Thurmon JC, Tranquilli WJ, Benson GJ. Lumb & Jones' Veterinary Anesthesia. Williams and Wilkins, Baltimore. 1996.
5. Trostel CT, Pool RR, McLaughlin RM. Canine Lameness Caused by Developmental orthopedic Diseases, in Compendium volume 25(4), 2003:282-293.

NOTES

This section considers appropriate chemical restraint and analgesia for several specific procedures that are often required in an emergency or critical care situation.

Specific Procedures List

- Venous Cut-Down
- Percutaneous Intra-Arterial or IV Catheter Placement
- Thoracocentesis
- Chest Tube Placement
- Placement of a Urinary Catheter
- Wound Management/Bandage Change
- Abdominal Ultrasonographic Examination and Biopsy

In compromised patients (i.e., hypotension, hypoxemia), stabilization through oxygen and fluid delivery takes priority over chemical restraint and diagnostic procedures; however, analgesia must be considered a priority, as outlined in Chemical Restraint for Specific Emergencies.

In unconscious patients chemical restraint is not necessary. Many stuporous or shock patients may not require chemical restraint. However, individual consideration is required. Although other patients will need some chemical restraint, it is wise to use lower drug dosages when animals are geriatric, depressed, recently traumatized, or cardiovascularly compromised. If the degree of restraint or analgesia is inadequate, additional doses may be administered. Opioids have the advantage of fast reversal at the end of the procedure, or at any time should adverse effects be noted. Naloxone can be administered to achieve either partial (titration of a low dose to the desired effect) or total reversal, as desired. Infiltration of a local anesthetic should be considered for potentially painful procedures (e.g., cut down for IV access, suturing wounds, stabilizing fractured ribs, etc.) in any animal, but particularly so where higher drug doses may compromise the patient further.

Some drugs are contraindicated in certain cases. Sedatives, such as acepromazine or medetomidine, are rarely required in the compromised animal and may be associated with significant adverse effects (*see Analgesics/Sedatives p. 93/94*). Avoid ketamine in cats with renal insufficiency, or with potentially significant renal compromise from long-standing urethral obstruction.

Within this section, the term profound mu agonists will be used to refer to all mu agonists except meperidine (hydromorphone, oxymorphone, fentanyl are most common). Better sedation and excellent dose-related analgesia are expected with their use (compared to the reduced/more mild effect of meperidine, butorphanol or buprenorphine). The dose range of **oxymorphone is 0.03 – 0.1 mg/kg, hydromorphone is the same, but as high as 0.2 mg/kg can be used for better restraint and the fentanyl dose range is 1 – 5 μg/kg.**

A. Venous Cut-Down

When venous cutdown is required for catheter access in hypovolemic/hypotensive patients the animal is usually in shock. Therefore, avoid chemical restraint. If this procedure is required in more stable patients, mild restraint can be used if necessary (opioid alone usually).

1. Infiltrate skin and subcutaneous tissue with **0.5 – 1.0 mL of 0.5 – 1% lidocaine** (allowing 5 minutes for full effect) prior to performing this procedure.
2. Where the patient may not tolerate the 'sting' of lidocaine or where a bleeding disorder exists (to avoid further bleeding in the area of the cut-down), apply **EMLA cream** (Astra) over the previously cleansed venous access site 30 minutes prior to injection of lidocaine or cut-down. **EMLA cream** alone may not be adequate, as it does not penetrate the subcutaneous tissue.
3. Animals that are very stressed and resistant to handling can be given an IM **opioid** alone, or **sedative** (pentobarbital 5 mg/kg, midazolam 0.2 mg/kg, 0.2 – 0.5 mg/kg in cats), with or without an opioid, or low dose ketamine 5 mg/kg in cats.

B. Percutaneous Intra-Arterial or IV Catheter Placement

Usually performed without chemical restraint, unless jugular catheter placement is required.

1. **Sedation** may be required in difficult patients. It is usually beneficial for most jugular catheter placements.
   a. **Butorphanol 0.2 – 0.4 mg/kg** may suffice if profound mu opioid analgesia is not needed for other procedures.

      b. A profound mu agonist will produce better restraint.

      c. Diazepam or midazolam 0.2 – 0.5 mg/kg can enhance the opioid effect.

      d. Profound chemical restraint with **ketamine 10 mg/kg/midazolam 0.2 – 0.5 mg/kg IM** may be required in cats.

2. **Lidocaine 0.5 – 1.0 mL of 0.5 – 1%,** local subcutaneous infiltration (allowing 5 minutes for full effect) will facilitate jugular catheter placement and allow lower levels of anesthesia (when required). EMLA cream (Astra) placed over the previously cleansed arterial, or venipuncture site, eliminates the pain of catheter placement (30 minutes to reach full effect). This is especially useful where the procedure (such as Seldinger technique) will take time to complete.

3. **Inhalational Anesthesia** (by mask or induction chamber) may be preferred in some more aggressive cats (when ketamine is contraindicated), or to provide more controlled conditions for jugular catheter placement. Intubation is not necessary but careful monitoring to ensure a patent airway, adequate ventilation, and oxygenation is required.

C. Thoracocentesis

For diagnostic or therapeutic purposes, needle thoracocentesis usually requires no analgesia or sedation.

1. Provide nasal or face mask oxygen supplementation and monitor carefully.

2. **Lidocaine 0.5 – 1.0 mL of 1% solution** is required for local infiltration of the skin, intercostal muscles, and pleura where the teat cannula technique is used.

3. If the patient cannot be restrained calmly, the stress associated with struggling and excessive manual restraint can be associated with hypoxia; therefore chemical restraint is necessary (*see Chemical Restraint for Respiratory Compromise p. 101*).

D. Chest Tube Placement

Chest tube placement can be performed with local infiltration of lidocaine (as above), with opioids with or without sedatives, or with inhalational anesthesia. Patient assessment will dictate which and how much restraint is necessary.

1. Provide nasal or face mask **oxygen** supplementation and monitor carefully.

2. **Local anesthesia** should always be performed to reduce the requirements of additional drugs.

3. **Sedative/analgesia.** Refer to Chemical Restraint for *Respiratory Compromise p. 101* for safe selection.

4. **Inhalational (general) anesthesia** is required for cats, unless severely depressed, due to chest wall compliance and the degree of restraint required for this procedure. Opioids and neuroleptanalgesia are inadequate to achieve this degree of restraint.

E. Placement of a Urinary Catheter

Unless the canine penile urethra is obstructed, catheterization is performed without chemical restraint. Female dogs and cats (unless significantly depressed) require sedation/analgesia to facilitate passage of the urinary catheter and reduce the risk of catheter contamination. Drug selection may not be critical in these cases, but choices should consider the clinical condition of the patient (e.g., renal function in cats and liver function in dogs, if ketamine is considered).

1. **Butorphanol with acepromazine or diazepam** is usually sufficient. Additional **ketamine** may be needed in the cat.

2. **A sterile 2% lidocaine gel,** in a tapered-end cartridge (Astra), can be introduced into the vaginal vault. The area is desensitized in 5 minutes, facilitating passage of a urinary catheter. It is recommended that this be used in all female patients, even if depressed, as they will still feel the discomfort although too weak to resist.

F. Wound Management/Bandage Change

The major consideration is provision of adequate analgesia at the time of the procedure.

1. **Opioid** use at analgesic dosages is usually sufficient.

2. **Diazepam, midazolam, or acepromazine** (patient circumstances will dictate the most appropriate) act synergistically with opioids to increase the level of analgesia and sedation. Intravenous administration of lower drug doses will give more predictable restraint. The lower doses facilitate a more rapid recovery.

3. **Medetomidine 2 – 20 μg/kg IV** may occasionally be used in healthy animals with the advantage of complete reversal and rapid return to normal function. The higher dose ($>10\,\mu$g/kg) is reserved for cats.

4. **Propofol in 1 mg/kg boluses,** in healthy animals, may be titrated to effect sedation should 'breakthrough' struggling occur.

G. Abdominal Ultrasonographic Examination and Biopsy

Often these procedures are peformed in animals with abdominal masses, kidney or liver disease. Pregnant animals may require ultrasonographic examination to assess fetal status or numbers. If sedation is required, the choice is not critical as long as hypotension or hypoxia is not produced.

1. **Butorphanol with diazepam** is recommended as the underlying condition may be associated with some degree of depression. Other opioids are associated with panting, which can make the procedure more difficult.
2. **Local anesthetic** infiltration of the skin and deeper tissues is required prior to a biopsy procedure.
3. **General anesthesia** may be required for difficult to restrain patients.
4. **Propofol 0.5 – 1 mg/kg IV increments** is useful as needed to enhance the restraint, or achieve anesthesia, if required for a biopsy in patients with a stable cardiovascular system.

PHARMACOLOGY

See Analgesia and Sedatives.

SUGGESTED READING

1. Dyson DH. Chemical Restraint and Analgesia for Diagnostic and Emergency Procedures. Vet Clin North Am Small Anim Pract: 2000;885-898.
2. Mathews KA, Dyson D. PAIN HURTS CD. Mathews KA (ed). Jonkar Computer Systems, Guelph, ON. 2003.

NOTES

INTRODUCTION

Handling, examination and treatment of animals in emergency situations will often require analgesia, chemical restraint (mild sedation to profound neuroleptanalgesia), or anesthesia. The drug selection, dosage and administration will be determined by the nature of the emergency, the behaviour and medical condition of the patient, the assessment of pain, and the diagnostic and therapeutic procedures selected. Each case must be assessed and managed carefully on an individual basis, because particulars such as the behavior and size of a patient will influence doses. Therefore it is understood that these recommendations will require some adjustment in techniques, doses, and drugs suggested. Whenever possible, guidance will be provided to assist in modification of the suggested regimen.

This chapter consists of 7 sections:

SPECIFIC EMERGENCIES:

I. Respiratory Compromise
  A. Upper airway obstruction
  B. Respiratory muscle failure
  C. Lower respiratory disease
  D. Diaphragmatic hernia
  E. Major chest trauma

II. Cardiovascular Compromise
  A. Shock
  B. Dehydration
  C. Arrhythmias
  D. Cardiac disease

III. Gastrointestinal Compromise
  A. Gastric torsion dilation
  B. Esophageal foreign body
  C. Endoscopy
  D. Obstipation/ constipation in cats

IV. Neurological Compromise
  A. Head trauma
  B. Seizuring patient
  C. CSF tap

V. Generalized Trauma

VI. Cesarean Section

VII. Behavioural Challenges
  A. Aggression
  B. Anxiety

I. RESPIRATORY COMPROMISE

Respiratory compromise is usually apparent directly upon admission and is often associated with excitement, panic, or anxiety. If severe, it can progress rapidly to respiratory and cardiac arrest, and therefore must be dealt with immediately. Calming the animal will facilitate therapy in mild situations, but anesthesia may be necessary for immediate treatment in severely distressed patients. Preparation for intubation and ventilation should be carried out (equipment and drugs available, doses calculated) in advance. Personnel that might be involved should be properly briefed on monitoring these patients, and on their need to respond quickly and efficiently if deterioration should occur.

A. Management of Upper Airway Obstruction (UAO)
Obstruction can be caused by laryngeal paralysis, laryngeal or pharyngeal foreign bodies, tumors, inflammation or edema, brachycephalic syndrome, internal or external trauma and collapsing trachea. Usually rapid intervention is necessary to guarantee oxygen delivery. Handling the animal may result in increased stress and anxiety that can worsen the situation.

1. Calm the animal while attempting oxygen delivery by mask or 'flow by'. A mixture of **oxygen and helium** (Heliox) may be more effective due to ease of inspiration in the presence of increased airway resistance.

2. Chemical restraint may still be necessary. The IV route of the following drugs is preferred for the most rapid effect.
   a. Low dose of **acepromazine 0.01 – 0.05 mg/kg (adjusted for size, age, condition)** can be beneficial, if not contraindicated (e.g., seizures, hypotension).
   b. **Butorphanol 0.05 – 0.2 mg/kg (adjusted for size)** can be beneficial (cats may benefit from a higher dose, up to 0.4 mg/kg).

3. Anesthetic induction (or profound restraint using low doses of these induction agents) is often necessary and may be attempted immediately or following unsuccessful relief with the sedation and treatment stated above. Our choices reflect the need to be able to titrate restraint, or induction to the desired effect.
   a. **Diazepam/Ketamine** (5 mg/100 mg per mL) **(0.02 – 0.03 mL/kg IV increments)** of mixture is chosen for the advantage of safe, slow induction to effect; although use of a 2:1 mixture would also be acceptable in cats. Because these animals may be very sensitive to the dose used, especially if a degree of hypoxia has been produced, **titrate** to the desired effect or until intubation is possible (when deemed necessary) by using 1/4 – 1/5 of typical induction doses repeated every 15 – 20 sec. Cardiovascular unstable patients may require a longer time between top up doses due to the slower circulation time.
   b. **Propofol 0.5 – 1.0 mg/kg IV increments** is also suitable for a slow induction. Titrate to affect using 1/4–1/5 of the typical induction doses repeated in 15 – 20 sec until intubation is possible. **Diazepam 0.2 mg/kg IV** can be given, following the initial dose of propofol, to reduce the dose of propofol required and possibly the resultant adverse cardiovascular effects (hypotension from vasodilation).

4. Once airway management has been secured,
   a **corticosteroid** administration and/or surgery is carried out as necessary. Recovery is managed by ensuring that an opioid effect persists for proper analgesia (if surgery was done), and/or an antitussive effect. This provides more and longer control of airway during recovery and results in less coughing and irritation.
   b. **Butorphanol 0.05 – 0.4 mg/kg IV, IM, OR**
   c. **oxymorphone or hydromorphone 0.03 – 0.05 mg/kg IV, IM, OR**
   d. **morphine 0.3 – 0.5 mg/kg IM OR**
   e. **meperidine 2 – 3 mg/kg IM** will provide an antitussive effect at recovery. Note, that although subanalgesic doses of butorphanol and meperidine are antitussive, analgesic doses of the profound mu agonists are required for an antitussive effect. Drug and dose selection should first be considered based on the analgesic needs. Ranges provided also reflect size considerations (e.g., lower doses in very large animals).

B. Management for Respiratory Muscle Failure

Animals with neuromuscular disorders (i.e., polyradiculoneuritis) or high spinal cord injuries affecting the muscles of respiration can progress to a point where the effort of breathing is excessive, tiring and stressful. Profound chemical restraint, close to surgical anesthesia, is required to allow intubation and maintenance on a ventilator. The anesthetic choice for induction is not critical unless there are other problems such as cardiac disease (see Cardiac Disease in this section) and hypotension (see Cardiovascular Compromise in this section). Where high intracranial pressure (see Neurological Compromise in this section), renal (avoid ketamine in cats), or liver disease (avoid ketamine in dogs) are present, propofol or inhalant induction is ideal.

1. **Preoxygenation** is beneficial to avoid rapid desaturation if induction apnea occurs.

2. Premedication with an opioid prior to induction is recommended. **Oxymorphone** OR **hydromorphone 0.03 – 0.05 mg/kg IV, IM** OR **morphine or methadone 0.3 – 0.5 mg/kg IM.**

3. Anesthesia may be induced by any of the following, which have been selected based on clinician familiarity, smoothness and short duration.
   a. **Propofol 4 – 8 mg/kg**
   b. 1:1 mixture of **diazepam/ ketamine 0.1 – 0.2 mL/kg (see A2a C1)** or even
   c. **thiopental 10 – 12 mg/kg IV** are the most common. Thiopental induction must be preceded by premedication, although the first two choices may not; the dose ranges noted considers this. While these doses are recommended, lower (one-half) doses should be used with titration-to-effect if cardiovascular compromise is also a concern. For long term maintenance of anesthesia, pentobarbital may be used as an induction agent and is only recommended for those familiar with its use.

4. Maintenance of anesthesia while on a ventilator includes continuous opioid sedation /analgesia using
   a. **oxymorphone** OR **hydromorphone 0.03 – 0.05 mg/kg/q3–4h**
   b. **morphine** OR **methadone 0.3 – 0.5 mg/kg q4h** OR
   c. **fentanyl 30 – 50 μg/kg/h** in combination with
   d. **pentobarbital 1 – 5 mg/kg/h** OR
   e. **propofol 0.1 – 0.4 mg/kg/min** infusion. These drugs and dosages are given as guidelines, the condition and requirements of the patient will dictate the most appropriate selection and dose required for maintenance on the ventilator.

C. Lower Respiratory Disease

Patients presenting with pneumonia (fungal, bacterial, aspiration), edema, neoplasia, hemorrhage, severe contusions, status asmaticus, are frequently hypoxemic ± hypercarbic and may have associated cardiovascular compromise (i.e., chest trauma). Chemical restraint may be required to facilitate placement of a nasal oxygen canula or chest tubes, for radiographic examination or to perform transtracheal wash or obtain biopsies. The method of restraint selected should be the minimal required for the procedure.

1. Ensure supplemental **oxygen** is provided before, during and after the procedure. Five minutes of preoxygenation is recommended prior to IV anesthetic induction.

2. **Local anesthetic** should be considered where applicable. This may be all that is required, or may be combined with the restraint techniques below to improve their effectiveness.
   a. Generous instillation of an ophthalmic local anesthetic into the nasal meatus is adequate for oxygen canula placement.
   b. Infiltration of **lidocaine 1%** (equal volumes of 2% and saline) 1 – 2 mg/kg should be used prior to pleural space evacuation with large catheter, chest tube placement or performing a transtracheal wash.

3. Low dose acepromazine 0.01 – 0.02 mg/kg or diazepam 0.2 mg/kg may be effective alone or combined with opioids.

4. **Opioids:** (**Butorphanol 0.05 – 0.4 mg/kg IV, IM, oxymorphone** or **hydromorphone 0.03 – 0.05 mg/kg IV, IM, morphine or methadone 0.3 – 0.5 mg/kg** to calm the patient and reduce oxygen requirements. Lower doses are advised initially, then increase if required.

5. Short-term anesthesia may be required for these procedures in cats (often more resistant to the effects of neuroleptanalgesia and physical restraint) and lung biopsies in cats and dogs.
   a. **Propofol 2 – 8 mg/kg IV** induction and **isoflurane** maintenance is preferred for such a short procedure due to the rapid recovery.
   b. **Ketamine** at 2 mg/kg IV given in incremental doses to effect, OR slow titration with **diazepam/ketamine** 0.1 – 0.2 mL/kg IV (*see upper airway obstruction 3a p. 101*), is a safe approach in cats with severe respiratory compromise and unknown cardiovascular status.
   c. Mask **isoflurane** or **sevoflurane** (less breath holding) anesthesia works well if a slower induction is not contraindicated (e.g., brachycephalic breed). Advance preoxygenation is not required since the drug effect occurs so slowly and is in the presence of oxygen.

D. Management of Diaphragmatic Hernia

Oxygen supplementation is critical to the safe management of this case. Any fluid accumulation in the chest should be removed prior to anesthetic induction since it will add to ventilatory and oxygenation impairment. Significant cardiovascular compromise is also possible in these patients and replacement of fluid deficits is important (refer to Cardiovascular Compromise later in this section). Special concerns related to gastrointestinal compromise (presented later) should be consulted if intestinal incarceration exists. Restraint may be required for radiography or thoracocentesis. Since these patients often overlap with those with major chest trauma, see recommendations below.

E. Management of Major Chest Trauma

Oxygen supplementation is a vital part of the treatment in such patients. These animals also need analgesia with some associated sedation to reduce movement and subsequent pain.

1. Dependent on the degree of pain associated with the injury, **butorphanol 0.2 – 0.4 mg/kg, oxymorphone 0.03 – 0.1 mg/kg, hydromorphone 0.05 – 0.1 mg/kg, or morphine 0.3 – 0.5 mg/kg (in dogs), 0.1 – 0.2 mg/kg (in cats)** can be used. Doses selected are primarily size related (smaller dose/kg for bigger dogs), and titrated slowly to effect. An increased respiratory rate may be an early sign of a mild overdose. In the event of increased respiratory rate the administration of the opioid can be stopped before panting occurs. Although morphine can be given very slowly IV, the possibility of histamine release can be a significant concern with this route of administration. In this case, IM administration is recommended (except if an infusion is used). This is more of a concern in the trauma patient where hypovolemia is frequently present

2. **Diazepam 0.2 mg/kg IV** can enhance the restraint if required for a diagnostic or short emergency procedure.

3. **Ketamine** can also be used
    a. At **1 – 2 mg/kg IV** as it can provide short-term analgesia if intramuscular morphine is selected for the long-term analgesic (bridging the gap until IM morphine can take over).
    b. At **7 – 10 mg/kg** it can be squirted in to the mouth of a fractious cat or dog for initial restraint and management, and to allow administration of other analgesic agents.

4. Consider the use of **local anesthesia** to supplement systemic analgesia. **Intercostal nerve blocks** using **0.2 mL/kg of 0.5% bupivacaine** divided amongst 4 – 6 nerves can provide excellent analgesia for 3 – 6 hours. Repeat as needed for rib fractures or lateral thoracotomy incisions (*see Regional Analgesia and Local Anesthetics p. 125*). **Epidural analgesia** with low doses of morphine can impart reasonable analgesia in the thorax with limited adverse systemic effects (*see Epidural Analgesia p. 112*).

5. Before **general anesthesia** is considered, evacuation of air or fluid from the chest is recommended to reduce ventilatory impairment, atelectasis, and potential compromise of oxygenation. Any fluid deficits should be addressed to avoid associated hypotension. Whenever possible half of the fluid deficit should be corrected in advance of anesthesia. See Cardiovascular Compromise in this section if concurrent concerns exist. With these recommendations in mind, the risk associated with anesthesia becomes less. Induction as described assumes analgesia (above) has been administered.
    a. Following preoxygenation, a typical induction with **thiopental or propofol** can begin. **Diazepam 0.2 mg/kg** can be given in advance of, or following, the initial injection and should reduce cardiovascular depression by a dose-sparing effect. **Diazepam/ ketamine 0.1 – 0.2 mL/kg** (*see upper airway obstruction 3a p. 101*) can also be used.
    b. If **mask isoflurane** is chosen for induction, a very low dose of **propofol 0.5 – 1.0 mg/kg** or **diazepam 0.2 mg/kg** may assist in preventing excitement. This dose of propofol does not appear to produce significant hypotension as can occur during a typical propofol induction.

II. CARDIOVASCULAR COMPROMISE

Avoid unnecessary sedation and anesthesia where possible; however, excessive manual restraint with accompanying stress can be associated with epinephrine release and potential adverse effects. Monitoring of both oxygenation and perfusion of the patient is critical to avoid metabolic acidosis, prolonged CNS depression or excessive anesthetic depth, arrhythmias and cardiac arrest. Blood pressure and heart rate should be closely monitored, and problems managed, as they arise.

Initial drug doses should be low with subsequent titration to effect (IV or inhalant administration). **Any opioid** alone is reasonable for sedation. **Diazepam 0.2 mg/kg IV** can be added if needed. The adverse effects of opioids are usually minimal. If bradycardia results, use an anticholinergic; **glycopyrrolate 0.005 – 0.01 mg/kg IV** should be given to maintain cardiac output. Acepromazine is usually avoided, unless very minor concerns exist, due to vasodilation and potential for hypotension. Low dose **ketamine 2 – 4 mg/kg with diazepam dose** can be used to sedate cats. Propofol should not be used alone due to the potential for significant hypotension at induction doses. Opioids are generally considered the safest anesthetic supplement and most effective in reducing the dose of other agents used for restraint, induction, or maintenance. Although isoflurane is the inhalant of choice, reducing the dose of this inhalant by concurrent opioid administration is highly recommended. Oxymorphone, hydromorphone, fentanyl, alfentanyl or sufentanyl are the drugs most widely accepted as safe in patients with cardiovascular compromise. Butorphanol has **not** been shown to have significant MAC sparing effects in dogs. Hydromorphone is a good choice as it reduces MAC and has a similar safety profile to oxymorphone in hypovolemic dogs. Morphine, although reduces MAC, is generally not advised due to its venodilation and potential for histamine release. In most patients with significant cardiac compromise, other than hypertrophic cardiomyopathy, **dopamine** 5 – 10 μg/kg/min or **dobutamine** 5 μg/kg/min are beneficial inotropic agents to improve cardiac output.

A. Shock

These animals may be 10 – 15% dehydrated or have experienced a 30 – 45% intravascular fluid volume loss (*see Fluid Therapy p. 347*).

1. Provide **oxygen** by facemask, nasal cannula, tent, or 'flow by' while proceeding with assessments and treatment.

2. **Fluid** resuscitation, up to 100 – 150 mL/kg of crystalloid should be administered before profound chemical restraint or anesthesia is performed. CNS depression occurs with shock and is usually sufficient to enable catheter placement without any analgesia.

   a. See recommendations for venous cut down or percutaneous catheter placement in the section on Diagnostic and Minor Procedures if either are required

   b. The crystalloid fluids should then be started at **60 (cats, older dogs), 90 (younger dogs) mL/kg/h** and continued at this rate until the animal is showing signs of responding. In profound hypotension synthetic **colloids 5 – 10 mL/kg cats, 10 – 20 mL/kg dogs administered over 15 minutes** is preferred to crystalloids alone. A reduction of crystalloids by up to 50% is recommended with concurrent colloid administration. A more rapid replacement of vascular volume is possible if **hypertonic saline (5 – 7%) (2 mL/kg cats, 4 mL/kg dogs** in 5 – 10 min) or colloid plus 5% hypertonic saline is used. If hypothermic *see p. 293* and Fluid Therapy *p. 348* for guidance in fluid therapy.

   c. A blood sample for packed cell volume (PCV) and total solids (TS) should be measured as a guide to administration of whole blood, packed red blood cells, plasma or synthetic colloid. Attempt to maintain PCV and TS higher than 20% and 35 g/L (3.5 g/dl) respectively, recognizing that a shock volume of fluid will reduce baseline levels by approximately 33%.

3. Once the animal is starting to respond, consider the need for **analgesia** (as noted above). The persistent catecholamine release associated with pain will further reduce oxygen delivery to the tissues as well as increase oxygen demand and this detrimental effect is of greater concern than any adverse opioid effect. If any problem arises, partial reversal with **naloxone** 0.1 – 0.25 mL of 0.4 mg/mL solution diluted in 10 mLs saline titrated in 1 mL increments to reduce the adverse effects, while maintaining analgesia, should alleviate the veterinarian's fear of using opioids for analgesia. Anesthesia should be delayed until the animal is stable. See recommendations on dehydration, below.

B. Dehydration

1. Fluid therapy. Calculate fluid deficits and replace rapidly (*see Fluid Therapy p. 351*) to enable earlier surgical intervention, or at least start the correction at shock rate before induction, and continue at this rate following induction until the deficit is corrected. Even subclinical (<5%) dehydration can result in hypotension with chemical restraint or anesthesia

2. Analgesia or restraint is possible using an appropriate opioid; add **diazepam** or **midazolam 0.2 mg/kg IV** if needed to facilitate handling.

3. **Anesthesia** is more safely induced using a titration technique if dehydration cannot be completely corrected before anesthesia and surgery is necessary.

4. **Propofol 1.0 mg/kg IV increments** followed after the first dose with **diazepam 0.2 mg/kg IV** allows a smooth induction using a lower overall dose of propofol in compromised patients and causes little change in cardiovascular status.

   a. **Diazepam/ketamine** titration (1:1 mixture) at **0.02 mL/kg IV increments** is considered very safe.
   b. **Mask isoflurane or sevoflurane** is safe, but is more stressful with no added benefits.

C. Arrhythmias

Premature ventricular contractions (>15/min or multifocal) should be controlled or reduced with lidocaine prior to administration of profound chemical restraint or anesthesia. A therapeutic dose of lidocaine may reduce the chance of a fatal arrhythmia even when some arrhythmias persist. Correct hypoxemia, pain, stress, hypokalemia (*see p. 395*) or metabolic acidosis (*see p. 410*), which may contribute to ventricular arrhythmias.

   a. **Lidocaine 2 mg/kg bolus (dogs),** repeat if necessary within 10 minutes (typically given as 2 boluses of 2 mg/kg in the first 10 minutes) and then **120 µg/kg/min** to provide therapeutic levels during isoflurane anesthesia. Reduce after 1 h to 40 – 80 µg/kg/min. The purpose of treating arrhythmia prior to anesthesia

is to reduce potential of a fatal arrhythmia and maximize cardiac output. Added benefits of mild sedation, analgesia and a MAC sparing effect occur with therapeutic levels of lidocaine.

    b. **Procainamide 6 – 15 mg/kg IV** administration over 20 minutes to avoid hypotension may be required if there is no response to lidocaine.

    c. **Anesthesia** can be carried out as noted above for patients with Cardiovascular Compromise, if required, with little concern once the arrhythmias are under control.

2. **Bradycardia** may be caused by end-stage hypoxia or hyperkalemia, but more frequently due to enhanced vagal tone.
       a. **Glycopyrrolate 0.005 – 0.01 mg/kg IV** should be administered to
         i. **awake dogs** if heart rate is <50 – 60 beats/min in dogs or <80 – 100 beats/min in cats, or if escape beats (ventricular beats following a period of sinus arrest) are present.
         ii. **anesthetized animals** with heart rates <65 – 80 beats/min (in large and small dogs respectively) or <120 beats/min in cats.
       b. **Diazepam/ketamine mixture (1:1) 0.02 mL/kg** is the induction regimen of choice for pacemaker placement in **sick sinus syndrome** (unlikely to respond to anticholinergic therapy). It is ideally continued for maintenance of anesthesia. Minimal or no inhalant should be used to prevent a further reduction in heart rate. Isoproterenol is recommended as a chronotrope, if required.

3. **Tachyarrhythmias** are often related to insufficient management of pain, hypovolemia and hypoxemia. Assess the animal to determine the cause.
       a. **Opioids** are recommended when pain is involved for the dual effects of pain control and increased vagal tone.

C. Cardiac Disease

It is often necessary to sedate patients with cardiovascular disease to perform minor tasks such as blood collection, IV catheter placement, or radiographic/ultrasonographic examination, because these tasks may unduly stress the patient. Struggling with an animal in heart failure can be more dangerous than the potential adverse effects of the appropriate drug. Short-acting, reversible sedative regimens are preferred. Avoid using drugs and dosages that will cause respiratory depression (if sedation alone is desired) or increase susceptibility to arrhythmias. Where hypotension is a concern, monitor blood pressure continuously. The IV route for drug administration is advised to allow titration to effect when sedation is needed. If IV access cannot be obtained, low dose IM administration is an alternative; the slower absorption potentially being advantageous.

1. **Opioid** and **benzodiazepine** derivative drugs either alone or in combination are preferred. **Butorphanol** is the opioid of choice for minor procedures. **Meperidine** at **3 – 5 mg/kg IM** can also produce reasonable sedation and may be used instead of butorphanol. For more painful patients, or procedures, mu agonists are recommended. Do not administer meperidine or morphine IV.

2. Formulate an **anesthetic plan** that is balanced (several drugs targeting specific needs to reduce the negative cardiovascular effects of the inhalant). Isoflurane is the most compromising drug used in this setting and should be kept to a minimum.
       a. **Less critical cases** should receive high dose **opioid** premedication and preoxygenation; induced with **ketamine/ diazepam** and maintained on isoflurane. **Local anesthesia blocks,** where appropriate, also reduces inhalant dose.
       b. **More critical cases** require preoxygenation and induction of anesthesia with high dose opioid/ benzodiazepine combination. Local anesthesitic blocks or **lidocaine** 120 μg/kg/min – (*see previous under Arrhythmias*) and/or **ketamine** infusions 2 mg/kg/h may be considered to reduce inhalant requirements. **Fentanyl/midazolam infusion** 0.8 μg/kg/min + 8 μg/kg/min, respectively, is a more stable means of reducing MAC than intermittent opioid injections. Muscle relaxation using **atracurium** 0.1 mg/kg may also facilitate MAC reduction
       c. As both techniques above require high doses of mu agonists, positive pressure ventilation will be required, especially in the more critical patient protocol described.

3. In cats with hypertrophic cardiomyopathy maintain lower heart rates, using analgesics and adequate anesthetic depth . Mask isoflurane induction in well-sedated cats **(opioid + benzodiazepine)** is preferred. To avoid the stress of this technique, add a low dose of **propofol 0.05 mg/kg IV increments** as needed to improve acceptance of the mask and/or bypass the excitement stage. Induction of anesthesia with ketamine is avoided due to potential for higher heart rates and enhanced output obstruction.
       a. **Methoxamine or ephedrine 0.2 mg/kg IV** may be suitable adjunct agents where hypotension exists to counter the vasodilation associated with isoflurane.

III. GASTROINTESTINAL COMPROMISE

Alpha-2 agonists, hydromorphone and morphine have a high incidence of vomiting when used for premedication or analgesia in the awake animal; therefore, these drugs should be avoided where a foreign body or other obstruction is suspected as potential gastrointestinal rupture may occur.

A. Gastric/Dilation Volvulus (GDV)

Cardiovascular compromise can present as a primary problem in these cases if shock, dehydration or arrhythmias are present (refer to previous recommendations under Cardiovascular Compromise). With advanced GDV, metabolic acidosis and hypokalemia are common and should be managed before anesthesia. Occasionally respiratory compromise may co-exist due to abdominal enlargement and pressure on the diaphragm.

1. **Oxymorphone 0.03 – 0.04 mg/kg IV** (with or without **diazepam**) is suggested for analgesia and pre-medication. Many of these dogs are very large and the effective dose will be lower than typically used, especially if cardiovascular compromise exists. The drug can be diluted in saline and slowly given over 5 min until the desired effect is reached. Analgesia can produce an antiarrhythmic effect by reducing catecholamine release and increasing vagal tone. If oxymorphone is not available, meperidine **3 – 5 mg/kg IM** can be used for mild, short duration analgesia. The more profound mu opioid available (**hydromorphone, fentanyl, morphine or methadone**) can be given after induction (for better and longer analgesic effect) when the vomiting center is less receptive to the opioid due to the depressant effects of general anesthesia at this site.

2. Due to the potential for arrhythmias, administer **lidocaine 4 mg/kg within 10 minutes** (typically given as 2 boluses of 2 mg/kg in the first 10 minutes), followed by a CRI **120 μg/kg/min** in dogs (as noted above). Prevention of arrhythmias reduces the chance of a fatal arrhythmia, adds mild sedation, analgesia and a MAC sparing effect.

3. **Induce anesthesia** using **diazepam/ketamine** titration, **mask isoflurane** or **high dose oxymorphone or hydromorphone administered with diazepam.** All are considered safe (if arrhythmias are managed), but diazepam/ketamine is the author's preference. Vomiting is not a concern with the opioid induction due to the rapid effect when given IV with diazepam.

B. Esophageal Foreign Body

Premedication can often be eliminated for a more rapid induction when esophageal foreign body removal is required immediately. If the situation is not critical, premedication, induction and maintenance according to the animal's health and age is indicated.

1. Since these cases are usually healthy outpatients, the convenience of **propofol** and **isoflurane** makes them appropriate choices. **Diazepam/ketamine** induction is also reasonable, but recovery will be smoother in healthy animals if **acepromazine 0.02 – 0.1 mg/kg (given before) or 0.01 – 0.05 mg/kg (during) anesthesia.**

2. **Butorphanol 0.1 – 0.2 mg/kg** for analgesia is usually adequate if esophageal or oral irritation exists. With esophageal erosions, and especially ulceration, a mu agonist may be required.

C. Endoscopy

For upper gastrointestinal procedures the drugs selected are based on patient status and age, with a few notes of precaution. Assess hydration status as persistent vomiting may be the reason for endoscopy.

1. Stabilize if dehydrated (*see Dehydration recommendations previous*).

2. Premedication will vary based on the patient's hydration state and attitude.

    a. If examination and biopsy of the duodenum is to be included, **butorphanol** is recommend as sphincter tone is not affected. Profound mu opioids, especially morphine, and atropine, will increase sphincter tone potentially making scoping of the duodenum difficult. If not dehydrated and more restraint is desirable, **acepromazine 0.01 – 0.05 mg/kg** can be used (dose based on patient age, size and condition). However it should be avoided in a dehydrated patient as hypotension may occur.

    b. **Diazepam** or **midazolam** may be a suitable alternative, although the effect is rarely profound unless significant patient depression is present.

    c. **Pentobarbital 3 – 5 mg/kg IM** is an alternative to acepromazine producing some sedation, without vasodilation, and reducing the doses of other anesthetic agents used.

    d. If cardiovascular status is such that mu opioid/diazepam induction is indicated (*see Cardiac Disease previous*), the animal's safety takes priority over ease of induction.

3. Hypotension should be treated with **crystalloids 20 – 40 mL/kg**, or **colloids 5 mL/kg** and/or **ephedrine 0.2 mg/kg IV** in patients that are either dehydrated or may have excessive vasodilation from acepromazine use or isoflurane. **Dopamine 5 – 10 μg/kg/min** is a safe choice (if inotropic support is needed) along with fluids in animals with cardiac disease.

4. Assess the requirement for a mild **analgesic** or an **antitussive** agent at the end of this procedure if none was administered preoperatively. An antitussive agent is valuable in brachycephalic dogs, and also in cats, to reduce complications associated with laryngeal irritation and swelling at recovery.

   For rectocolic endoscopic procedures, the animal is often anesthetized for restraint and convenience with the selection of drugs based on the patient's condition and age. It is possible to carry out this procedure with profound chemical restraint alone. An alpha-2 agonist or acepromazine, combined with hydromorphone or morphine (dogs), or diazepam/ketamine (cats), would be most effective, if not contraindicated (*see recommended doses under Aggression VII A p. 109*).

D. Obstipation or Constipation

Frequently restraint is required to evacuate the colon in cats with severe constipation or obstipation. The procedure can take a long time to accomplish, sometimes up to 2 hours.

1. In cats with good renal function, the author prefers to use chemical restraint (rather than inhalant or general anesthesia) using **diazepam/ ketamine** to a level of heavy sedation. The patient is able to assist in evacuating the feces as it is broken up. Be cautious, titrate low doses **(0.02 mL/kg IV increments)** to achieve, and then maintain, a state of restraint that retains full laryngeal and swallowing reflexes. These reflexes are not maintained sufficiently to avoid aspiration if a state of anesthesia is approached with this combination.

2. If **general anesthesia** is more desirable, due to potential for vomiting, or if renal function is a concern, an appropriate anesthetic protocol can be chosen (diazepam/ketamine induction with isoflurane maintenance; isoflurane or propofol induction and isoflurane maintenance, respectively), which must include intubation due to the risk of aspiration.

IV. NEUROLOGICAL COMPROMISE

Significant CNS depression can be present in cases admitted for emergency care and diagnostic assessments. These animals may be victims of trauma or CNS disease.

A. CNS Trauma

1. It is critical to provide **oxygen** and determine if **positive pressure ventilation** is required. Increased respiratory depression with resultant increased $PaCO_2$ from drug therapy can result in a rise in CSF pressure and could eventually result in brain herniation, if not addressed. Avoid stress or pain in these animals as this can also raises CSF pressure.

2. Animals that are unconscious due to shock should be **stabilized** (*see Head Trauma p. 694*).

3. If **analgesia** is necessary, titrate low doses to effect regardless of potential respiratory depression. Commence positive pressure ventilation, if this risk exists. Do not assume that analgesia is adequate based on mild CNS depression caused by the condition. Pain also raises CSF pressure and careful assessment for this is required. Use of mild analgesics (**meperidine** 3 – 5 mg/kg IM or **butorphanol** 0.1 – 0.4 mg/kg IV) initially, if deemed necessary, is wise in more critical cases. Response to these drugs must be monitored cautiously. Fentanyl constant rate infusion in both cats and dogs is recommended for moderate to severe pain. As fentanyl has a short (~20 min) duration of action, administration can be stopped periodically to allow for neurologic assessment. Titration of opiates is required to avoid vomiting; vomiting increases intracranial pressure, which worsens the neurological condition.

4. Reduction in intracranial pressure may also be obtained by administration of hypertonic saline (*p. 696*) **mannitol 0.25 g/kg** over 1 min and/or (depending on availability of medication) **1 mg/kg lidocaine IV** rapidly, repeated if necessary. (K. Mathews personal observation).

5. Where indicated, **local anesthesia** for analgesia may be used to avoid higher doses of opioids for the first 24 hours.

B. Collection of Cerebrospinal Fluid (CSF)
All patients will require general anesthesia for this procedure.

1. Premedication can be given if severe CNS depression is not present. **Meperidine 3 – 5 mg/kg IM** is effective in reducing the anesthetic agent and to smooth induction and recovery. Meperidine is safe in animals receiving anti-epileptics. Most animals can be induced with thiopental or propofol. The short duration of effect of meperidine and propofol is appropriate for this procedure and allows rapid recovery and evaluation. When significant CNS depression exists, no premedication is required, and induction should be carried out with **propofol** slowly titrated to effect (if cardiovascular status is not a concern), or mask induction with **isoflurane** in more critical patients as long as stress is minimized. If the patient is stressed use propofol 0.5 – 1 mg/kg to smooth induction. Mask induction is more likely to be associated with a rise in CSF pressure and may be a risk to the patient.

2. Positive pressure ventilation should be commenced immediately, and the patient should not be allowed to breathe spontaneously until the anesthetic is turned off and a medial palpebral reflex and/or jaw tone exists. At this point, spontaneous ventilation will resume quickly and the level of CO_2 should not rise to adversely affect CSF pressure. In patients showing mild CNS signs with little risk of high CSF pressure, positive pressure ventilation may not be required.

C. Patients with a History of Seizures
These patients may require restraint or anesthesia for emergency procedures. The sedation, analgesia, and anesthesia used are primarily determined by the presenting condition. The only drug that is a potential risk is **acepromazine,** which may decrease the seizure threshold. Concurrent anti-seizure medication has little influence on drug choices. If this medication results in sedation or depression in the animal, then lower doses of premedication may be appropriate.

V. GENERALIZED TRAUMA

Traumatized patients will often present with major chest trauma (*see Respiratory Complications I previous*), blood loss to the extent of being in shock (*see Cardiovascular Complications II previous*) and occasionally head trauma (*see Neurological Complications IV previous*). When these issues are not significant, consider the following recommendations.

A. **Control bleeding** into tissues, abdomen or from wounds with the use of pressure bandages. Recognize that a large amount of blood can be lost from the circulation into the area of trauma (i.e., fracture with resultant swelling due to vessel rupture and hemorrhage). *See Hemorrhage p. 623.*

B. Provide **analgesia:** (hydromorphone, oxymorphone, fentanyl for moderate to severe pain; low dosages of these or butorphanol for mild to moderate pain. Also consider applying a **fentanyl patch** that will provide underlying constant analgesia within 12–24h (recognizing that it will have minimal to no effect before this time, and no guarantee of complete effectiveness after).

C. Supportive therapy needs to be considered.
   a. **Support unstable fractures** to reduce the added pain associated with movement.
   b. **Nursing care** to ensure **patient comfort** (i.e., turn to avoid pressure sores; dry, padded and clean bedding).
   c. Prevent urine scalding
   d. **Monitor for other concerns** (i.e., arrhythmias may occur at 12– 48h after insult, pneumothorax, worsening pulmonary contusions and hemorrhage – *see The Trauma Patient p. 682.*

D. Should **anesthesia** be required to manage an emergent problem where possible ensure that the cardiovascular system is stable (*see Cardiovascular Compromise II previous*).

E. Refer to other sections if significant concerns have been addressed or persist. If no concerns exist, other than the pain related to the trauma, anesthetic selection is not critical, except for appropriate management of pain.

F. If hypothermia (<36°C, 97°F) is noted, *see Hypothermia p. 293.*

VI. CESAREAN SECTION

Cesarean section is a common emergency requiring immediate anesthesia. However, the bitch or queen may need stabilization prior to anesthesia (*see Cardiovascular Compromise previous II*).

A. Premedication with **meperidine 3 – 5 mg/kg; butorphanol 0.2 – 0.4 mg/kg; hydromorphone or oxymorphone 0.03 – 0.05 mg/kg; or morphine or methadone 3 – 5 mg/kg** is advised to reduce the anesthesia induction and maintenance drug doses, and their associated adverse effects.

B. If further restraint is needed, a **benzodiazepine** is preferred, but low dose **acepromazine 0.01 – 0.02 mg/kg** may be selected for the elective, stable Cesarean section. Benzodiazepines may cause muscle relaxation in the newborn and owners should be cognizant of this.

C. **Propofol 2 – 6 mg/kg IV** is a safe and easy induction OR **mask inhalant induction** with **isoflurane** or **sevoflurane** is possible, but due to the stress and inconvenience, this offers no advantage except for the most critical case.

D. **Local anesthetic blocks** (epidural or line) are recommended in more critical cases to reduce inhalant needs (*see Regional Analgesia with Local Anesthesia p. 124 or Epidural Analgesia p. 112*). Local anesthetic line blocks can be considered in any patient, although care to avoid the mammary glands is required.

E. **Naloxone 0.4 mg/mL** one drop sublingually in the newborn may be required in spite of the low dose of opioid administered to the bitch/queen. A repeat dose can be sent home with the owner if concern for renarcotization exists. It is rare that analgesic levels of butorphanol or meperidine will cause depression in the newborn.

F. If meperidine was given or low dose of other mu agonists were chosen, a profound mu agonist can be given once pups or kittens are removed. A single dose of a **nonsteroidal anti-inflammatory analgesic** (NSAIA) such as meloxicam 0.1 mg/kg (dog or cat), or carprofen 4 mg/kg (dog), 2 mg/kg (cat) can be administered, if not contraindicated. If butorphanol is selected as the premedication, an additional dose should be administered at the same time the NSAIA is administered, as the NSAIA requires 45 – 60 min for adequate effect.

VII. BEHAVIOURAL CHALLENGES

A. Aggression upon Admission

It is not uncommon for patients to be aggressive on presentation, preventing even the simplest of assessments or treatments. These animals may be in a reasonably stable condition, but this assumption should not be made hastily. The animal should be cautiously assessed from afar, and a thorough history obtained to include current and past medical conditions, before selecting a method of restraint. Chemical restraint rather than force is the humane, and often safer way, to deal with these animals. Once the reason for the aggression has been identified, a more direct approach to management is possible. Aggression may be secondary to significant pain and fear in traumatized animals. Respiratory distress may appear as a combination of panic and aggression. Endorphin and epinephrine release can mask the seriousness of the patient's clinical condition. Cats are very likely to be aggressive in a strange environment and following a car trip. In the authors' experience a cat with severe dehydration can be so difficult to handle that a proper assessment is impossible without some chemical restraint.

1. Provide 'flow by' **oxygen,** when stress, poor perfusion or respiratory compromise could exist. However, an oxygen mask will provide a degree of protection to the handler as a type of muzzle for dogs and may be a better option than 'flow-by'. The aggressive cat should be allowed to settle down in an induction chamber with oxygen administration.

2. If pain is a component of the aggression, **opioid** administration is a safe, effective approach to management. Opioids are considered extremely safe from the cardiovascular standpoint. Any adverse effects are easy to treat (anticholinergic administration in the case of bradycardia or titration of naloxone should other unwanted effects occur). Refer to analgesic recommendations above according to the suspected condition in this patient.

3. Supplemental sedation (in addition to the opioids) is often needed.
   a. The safest supplement to opioid sedation is **midazolam or diazepam at 0.2 – 0.5 mg/kg.** Midazolam is better absorbed than diazepam due to the solubility characteristics (it is also less painful), and is preferred when an IM route is chosen.
   b. A minimally compromised, non-geriatric aggressive animal can be most effectively sedated with a profound mu opioid and **acepromazine 0.02 – 0.05 mg/kg (dogs), 0.05 – 0.15 mg/kg (cats).**

c. Aggressive cats can be restrained effectively and easily with **ketamine 2 – 10 mg/kg** by any route including squirting a dose into the mouth. Ketamine should be combined with midazolam, diazepam or acepromazine when administered IM for better restraint and relaxation. Lower doses of ketamine can be used with this combination. Avoid ketamine in cats if significant renal compromise may exist.

d. **Alpha-2 agonists** can be used in low doses with opioids to provide dependable and profound restraint in healthy animals. It is important to stress both "low doses" and "healthy animals" as arrhythmias, cardiac output depression, and mortality have been associated with the use of xylazine in small animals prior to anesthesia. Although the newer drugs in this class (medetomidine, romifidine) depress cardiac output and heart rate, they may prove useful when used judiciously, and combined with opioids to reduce the dose required for effect. An IV administration is more predictable in the level of restraint achieved (compared to IM). Healthy animals can be given **medetomidine 2 – 20 μg/kg** with low to moderate doses of opioids. The ability to reverse these drugs provides added safety and convenience for outpatients.

4. **Anesthesia** may be required, but an aggressive animal with unknown health status should not be given IM doses of any drug at doses capable of producing anesthesia.

   a. Attempt mild to moderate restraint with initial drug therapy and then if the animal proves to be sensitive to the drugs, there is less chance of adverse effects or overdose. If you have achieved some restraint, carry out a thorough evaluation of the patient allowing you to formulate a safe anesthetic plan.

   b. As some very sick cats remain aggressive in spite of opioid administration, and restraint for an IM injection may be difficult and stressful, **chamber inhalant induction** is often required. This is a good choice in aggressive cats with suspected renal failure or older cats with an unknown medical condition. Allow the animal to calm down in the tank before turning on the inhalant. Oxygen should be provided and initially a towel over the chamber may help reduce the animal's stress. Observe the animal frequently during induction and move the tank to assess level of restraint achieved. Remove the cat and transfer to a mask as soon as possible to allow evaluation of depth of anesthesia. **Isoflurane** is the drug of choice for induction, but should not be started until the cat is relaxed (minimal epinephrine release). Complete anesthetic induction is not always required for restraint, and sedation alone is possible with isoflurane. If respiratory depression or obstruction occurs with this degree of restraint, then complete induction and intubation will be required, so be prepared. The patient requires cautious monitoring during this time (whether restraint or anesthesia is provided) while catheter placement, blood samples and other diagnostic assessments are conducted. An appropriate analgesic can be given following restraint if pain is a component of the problem or diagnostic procedures are performed. The inhalant percent dialed should be reduced within 5 min of administration to avoid a deepened plane of anesthesia. If the cat is induced more rapidly (in 2 – 3 min) than expected, this implies that significant cardiac output depression may be present; **rapid crystalloid** (20 – 30 mL/kg) or **synthetic colloid** (2 – 10 mL/kg) administration over 20 – 30 min, is advised. Inotropic support (**dopamine** at 10 μg/kg/min, or to effect) may be required.

B. Aggression Acquired

Animals may acquire aggressive behaviour while in hospital and being subjected to repeated manipulations. This is especially true when pain is not managed appropriately. Unfortunately, appetite and normal gastrointestinal function can be impaired through repeated sedation for bandage changes and other procedures. Changing the drug regimen for restraint and use of rapid acting, short-term drugs is advised.

1. The use of **fentanyl patches** has been beneficial; however analgesia cannot be guaranteed due to variation in absorption.

2. **Maintenance of an IV access** is necessary to facilitate administration of low dose drugs and reversal agents.

3. **Propofol** has become popular for sedation or anesthesia in these circumstances and shows little compromise when administered slowly and at doses appropriate for the associated illness. Cats can develop Heinz body formation with repeated propofol anesthetics; the resulting anorexia and depression is quickly reversed following cessation of propofol treatments.

4. **Alpha-2 agonists** are a good choice in healthy animals. There is little residual depression following reversal, or the typical duration of effect, with rapid return to normal appetite and behavior. When the patient is fairly healthy, this can be a good choice.

C. Anxiety

It may not be necessary to treat anxiety in animals, although it remains a significant component of therapy in human medicine.

1. Veterinarians try to deal with this aspect more through gentle handling, patient comfort, holding, petting and soothing words.

2. It may be possible to provide temporary anxiolytic treatment with **diazepam 0.2 mg/kg IV** for procedures that are not painful. Unfortunately, diazepam is unpredictable and excitement and vocalization may occur. This may be less common if anxiety is the actual problem and when administered very slowly.

3. If anesthesia required, induction should be preceded by **oxygen** administration by mask.

   a. The easiest induction is with **propofol** given as a typical induction (in the stable patient) or titrated to effect cautiously (in the less stable patient). The addition of **diazepam 0.2 mg/kg IV** will reduce dose requirements further. Maintenance is then continued with **isoflurane** or **sevoflurane.**

PHARMACOLOGY

See Analgesics and Sedatives.

SUGGESTED READING

1. Dyson DH. Chemical Restraint and Analgesia for Diagnostic and Emergency Procedures. Vet Clin North Am Small Anim Pract: 2000:885-898.
2. Mathews KA, Dyson D. PAIN HURTS CD. Mathews KA (ed). Jonkar Computer Systems, Guelph, ON. 2003.

NOTES

INTRODUCTION

Analgesics or local anesthetics placed in the epidural space provide intraoperative analgesia, reduce anesthetic demands, provide total anesthesia for procedures performed that are caudal to T_{13} innervation (when local anesthetics are used) and provide postoperative analgesia. Occasionally, epidural analgesia may be chosen for the awake animal for long duration analgesia, reducing or eliminating the requirement for systemic analgesics. Local skin sensitivity, itch and slower hair growth at the site of injection, have been reported and may not be related to the drug used. Skin infection near the site for injection, sepsis, coagulation disorders or spinal trauma (that may interfere with placement or spread of the drugs) increases the risks beyond the benefits.

Opioid Use

Opioid respiratory depression and other effects are dose related. Respiratory depression is minimal in the awake animal if pain is present, although it may be a concern in the anesthetized animal, requiring positive pressure ventilation when high doses of opioids are used. When placed in the epidural space, lower doses are required than when given systemically, so although epidural systemic absorption occurs to a similar degree to an IM injection, the effects are minor. Migration within the CSF to the respiratory center is also minimal since opioids are highly bound to spinal tissue. However, urinary retention is common and may result in some discomfort, especially with high fluid rates and in patients with a history of polyuria. Bladder evacuation is recommended upon completion of the surgical procedure.

Local Anesthesia Use

Local anesthesia will result in paralysis. Postoperative ataxia is present for the duration of blockade, and may be extended in duration with opioid and local anesthesia combination. Animals should be carefully observed, sedated or assisted as necessary to avoid injury. Other adverse effects are not significant in small animals. According to studies done in dogs, vasodilation from sympathetic ganglionic blockade is not present during anesthesia if the MAC sparing effect of epidural use is taken into consideration.

Technique

This manual does not intend to describe the technical details of an epidural injection, but the following points are worth keeping in mind.

A. Aseptic technique is mandatory. Avoid multidose vials of opioid or local anesthesia unless great care is taken to maintain their sterility (e.g., reserved for epidurals only).

B. If local anesthetics are used, it is essential to ensure a very slow injection rate to provide an even spread of the solution within the epidural space, thus avoiding a patchy block. Positioning for injections is not critical (usually a personal preference), but to maximize anesthesia, it is recommended that the proposed surgical site be placed in a dependent position for 5 minutes following injection to maximize local anesthetic spread to the side to be anesthetized. If this is not possible (e.g., unstable fracture) then place the patient in a dorsal or sternal position to allow even spread of the local anesthetic.

C. Inadvertent subarachnoid puncture is rare, except in puppies and cats where the spinal cord and dural sac end further caudally. Although slight needle repositioning may suffice to avoid a subarachnoid injection when CSF is noted, often replacement of the needle is attempted. If injection is made into the CSF, generally a dose reduction of 40 – 50% is recommended. Concern for anterior spread of any local anesthesia used requires observation for respiratory depression. Since local anesthesia is typically used during anesthesia (not the awake animal), it is simple to use positive pressure ventilation during the time of concern.

D. A volume of **1.0 mL/5 kg** is recommended for most epidural injections and is obtained by adding sterile saline or local anesthetic to opioid dose. Smaller volumes may be effective in the larger patient, especially when the effect required is limited to the tail, perineum and hind limbs (6 mL maximum is adequate). Volumes up to **1.0 mL/3 kg** are used when anterior abdominal local anesthesia effects are required, although this volume should be avoided in patients with increased intra-abdominal pressure (e.g., pregnancy, ascites, large tumours, etc.).

Drug Selection

A. Local anesthesia is beneficial for immediate (5 – 15 min) sensation and motor blockade caudal to the lower thoracic segments (approaching the anterior abdomen). Absorption from the epidural site should be considered to produce similar systemic effects as that expected from an IM injection of the same dose. Note the dose used and expect dose related systemic effects. Respiratory depression in the anesthetized patient and bradycardia are possible with epidural opioid use when doses close to that used systemically are placed epidurally.

B. **Morphine** produces an effect (by 30 min) as far forward as the front limbs, and is unlikely to produce any respiratory effects (note very low doses used).

C. **Oxymorphone** is highly bound at the area of placement and therefore tends to limit the analgesic effects to the posterior part of the body (onset by 30 min, although systemic effects are significant in 5 min due to the use of systemically effective doses). The effects may be more profound than morphine.

The duration of analgesia from opioids is 10 – 24 hours in canine studies. Some variability is expected, which in part, will be inversely proportional to the degree of painful stimulus. Expect the patient to require additional systemic analgesia in cases exhibiting moderate to severe pain. Research indicates that a slight improvement in postoperative analgesic effect is produced with the combination of opioid and local anesthetic which may be due to the effect of excellent pre-emptive analgesia.

TABLE 1. Local Anesthetics Used for Epidural Anesthesia

Local Anesthetic Agent	Dose	Duration of Action	Time to Onset of Action
Lidocaine 2%	0.2 mL/kg	45 – 90 min	5 min
Mepivacaine 2%	0.2 mL/kg	60 – 90 min	5 min
Bupivacaine 0.5%	0.2 mL/kg	120 – 360 min	20 min
Ropivacaine 0.2%	0.5 mL/kg	90 – 420 min	15 min

TABLE 2. Opioids Used for Epidural Analgesia

Opioid	Dose
Morphine	0.1 – 0.3 mg/kg
Oxymorphone	0.03 – 0.05 mg/kg
Hydromorphone	0.02 – 0.04 mg/kg
Fentanyl	0.005 – 0.01 mg/kg

INTRODUCTION

This section is not intended to be a comprehensive pharmacology or anesthesia textbook. The material included should assist in decision-making, as most of the key applied information on the drugs and their use is included. Please refer to more in depth resources as needed. The previous section on Analgesics and Sedatives should be consulted as well to manage the complete perianesthetic period.

I. INDUCTION

A. Diazepam/Ketamine

Diazepam in combination with ketamine is made simply by mixing equal volumes of diazepam 5 mg/mL: ketamine 100 mg/mL; titrated to effect in more critical animals or given as a partial bolus (1/2 – 2/3 of dose based on the guideline dose of **0.15 mL/kg IV**) and then to effect in healthier patients. Low doses can produce sedation or profound restraint. Older animals, depressed patients, very large dogs and premedicated animals will usually be induced with the lower doses. Dogs appear to recover faster than cats. Younger, healthy animals have a smoother recovery when premedicated appropriately.

1. **Advantages:** Maintains good cardiovascular stability by sympathetic stimulation produced by the ketamine.
2. **Concerns:** Sympathetic drive may be a concern in animals with hypertrophic cardiomyopathy, cardiac arrhythmias, head trauma or with a history of seizures. Occasionally tachycardia may be produced and persist during anesthesia. Normal renal function is required in cats for elimination and recovery from ketamine (not a concern in dogs where normal liver function is required for elimination). Benzodiazepines are contraindicated in significant liver disease.

Midazolam/Ketamine

Refer to comments on Diazepam/Ketamine above. Predictable IM advantage to administration.

B. Thiopental

An ultrashort acting barbiturate for IV use only. This is best given after appropriate premedication according to individual patient requirements (sedative, analgesic or combination) given as a partial bolus (1/2 – 2/3 of dose based on the guideline dose of **10 – 12 mg/kg**) and then to effect.

1. **Advantages:** cheap and reasonable in healthy patients.
2. **Concerns:** Excitement may occur on induction when initial bolus is too low or given too slowly. It is inappropriate for maintenance of anesthesia greater than 30 min due to the long and rough recovery that can occur. Smoothness of recovery is dependant upon appropriate sedation from premedication. If an alpha-2 agonist is used for premedication, the initial partial bolus is 1/4 of the guideline dose and drug effects will take 1 min, rather than the 15 – 20 sec with all other premedication. The dose required following an alpha-2 agonist is typically 25 – 50% of the guideline dose.

C. Propofol

An ultrashort acting induction agent for IV use only, made as an emulsion of diisopropylphenol. Induction can be carried out in a similar fashion to thiopental, above (based on the guideline dose of **4.0 mg/kg in dogs, 6.0 mg/kg in cats**), or gradual titration to effect is possible without concern for undesirable excitement. Induction and recovery is smooth, even in the unpremedicated animal (guideline dose is higher **if no premedication – 6.0 mg/kg in dogs, 8.0 mg/kg in cats**).

1. **Advantages:** Recovery is rapid following extended administration due to rapid redistribution and excellent metabolism. Facilitates emergency induction of unpremedicated patients with rapid, hang-over-free recovery. Ability to titrate to effect and therefore, selection of **the appropriate dose without excess and may lessen potential adverse cardiovascular/respiratory effects.**
2. **Concerns:** Use with caution in geriatric and debilitated patients due to resultant cardiovascular and respiratory depression of a similar degree to that apparent with thiopental. Reduce the adverse effects by preoxygenation, very slow titration to the desired level, (thus lowest dose used) and administering **diazepam** at **0.2 mg/kg** following the initial dose to further reduce the dose of propofol required (shown to be safe in hypovolemic patients with this technique). Propofol contains no preservative so it must be used on the day that the vial is opened.

D. Pentobarbital

This short acting oxybarbiturate is rarely used as an anesthetic in small animals. However, in chronic maintenance of restraint that may be required for ventilatory support, pentobarbital is given to effect (initially at **15.0 – 30.0 mg/kg** over 3 – 5 min – dose based on presence, or not, of premedication). A longer time (15 min) may be required for transfer to pentobarbital when induction has been produced with thiopental or propofol or has been previously maintained with inhalant anesthesia. These more familiar agents may be preferred for induction since the transfer to pentobarbital may be carried out more smoothly than an unfamiliar induction with its risk of excitement or overdose. Following full transfer to pentobarbital, a dose of **1.0 – 5.0 mg/kg/h** or higher can be given by infusion to maintain the restraint required. Diazepam and/or opioids must be given, to reduce the dose, enhance sedation or produce an antitussive effect.

1. **Advantages:** Cheap. Slow plane changes allowing easier long term maintenance.
2. **Concerns:** It is contraindicated in cats due to their poor metabolism of this drug. It is very slow to take effect and must be given cautiously to avoid overdose, allowing 1 min to see full effect of each dose administered. Induction excitement is possible if no premedication is used or too low a dose is given as the initial bolus. Very slow recovery and can be rough if not enough sedation present. Normal liver function is required for metabolism. No analgesia is present (only achieved with surgical levels).

E. Inhalant Anesthesia

Mask or tank induction with either isoflurane, sevoflurane or halothane is possible in either the unpremedicated animal or where chemical restraint (as described in the previous section) tried alone was ineffective for the procedure. Induction requires 4 – 5% administration initially (up to 8% with sevoflurane), to the desired effect, and maintenance with the **0.5 – 1.5 times MAC** (minimum alveolar concentration) (MAC of isoflurane:1.2%, sevoflurane:2.4%, or halothane:0.8%) dependant upon the patient's level of depression or stimulation. Recovery is rapid following cessation. Premedication and/or analgesics may be required to guarantee a smooth emergence from anesthesia.

1. **Isoflurane** is preferable in the older or cardiovascular compromised patient, pediatric patients, severely stressed patients, the animal with liver disease or in shock. Animals prone to, or demonstrating, arrhythmias (dogs with gastric torsion, cats with urethral obstruction, animals with myocardial contusions) will be less likely to develop a fatal arrhythmia during isoflurane administration. It is also desirable in patients with renal compromise, resulting in better renal blood flow due to improved cardiac output. Recovery is more rapid with less hangover than noted with halothane.
2. **Sevoflurane** is a safe alternative to isoflurane, with similar properties. It is less pungent, and thus patients may be less inclined to breath-hold during induction.

II. INTUBATION

This may not be necessary for short-term maintenance of anesthesia. The risks associated with intubation, especially in cats, may outweigh the benefits for 5 – 10 min procedures. It is very important that these animals are monitored more carefully for adequate ventilation, since problems are less apparent when the face is covered by a mask, and movement of the rebreathing bag may not be as obvious.

Intubation should always be carried out atraumatically. This is benefited by the use of a laryngoscope in most animals, but especially cats, small dogs and brachycephalic animals. **Laryngeal spray (10% lidocaine)** or **2% lidocaine solution 2.0 mg/kg** should be applied to the larynx of all cats and in any dog where intubation is being attempted with strong chemical restraint alone, or in a very light plane of anesthesia.

III. MAINTENANCE

A. This is best carried out with an inhalant (selection based on considerations noted previuosly under Induction), due to the rapid recovery following cessation of anesthetic administration.

B. **Propofol** (0.1 – 0.5 mg/kg/min) CRI is appropriate when inhalants are not possible. There is no limit to the duration of anesthesia allowed with propofol, as rapid metabolism occurs after redistribution sites are saturated.

C. Diazepam/ketamine (I. A previously) is not unreasonable for long-term maintenance in cats, but the recovery period is prolonged compared to the first choices listed. This combination, with fentanyl, has been used to maintain a cat on mechanical ventilation for several days. **Fentanyl (2 – 6 μg/kg/min)** was maintained until the day of weaning off the ventilator. Ketamine was discontinued prior to discontinuing diazepam. It is advised to reduce diazepam at least 24 – 36 hours prior to weaning. Propofol can be added as needed to allow a longer weaning time from these drugs.

D. Thiopental is limited to short procedures only and pentobarbital is inappropriate for all but chronic maintenance of anesthesia in dogs (i.e., ventilator cases).

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1. Matthews NS. Clinical Anesthesia. Vet Clin North Am Small Anim Pract. WB Saunders, Toronto, 1999.

NOTES

INTRODUCTION

Pain is present in all surgical, traumatic and many medical conditions. The demonstration of pain is not always obvious, therefore an animal should be assumed to be experiencing pain in any condition expected to produce pain in humans. Response to analgesic administration (as with any other therapy-directed treatment of a problem) can guide the veterinarian in the management of pain (or presumed pain). Return of normal behaviour, including eating, sleeping, dreaming, yawning, 'normal stretching', grooming and a general appearance of well-being, is the goal to achieve. This practice will allow the practitioner to gain experience in recognizing and treating pain in cats and dogs. Administration of opioid analgesics is frequently withheld in ill or injured animals as it is the belief that these drugs will "mask" the signs of deterioration. This is not so. In fact, the opposite occurs where alleviating pain and reducing the associated response of the sympathetic nervous system to pain, will allow the practitioner to focus on other causes of tachycardia, tachypnea, pale mucous membranes and weak pulses. If hypovolemia or hypotension are not present, these parameters frequently return to normal after administration of analgesics.

IN GENERAL, dogs may continue to wag their tail in response to touch or commands even though they may be experiencing moderate to severe pain. Therefore, a tail wag should not be used to judge a pain-free situation. Cats typically remain quiet and motionless, but occasionally may growl, when in mild to moderate pain and may thrash, growl and scream when pain is severe. Cats may still purr when painful to any degree and, in fact, up until death. The term 'depressed' in this text means slow or a 'hang-dog' response to a situation where the dog or cat would normally act as described in pain level 0. They may appear 'tired', the palpebral fissures may be incompletely open, with a low carriage of the head. The level of depression may vary from that just described to poorly or non-responsive to caregiver.

Painful sensations such as dull aching, sharp shooting, throbbing, stinging – we have all experienced these at some time – can be experienced in any individual as a single or multiple experience. A single patient can experience a combination of these painful sensations after trauma or after major orthopedic surgery. Combinations of different classes of analgesics are recommended in these animals, as one analgesic class alone is usually not adequate to control all types of pain.

NOTE: Where **NSAIAs** are recommended it is assumed that there is **no contraindications** for their use (*see Analgesics and Sedatives p. 87*).

Pregnant and Nursing Animals. The diagnosis and assessment of pain in pregnant and nursing animals is based on the problem at hand and is similar to other mature animals. The dose of analgesic used in the pregnant animal should be based on lean (non-pregnant) weight; dosages recommended in Tables 1 – 3 may be used as a guide. However, the goal is to relieve pain so titration to effect would be the most prudent method of dosing. Inadequate analgesia in nursing mothers may cause aggressive behaviour towards the young. The non-steroidal anti-inflammatory analgesics must be avoided in these animals due to several potential problems (*see Suggested Reading 2*). A single injection post-caesarian section is acceptable. Currently, fentanyl, hydromorphone, oxymorphone, morphine, methadone, buprenorphine or butorphanol and local anesthetics are the analgesics of choice in both pregnant and lactating animals. To avoid potential for drug side effects in suckling kittens and puppies, avoid nursing during peak drug levels and where possible, time nursing immediately prior to the next dose. One drop of naloxone can be administered (sublingual) to puppies and kittens if depression is noted. Short-term pain management using a fentanyl patch may be a problem due to the puppies or kittens chewing on the patch and is therefore not recommended. Avoid sedatives with long half-lives

Neonates, Infants, Weanlings and Pediatric Patients. Management of pain is extremely important in all animals but especially the very young where a permanent hyperalgesic response to pain may exist with inadequate therapy. The age demarcation of neonates (0 – 2 weeks), infants (2 – 6 weeks) weanlings (6 – 12 weeks) and juveniles (3 – 6 months), is necessary due to the metabolic changes that occur during these periods of maturation. Neonates, and potentially infants, may require lower doses of **fentanyl or morphine** for analgesia. They are also more sensitive to the sedative and respiratory depressant affects of opioids; fentanyl is preferred in the very young, especially, the neonate. Weanlings and pediatric patients may require an adult dose, or even higher, of opioid due to increased metbolism (*see Suggested Reading 2*). This author emphasizes that titration of the opioid to effect, rather than a pre-determined dose, is the most important method by which to manage pain. Starting at lower dosages and increasing to effect is recommended for analgesia. As the effects of the opioid occurs quite rapidly after administration, it is wise to monitor for potential adverse effects rather than ignore appropriate analgesia for a 'potential' problem which may not happen. Should overdose be a concern, the opioids can be reversed with naloxone (depending on the size of the animal, 0.05 – 0.1 mL naloxone [0.4 mg/mL] diluted in 5 mL saline, administered at 0.5 mL/min and titrated to effect). There are no published veterinary studies investigating the pharmacokinetics of fentanyl transdermal patches in this young group of patients. Also, the potential of other littermates chewing the patch is a reason for not using this method of analgesia. The use of sedatives should be used with caution in young animals, especially when less than 12 weeks of age. The phenothiazine tranquilizers (i.e., acepromazine) undergo minimal hepatic biotransformation and may cause prolonged CNS depression. If this drug is required, reduce the dose to 0.005 – 0.025 mg/kg IM or SC. Opioids have sedating effects, especially in young animals; therefore, if these drugs are required the addition of a sedative may not be necessary in animals younger than 4 months. Local anesthetics at half the adult dose in neonates and infants may be suitable to prevent pain during various emergency procedures. Refer to local anesthesia for details on preparation. **Non-steroidal anti-inflammatory analgesics** are not recommended for animals less than 6 weeks of age based on developing hepatorenal system.

TABLE 1. Suggested Analgesics for the Initial Management of Acute Pain

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Severe to excruciating pain:

Requires high dose opioids and titration to effect is recommended. Oxymorphone or hydromorphone 0.2 mg/kg IV, IM (dogs & cats) OR morphine or methadone at 1 mg/kg (dogs), and 0.2 – 0.5 mg/kg in cats IM or careful IV titration to effect **over 3 – 5 minutes.** Use the effective dose of the opioid, divided by 2 – 4 to establish an hourly SC or IV CRI; OR fentanyl 10 – 50 μg/kg IV titrated to effect (cats & dogs), continuing with the effective dose as an hourly CRI, + **NSAIAs** where not contraindicated.

ketamine 1 – 4 mg/kg as a bolus combined with the opioid above (dogs & cats)

lidocaine 2 – 4 mg/kg bolus followed by 2 – 4 mg/kg/h CRI (dogs); 0.25 -1 mg/kg bolus then 0.5 – 2 mg/kg/h (cats). The author has no experience with lidocaine CRI in cats. Lidocaine should not be included if local anesthetics have been administered via a different route. Do not overdose with local anesthetic. Tachycardia may persist, rule out other causes (e.g., hypoxemia, hypotension, hypercarbia). It may be impossible to control the pain. Consider combining the above analgesics with **epidurally placed analgesics** or **local blocks,** or **anesthetize** the patient while attempting to find or treat the inciting cause. Remove the inciting cause immediately. **This degree of pain can cause death.**

Drug	Dose	Duration of Action or Dosing Interval
Moderate to severe pain:		
Morphine or Methadone Use low end of the dose for moderate pain	Cat: 0.1 – 0.2 + mg/kg IM, SC Dog: 0.5 – 1+ mg/kg IM, SC For IV dosing use half the low end dose, titrate over 3 – 5 minutes	2 – 6 h IM, SC 1 – 4 h IV
Oxymorphone Use low end of the dose for moderate pain	Cat: 0.02 – 0.1 + mg/kg IV, IM Dog: 0.05 – 0.2 + mg/kg IV, IM	2 – 6 h
Hydromorphone Use low end of the dose for moderate pain	Cat & Dog: 0.02 – 0.1+ mg/kg IV, IM, SC	2 – 6 h
Fentanyl Use low end of the dose for moderate pain	Cat & Dog: 0.001 – 0.01+ mg/kg	0.3 h
#Ketamine Use low end of the dose for moderate pain	Cat & Dog: 0.2 – 4 mg/kg IV Cat & Dog: 2 – 10 mg/kg PO	Prn (~0.5 h)
NOTE: Opioids should be given to effect even beyond dosing and frequency noted if necessary.		
Mild to Moderate pain:		
*Opioids listed above for moderate pain.		
Butorphanol Use low end of dose for mild pain	Low end of dosage range for both cats and dogs Cat & dog: 0.1 – 0.4 IV, Cat: 0.4 – 0.8 mg/kg IM, SC Dog: 0.1 – 0.4 mg/kg IM, SC	0.25 – 1 h 2 – 4 h 1 – 2 (3) h
Buprenorphine Use low end of dose for mild pain	Cat: 0.005 – 0.01 mg/kg IV, IM 0.02 mg/kg sublingual Dog: 0.005 – 0.02 mg/kg IV, IM	4 – 8 h 7 h 4 – 8 h
Meperidine (pethidine)	Cat & Dog: 5 – 10 mg/kg IM, SC	20 – 30 min

TABLE 2. Suggested Analgesia for Various Levels of Ongoing Pain

Severe to excruciating pain:
See Table 1 for suggestions. NOTE: Opioids, ketamine, lidocaine as a CRI can be combined in IV crystalloid fluids (lactated Ringer's or Ringer's may not be compatible due to calcium content. See individual drug charts for hourly dosing). It is recommended to place the medication in a burette in-line with the maintenance fluid rate. Additional individual drug can be placed in the burette, or additional fluids can be added to dilute if reduction is required. A set dosing regimen does not work, individual drug dosing is necessary.

Drug	Dose	Duration of Action or Dosing Interval
Moderate to severe pain:		
Morphine or Methadone	Cat: 0.1 – 0.2+ mg/kg IV titrate to effect over 3 – 5 minutes 0.1 – 0.5 IM, SC Dog: 0.3 – 1 mg/kg IV, IM, SC Administer intermittently or follow with a CRI with effective dose over dosing interval	1 – 4h 2 – 6 h 2 – 4h
Oxymorphone or Hydromorphone	Cat: 0.02 – 0.1+ mg/kg IV, IM, SC Dog: 0.05 – 0.2 mg/kg IV, IM, SC Administer intermittently or follow with a CRI with effective dose over dosing interval	2 – 4h 2 – 4h
Fentanyl	Cat & Dog: 0.004 – 0.01+ mg/kg IV bolus 0.001 – 0.010 + mg/kg/h	0.3 h CRI
Fentanyl patch	Cat & <10kg Dog: 25 µg/h Dogs: 10 – 20 kg – 50 µg/h 20 – 30 kg – 75 µg/h >30 kg – 100 µg/h	*See Analgesics and Sedatives p. 83 for details*
#Ketamine combined with an opioid or sedative	Cat & Dog: 1 – 4 + mg/kg/h IV, SC 0.2 – 4 mg/kg IV	Bolus CRI
Ketoprofen★ *Do not use if hemorrhage is a concern*	Cat: ≤ 2 mg/kg SC Then ≤ 1 mg/kg Dog: ≤ 2 mg/kg IV, IM, SC, PO then ≤ 1 mg/kg	Once, then Every 24h up to 4 days Once, then Every 24h up to 4 days
Meloxicam★	Cats: ≤ 0.2 mg/kg SC, PO then ≤ 0.1 mg/kg Dogs: ≤ 0.2 mg/kg IV, SC, PO then ≤ 0.1 mg/kg	Once, then Every 24h up to 3 days Once, then Every 24h
Carprofen★	Cats: ≤ 4 (2 suggested) mg/kg SC Dogs: ≤ 4 mg/kg SC, IV, PO then ≤ 2.2 mg/kg	Once Once, then Every 12h, preferably q24h
Flunixin meglumine★ *Do not use if hemorrhage is a concern*	Cat & Dog: 1 mg/kg SC	Once
Ketorolac tromethamine★ *Do not use if hemorrhage is a concern*	Cat: 0.25 mg/kg IM Dog: 0.3 – 0.5 mg/kg IM, IV	Repeat once in 8 – 12h Repeat once in 8 – 12h
Etodolac★	Dog: ≤10 – 15 mg/kg PO	Every 24h
Bupivacaine 0.5%	Intra-pleural and peritoneal use: 1 mg/kg (0.2 mL/kg lean weight) + 0.01 mEq/kg sodium bicarbonate diluted to 6 or12 mL (depending on size of the animal) with saline. For intra-pleural flush this through tube with volume of 0.9% saline equal to volume of chest drain.	6 h

Mild to moderate pain:		
Opioids above	Low dosages	Titrate down to lowest effective dose
Buprenorphine	Cat: 0.005 – 0.01 mg/kg IV, IM 0.01 – 0.002 mg/kg sublingual Dog: 0.005 – 0.02 mg/kg IV, IM	4 – 8h 7h 4 – 8h
NSAIAs above	Low dosages	Titrate down to lowest effective dose
Butorphanol	Cat & Dog 0.1 – 0.4 mg/kg IV, IM, SC Administer intermittently or follow with a CRI with effective dose over dosing interval	2 h
Meperidine (pethidine)	5 – 10 mg/kg IM, SC for short duration analgesia or administered at time of NSAIA injection.	20 – 30 minutes
Morphine syrup	0.5 mg/kg PO- titrate to effect	Every 4 – 6 h
Codeine	0.5 – 2 mg/kg PO- titrate to effect	Every 6 – 12 h
Bupivacaine 0.5%	intra-pleural and peritoneal use: 1 mg/kg (0.2 mL/kg lean weight) + 0.01 mEq/kg sodium bicarbonate diluted to, 6 or12 mL (depending on size of the animal) with saline. For intra-pleural flush this through tube with volume of 0.9% saline equal to volume of chest drain.	6 h
Sedatives to combine with opioiods:		
Midazolam	Cat & Dog: 0.1 – 0.5 mg/kg IV, IM	Dog: up to 6h Cat: can be >6h
Diazepam	Cat & Dog: 0.1 – 0.5 mg/kg IV	Dog: up to 6h Cat: can be >6h
Acepromazine	Cat & Dog: 0.01 – 0.05 mg/kg IV Cat & Dog: 0.02 – 0.1 mg/kg IM, SC	1 – 2 h 2 – 6 h
Medetonmidine	0.002 –0.004 mg/kg IM, SC	6 h

Not first line but may be beneficial in difficult to manage cases.

* *See NSAIAs in Analgesics and Sedatives p. 87* for safety information. It is not always necessary to administer the recommended loading dose. The dose is determined based on the degree of pain assessed. It is advised that a dose as low as possible is used to manage the varying degrees of pain. This will reduce the potential for adverse effects.

Not first line but may be beneficial in difficult to manage cases.

NOTE: The drugs and doses given are suggestions. If the pain is not being managed, then increase to effect (not NSAIAs). If administered IV, morphine must be administered slowly to prevent hypotension in all animals. Ketamine 2 – 4+ mg/kg IV or 10 mg/kg **per os,** may be an alternative to control pain quickly if opioids are not available and renal function or hypertrophic cardiomyopathy is not a concern. For severe to excruciating pain, in cats with normal renal function and dogs with normal liver function, and after appropriate dosing with an opioid agonist, ketamine (100 mg/L) and diazepam (5 mg/mL) or midazolam (5 mg/mL) mixed 1:1 and administered at 0.05 – 0.15 mL/kg, to effect should also be considered. General anesthesia is another alternative.

As pain sensation is an individual experience, one animal appearing more painful than another with a similar condition, an individual approach to pain management is required. While suggestions for treatment can be made for mild, moderate and severe pain, response to analgesic therapy is the best approach. If the animal is still considered painful, increase the dose or add another type of analgesic. Assigning the severity of trauma or degree of surgical invasiveness and tissue manipulation to a case may guide you as to which analgesic and how much to give, but even this has its variability. Surgical 'trauma' (tissue handling) and duration of the surgical procedure will influence the degree of post-operative pain. The combination of NSAIAs and opioids confers excellent analgesia for moderate to severe orthopedic procedures and certain soft tissue injury (including surgical) where inflammation is a feature.

TABLE 3. Suggested Analgesic Regimens Associated with Behaviour

Pain Value	Pain Description
0	**No pain**. Patient is running, playing, eating, jumping, bouncy. Sitting or walking normally. Sleeping comfortably with dreaming. Normal, affectionate response to caregiver. Heart rate should be normal, but if elevated, it is due to excitement. Cats will rub their face on the caregiver's hand or cage, may roll over and purr. Cats and dogs will groom themselves when free of pain. Appetite is normal. Behaviour different from this, not associated with pain, may be associated with apprehension or anxiety. Apprehension/anxiety can be a feature of hospitalized patients.
1	**Probably no pain**. Patient appears to be normal but condition is not as clear-cut as above. Heart rate should be normal, or slightly increased due to excitement. Cats may still purr.
2	**Mild discomfort**. Patient will still eat or sleep but may not dream. <u>May</u> limp slightly or resist palpation of the surgical wound, but otherwise shows no other signs of discomfort. Not depressed. There may be a slight increase in respiratory rate; heart rate may or may not be increased. Dogs may continue to wag their tail and cats may still purr. **Reassess within the hour; give an analgesic if condition appears worse.**
3	**Mild pain or discomfort**. Patient will limp or guard incision or the abdomen may be slightly tucked up if abdominal surgery was performed. Looks a little depressed. Cannot get comfortable. May tremble or shake. Appears to be interested in food and may still eat a little but somewhat picky. This could be a transition from 2 above, a change from being comfortable to becoming restless, as though the analgesia is wearing off. Respiratory rate may be increased and a little shallow. Heart rate may be increased or normal, depending on whether an opioid was given previously. Cats may continue to purr and dogs may wag their tail, even when they are in pain, therefore disregard these behavioural patterns as indicators of comfort. **Needs analgesia.** The analgesic selected will depend on whether **(i)** it is a repeat in a patient with moderate to severe pain (fracture repair), **or (ii)** the patient has a problem resulting in mild to moderate pain. **Analgesia**: **If (i),** then continue with morphine IM, SC (Dogs: 0.3 – 0.5 mg/kg, Cats: 0.2 – 0.3+ mg/kg) or oxymorphone or hydromorphone 0.05 – 0.1 mg/kg IV,IM dogs & cats, or methadone at 0.2 – 0.5 mg/kg IV,IM,SC or an injectable NSAIA, if not contraindicated). **If (ii),** then administer butorphanol 0.2 – 0.4 mg/kg, or buprenorphine 0.005 mg/kg, Dog & Cat, or NSAIA where appropriate. If this is a mild to moderate pain situation, oxymorphone, hydromorphone or morphine is not necessary as the patient may become dysphoric.
4	**Mild to moderate pain** with the patient resisting touching of the operative site, injured area, painful abdomen, or neck, etc. Guarding or splinting of the abdomen or stretch all four legs. May look, lick or chew, at the painful area. The patient may sit or lie in an abnormal position and is not curled up or relaxed. May tremble or shake. May or may not appear interested in food. May start to eat and then stop after 1 or 2 bites. Respiratory rate may be increased or shallow. Heart rate may be increased or normal. Pupils may be dilated. May whimper (dogs) or cry (cats) occasionally, be slow to rise and, hang the tail down. There may be no weight bearing or a toe touch on the operated limb. Will be somewhat depressed with reduced response to caregiver. Cats may lie quietly and not move for prolonged periods. **Analgesia.** As for 3 above but at high end of the range dosages. If patient has already received an opioid, consider a NSAIA as an adjunct to opioid.
5	**Moderate pain**. As above but condition progressing from above. Patient may be reluctant to move, depressed, inappetant and may bite or attempt to bite when the caregiver approaches the painful area. Trembling or shaking with head down may be a feature, depressed. The patient may vocalize when caregiver attempts to move them or when it is approached. There is definite splinting of the abdomen if affected (ie peritonitis, pancreatitis, hepatitis, incision), or the patient is unable to bear weight on an injured or operative limb. The ears may be pulled back. The heart and respiratory rates **may** be increased. Pupils may be dilated. The patient is not interested in food, will lie down but does not really sleep, and may stand in the praying position if there is abdominal pain. Cats may lie quietly and not move. **Analgesia.** Butorphanol at 0.4 mg/kg, q2-4h for soft tissue surgical (ie laparotomy), or buprenorphine (Cat: 0.01 mg/kg, Dog: 0.02 mg/kg), or oxymorphone or hydromorphone at 0.05 – 0.1 mg/kg, or morphine (dogs: 0.3 – 0.5 mg/kg, cats: 0.2 – 0.5 mg/kg), or methadone 0.2 – 0.5 mg/kg q 3 – 6h, for soft tissue or orthopedic problems. Consider an injectable NSAIA, either alone or as adjunct to opioids, if orthopedic and soft tissue surgery or injury, where there are no contraindications.

6	**Increased moderate pain. As above** (5), but patient **may** vocalize or whine frequently, without provocation and when attempting to move. Heart rate may be increased or within normal limits if an opioid was administered previously. Respiratory rate may be increased with an abdominal lift. Pupils may be dilated. **Analgesia.** Oxymorphone or hydromorphone 0.1 – 0.2 mg/kg, or methadone or morphine 0.3 – 0.5 mg/kg IM, SC or slow push IV q3–6h; OR morphine 0.1 – 0.2 mg/kg/h or fentanyl 3 – 5 μg/kg/h (dogs & cats) constant rate infusion (CRI). If butorphanol was given within the last 20 min, and the condition is still painful, then a higher dose of pure μ agonist is usually required due to the antagonistic effects of butorphanol; alternatively, give an injectable NSAIA, especially if the pain is associated with an orthopedic problem and there are no contraindications.
7	**Moderate to severe pain** (include signs from 5 & 6 above). The patient is very depressed and is not concerned with its surroundings but usually responds to direct voice (this may be a stop in whining, turning of the head or eyes). The patient will urinate and defecate (if diarrhea) without attempting to move, will cry out when moved or will spontaneously or continually whimper. Occasionally an animal doesn't vocalize. Heart and respiratory rates may be increased. Hypertension may also be present. Pupils may be dilated. **Analgesia:** Patients require a higher dose of morphine, fentanyl, oxymorphone, hydromorphone, or methadone; give any of these opioids to effect. OR a NSAIA alone , especially if orthopedic pain, or a combination of a NSAIA and an opioid. Addition of a bolus 1 – 2 mg/kg and CRI of ketamine 0.25 – 2 mg/kg/h should be considered in addition to the opioid and NSAIA (where appropriate) if pain is not controlled. Also consider adding lidocaine 1 – 2 mg/kg bolus followed with 1 – 2 mg/kg /h CRI (dogs), 0.25 – 1 mg/kg bolus and 0.5 – 1 mg/kg/h CRI (cats). Epidural and/or Local analgesia/anesthesia should be considered where indicated. Both parenteral and epidural routes should not be administered simultaneously.
8	**Severe pain**. Signs as above (7). Vocalizing may be more of a feature, or so consumed with pain the patient will not notice your presence and just lie there. The patient may thrash around in the cage intermittently. If it is traumatic or neurological pain, the patient may scream, especially cats, when being approached. Tachycardia, $\pm$ tachypnea with increased abdominal effort and hypertension are usually present even if an opioid was previously given, although these can be unreliable parameters if not present. **Analgesia: High dose** oxymorphone, hydromorphone or morphine IM, SC or CRI, to effect, or fentanyl (induce with 5 – 10 μg/kg and maintain on up to 50 μg/kg/h) CRI dogs and cats. Add an injectable NSAIA especially if orthopedic pain, with no contraindications, add ketamine 1 – 4 mg/kg bolus followed by 0.5 – 2 mg/kg/h CRI $\pm$ lidocaine 1 – 2 mg/kg bolus followed with 1 – 2 mg/kg /h CRI (dogs), 0.25 – 1 mg/kg bolus and 0.5 – 1 mg/kg/h CRI (cats). Epidural and/or Local analgesia/anesthesia should be considered where indicated. Both parenteral and epidural routes should not be administered simultaneously. Epidural and/or Local analgesia/anesthesia should be considered where indicated.
9	**Severe to excruciating**. As above (8), but patient is hyperesthetic. The patient will tremble involuntarily when any part of the body in close proximity to wound, injury, etc. is touched. Neuropathic pain (entrapped nerve or inflammation around the nerve) or extensive inflammation anywhere (ie peritonitis, pleuritis, fasciitis, myositis, especially when caused by a streptococcal organism; severe necrotizing pancreatitis). **Analgesia: Requires high dose** oxymorphone, hydromorphone IM, SC or CRI given to effect or morphine IM, SC or CRI (dogs & cats); OR fentanyl up to 50 μg/kh/h CRI (cats & dogs); $\pm$ NSAIAs where not contraindicated; or $\pm$ 2 – 4 mg/kg ketamine IV bolus followed by 2 – 4mg/kg CRI; $\pm$ lidocaine 2 – 4 mg/kg bolus followed by a 2 – 4 mg/g/hr CRI (dogs); 0.25 –1 mg/kg bolus then 0.5 – 2 mg/kg/h (cats). Lidocaine by this route cannot be used if local anesthetics are being administered via another route as the dose of lidocaine will likely exceed the safe limit, especially in cats. Tachycardia may persist and may be impossible to control the pain. Consider combining analgesics with epidurally placed analgesics or local blocks, or anesthetize the patient while attempting to find or treat the inciting cause. Remove the inciting cause immediately. **This degree of pain can cause death.**
10	**As above (9), but patient emitting piercing screams or almost comatose.** The patient is hyperesthetic/hyperalgesic, pain is elicited wherever you touch the patient **Analgesia:** Very high doses of opioids do not relieve this pain; however, you must give at least 0.2+ mg/kg (dogs), 0.1 mg/kg (cats) oxymorphone; 0.3 – 0.4 mg/kg hydromorphone or morphine 1 mg/kg (dogs), 0.5 mg/kg VERY slowly IV (cats, give more if needed, to effect) or fentanyl (induce with 5 – 10 μg/kg and maintain on 50 μg/kg/h) and consider combining this with NSAIAs where not contraindicated, epidurally placed analgesics or local blocks where appropriate, 1 – 4 mg/kg ketamine bolus followed by 1 – 4mg/kg/h CRI or anesthetize the patient while attempting to find or treat the inciting cause. Consider addition of lidocaine 2 – 4 mg/kg IV bolus and 2 – 3 mg/kg/h IV CRI (dogs), 0.25 – 1 mg/kg bolus and 0.5 – 2 mg/kg/h CRI (cats). Epidural and/or Local analgesia/anesthesia should be considered where indicated. Do not administer both parenteral and epidural local anesthetics simultaneously. **This degree of pain can cause death.**

If the pain is not being managed, then increase to effect (opioids and ketamine). In the author's experience, there have been minimal or no side effects with high dose opioids when animals are painful.

Neuropathic Pain may be associated with a variety of surgical procedures or medical conditions.
Gabapentin is a useful adjunctive analgesic for neuropathic pain. Pain associated with neuritis, nerve entrapment secondary to trauma, cervical or thoracolumbar disc disease or post-laminectomy can be responsive to gabapentin. Gabapentin can be used in combination with opioids. Post-seizure or CPR vocalization, if relentless, may also be managed with gabapentin. Suggested range in cats is 2.5 – 5 mg/kg q12h, and in dogs 5 – 25 mg/kg q8h for pain. This author starts at 10 mg/kg and increase if no effect seen in 2 hours. There may be a requirement for up to 12 mg/kg q6h for post-seizure or post-CPR vocalization and thrashing. Wean off slowly otherwise the patient will experience worse pain. Reduce in renal insufficiency. Usually the limit of dosing is reached when the animal is sedated which may be up to 25 mg/kg q8h.

TABLE 4. Adjunctive Analgesics Suggested Dosages

Drug	Species	Dosage (mg/kg)	Route of Admin	Duration
Ketamine	Dogs & Cats	0.5 – 4 0.5 – 4 mg/kg/h	IV IV	bolus for control followed by CRI depending on severity of pain
Lidocaine	Dogs Cats	1 – 4 1 – 3 mg/kg/h 0.25 – 1 0.5 – 2 mg/kg/h	IV IV IV IV	bolus followed by CRI depending on severity of pain bolus followed by CRI Limit 24 hours
Gabapentin	Cats Dogs	2.5 – 5 (10 rarely) 5 – 10 (25 rarely) up to 12	PO PO PO	q12h q8h for pain q6h for post-seizure or post-CPR vocalization and thrashing. Wean off slowly.
Amantadine	Dogs & Cats	3	PO	q24h
Tricyclic Antidepressants:				
Amitriptyline	Dog Cat	1 – 2 2.5 – 12.5 mg/cat	PO PO	q12–24h q24h
Imipramine	Dog Cat	0.5 – 1 2.5 – 5 mg/cat	PO PO	q8h q12h

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SUGGESTED READING

1. Gaynor JS, Muir III WW. Handbook of Veterinary Pain Management. Mosby, St. Louis, MO, 2002.
2. Mathews KA. Analgesia for the pregnant, lactating and neonatal to pediatric cat and dog. J Vet Emerg & Crit Care. 2005, December In press.
3. Mathews KA Ed. PAIN How to Understand Recognize Treat and Stop CDs/DVD (www.jonkar.com), Jonkar Computer Systems, Guelph, ON.

INTRODUCTION

The use of local anesthetics should be considered for analgesia when performing various procedures in awake and sedated animals. The various local anesthetic techniques are also useful to supplement general anesthesia, reducing the need for higher levels of inhalants, and/or higher doses of opioids, both of which may be associated with cardiovascular and/or respiratory depression. Local anesthetics are safe if used appropriately with careful calculation of dosages, especially in very small animals (*see below*). To prevent inadvertent arterial or venous injection, aspirate prior to administration.

Lidocaine is the most common local anesthetic, primarily used as a 2% solution – with or without epinephrine – but is also available as 0.5%, 1% solution, and as a gel and ointment. Onset of action occurs within 2 – 5 minutes, and duration of effect is between 30 – 60 minutes. Infiltration of lidocaine 2% is extremely painful. However, the pain may be reduced with lower concentrations, use of small needles (minor effect) and less volume delivered with pressure, warming (37 – 42°C)[98.6 – 107.6°F], slow administration, and buffering. When intrapleural use is carried out in the awake animal buffering is needed to reduce the pain (mix **2% lidocaine** with **saline** and **sodium bicarbonate [1 mEq/mL]**) at a 5:5:1 ratio = 10 mL **1% lidocaine** and 1 mL sodium bicarbonate). Administer **<1.0 mL/kg (dogs),** and **<0.6 mL/kg (cats). The maximum dose of lidocaine to be administered is** <10 mg/kg or <0.5 mL/kg (2%). This dose can be diluted to 1% to achieve a larger volume for local blocks.

Bupivacaine is the preferred local anesthetic due to its longer duration of action. It is primarily used as a 0.5% solution (also available in 0.25%), has a slower onset of action than lidocaine (15 minutes), and lasts for 3 – 6 hours in most local blocks. **The maximum dose of bupivacaine is 2 mg/kg, or <0.5 mL/kg (0.5%).** Dilution to 0.25% will increase volume for local blocks; 10 mL **0.25% bupivicaine** and 1 mL of 1.0 mEq/mL sodium bicarbonate, **administer at <1.0 mL/kg.** Note the similar maximum volumes for both lidocaine and bupivicaine, and the noted concentrations. If lidocaine is used to spray the larynx prior to intubation, the 10 mg dose must be factored into the total amount if administered within a one hour period.

PROCEDURES

Please refer to recommendations and maximum doses above.

A. Topical Techniques

1. Surface **anesthesia** results when the local anesthetic is applied to the skin or mucous membranes such as the mouth, eye, vaginal vault, and nose prior to various procedures. EMLA cream confers analgesia to the skin.
2. **Intrapleural and intraperitoneal block** is a useful adjunct to opioid analgesics for thoracic incisional pain or pleuritis, or pain associated with pancreatitis. Using aseptic technique, via chest drain for intrapleural, or via catheter for intraperitoneal analgesia, instill a mixture of bupivacaine to a maximum of **0.4 mL 0.5% bupivicaine,** prepared as above with sodium bicarbonate, then add 6 – 12 mL saline. Flush with a volume of saline equal to volume of chest drain to flush the local anesthetic into the pleural space. After intrapleural administration, the animal should be placed with the injured, or incision side, down for 5 minutes to enhance the effect at the desired site. The patient can also be rolled onto its back to allow the local anesthetic to flow into the paravertebral gutters to block nerves before entering the spinal cord. The diluted solution will result in sensory blockade but is unlikely to cause motor blockade. If the patient still appears uncomfortable, adjust their position to facilitate re-distribution of the local anesthetic. While the addition of sodium bicarbonate results in pain reduction, indications of pain may still appear, so be prepared for this.

B. Local Infiltration

1. Use **0.5 – 1% lidocaine (without epinephrine)** to infiltrate the area involved prior to chest tube placement, IV cut-down and other minor procedures. Longer duration of effect is produced with **bupivacaine 0.25 – 0.5%.** Healing may be adversely affected by the presence of local anesthetic at the site; if there is no other reason for delayed wound healing (i.e, non-sterile technique, tissue trauma), this should not be a significant problem.
2. **Soaker catheter technique.** For longer management of pain (up to 5 days), the continuous infiltration of a local anesthetic can be accomplished by using a commercial system (PainBuster Soaker® catheter, dj Orthopedics, Inc. Vista California) or can be made with IV tubing and catheter. The local anesthetic can be delivered intermittently, or continuously by a pump attached to the tubing and an in-dwelling sterile multipore catheter placed at the surgical site.

3. **Incisional line block.** This should be performed after surgical preparation. Insert a 25 ga needle subcutaneously, aspirate, deposit the drug until a small bleb is noticed, remove the needle, and then reinsert at the edge of the bleb. Continue this until the length of the proposed incision is complete. Prior to closing an incision not previously blocked, insert the needle subcutaneously and deposit the drug in a fanlike manner through the muscle, to the peritoneum, along the incision.

C. Ring Block

Placement of a local anesthetic by infiltrating around a digit or limb proximal to the incision or injury or infiltrating around a lump at a distance from the incision to reduce the potential of complications associated with healing. This is a useful technique when the location of specific nerves to site is not known. Recommendations are similar to infiltration (note: no epinephrine). Consider using for lacerations where the tissue trauma will contribute to delayed wound healing.

D. Nerve Blocks

Desensitization of specific nerves may be useful. Longer duration of effect is produced with bupivacaine. Use **0.25 – 0.5% bupivacaine** to block nerves by instilling 0.25 – 3 mL at the nerve site. **Note maximum dosages above.**

1. **Dental blocks** include infraorbital (upper premolar, canine, incisor teeth and from rostral midline to lateral muzzle), maxillary (hemimaxilla and palate), inferior alveolar (mandibular teeth and bone, half of tongue) and mental (mandibular canine, incisors and lip).
2. **Intercostal blocks** are dorsal to the site of surgery or injury and spanning at least 2 intercostal spaces each side of the incision. Typically 0.5% bupivacaine is infiltrated between the ribs (***note maximum dosages p. 124***). Take care to avoid the artery, situated caudal to the rib (Fig. 1).

   This technique is useful for providing analgesia after thoracotomy or traumatic rib fractures. The block may be placed prior to surgical incision percutaneously (pre-emptive approach) or intra-operatively, pre muscle incision or prior to closure. Two to three spaces cranial and caudal to the incision should be blocked. The nerves, along with the artery and vein, lie on the posterior aspect of the rib. The site to be blocked is the most proximal point of the rib on the caudal aspect (see figure below). Aspirate prior to depositing the drug. The dose of drug should be carefully calculated and divided amongst sites. Dilution with sterile saline to facilitate even distribution amongst sites is often necessary but may not be as effective. Operative patients should receive bupivacaine and awake patients should receive 1.5 mg/kg lidocaine and 1.5 mg/kg bupivacaine to ensure immediate pain control with lidocaine and longer duration with the bupivacaine.

FIGURE 1. Intercostal Nerve Block

Intercostal Nerve Block Site

Intercostal A.   Intercostal N.
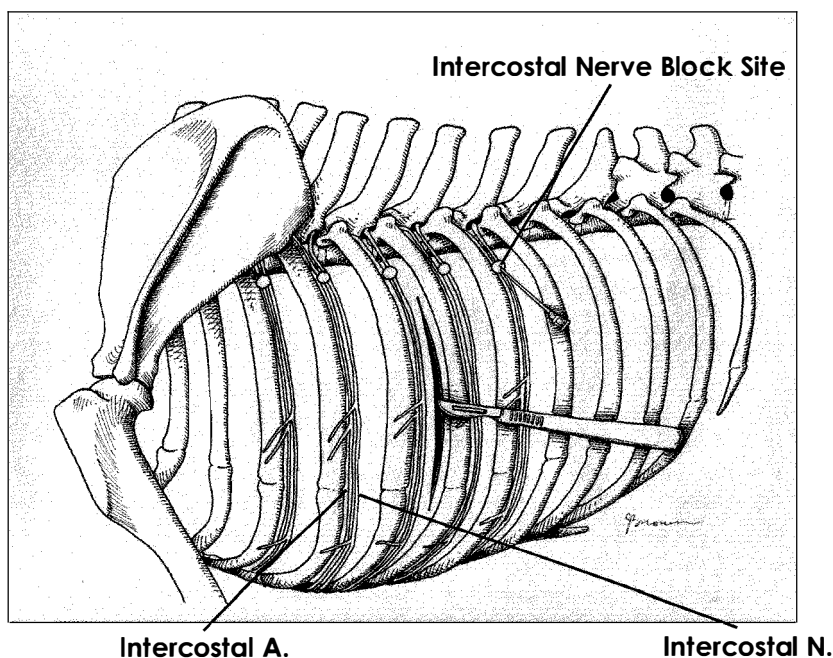
3. **Brachial plexus block** can be placed by infiltration of local anesthesia caudal to the point of the shoulder (abduct the leg and approach the site ventral and medial to the leg in the anesthetized animal. Fan the injection and avoid vessels) (needle 1 in Fig. 2). It is very effective for procedures performed from the elbow to distal limb, and when applied intraoperatively at least 5 (lidocaine) to 15 minutes (bupivacaine) prior to transection of the brachial plexus during forelimb amputation. A volume of 3 – 15 mL (calculating the dose of anaesthetic to avoid overdose) is required and should be deposited in multiple locations to improve the block. A long duration of effect is possible resulting in paralysis for 12 – 18 hours. The dog will require assistance to ambulate. Secondary injury may be a potential problem if care is not taken during this time. The block is not always complete, possibly due to multiple fascial planes in the area interfering with spread.

    a. A high block has been described that is paravertebral in location and involves blocking C_6, C_7, C_8 and T_1 nerves under the scapula as they exit from the vertebral foramen (0.5 – 2 mL/site) (needle 2 in Fig. 2). This block provides more complete analgesia of the entire forelimb.

FIGURE 2. Brachial Plexus Block
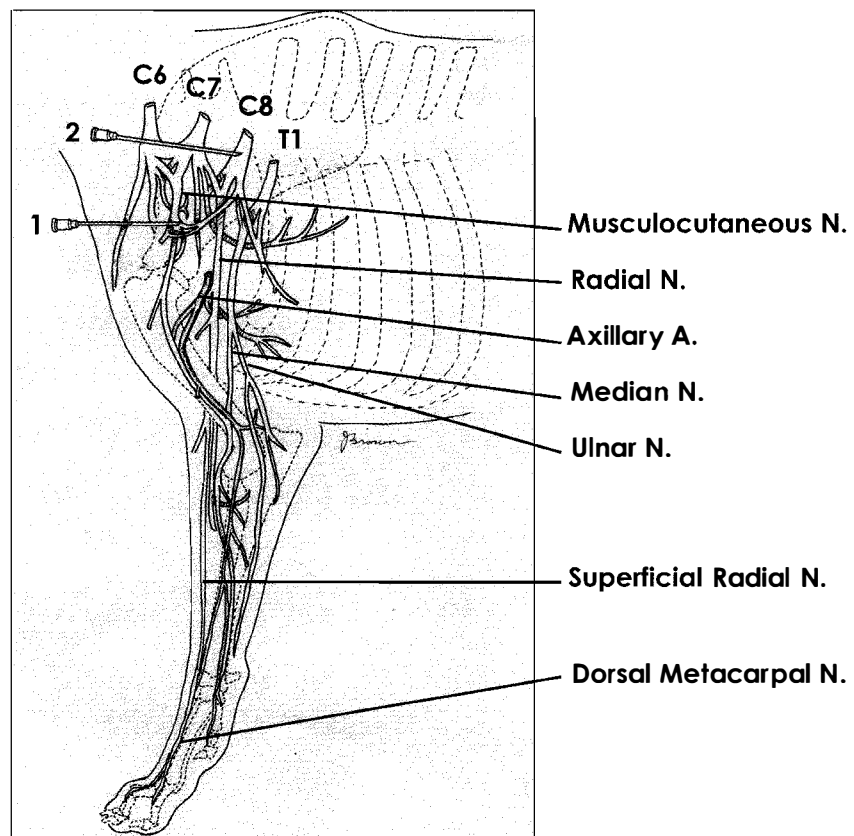
4. **Distal extremity block** (similar to that used for onychectomy) can be placed prior to onychectomy or managing injuries of the paw. For the fore paw, inject 0.2 mL of **1% lidocaine** or **0.25% bupivacaine** subcutaneously at each site of the dorsomedial aspect of the carpus, just proximal to the joint (blockade of the superficial branches of the radial nerve), and medial and lateral to the carpal pad (blockade of median nerve and palmar and dorsal cutaneous branches of the ulnar nerve). This will confer analgesia for approximately 60 minutes to four hours depending on the solution used. For the hind paw, inject subcutaneously on the dorsomedial aspect of the tarsus just distal to the joint (selective blockade of distal branches of the common peroneal and tibial nerves) and inject on the ventromedial aspect of the tarsus just distal to the joint (superficial branches of the tibial nerve are blocked) to give approximately 60 minutes to four hours of analgesia.

Auriculopalpebral Branch

Ear Canal

Parotid Gland

Facial N.

Greater Auricular N.

External Jugular V.

Mandibular Lymph Nodes

Mandibular Gland

1

2

External Acoustic Meatus

Auriculopalpebral Branch

Ear Canal

Dorsal Buccal Branch

Greater Auricular N.

Wing of the Atlas

Ventral Buccal Branch

Cervical Branch

2nd Cervical N.

1

2
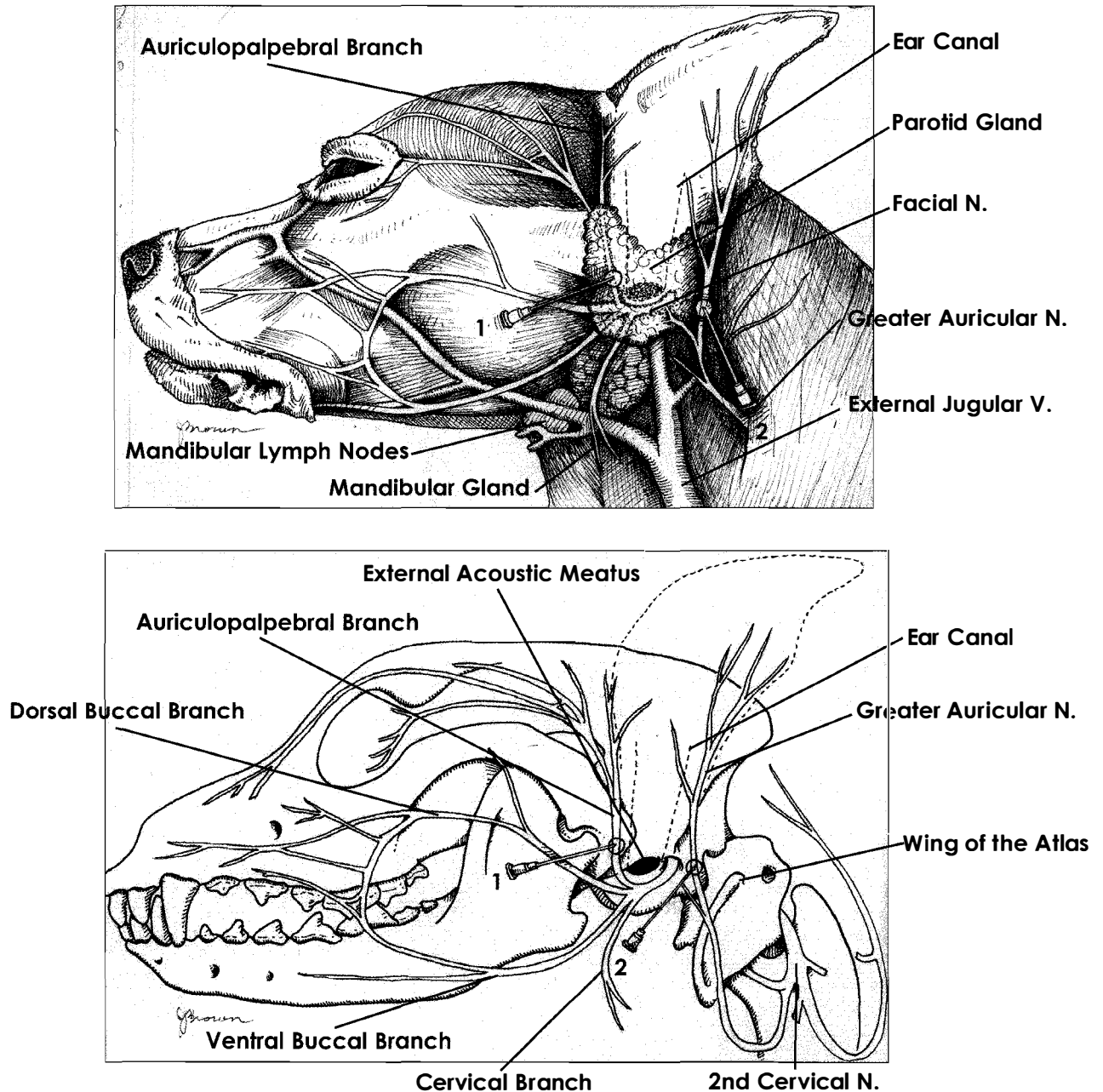
FIGURE 3. Aurioculopalpebral Block

5. **Auriculopalpebral block** is utilized prior to painful ear surgery (e.g., bulla osteotomy, total ear ablation), and has been shown to reduce maintenance anesthetic requirements and post-operative analgesia. In the emergency setting, this block may be used to reduce pain (i.e., acute severe otitis, injuries), or perform minor procedures (e.g., aural hematoma repair or suture laceration). Following anesthesia instill 0.25 – 3.0 mL 0.5% bupivicaine at points 1 & 2 (Fig. 3) – total volumes of bupivicaine are as those mentioned above.

All diagrams with permission Jonkar Computer Systems Ltd., Guelph, ON, Canada.

Intravenous Regional Block

Surgery of an extremity can be carried out following placement of an IV regional block. A tourniquet is required and limits the duration of the block. An IV injection of 5 – 10 mL of 1% lidocaine either cehalic or saphenous veins, in animals >5 kg will distribute in the area occluded by the tourniquet and block sensation until the tourniquet is released (no advantage to selecting bupivacaine and faster effect of lidocaine reduces overall tourniquet time). Smaller volumes should be used in smaller animals. This is an appropriate block in the animal that can be restrained adequately, and if vascular compromise, infection or fibrosis is not present in the affected limb. The use of a small gauge catheter or needle, and a slow injection technique employed while placing gentle pressure at the injection site, improve the effect of the block.

Intra-articular Block

Administration of bupivacaine into a joint prior to, or following, surgery will reduce post-operative pain. Bupivacaine (1 – 1.5 mg/kg), lidocaine (4 – 6 mg/kg) or morphine (0.1 – 0.5 mg/kg), or a combination of opioid and local anesthetic, may be placed into the stifle joint lateral to the parapatellar ligament, or the elbow joint, via catheter after surgery is complete. For the elbow, a tourniquet placed above the joint prior to injection and left in place for 5 – 10 min after injection has been suggested.

Epidural Block *(see section on Epidural Analgesia p. 112).*

SUGGESTED READING

1. Dyson D. PAIN HURTS CD. Mathews KA (ed). Jonkar Computer Systems, Guelph, ON, 2003.
2. Lemke KA, Dawson SD. Local and Regional Anesthesia. Vet Clin North AmSmall Anim Pract; 2000:839-85.
3. Tranquilli WJ, Grimm KA, Lamont LA. Pain Management for the Small Animal Practioner. Teton NewMedia, Jackson, WY. 2000.

NOTES

INTRODUCTION

In order to provide optimal patient care, including pain relief, veterinarians must include narcotics such as opiates, among their arsenal of treatment options. Veterinarians providing therapy to animals with neurological and behavioural issues must also use controlled substances, e.g., phenobarbital, and targeted drugs, e.g., diazepam. A common anesthetic induction agent in veterinary anesthesia is ketamine, which is a narcotic. Therefore veterinarians must use, and have at their practice location, targeted drugs, controlled substances and narcotics.

The storage and record keeping associated with controlled drugs and other regulated substances are frequently a source of stress for veterinarians. While caution and due diligence are required compliance is not as difficult as many practitioners perceive. In a sentence, what comes in and what goes out must balance and be recorded.

Legislation

Controlled drug substances and narcotics fall under Federal Legislation: The Food and Drugs Act & Regulations; The Controlled Drugs and Substances Act; and the Narcotic Control Regulations. Veterinarians are also responsible to fulfill the requirements of their provincial licensing body, for example in Ontario, The College of Veterinarians of Ontario (CVO). If the requirements conflict the more stringent requirement applies. It is the responsibility of the veterinarian to keep current on legislative requirements.

The simplest way to determine whether or not a drug is a targeted substance, e.g., benzodiazepines, a controlled drug substance, e.g., phenobarbital, or a narcotic, e.g., morphine, is to access the National Drug Schedules on the NAPRA (National Association of Pharmacy Regulatory Authorities) web site http://www.napra.org. Manufacturers generally indicate on their labels the status of a drug, although this cannot be relied on:

Targeted Substance   **Controlled Drug**   **Narcotic**

Although federal legislation stipulates different requirements for targeted substances, controlled drug substances and narcotics, provincial veterinary licensing bodies frequently do not and it is simplest to treat all 3 classes of drugs as though they were narcotics, i.e., follow the most stringent requirements. The following will therefore apply to all targeted substances, controlled drug substances and narcotics, referred to as controlled drug substances.

Records

All documentation relating to controlled drug substances must be maintained for a minimum of 2 years, as specified by federal legislation or the minimum specified by the provincial licensing body, which ever is longer. In Ontario it is a minimum of 5 years. All records must be readily accessible by a federal or provincial inspector.

Ordering

All suppliers require the signature of a licensed veterinarian. This can be supplied at the time the order is placed or within 5 working days of receipt of the order.

Receipt

A log must be maintained of receipt of all targeted substances, controlled drug substances and narcotics. This must include: date goods received; name strength quantity of drug; name and address of the supplier; purchase price; signature of the purchasing veterinarian. The simplest way to do this is for the purchasing veterinarian to sign and date the invoices, and to maintain the invoices in a file. Note, veterinary software that is designed to eliminate paper in a practice and make it completely electronic frequently fails to accommodate the signature requirement and is a source of non-compliance on inspection.

Use

Whether dispensing to a client to take home, or to use in the practice setting such as during surgery, a veterinarian must maintain a register of targeted substances, controlled drug substances and narcotic use. This register must show a running balance of how much drug substance has been received and given out. The balance shown in the register must reflect the amount of substance physically in the practice. Frequent audits or counts are advised. The sooner a discrepancy is detected the more likely the source of error or loss will be accurately determined.

Access to controlled drug substances must be under the specific direction of the veterinarian. Thus there must be a record that the veterinarian requested the controlled drug substance for a particular case. This could be accomplished by the veterinarian signing or initialling the controlled drug substance register for each withdrawal. If an employee of the veterinary hospital is withdrawing controlled drug substances on behalf of the veterinarian it is also wise to have that individual initial or sign the register. In many circumstances, the requirement for a witness is good practice, particularly for single use vials when there will be waste, or drug remaining. It is good practice to have separate sheets for each controlled drug substance used in the practice. Each sheet should have the drug name, manufacturer or trade name, and strength in the header.

A controlled substances register must contain: date of dispensing; client/patient information (name and address, or client ID number); name, strength and quantity of drug; current balance, and signature (as discussed above).

A Sample Log

ABC Veterinary Clinic
Controlled Drug Register

Sheet # _____

Drug name/manufacturer/strength

Balance Forward _____

Date	Received from/ Dispensed to	Quantity Received/Issued	Balance	Signature/Witness

Mixtures

If the controlled drug substance used is a pre-mix e.g. butorphanol/acepromazine/glycopyrrolate, the log must either clearly indicate the amount of controlled drug substance given or it must be readily apparent and easily calculated from the recipe or name of the mixture.

It is easiest when preparing a premix to indicate a decrease in amount in the controlled drug(s) used to prepare the mixture in the log and a corresponding increase in amount in the mixture. The amount of the mixture dispensed would then be tracked in the log.

Butorphanol/Wyeth/10 mg/mL
Name/manufacturer/strength

Balance Forward 100 mL

Date	Received from/ Dispensed to	Quantity Received/Issued	Balance	Signature/Witness
December 20, 2004	From Wyeth Ayerst	+100 mL	200 mL	XXXXXX
January 1, 2005	For Premix B.A.G. Lot #1234	10 mL	190 mL	XXXXXX

PREMIX B.A.G.
Name/manufacturer/strength

Balance Forward 0 mL

Date	Received from/ Dispensed to	Quantity Received/Issued	Balance	Signature/Witness
January 1, 2005	From ABC Vet Clinic Lot # 1234	+50 mL	50 mL	XXXXXX
January 2, 2005	Owner Smith "Rover" ID # C12345	2 mL	48 mL	XXXXXX

Note: It is possible to combine the controlled drug register with the prescription drug file provided the controlled drug requirements are met.

Loss

Any loss or theft must be reported to the local police immediately and Health Canada (613•954•1541) within 10 days of detection. Health Canada has standard forms that can be faxed to 613•957•0110.

Storage

Controlled drug substances must be stored in a manner that will protect them against loss or theft. In Ontario, Veterinary Legislation specifies that this must be a locked cupboard. This cupboard must be locked at all times other than when a controlled drug substance is being added or removed. Ideally this cupboard should be fixed and not readily removed. If it is possible to physically remove the locked cupboard it is advisable to keep the narcotic log separate from the narcotics in case of theft. This is an American Animal Hospital Association requirement. The cupboard should be reasonably accessible from the area of greatest use e.g., the surgery area, however the further it is from a means of entry/exit the longer it would take a potential thief to access the cupboard. The cupboard should not be visible from a window. Although more expensive, a safe that requires both a combination and a key, and is not easily moved, is more secure.

Disposal

Controlled drug substances that are no longer required or have expired should be returned to the manufacturer or supplier, depending upon company policy, or destroyed. Destruction requires permission from Health Canada. Items that are returned or destroyed should be removed from the controlled drug substance log with an appropriate entry e.g., Returned to Manufacturer, 100 mL, balance 0. All destruction and disposal of controlled drug substances must comply with municipal waste disposal laws.

Editor's Note: While the legislative details of this chapter are specifically those for Ontario, Canada, similar regulations apply elsewhere. As stated here, it is in the veterinarian's best interest to keep current on legislative requirements for the individual's province, state or country. Specific guidelines for the United States are published in the J Veterinary Emergency & Critical Care, December 2005.

This chapter is intended as a guide to help veterinarians apply controlled drug substance legislation in a practice setting, however it is not intended to, nor can it, replace the legislation.

NOTES

INTRODUCTION

Cardiopulmonary arrest (CPA) is a sudden cessation of functional ventilation and effective circulation. It can be precipitated by many situations (e.g., hypovolemia, acidemia, respiratory failure, trauma, anesthesia and other drugs, cardiac arrhythmias, vagal stimulation). Successful recovery is dependent on the patient's history, current health status, prior drug therapy, precipitating event, size of the patient, the operator's skill at performing cardiopulmonary-cerebral resuscitation (CPCR) and understanding of the pharmacological support available for various situations. At least 3 people are required to perform adequate resuscitative techniques. In the average veterinary practice all hospital personnel should be trained in some CPCR role. Preparedness is the key to initial response to a CPA. There should be a designated area where all drugs and equipment are available in a visible organized manner (*see Contents for Crash Cart p. 9*).

CPCR is divided into 3 stages, **Basic Cardiac Life Support (BCLS)** *p. 113* which is basic breathing and circulation, **Advanced Cardiac Life Support (ACLS)** *p. 136* which is the addition of drugs or procedures (i.e., defibrillation, open chest), and **post-CPCR management** *p. 139* which is crucial to reduce the chance of re-arrest. While BCLS and ACLS are stages of CPCR, ACLS must be anticipated and performed concurrently with BCLS when BCLS fails. The decision as to whether open chest CPCR, with direct (internal) cardiac massage, should be undertaken can be a difficult one. Open-chest CPCR has been advocated in patients weighing >15 kg where return of spontaneous circulation (ROSC) has not occurred after 2 minutes. It has been the author's experience that, with closed chest CPCR and epinephrine, some dogs >15 kg (some >30 kg) have ROSC with normal neurological outcome. These dogs were treated promptly and adequate pulse pressures were maintained for up to 8 minutes of resuscitation prior to ROSC; this has also been reported by others. However, not all resuscitative efforts have a successful outcome. In many situations, open-chest CPCR is necessary (see Management below). In these situations, the decision to open the chest should be made quickly. Prepare for open chest CPCR at the outset of most CPAs. Have all the instruments ready. Clippers and final skin prep solution should be in reach. A crash cart instrument kit should contain a scalpel handle with a protected blade in place, curved mayo scissors, kelly forceps, small and large balfour retractors, sterile gauze squares, suture material, needle drivers, rat-toothed tissue forceps, umbilical tape and penrose drain.

Successful resuscitation from CPA is up to 10% in veterinary patients. Similar success rates occur in humans with one report citing 25% with survival to discharge with normal neurological function at 19%. Survival to discharge is <10% for veterinary patients with majority being anesthetic arrests, or those situations where the underlying cause was easily recognized and reversible.

DIAGNOSIS

History/Signalment

- Identifying those patients at risk for CPA (i.e., brachycephalic breeds recovering from anesthesia and other potential respiratory compromised patients, hypotensive/hypovolemic, trauma patients, various breeds with arrhythmogenic cardiomyopathies) facilitate preparedness for CPA, and more importantly, prevention.
- Prior to instituting CPCR, critically assess the CPA either as a 'cardiopulmonary arrest' situation or inevitable 'death' from bad disease with a poor prognosis. CPCR should not be instituted in these individuals.
- In those patients where respiratory and/or cardiac function ceases unexpectedly and the underlying cause of the CPA can be reversed, CPCR should be instituted immediately. Cardiopulmonary arrest while under anesthesia, in the otherwise healthy patient, carries a good prognosis if resuscitative efforts are promptly instituted.
- Knowing what may have precipitated the CPA will aid in directing therapy.

Clinical Signs/Physical Examination

Respiratory and/or cardiac arrest in non-anesthetized patients is based on a loss of consciousness and cessation of normal ventilation. Gasping (effective ventilation) may occur a few seconds after cardiac arrest in both the anesthetized and awake animal.
- **Pupils** become fixed and dilated within 30 – 45 seconds.
- **Capillary refill time** (CRT) may continue to be normal (1 – 1.5 secs) for several minutes if vasomotor tone and vascular volume are normal at the time of CPA.

- **Mucous membranes** may be cyanotic, grey, dusty pink, pale pink, white or normal (if animal is receiving 100% oxygen, especially when anesthetized).
- **During surgery** there may be a lack of expected hemorrhage, no pulsations noted in vessels, and blood may appear dark if the arrest is due to poor oxygenation.
- **Absence of a palpable pulse.** This may also occur in hypovolemic/hypotensive patients with very weak cardiac function. Immediate CPCR with appropriate fluid, pressor and oxygen support usually results in a rapid response.
- **Electrocardiographic (ECG) findings. NOTE: do not use alcohol** for contact if defibrillation may be required (fire!), use ECG gel, ultrasound gel or K-Y Jelly. The ECG is necessary to guide therapy i.e.,
  - Asystole (probably the most common) almost always requires early epinephrine administration (if ventilation alone not successful).
  - Ventricular fibrillation (V fib), requires immediate defibrillation.
  - Pulseless electrical activity (PEA) a normal sinus appearing ECG tracing with no palpable pulse or audible heart beat, previously termed electromechanical dissociation (EMD). Treatment of the underlying cause, and atropine initially, is recommended.

MANAGEMENT

Appropriate and timely therapy, constant monitoring and rapid response to deterioration in a prepared setting, will ensure optimal management and improve outcome. While the following is a step-by-step guide, many steps will be performed simultaneously. IV access should be obtained as soon as possible but should not take precedence over airway, breathing and compressions (ABCs). If staff available, this can be performed simultaneously with the ABCs. When a CPA occurs immediately call for help! One person should take charge and 'conduct' the procedure.

I. BASIC CARDIAC LIFE SUPPORT (BCLS)

While obtaining an airway is of utmost importance, if cardiac arrest (not just respiratory arrest) is confirmed, chest compressions should begin immediately while preparing for (and during if possible) intubation.

A. **Airway patency.** Check and remove any obstruction. Intubate, in lateral or dorsal recumbancy, with a well fitting, cuffed endotracheal tube. Place in right lateral recumbancy in anticipation of entering the chest.

B. **Breath (ventilate) with 100% oxygen.** Place an **endotracheal tube** in ALL patients. Ensure correct placement of the endotracheal tube by observing chest excursion (not abdomen) while administering two "deep breaths" with 1.5 secs. inspiration. End-tidal CO_2 monitoring will also verify position and CPR progress. Continue at 25 – 30 normal breaths/minute initially to oxygenate and remove excess CO_2.

C. **Circulation, cardiac compressions.** (No alcohol on ECG clips). If possible also obtain IV access.

  1. If **V fib** try a precordial thump, (a clenched fist hit to the sternum appropriate for the size of the animal). Check ECG rhythm.
     a. If still V fib **go to II ACLS Management C, *p. 136*.**
     b. If ROSC with abnormal rhythm **go to II ACLS J, K, L, *p. 137*.**
  2. Palpate femoral pulse, if present then **respiratory arrest** only, ventilate the patient, post-arrest support may be all that is required. (Go to III Post-Resuscitation, *p. 139*).
  3. **Consider indications for internal cardiac massage (II ACLS I, *p. 137*).**
     a. If known **tension pneumophorax** and femoral **pulse still present** incise through to the pleural space, leave open to the atmosphere, place a large bore thoracotomy tube. Continue ventilation, check pulse; if improved go to III Post-Resuscitation below. If **pulse absent** open the chest for internal massage.
     b. **Trauma** case, unknown injuries.
     c. **Pleural fluid** of any kind, **pericardial effusion/tamponade, diaphragmatic hernia, chest wall or penetrating injuries** are present or suspected.
     d. **Massive blood loss (≥40%), or anaphylactic shock** causing CPA.
     e. **Large dogs.** The **actual size** depends on the ability (inability) of the operator to perform effective external technique.

4. **Chest compression.** If you are alone attempt two ventilations after every 10 – 12th compression. Alternatively pass a cannula (i.e., urinary catheter) via the endotracheal tube to the carina and deliver 100% oxygen at 150 mL/kg/min. If 2 or more people, follow (a) or (b).

   a. **Cardiac pump** (*details in Perfusion-enhancing techniques below p. 144*). For those weighing **<15 kg,** compress the chest directly over the heart. In very small patients, compress the heart with thumb and fingers at 100 – 110/minute. Avoid excessive force in thoracic compression in the small patient to prevent intrathoracic trauma. Airway pressures should not exceed 40 mmHg in order to prevent volu/barotrauma. Give 2 breaths (ventilate) after every 10 – 12th compression.

   b. **Thoracic pump** (*details in Perfusion-enhancing techniques below p. 144*). Patients weighing **>15 kg,** are placed in right lateral recumbency, ventilations should be coordinated with the systolic phase of compressions. Coincide peak inspiration (ventilation) with every fourth compression. Compressions to the widest area of the thorax (junction of the dorsal-middle third at the 7th intercostal space) should be delivered at 80 – 100/minute. Perform compression with a 'quick' motion so as to produce a "cough" (systole) and depress the thorax approximately 1/3. A 2 – 4 kg/kgBW force on the chest wall is required to produce an adequate increase in intrathoracic pressure. A 1:1 compression:relaxation cycle should be achieved. During relaxation (diastole), chest recoil and decrease in intrathoracic pressure facilitates venous return. It is essential to allow adequate refill time (without ventilation) to ensure coronary perfusion and filling of the ventricles. A great deal of pressure has to be applied in large dogs, but in the smaller animal, the appropriate, rather than excessive, external force must be delivered to avoid injury.

   c. In cases that are cyanotic at the time of CPA, adequate oxygenation and circulation results in mottling of the tongue initially which gradually becomes pink. A doppler probe placed on the eyeball will detect blood flow if there is adequate perfusion.

   d. Cease compressions for $\sim$ 2 seconds every 1 – 2 minutes to assess ECG rhythm; if present, assess femoral pulse for ROSC.

   e. If ROSC go to II I Post-Resuscitation below.

5. **Abdominal Compression.** (*details in Perfusion-enhancing techniques below p. 144*).

   a. **Interposed abdominal compression** is performed by compressing the abdomen during diastole (the non-thoracic compression interval). If performed caution is needed not to compress the abdomen at the same time as the chest compression as the liver is pushed forward under the ribs and is prone to laceration. For this reason the abdomen should not be bound during CPCR. This author has seen liver laceration and severe hemorrhage in laboratory exercise dogs using abdominal binding.

   b. **Abdominal compression** by placing a sandbag on the abdomen caudal to the ribs may be effective but care must be taken not to apply too much pressure forcing the liver cranially. Binding the hind limbs with a tensor bandage to mid-abdomen over a rolled towel between the legs and along the ventral abdomen with moderate pressure may be helpful. The bandage should be no tighter than a hand space between the bandage and the abdomen. Time and personnel are required for this.

6. **Obtain IV access. II ACLS A** (*p. 135*) a short catheter, largest bore possible should be used. If difficult perform cutdown (*p. 372*) preferably into the jugular vein, or cephalic vein.

7. **Fluid therapy II ACLS B** below should be administered according to circumstances surrounding the CPA.

8. If ROSC **does not return,** continue CPCR with the addition of the appropriate drug to treat the abnormal ECG rhythm (see **II ACLS** below *p.136*).

9. Once **successful resuscitation** has been established, continue to ventilate the patient. Hyperventilate (30 breaths/min) for 2 min to remove excess CO_2 then continue at 12 – 15/min. If spontaneous ventilation does not return reduce ventilatory rate to 6 – 8/min for 2 min, insert a 25 – 28 gauge needle into the base of the midline of the nasal philtrum and twist it rubbing the maxillary periosteum. Maintain $PvCO_2$ at $\sim$38 – 42 mmHg, $PaCO_2$ at $\sim$35 – 38 mmHg or $ETCO_2$ at $\sim$30 – 35 mmHg.

10. **Assess ECG rhythm.** Treat any abnormality (see **II ACLS below J, K, L** *p. 138*).

11. Seek etiology of CPA.

12. **Monitor and support** the patient (see **III Post-Resuscitation** *p. 139*).

II. ADVANCED CARDIAC LIFE SUPPORT (ACLS)

DRUG ADMINISTRATION through IV or IO catheter. When drugs are being administered into a vein, follow with a bolus of fluids of an adequate volume that will drive it to the heart (5 – 50 mL), depending on the size of the patient and distance to travel (peripheral vs central catheter). If IV access not available, **intra-tracheal route may be used for administration of atropine, epinephrine, and lidocaine only.** Pass a urinary catheter or small Fr red rubber tube into the trachea to the carina. Double the dose and flush with 5 mL saline. Ventilate with two full breaths. Intracardiac administration should be avoided due to potential for laceration of coronary arteries or myocardium and ventricular fibrillation. If pulmonary involvement (hemorrhage, edema) requiring suction, administer these drugs through the lingual vein or into the tongue parenchyma at double the dose.

As a rule of thumb the **volume in mL** to be delivered, of drugs listed below, is one-tenth the body weight in kgs (i.e., 5 kg = 0.5 mL). With this volume, some modifications can be made depending on the circumstances. **Epinephrine (1.0 mg/mL, 1:1000)** used for non-anesthetic arrest (**D1, E & F** *p. 136*) but modified for immediate (<1 min) arrest by giving half the epinephrine dose initially. For **anesthetic arrest, V fib arrest or ventricular tachycardia (V tach) arrest, dilute the epinephrine to 1:10,000 by taking 1 mL of 1.0 mg/mL and add 9 mL 0.9% saline** and administer volume as one-tenth body weight in kg. Repeat the dose in 1 minute if no response. Give **lidocaine 2%** (20 mg/mL), one-tenth body weight in kg as a ONE-time bolus following epinephrine. **Atropine (0.5 mg/mL USA, Europe, or 0.6 mg/mL Canada),** retrieve the one-tenth volume but only give one-half of this dose and repeat almost immediately if no response for **vagally-mediated cardiac arrest.** This is to avoid tachycardia should the full dose not be required. Conflicting recommendations suggest an atropine dose up to 0.12 mg/kg in a known vagally-mediated arrest.

NOTE: In our experience V tach at rates of 300 have occurred in some dogs after epinephrine resuscitation. The incidence of V fib is reduced if **lidocaine 2 mg/kg IV** is administered as a bolus immediately after the epinephrine has been administered. ADMINISTER ONCE, DO NOT REPEAT UNLESS INDICATED AFTER RESUSCITATION (*see J p. 138*). High dose lidocaine raises the defibrillation threshold and may decrease effectiveness of countershock therapy if fibrillation occurs.

NOTE: *Vasopressin is included in this protocol as it has recently been introduced into the human CPCR protocol. In the research setting vasopressin may be superior to epinephrine. In this author's experience with 8 randomly selected dogs in the laboratory setting, 2/4 vasopressin treated dogs and 2/4 epinephrine treated dogs had ROSC. Currently there is no clinical data or approved guidelines in veterinary medicine on the use of vasopressin in the CPCR setting. *Amiodarone** is included in this protocol as it has recently been recommended for countershock refractory V tach/V fib in humans; however, there is no clinical veterinary data or approved guidelines on its use in the CPCR setting. In the failing CPCR setting, you have nothing to lose! **CAUTION** see PHARMACOLGY Antiarrhythmics 1 *p. 142.* prior to use for specific details on administration.

A. **Obtain IV access.** A short catheter, largest bore possible should be used. If difficult, perform cutdown (*p. 372*) preferably into the jugular vein (preferred in pups and kittens), cephalic and lastly saphenous. Intraosseous (proximal humerus, tibial crest, trochanteric fossa) are alternatives to jugular vein in young animals.

B. **IV fluid** therapy should be administered according to circumstances surrounding the CPA. If arrest was due to
   1. **Hypovolemia/Hemorrhage,** delegate someone to rapidly **obtain PCV and TS** and deliver fluids rapidly.
      a. Initially, rapidly administer isotonic, alkalinizing, crystalloid fluids in **aliquots of 20 – 40 mL/kg (dog); 10 – 20 mL/kg (cat).** In addition,
      b. If **moderate to severe blood loss (PCV ≤25 – will be higher in peracute loss)** administer
         i. whole blood 10 – 20 mL/kg (dog & cat), based on degree of blood loss, OR
         ii. Oxyglobin 2 mL/kg aliquots (dogs), 1 mL/kg (cats) up to 4 aliquots if blood not available.
      c. If **moderate to severe hypoproteinemia (TS <5.0)**
         i. aliquots of **synthetic colloids (dextran 70, 6% hetastarch, 6% pentastarch)** at 5 – 10 mL/kg (dog) or 2 – 5 mL/kg (cat) to a maximum of 20 mL/kg (dog), 10 mL/kg (cat), OR
         ii. 25% Human Serum albumin 2 mL/kg (dog & cat). Where synthetic or natural colloids are administered, reduce the crysalloid volume by half.
         iii. Plasma 10 – 20 mL/kg (dog & cat) may also be an option, however thawing time precludes its immediate use but may be administered when thawed.
   2. **Euvolemia,** a crystalloid bolus of **10 – 20 mL/kg (dog); 5 – 10 mL/kg (cat)** followed by maintenance levels (**10 mL/kg/h, includes bolus after drug administration**). It is important not to overload the patient with fluids, which ultimately can result in severe pulmonary edema, decreased myocardial and cerebral perfusion pressures. A burette should be placed in line when delivering fluids to small patients (<10 kg) to avoid pulmonary overload.

C. **Ventricular fibrillation (V fib). Electrical defibrillation** (*see 8 below for chemical defib*).

1. **Clip** fur on both sides of the chest. **Use defibrillator gel (gritty),** not ultrasound gel.

2. With patient in dorsal recumbency, if in a trough, or a position where the patient's limbs will not touch the operator and the operator will not touch the table (dorso-lateral?); **apply paddles very firmly, one on each side of the chest. Be sure there is no open oxygen source.** Keep oxygen source connected to the ambubag and oxygen flowing in a closed system to avoid fire from a spark.

3. **Give 3 consecutive countershocks (higher energy for big dogs):**
   a. 3 – 5 Joules/kg initially, 5 – 7 J/kg, then 7 – 10 J/kg
   b. The pause between countershocks should only be to re-charge defibrillator and assess ECG. If ROSC occurs then no further countershocks are required.
   c. **Internal defibrillation,** one-tenth the above dose using saline-soaked sponge between paddle and epicardium.

4. If not successful, resume CPCR for 60 – 90 seconds (*see 8 & 12 below*).

5. Resume countershock at **5 – 10 J/kg increasing to highest dose during 3 consecutive countershocks.**

6. Administer low dose **epinephrine 0.01 mg/kg (0.1 mL/kg of 1:10,000)** OR ***vasopressin 0.8 U/kg IV once.**

7. **Follow with Lidocaine 2 mg/kg (0.1 mL/kg) IV. If no response go to 8.**

8. **If no response give magnesium sulphate (200 mg/mL) 30 mg/kg (0.12 mmol/kg [0.25 mEq/kg])** with counter shock. **If countershock not available** try magnesium 1 – 2 g total IV over 2 min. **CAUTION:** if hypocalcemic administer calcium chloride 10% 0.1 – 0.3 mL/kg or calcium gluconate 10% 0.5 – 1.0 mL/kg when magnesium is administered.

9. Consider ***amiodarone 5 – 10 mg/kg IV** (dilute to 5 mg/mL in D5W. **Note: MUST** refer to Pharmacology 1 *p. 142*. There are no veterinary clinical reports of amiodarone use in CPCR, just guidelines). If no ROSC, then;

10. Defibrillate twice more at double the initial dose if necessary. Continue BCLS between defibrillation.

11. V fib may not be sustained in hearts of animals <3 – 5 kg, therefore, CPCR should continue to support these patients until the arrhythmia resolves (~ 20 min).

12. Consider **sodium bicarbonate 0.5 – 1.0 mEq/kg** if the arrest time is >10 minutes or the underlying disease has resulted in acidosis.

D. Asystole

1. **Non-anesthetic arrest.** (a, b or c initially)
   a. If **vagal arrest suspected give atropine USA & Europe: 0.025 mg/kg** (1/2 the one-tenth rule) **or Canada: 0.03 mg/kg** (1/2 one-tenth rule Canada) **IV**. If no response repeat; if no response go to (b).
   b. If vagal arrest not suspected administer **epinephrine 0.1 mg/kg (0.1 mL/kg of 1 mg/mL).** If within 1 minute of arrest give **half dose initially,** repeat in 1 – 2 min. If no response, repeat 0.1 mg/kg dose in 1 – 2 min. If no response after 2 doses (5 min) consider (d–h below), **OR**
   c. ***Vasopressin 0.8 U/kg ONCE**
   d. **Sodium bicarbonate 0.5 – 1.0 mEq/kg** and continue compressions for 1 – 2 min
   e. **Internal cardiac massage (II ACLS I** *p. 137*). If not able, then f – h below
   f. **Electrical countershock (C above).** Probably won't work but has been suggested as a last option. **Repeat epinephrine OR**
   g. **Phenylephrine 0.01 – 0.1 mg/kg (repeat q 3 – 5 min) OR**
   h. **Methoxamine 0.1 – 0.2 mg/kg.**

2. **Anesthetic arrest.**
   a. **Turn vaporizer off, empty rebreathing bag** into the room or get ambubag with oxygen supply.
   b. Consider peri-operative drugs precipitating arrests.
   c. **Opiate** – reverse with **naloxone 0.02 mg/kg IV.**
   d. **Benzodiazepine** – reverse with **flumazenil 0.02 mg/kg 0.2 mg total dose.**
   e. **Medetomidine** – reverse with **atipamezole 0.1 – 02 mg/kg IV slowly.**
   f. **Go to 3 or 4 below.**

3. **Halothane anesthetic-associated arrests.** [Drugs (b below) and D 1 (a), (c) – (h) *p. 136*]
   a. **Internal cardiac massage,** access **through the diaphragm** if CPA occurs during laparotomy
   b. **Epinephrine: 0.01 – 0.02 mg/kg (0.1 mL – 0.2 mL/kg 1:10,000 solution or 'homemade'** [add 1 mL 1:1000 epinephrine to 9 mL 0.9% NaCl]). Repeat in 1 min if no response. **Caution with higher dosages due to V fib.** When acepromazine has been used for premedication, ventricular fibrillation may be difficult to induce even when higher doses of epinephrine are used. **Lidocaine 2 mg/kg (0.1 mL/kg of 2%), one dose only,** given immediately after first dose epinephrine may prevent fibrillation. Repeat dosing of epinephrine may be required and at 1 minute intervals to achieve the effect epinephrine has on arterial pressure and patency. If after 5 mins there is no response consider,
   c. **Sodium bicarbonate 0.5 – 1.0 mEq/kg** and continue compressions for 1 – 2 min
   d. **Internal cardiac massage,** via thoractomy **(II ACLS I below) OR**
   e. **Repeat epinephrine** if no response **OR**
   f. **Atropine, vasopressin, phenylephrine or methoxamine as in** D1(a), (c) – (h) *p. 136*.

4. **Isoflurane anesthetic-associated arrests.** As halothane **3a – f** above but commence with **epinephrine 0.02 mg/kg.** Isoflurane is less arrythmogenic than halothane and a higher dose of epinephrine may be given.

E. **Pulseless Electrical Activity (PEA).** Sinus-like rhythm with no mechanical activity (no detectable pulse or audible heart sound).
   1. **Atropine 0.025 mg/kg** (1/2 the one-tenth rule USA) **or 0.03 mg/kg** (1/2 one-tenth rule Canada) **IV,** if no response repeat immediately; then if no response,
   2. **Epinephrine** (low dose) **0.01 – 0.02 mg/kg** (0.1 mL – 0.2 mL/kg of 1:10,000 solution, or 'homemade' [add 1 mL [1 mg/mL] 1:1000 epinephrine to 9 mL 0.9% NaCl]).
   3. If no response, repeat **epinephrine 0.02 mg/kg q1–2min OR**
   4. ★**Vasopressin 0.8 U/kg once**
   5. Seek underlying cause (i.e., vagally mediated, hypoxemia, acidosis, tension pneumothorax) and treat.
   6. **Sodium bicarbonate 1 – 2 mEq/kg for non-respiratory (metabolic) acidosis,**
   7. **Calcium chloride 10%** is equal to 100 mg/mL, **2 – 4 mg/kg (0.02 – 0.04 mL/kg) IV, OR Calcium gluconate 10%, 10 – 15 mg/kg (0.5 – 1.0 mL/kg) IV** repeated as necessary at 10 minute intervals may reverse this arrhythmia in patients receiving calcium channel blockers. In CPCR calcium chloride is preferred as it produces higher and more predictable levels of ionized calcium in plasma.
      a. **Precautions:** If the heart is beating, rapid administration of calcium can produce slowing of the cardiac rate. Calcium must be used cautiously in the digitalized patient because it increases ventricular irritability and may precipitate digitalis toxicity.
      b. In the **presence of sodium bicarbonate,** calcium salts will precipitate as carbonates. Thus, these drugs cannot be administered together. Calcium may produce vasospasm in coronary and cerebral arteries and is therefore, only recommended as a treatment for hypocalcemia.

F. **Severe bradycardia that is vagally mediated,** precipitating the CPA frequently responds to a very low dose of **atropine (0.01 mg/kg).** However, this dose may result in a transient exacerbation of bradycardia; repeat the dose immediately should this occur. Doses up to 0.12 mg/kg have been recommended. Administer oxygen. Chest compressions are usually not required. If a full CPA occurs go to II ACLS **E above.** The low dose atropine is to avoid sinus tachycardia with higher doses.

G. If no ROSC after 3 – 5 minutes consider internal cardiac massage (**I below**). External compressions and appropriate drug therapy should continue until ready for thoracotomy to be performed by 6 – 8 minutes (or sooner depending on the size of dog and if there is no evidence of adequate perfusion with external methods).
   1. **Reasons for failure** are inadequate perfusion (i.e., dog is too big for the operator, inadequate compressions), pleural space problems not identified, acidemic, fibrillation not identified, inadequate oxygenation, inadequate drug therapy, 'dead' patient (unwitnessed arrest, irreversible illness).

H. If resuscitation **successful, assess ECG** and go to **J, K, L and III Post-Resuscitation** *p. 139.*

I. **Internal Cardiac massage. Indications in I BCLS C** *p. 133.*
   1. A rapid shave (with clippers!) from dorsal to ventral midline over **sixth** intercostal space followed by a 'squirt' of aqueous chlorhexidine or other non-alcohol based solution. Incise skin, subcutaneous and muscle layers,

down to pleura, in a single motion from costovertebral junction (proximal) to sternum (ventral). **Stop ventilations.** Use the curved mayo scissors, with the curve pointing cranially, and penetrate the pleura ventrally. Open the scissors, place the lower blade into the chest ventral to the costochondral junction, elevate and push dorsally. Avoid laceration of the internal thoracic artery (very ventral) and intercostal arteries caudal to ribs, and lung. Cut the pericardium at the sternopericardiac-ligament. Open the pericardium and incise ventral to the phrenic nerve. Elevate the heart and massage from apex to base at 80 – 100/min. You should feel filling and emptying of the ventricles. Place Balfour retractors to retract ribs. Ventilate after every 10th manual contraction (diastole). Identify the descending aorta and occlude with downward pressure of thumb or forefinger of opposite hand or pass umbilical tape or red rubber feeding tube around the aorta and occlude temporarily (< 10 min).

2. Fluids may be delivered through a large bore catheter placed into the right auricle through a small incision, stablize with your fingers, bolus fluids if hypotensive/hypovolemic **(see II ACLS B 1 & 2 p. 135)**. **Perform cardiac compressions with opposite hand.** Then pursestring around the catheter. Continue with resuscitation.

3. After resuscitation is established, move into the surgery area and lavage the thorax with several litres (varies with the size of the patient) of warm saline. Leave the pericardium open. Close the thorax routinely. Place a chest drain. Be prepared to administer **fentanyl 10 – 50 μg/kg/h CRI** or other opioid, or **propofol 0.1 – 0.2 mg/kg/min CRI with 0.5 – 1 mg/kg top up dose** if an anesthetic arrest, or isoflurane anesthesia if not.

J. **Ventricular ectopy** (for **detailed therapy** *see VPCs V tach p. 181*). If a slow ventricular or sinus rhythm is present, lidocaine should not be used. Only use if rate > 180/min, multiform or no isoelectric shelf is present between complexes.
  1. Lidocaine
    a. **2 – 4 mg/kg IV bolus (dog),** repeat if necessary; **0.75 – 1.0 mg/kg (cats)** IV bolus ONCE
    b. **2 – 3 mg/kg/h (dogs)** (*see Lidocaine Infusion p. 181*); **0.5 – 2 mg/kg/h (cats).** Use lowest dose possible.

  2. Procainamide
    a. **Dogs: 5 – 15 mg/kg (start with 10 mg/kg over 15 min) IV** followed by **25 – 40 μg/kg/min CRI** OR
      8 – 20 mg/kg (start with 10 mg/kg) q4–6h IM.
    b. **Cats: 5 – 10 mg/kg (start with 7 mg/kg over 15 min) IV q8h.**
      i. Cats rarely get V tach. *See Ventricular Arrhythmias p. 182* for further guidance if unsuccessful.

  3. ***Amiodarone see PHARMACOLOGY 1. for details** OR

  4. **Magnesium sulfate 30 – 40 mg/kg of ≤ 20% solution** IV CRI over 2 – 4 hours.

  5. **Treat hypokalemia, aim for high normal values.**

K. Bradycardia (for ***detailed therapy*** *see p. 168*).
  1. Rule out underlying cause *p. 164.*

  2. **Atropine 0.02 – 0.04 mg/kg IV.** Repeat rapidly (may require 0.12 mg/kg) if no response.

L. Supraventricular tachycardia (for ***detailed therapy*** *see p. 174*).
  1. Diltiazem
    a. **Dogs: IV boluses of 0.1 – 0.25 mg/kg q 3min to max dose of 0.5 mg/kg., then 1 – 5 μg/kg/min CRI**
    b. **Cats: 0.1 – 0.2 mg/kg IV bolus, then CRI as per dogs.**
      Preferred as may offer cellular protection.

  2. Procainamide
    a. **Dogs: 5 – 15 mg/kg (start with 10 mg/kg) slowly IV** followed by **25 – 40 μg/kg/min CRI.**   OR
    b. **8 – 20 mg/kg (start with 10 mg/kg) q4–6h IM.**
    c. **Cats: 5 – 10 mg/kg (start with 7 mg/kg over 15 min) IV q8h.**

III. POST-RESUSCITATION MANAGEMENT

A. Apply or leave ECG leads attached to patient and monitor rate and rhythm continuously. If a slow ventricular or sinus rhythm is present, lidocaine should not be used.

B. If **spontaneous breathing** with normal ventilatory movements, sinus rhythm or fast V tach and concern for increased intracranial pressure, give **lidocaine 1 mg/kg prior to extubation** (reduce ICP). Avoid lidocaine if slow V tach. Administer supplemental oxygen with nasal prongs or cannula (desensitize the nasal meatus extremely well to avoid sneezing and an increase in intracranial pressure). If spontaneous ventilation does not return, reduce ventilatory rate to 6 – 8/min for 2 min, insert a 25 – 28 gauge needle into the base of the midline of the nasal philtrum and twist it rubbing the maxillary periosteum. Maintain $PvCO_2$ at ~38 – 42 mmHg, $PaCO_2$ at ~35 – 38 mmHg or $ETCO_2$ at ~30 – 35 mmHg. If not successful, go to P. below.

C. Avoid glucose-containing fluids unless hypoglycemic. Ensure only a small volume is infused with the pressor agent.

D. If **hypotension exists without hypovolemia** (systolic BP less than 90 mm Hg, poor capillary refill time, oliguria or mental status change),

   1. An infusion of **dopamine 5 µg/kg/min** initially (*see Dopamine Infusion Chart for CRI dosing p. 233*), which may have to be increased or decreased to a goal of 120/80 (MAP 100) mmHg to improve cerebral perfusion. If heart rate increases this may exacerbate arrhythmias necessitating a reduction in the infusion rate.

   2. If further improvement in cardiac output is required without producing tachycardia, try

   3. **Dobutamine at 5 µg/kg/min (dogs only)** *see Dobutamine Infusion Chart for CRI dosing p. 231,* alone or with dopamine, may improve cardiac output and cerebral perfusion.

   4. **Norepinephrine** (*see Norepinephrine Infusion Chart for CRI dosing p. 253*) **as an alternative to 1 & 2 above.**

   5. **Slowly taper** inotropic and vasopressor agents as soon as the patient is stable.

   6. **If hypotension due to hypovolemia,** refer to **II ACLS B** *p. 135* or *Fluid therapy p. 350*. To optimize oxygen delivery and cerebral perfusion, whole blood or plasma should be administered to achieve a PCV > 25 and total solids of 50 g/L.

E. If pulmonary edema (consider pulmonary contusions due to CPCR) identified, give furosemide 1mg/kg and reasses further dosing (*see Furosemide Infusion Chart for CRI dosing p. 239*). Avoid hypovolemia.

F. **Pain Management.** The patient may be painful due to the underlying problem (i.e., surgical procedure) or from the CPCR procedure; external and internal. Select the appropriate analgesic and *see p. 81* for combination therapy if required.

   1. **Morphine 0.1 – 0.5 mg/kg IM followed by a 0.1 mg/kg/hr constant rate infusion** (cat & dog) (*see Morphine Infusion Chart for CRI dosing p. 251*), OR

   2. **Methadone 0.1 – 0.5 mg/kg IV,q4h OR**

   3. **Butorphanol 0.1 – 0.4 mg/kg IV q2–3h** (cat and dog) OR

   4. **Hydromorphone 0.01 – 0.05 mg/kg q3–4h** (cat and dog). OR

   5. **Fentanyl 2 – 4 µg/kg/h CRI**

G. Seek the precipitating cause of the cardiac arrest and treat appropriately.

H. Continue to assess the hemodynamic status, auscultate the heart and lung fields. Chest radiograph may be warranted.

I. Monitor urine output (1 – 2 mL/kg/h) (*see Acute Renal Failure p. 714*) if necessary.

J. Ensure maintenance fluid administration (*p. 356*), using a balanced electrolyte solution, with special attention to possible pulmonary edema. CVP monitoring may be necessary, however, caution should be used with placing a CVP line as increased intracranial pressure (ICP) may be present and a central catheter may increase ICP further. Diuretics, inotropes or vasodilators may be indicated, however, this will require ruling out cardiogenic vs non-cardiogenic pulmonary congestion (*see Congestive Heart Failure p. 149*).

K. Where possible, monitor **blood gases (*p. 406*)** and **electrolytes (see specific sections)** and make appropriate corrections.

L. Maintain head and shoulders (as a unit) at 15 – 20° and don't allow the head to drop below the body.

M. Keep body temperature at 37 – 38°C (98.6 – 101°F) (*see Hyperthermia p. 297*).

N. Consider **R. below.**

O. Should the patient be difficult to manage in your practice, consider transfer to a special care unit where all the above and 24 hour care can be given.

P. **Neurologically Impairment.** Poorly responsive or comatose (*see Neurological examination in Head Trauma p. 698*), with or without other organ system failure.

  1. If **not breathing** or has poor ventilatory movements, mechanical ventilation is necessary to guarantee adequate oxygenation and prevent hypercarbia. Maintain $PaCO_2$ values between 35 – 40 mmHg (normal values) and PaO_2 values between 80 – 100 mmHg. Attempt hyperventilation to $PaCO_2/PvCO_2$ at 20 mmHg – 25mmHg for a few minutes if tentorial herniation suspected. Assess asymmetry of the globe and pupils and pupillary response (may be dilated and non-responsive for up to 18 hours if atropine has been administered). Pupillary responses are not affected if ischemia to the visual cortex has occurred. Do not maintain this hyperventilation and low CO_2 for more than 1 – 2 minutes.

  2. Conditions that increase the brain's oxygen requirements such as **seizure activity** (*Dogs p. 460 & Cats p. 456*) and **hyperthermia. If hyperthermic** treat immediately (*see Hyperthermia p. 300*).

  3. Continuous **ECG monitoring.** Treat specific arrhythmias (**II ACLS J,K,L *p. 138*** and *see Supraventricular p. 170, Ventricular Arrhythmias p. 172, Bradyarrhythmias p. 165*).

  4. **Cerebral resuscitation.** Cerebral damage often occurs in CPA survivors and is a major factor in post-resuscitation mortality.
     a. Any reduction in cerebral perfusion pressure (CPP) will contribute to a further decrease in cerebral blood flow, therefore systolic blood pressure should be maintained at 120 mmHg (mean arterial pressure 80 – 100 mmHg). See **III D4 & 5 above. If hypovolemic go to IIB 1, above.**
     b. To optimize oxygen delivery and cerebral perfusion, whole blood or plasma should be administered to achieve a PCV >25 and total solids of 50 g/L.
     c. An initial dose of **dexamethasone sodium phosphate 0.25 mg/kg** once daily for one or two days may prevent worsening of cerebral edema.
     d. If the patient is euvolemic, systolic pressure is ~120 mmHg, neurological signs are moderate to severe or are worsening, and

        i. **Hypertonic saline 5% (6 – 10 mL/kg max), OR 7.5% (4 – 8 mL/kg max) at 1 mL/kg/min** for dogs, **quarter of this for cats,** [respiratory arrest and/or vagoreflex bradycardia may occur, treat with 0.02 mg/kg atropine], may be **preferred to mannitol.** If HS not available, see ii below.
        ii. **Not** hypotensive, overhydrated, oliguric or anuric (*p. 718*), and pulmonary edema or congestive heart failure (*p. 149*) **have been ruled out,** give **mannitol 0.1 – 0.25 g/kg (100 – 250 mg/kg)** over 10 minutes.
        iii. **Repeat mannitol q4–6h** for two more treatments if required. Higher doses of mannitol are not recommended.
        iv. **Overhydration and pulmonary edema go to (i) hypertonic saline above, OR** treat with **2 mg/kg furosemide IV.** As soon as possible after edema has resolved, give mannitol as above providing the patient is normotensive and signs are not improved.

  5. **Vocalization, dementia, extreme restlessness (rule out pain, hypoxia etc.), 'discombobulation', consider gabapentin 5 – 25 mg/kg PO q8–12h,** 10 mg/kg preferred to start; adjust dosage according to level of sedation. Very effective. Reduce dose in renal failure (eliminated by kidneys), wean off slowly over days.

Q. The patient should be referred to a 24-hour specialty unit for support if possible. Most patients who ultimately recover full neurologic function will awaken and improve dramatically in the first 48 hours following resuscitation. If the patient remains totally unresponsive with no evidence of either cognitive or motor recovery

after this time, the chance of regaining meaningful cerebral function is almost nil. Patients have survived beyond this period of time, however, these pets require extensive nursing care initially and rarely recover their pre-arrest behavioural characteristics and personality (*see Neurological Examination in Head Trauma p. 698*).

R. **Reperfusion Injury** obviously occurs in the CPCR setting. Of potential benefit is **lidocaine 2 mg/kg followed by 3 mg/kg/h.** CAUTION: If a **slow** ventricular or sinus rhythm is present, lidocaine should not be used; close monitoring is advised and infusion stopped should this occur. While administration prior to reperfusion is advised this is not always possible nor recommended routinely. It has been this author's experience that severe V tach, V flutter and V fib may be halted, (especially if V tach noted at some point prior to full CPA) with a single dose **lidocaine 2 mg/kg** administration immediately following epinephrine administration.

PHARMACOLOGY

Inotropes and vasopressors

1) **Epinephrine** is an endogenous catecholamine with both alpha and beta-adrenergic activity. The cardiovascular responses expected from the dosages used during resuscitation are increased systemic vascular resistance, increased arterial blood pressure, increased heart rate, increased coronary and cerebral blood flow, increased myocardial, contraction, increased myocardial oxygen requirements and increased automaticity. Epinephrine's potent alpha adrenergic effects improve cerebral and coronary blood flow by preventing arterial lumen collapse and increasing peripheral vasoconstriction. In veterinary patients the dose of epinephrine depends on individual circumstances. Epinephrine can cause V fib (VF). Dogs are much more difficult to defibrillate than people.

2) **Dopamine** is a chemical precursor of norepinephrine. It stimulates dopaminergic, beta-2-(1 at higher doses) adrenergic, and alpha-adrenergic receptors in a dose-dependent fashion. It also stimulates the release of norepinephrine. In low dosages (1 – 4 μg/kg/min) dopamine produces vasodilation of renal, mesenteric and cerebral arteries by stimulation of dopaminergic receptors. In the dosage range of 4 – 10 μg/kg/min, dopamine stimulates both beta-1 and alpha-adrenergic receptors. Increases in cardiac output, due to the enhanced myocardial contractility induced by beta-adrenergic stimulation, reflexly antagonize, in part, alpha-adrenergic-mediated vasoconstriction. This results in enhanced cardiac output and only modest increases in systemic vascular resistance and afterload. At doses above 10 μg/kg/min, the alpha-adrenergic effects of dopamine predominate. This results in renal, mesenteric and peripheral arterial and venous vasoconstriction with marked increases in systemic vascular resistance and afterload. Doses above 20 μg/kg/min produce hemodynamic effects that are similar to those of norepinephrine. As with all vasoactive agents, there is substantial variability in response to dopamine. Therefore the drug must be titrated to hemodynamic effect. Dopamine increases myocardial work without significantly increasing coronary blood flow in a compensatory manner. The imbalance between oxygen supply and demand may result in myocardial ischemia. The **primary indication** for dopamine is hemodynamically significant hypotension (systolic arterial pressure of less than 90 mmHg accompanied by evidence of poor tissue perfusion, oliguria or mental status changes) in the absence of hypovolemia. Dopamine should be used at the lowest dose necessary to ensure adequate perfusion of vital organs. In the immediate postresuscitation period, higher doses may be required to induce the transient hypertension recommended to improve cerebral perfusion. Dopamine's vasopressor effects at higher infusion rates elevate the pulmonary artery occlusive pressure and may induce or exacerbate pulmonary congestion despite a rise in cardiac output. Vasodilators can be used to reduce preload and improve cardiac output by antagonizing the increased vascular resistance induced by dopamine. Dopamine is available for intravenous use only. The contents of a 200 mg ampule should be mixed in 500 mL of 5% dextrose or 0.9% sodium chloride. This yields a concentration of 400 μg/mL. **The initial rate of infusion is from 2 – 5 μg/kg/min** *see Dopamine Infusion Chart p.* **.** This rate may be increased until blood pressure, urine output and other parameters of organ perfusion improve. The lowest infusion rate that results in satisfactory hemodynamic performance should be used to minimize side effects. Dopamine should be administered via a volumetric infusion pump to ensure precise flow rates. **Precautions:** Dopamine will increase heart rate and may induce or exacerbate supraventricular and ventricular arrhythmias. On occasion, these effects may require reduction in the dose of therapy or even discontinuation of the infusion. Nausea and vomiting may occur. Dopamine may produce cutaneous tissue necrosis and sloughing if interstitial extravasation occurs. Treatment is phenotolamine, 5 – 10 mg diluted in 10 – 15 mL saline solution and infiltrated into the area to antagonize vasoconstriction and to minimize necrosis and sloughing. Patients receiving phenytoin may experience hypotension during concomitant administration of dopamine. Do not add to alkaline solutions. Dopamine should be tapered slowly over several hours to avoid an acute hypotensive response, unless tachycardic or hypertensive.

3) **Dobutamine** has potent inotropic effects. It stimulates beta-1-and alpha-adrenergic receptors in the myocardium. Its minor stimulation of peripheral alpha receptors is antagonized by more potent beta-2 stimulation. Thus mild vasodilation is usually induced. Peripheral resistance also falls in response to increases in cardiac output. In conventional clinical doses dobutamine is less apt to induce tachycardia than dopamine. However, dobutamine will increase heart rate at higher dosages. Renal and mesenteric blood flow usually increase as cardiac output increases but unlike dopamine, dobutamine does not produce renal and mesenteric vasodilation via dopaminergic receptors. Pulmonary occlusive pressure decreases. The net hemodynamic effects of dobutamine are similar to those of dopamine combined with a vasodilator such as nitroprusside. Cardiac output increases

and peripheral resistance and the pulmonary occlusive pressure decreases. Dobutamine's beneficial hemodynamic effects and non-induction of endogenous norepinephrine release minimize its effects on myocardial oxygen demand. This results in a more favorable balance between oxygen supply and demand than with either norepinephrine or dopamine. Dobutamine's positive inotropic effect is balanced by increased coronary blood flow. Since vasodilation occurs in response to increased cardiac output, blood pressure changes very little. Direct measurement of central hemodynamics are required to accurately assess the response to dobutamine. **Dopamine and dobutamine** have been used together and may result in better hemodynamics in patients with cardiogenic shock. **Indications** for dobutamine are in the treatment of pulmonary congestion and low cardiac output or hypotensive states where vasodilators cannot be used for fear of further lowering of the blood pressure. **Dosage: Start at 5 μg/kg/min and increase or decrease to effect.** *See Dobutamine Infusion Chart for CRI dosing p. 231.* **Precautions:** Dobutamine may cause tachycardia, arrhythmias and fluctuation in the blood pressure which can provoke myocardial ischemia, especially at higher doses. Other side effects include headache, nausea and tremor.

Inotropic and vasoactive agents should be tapered gradually over several hours, under close supervision, to avoid hypotension. If the patient is tachycardic or hypertensive, reduction may be more rapidly titrated to desired levels.

4) **Norepinephrine** has both alpha and beta-adrenergic properties. It is a powerful peripheral vasoconstrictor (alpha) and a potent inotrope (beta). Both these actions result in an increase in systemic blood pressure and coronary artery blood flow. Norepinephrine results in dilation of the coronary vessels approximately 2.5 times that of epinephrine, which also enhances coronary flow. The glycemic effects are less than that of epinephrine. Bradycardia may be associated with norepinephine should the systemic blood pressure increase to normal. **Precautions:** Norepinephrine will cause severe vasoconstriction and sloughing should it extravasate. Blood pressure and IV site must be checked frequently. Blood pressure should receive moment-to-moment monitoring until stabilized. Splanchnic perfusion may be reduced should hypertension occur. **Dosage: Start at 0.05 μg/kg/min and increase q1–2min until low normal, or decrease quickly if too high** *see Norephinephrine Infusion Chart for CRI dosing p. 253.*

5) **Vasopressin** is one of the most potent endogenous vasocontrictors via its interaction with V1a receptors on vascular smooth muscle. Its effects are not altered by acidosis, and it increases blood pressure and systemic vascular resistance. Its half-life in the intact circulation is 10 – 20 minutes and at least 5 minutes during CPCR, therefore only one dosing is recommended. This effect is longer than epinephrine. As there is no beta adrenergic activity it is not associated with increased myocardial demand following return of spontaneous circulation. Vasopressin has been recommended for shock-refractory V fib or pulseless V tach and may show benefit as a vasopressor for asystolic or PEA arrests. The dose suggested for veterinary patients is 0.8 U/kg.

6) **Phenylephrine,** an alpha agonist.

7) **Methoxamine,** an alpha agonist.

Antiarrhythmics

1) **Amiodarone** is classified as a class III antiarrhythmic agent, however, it possesses class I, II, III and IV actions. Its use in CPCR in veterinary medicine has recently been included in the guidelines based on human recommendations. This author has no experience using amiodarone in a CPCR protocol. The clinical pharmacology of amiodarone is not well understood with a large volume of distribution and long half-life (53 days). Amiodarone is well tolerated hemodynamically with minimal negative inotropic effects. It can be used in patients with CHF. IV amiodarone can cause drug-induced hypotension. Potentially, critically unwell patients, fully dependant on sympathetic drive can decompensate when recieving the added insult of Polysorbate 80 (vehicle), in addition to that of amiodarone itself. The vehicle for intravenous amiodarone (Cordarone X) is polysorbate 80 (polyethylene sorbitan monoleate), which is used for solubilising, emulsifying and wetting medicinal products. The intravenous form of amiodarone contains 150 mg amiodarone and 300 mg polysorbate 80. Polysorbate 80 is known to have vasodilatory and negative inotropic effects. In addition to haemodynamic effects, Polysorbate 80 has been suggested as a cause for the acute hepatotoxicity of amiodarone and has also been implicated in the E-ferol syndrome.

Intravenously, amiodarone slows heart rate and prolongs AV nodal refractoriness. Its acute effects may be partially explained by its sympatholytic and calcium channel blocking effects. Intravenous amiodarone controls life-threatening ventricular arrhythmias and is also effective in slowing AV nodal conduction in patients with rapid atrial tachyarrhythmias. If amiodarone does not adequately control the ventricular response, then DC cardioversion should be considered. Amiodarone may help to maintain sinus rhythm if cardioversion is successful. It interacts with digoxin, warfarin, quinidine, procainamide and flecainide, necessitating lower doses of these drugs. Pharmacokinetics are complex. Extrapolating from its use in humans, the following empirical protocol has been utilized in several cases:

   a. **Premedicate** with
      i. **diphenhydramine 0.5 – 2.0 mg/kg,** max total dose 50 mg IM **and**
      ii. **dexamethasone 0.5 – 1.0 mg/kg** IV as urticaria and angioedema frequently occur.
   b. **Amiodarone** should be administered in a central line and **diluted to 1 mg/mL in Dextrose 5% in water.**
      i. **Bolus 2 – 5 mg/kg** over 10 minutes.
      ii. **Begin CRI 1.0 mg/kg/h** for 6 hours, then 0.5 mg/kg/h for the remaining 18 hours.
   c. **Repeat boluses (2 – 5 mg/kg)** over 10 minutes can be given if inadequate response or if breakthrough arrhythmias occur. Do not exceed 10 mg/kg/h.
   d. **EKG** should be continuously monitored as the heart rate can drop quite dramatically but the time when this occurs can not be predicted.

2) **Lidocaine** suppresses ventricular arrhythmias by reducing automaticity. In some studies lidocaine has been shown to elevate the fibrillation threshold. Higher plasma lidocaine concentrations are required to achieve an antifibrillatory effect than to control ventricular ectopy. Lidocaine usually does not affect myocardial contractility, arterial blood pressure, atrial arrhythmogenesis or intra-ventricular conduction. It can, on occasion, facilitate atrioventricular conduction. Lidocaine is the drug of choice for the suppression of ventricular ectopy, including ventricular fibrillation. Lidocaine is also reported to reduce reperfusion injury. *See also Ventricular Arrhythmias p. 181 and Lidocaine Infusion Chart for CRI dosing p. 247.*

3) **Atropine sulphate** is a parasympatholytic drug that enhances both sinus node automaticity and atrioventricular conduction via its direct vagolytic action. Atropine may restore normal AV nodal conduction and initiate electrical activity during asystolic cardiac arrest. Atropine's beneficial effects in treating asystole or pulseless idioventricular rhythms is suspected but unproven. A dose of 0.02 to 0.06 mg/kg IV or intra-tracheal (IT) mixed with 3 – 10 mL sterile saline, is recommended. Repeat after 2 minutes if desired effect is not achieved. Caution – doses smaller than those recommended can produce a paradoxical bradycardia due to the central and/or peripheral parasympathomimetic effects. Atropine may produce tachycardia or ventricular fibrillation after IV administration, therefore start at the low dose and titrate to effect.

4) **Diltiazem** is a calcium channel blocking agent. It is a Class IV antiarrhythmic drugs that depresses the slow inward $Ca++$ current by blocking the slow L-type calcium channel. It has "use-dependent" action on AV nodal conduction that leads to greater therapeutic effects at faster heart rates. Diltiazem also has a direct effect on reducing vascular tone. Following a hypoxic event, the 'health' of any organ is jeopardized; diltiazem prevents calcium cytosolic and mitochondrial calcium accumulation and inhibition of Ca-dependent and calmoldulin-regulated enzyme activity thus reducing the generation of reactive oxygen metabolites and other radicals resulting in cell death. This latter effect may be useful following ischemia-reperfusion in CPCR.

Miscellaneous

1) **Dexamethasone sodium phosphate** has been recommended in the past for pulseless electrical activity. It is believed to act by inducing the release of ATP stores from mitochondria. This normalizes membrane polarization and increases production of cyclic adenosine monophosphate (AMP). However, it does not appear to be successful in the clinical setting. It may, however, have a beneficial affect on reducing cerebral edema. Although this has not been proven.

2) **Calcium chloride** should not be used routinely during cardiopulmonary resuscitation. The high levels of calcium in the blood induced by the administration of calcium salts may induce reperfusion injury and may adversely effect the neurologic outcome of the patient. Calcium salts should only be considered for the treatment of acute hyperkalemia, hypocalcemia or calcium channel blocker toxicity and hypermagnesemia or in those cases non-responsive to other therapeutic modalities. Calcium increases myocardial contractile function. Calcium's positive inotropic effects are modulated by its action on systemic vascular resistance. Calcium may either increase or decrease systemic vascular resistance. In normal health vasoconstricting effects produce a predictable rise in systemic arterial pressure.

3) **Sodium bicarbonate.** The absence of proven efficacy and the numerous adverse effects associated with sodium bicarbonate have led to a reconsideration of its role in cardiac resuscitation. Sodium bicarbonate should be used, after 8 – 10 minutes of CPCR or in specific clinical circumstances such as documented preexisting non-respiratory acidosis with or without hyperkalemia. The major problem with its use is that it has a high carbon dioxide content (260 – 280 mmHg for each 50 mEq). The carbon dioxide crosses rapidly into cells causing a paradoxical worsening of intracellular hypercarbia and acidosis. Bicarbonate crosses into cells much more slowly. However, sodium bicarbonate may be effective and is indicated in acidemic states. **Precautions:** Sodium bicarbonate administration results in the rapid generation of carbon dioxide and carbon dioxide is a rapidly acting and potent negative inotrope. The performance of the ischemic heart is closely related to tissue PCO_2 and is minimally related to the level of extracellular pH. Cardiac muscle performance is depressed by increases in arterial PCO_2 presumably due to the paradoxical intracellular acidosis that is induced. Other adverse effects include, hypernatremia and hyperosmolality. Shift in the oxyhemoglobin saturation curve caused by sodium bicarbonate can inhibit oxygen release to the tissues. **Dosage:** When sodium bicarbonate is used 0.5 – 1 mEq/kg should be given initially. A maximum of one-half this dose may be given for subsequent doses which should not be given more frequently than every 10 minutes.

4) **Morphine** is effective in treating ischemic chest pain and for acute pulmonary edema both of which could be present in the post-resuscitation period in dogs. Morphine manifests both analgesic and hemodynamic effects. It increases venous capacitance and reduces systemic vascular resistance, relieving pulmonary congestion. It reduces intramyocardial wall tension which decreases myocardial oxygen requirements. Morphine's hemodynamic effects may be mediated by sympatholytic effects on the central nervous system since they are most pronounced in patients with heightened sympathetic activity. **Precautions:** Morphine, like many other narcotic analgesics, can cause respiratory depression in non-painful conditions. Excessive narcosis occurs prior to respiratory depression which can be reversed by titrating 1mL aliquots of naloxone (dilute 0.1 mL or 0.25 mL [0.4 mg/mL naloxone], depending on size of patient, with 10 mLs saline] to effect. Hypotension is most common and most severe in volume depleted patients and in patients who are dependent on elevated systemic vascular resistance for maintenance of blood pressure. Use caution when administering morphine to these cases. Hypotension and an inappropriate heart rate (bradycardia) which appears to be vagally mediated may occur. If pain management is necessary, do not reverse the morphine but administer glycopyrrolate 0.005 mg/kg (large dogs) to 0.010 mg/kg (small dogs and cats). **Dosage:** The IM route of administration is preferred due to the hypotensive effects of morphine when given IV. A loading dose of 0.3 mg/kg IM can be given IM followed by a CRI of 0.1 mg/kg/h in the dog and cat.

5) **Gabapentin** is an antiepileptic and analgesic agent. It has been suggested that the antiallodynic actions of gabapentin involve a central mechanism of action by binding with the high affinity a2d subunits of voltage dependent calcium channels, blocking calcium currents in cortical neurons and blocking maintenance of spinal cord central sensitization. Gabapentin is excreted by the kidneys; animals with renal insufficiency may require less frequent dosing due to slower elimination. As dosing to effect is the method by which the appropriate dose is selected. Once this effect is reached, twice a day rather than three times daily treatment may suffice. Nephrotoxicity is not an issue. The author has found gabapentin useful in treating animals following cardiopulmonary arrest or seizures that are extremely restless, disoriented, vocalizing and/or manic. Signs of overdose are reduced activity and excessive sleepiness, progressing to depression. Tapering the dose down is important, as stopping the drug abruptly may lead to rebound pain which may be severe.

6) **Bretylium.** No longer available.

Perfusion Enhancing Techniques

1) **Thoracic Pump Technique:** The high intrathoracic pressure created by simultaneous compression and ventilation, generates an extrathoracic arterial-venous pressure gradient. With compression (systole) during ventilation the lungs are expanded and the airway pressure is high (up to 80 mmHg). This pressure (air) cannot be evacuated from the thorax (trachea), therefore, the increased intrathoracic pressure generated by the compression can only be 'vented' by blood leaving the intrathoracic vessels. As backflow of blood into veins is prevented by the venous valves and the increased intrathoracic pressure compresses the veins, the thoracic pump technique enhances the flow of blood through the arteries. This greater forward flow, and thus increased arterial (aortic and carotid) flow, improves cerebral and myocardial perfusion. *Pressure, is enhanced when sudden, forcible compression (simulate a cough) is applied to the thorax.*

2) **Abdominal Compression:** Abdominal compression or binding reduces the vascular tank. This increases available blood centrally. It is a valuable adjunct to CPCR in certain situations, however the following points must be considered:

   a. Abdominal binding during CPCR, with simultaneous compression-ventilation and epinephrine, increases atrial diastolic pressure. This leads to a smaller aortic-right atrial pressure gradient for myocardial perfusion. Abdominal binding also increases intra-cranial pressure by augmenting the transmission of intrathoracic pressure into the cranial vault. This reduces cerebral perfusion pressure.

   b. CPCR with epinephrine, and chest compression-ventilation but without binding, produces higher aortic diastolic pressures, lower jugular and intracranial pressures and increased cerebral blood flow. This relates to increased myocardial and cerebral perfusions.

   c. When compressing the abdomen, care must be taken not to apply too much pressure forcing the liver cranially into the region of chest compression where it is prone to laceration, and associated hemorrhage. Binding the hind limbs with a tensor bandage to mid-abdomen over a rolled towel between the legs and along the ventral abdomen with moderate pressure may be helpful. The bandage should be no tighter than a hand space between the bandage and the abdomen. Time and personnel are required for this.

   d. Cardiopulmonary resuscitation with **interposed abdominal compression** (IAC) (abdominal pressure/pulsation 180° out of phase with chest compression) has been shown to augment aortic diastolic pressure probably by squeezing blood retrograde toward the heart and brain and by priming the intrathoracic pump mechanism. Increased cardiac output, diastolic pressure and arteriovenous pressure differences were produced, resulting in increased coronary and cerebral perfusion pressures, when IAC was added to standard CPCR in experimental dogs. IAC is performed by compressing the abdomen during diastole (the upward phase of thoracic compression). In clinical practice, however, this may still cause laceration of the liver with subsequent hemorrhage if both chest and abdominal compressions inadvertently occur simultaneously. This technique requires an additional person to be effective.

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INTRODUCTION

Cardiac tamponade (intrapericardial pressure ≥ right ventricular diastolic pressure) due to pericardial effusion, is not uncommon in dogs but rare in cats. Rapid fluid accumulation, such as hemorrhage associated with trauma (i.e., right atrial rupture) can raise intrapericardial pressures with very small volumes of blood, whereas slow accumulation associated with idiopathic pericarditis allows for stretch of the pericardium with large accumulations of fluid. In both situations, progressive cardiac compression reduces cardiac filling, subsequent cardiac output and arterial blood pressure, resulting in eventual cardiogenic shock. **In dogs,** diseases most commonly associated with pericardial effusions are idiopathic pericarditis, or cardiac/extracardiac neoplasms such as right atrial hemangiosarcoma (increased prevalence in Golden retrievers and German shepherd dogs) or heartbase tumours. Other less common causes are infective pericarditis, hemorrhage into the pericardial space from trauma, left atrial rupture or a systemic coagulopathy, congestive heart failure, chronic uremia or iatrogenic. Feline infectious peritonitis, bacterial infections, neoplasia (i.e., lymphoma) and congestive heart failure are the most common reported causes **in the cat.** Prognosis depends on the etiology and potential for treatment. Animals with cardiac tamponade may present with similar presenting signs as those with congestive heart failure or pulmonary thromboemboli. However, the treatment is quite different, therefore an accurate diagnosis must be made quickly. Heart murmurs are not a feature of pericardial effusion unless associated with concurrent heart disease. **The mortality is 100% in patients with severe clinical signs if the pericardial effusion is not removed.** The time to death varies with the underlying cause and acuity of signs, but can be rapid. The morbidity associated with pericardiocentesis is low. Therefore, the risk:benefit ratio is very low even when performed by an inexperienced person. Pericardiocentesis can be performed subsequent to a history indicative of, and a physical examination suggestive of, a pericardial effusion (or tamponade) even if echocardiography or ECG is not available as is the case in many practices. Even a small volume of fluid removed may be lifesaving.

DIAGNOSIS

History

While administering oxygen, question the owner with regards to history, known medical diseases and current medication. With acute onset the owners may report no premonitary signs, or recent trauma, or recent depression and anorexia if associated with infectious causes. With sub-acute to chronic onset, owners may report a period of progressive weakness, exercise intolerance, lethargy, tachypnea, syncope, cough, abdominal enlargement, or muscle wasting.

Clinical Signs/Physical Examination

Animals with **acute pericardial effusion** present with:
- Severe dyspnea (increased breath sounds due to the effort of breathing) but no abnormal breath sounds are heard unless there is chronicity of effusion leading to bi-ventricular heart failure and pulmonary edema (rare).
- Heart sounds most commonly are muffled to absent, even with small volumes of hemorrhage; however these are rare exceptions.
- Signs of cardiogenic shock
  - tachycardia
  - hypotension
  - weak to absent peripheral pulses; femoral pulses may still be palpable
  - may have pulsus paradoxus (pulse during expiration stronger than pulse during inspiration)
  - distended jugular veins, jugular pulse
  - pale to gray mucous membranes with CRT > 2 sec
  - rectal temperature below normal unless infective pericarditis
- Animals with **sub-acute to chronic pericardial effusion** present with:
  - tachypnea or dyspnea as the acute case
  - lung sounds muffled if pleural effusion present
  - jugular vein distension ± jugular pulse

- heart sounds soft, muffled, or absent
- most cats and dogs show signs of right ventricular congestive failure such as pleural effusion and ascites, hepatomegaly
- biventricular signs may also be present with the addition of abnormal breath sounds due to pulmonary edema (rare)
- cardiogenic shock (as above for acute)

Laboratory/Imaging Evaluation

Stat

Administer oxygen. As IV (cephalic) access should be obtained, collect blood from the catheter.

- **ACT** to rule out coagulopathy as a cause.
- **PCV/TS** to assess degree of blood loss and for comparison to effusion.
- **Stick BUN** to assess renal perfusion (pre-renal azotemia).
- **Serum electrolytes** to identify potential abnormalities and for fluid selection.
- **Venous blood gases** (or total CO_2) to assess perfusion status.
- **Lactate** to assess perfusion status.
- **ECG** findings are not sensitive or specific and may include small (<1mV in dogs) QRS complexes, electrical alternans (alternating sizes of QRS complex or occasionally T-wave), ST segment elevation, tachycardia with normal QRS complexes and atrial or ventricular arrhythmias depending on the degree of myocardial ischemia. Acute effusion may not result in alteration of complex size.
- **Chest radiographs** (if doesn't unduly stress the patient). The cardiac silhouette may appear normal (especially with peracute, small volume, hemorrhage in trauma), or globose on chest radiographs. Various cardiac contours, especially atrial shadows, may not be easily visualized as fluid silhouettes out the angles and waists. Distension of the caudal vena cava and pleural fluid are often present with chronic pericardial effusion. Pulmonary densities typical of pulmonary edema and distended pulmonary veins are infrequent.
- **Echocardiography** is required to rapidly confirm the presence of pericardial effusion, however, it is not necessary prior to management when physical findings are indicative of effusion. Pericardial effusion is identified as a lucency around the heart, the size of which depends on the volume of fluid present. Where possible, echocardiograhic examination is advised prior to fluid removal as identification of intrapericadial masses are more easily visualized. While identification of a mass as a cause of effusion is required, do not jeopardize the patient's life by not removing the effusion. Frequently, a small residual amount of effusion remains post-pericardiocentesis facilitating identification of tumours. In the acute situation volumes as small as 50 mL or less in a large dog can cause shock and death. With chronic effusions, volumes of greater than a litre may be present in large dogs. There is diminished contraction of the heart, and compression or collapse (cyclic) of cardiac chambers. An intracardiac mass may be seen.
- **Pericardial fluid assessment:**
  - **pH** is unreliable in distinguishing idiopathic from neoplastic effusions.
    1) **Cytological examination** may reveal an inflammatory, septic or neoplastic cause for the effusion, however reactive mesothelial cells may resemble neoplastic cells.
    2) **Culture pericardial** for bacteria and for fungi (coccidiodomycoses) where indicated.
    3) **PCV/TS,** when compared to peripheral PCV/TS, defines whether hemorrhage or non-hemorrhage is the cause of effusion. A **high PCV** can be seen with: atrial tear, cardiac neoplasia and benign idiopathic effusions.

Extended Laboratory/Imaging Data Base

- **CBC.** A leukocytosis may be present in inflammatory, infectious and occasionally neoplastic states, or normal in trauma, most neoplasia, ruptured atria or idiopathic pericardial effusion. Schistocytes, nucleated red blood cells, a regenerative anemia and thrombocytopenia may be present in cases of hemangiosarcoma.
- **Biochemical profile** is usually non-specific and will vary with the etiology. Azotemia and increased ALT may be present depending on degree of chronicity and poor perfusion.
- **Serum electrolytes** may be normal or a hyponatremia may be present in very low cardiac output states. This is due to increased ADH and water retention in excess of sodium.
- **Mild hypoalbuminemia** may be present with pericardial, pleural or peritoneal effusions.
- **PT and PTT** if coagulopathy suspected.
- **Abdominal radiographs.** Hepatomegaly and ascites may be present on abdominal radiographs.
- **Echocardiographic** examination (if not yet performed) to confirm pericardial effusion and identify primary cause (*see introduction and stat evaluation above*).
- **Serologic titres** for fungi (coccidiodomycoses) where indicated.

MANAGEMENT

A. Oxygen 100% by mask or flowby.

B. IV access and fluids. Administer balanced electrolyte solution if in shock. A definitive rate cannot be given, however attempts at shock management should be initiated with constant vigilance as to tolerance (respiratory rate, heart rate, signs of anxiety). Unlike congestive heart failure, cardiac tamponade is not a disease of primary myocardial failure but one of inadequate diastolic filling, thus fluids are necessary to improve this until pericardiocentesis can be performed.

DO NOT USE ARTERIAL OR VENODILATORS, DIURETICS OR POSITIVE INOTROPES. SIGNS RESOLVE WITH PERICARDIOCENTESIS.

C. Pericardiocentesis is a lifesaving procedure and is **necessary** for initial stabilization.

Materials
> 60 cc syringe
> 3-way stopcock
> IV fluid extension line
> 16 G 3 1/4"(small animals) or 14G 5" over-the-needle Angiocath catheter. Consider making additional holes in the side of the tip of the catheter (stagger holes to prevent weakening) for additional drainage (the tip may clot)
> Sterile gloves
> Lidocaine for local anesthesia
> Scalpel blade

Technique
1. Connect the syringe to the 3-way stopcock and an IV extension tubing. Keep sterile.
2. The procedure is performed with the animal standing, in sternal or left lateral recumbency.
3. If sedation is needed (rarely) **do not use** hypotensive drugs such as acepromazine. **Butorphanol 0.2 mg/kg in combination with midazolam 0.1 – 0.2 mg/kg IV** is adequate.
4. **ECG** monitoring is recommended to assess needle contact with the myocardium (VPCs frequently occur).
5. Surgically prepare the ventral third of the **right** hemithorax from the 3rd to the 8th intercostal space. The right side is preferred so as to avoid the coronary vessels and reduce injury to the lung. Have an assistant pull the skin forward and hold in this position. Infiltrate the skin over the 5th or 6th intercostal space, at the level of the costochondral junction, down to, and including, the parietal pleura, with **2 mL of 1% lidocaine (mix 1:1 2% lidocaine with 0.9% saline** to reduce the 'sting'). Make a 0.3 cm incision in the skin at this point.
6. The catheter is advanced slowly through the small incision, with a slight upward angulation, cranial to the rib to avoid injury of the intercostal vessels. In most instances, one cannot detect when the catheter has passed through the pericardium. Fluid should appear in the hub of the needle when in the pericardial sac. However, this may also be pleural fluid. With longstanding effusions, the pericardium may be fibrous and a 'pop' may be experienced as the catheter penetrates it. Observe the ECG tracing while advancing with the needle and catheter. The appearance of VPCs, if not present previously, indicate you are touching the myocardium; these are usually transient Advance the catheter over the needle as the needle is removed. Connect the IV extension to the catheter and instruct the assistant to aspirate slowly.
7. Where pericardial and pleural effusion coexist, advance the catheter and needle until you can feel the heart, then remove the needle immediately and connect the IV extension to the catheter.
8. If sustained ventricular tachycardia occurs, retract the catheter slightly; if persists administer **lidocaine 2 mg/kg** (without epinephrine) intravenously and then refer to *p. 181* for further treatment of ventricular arrhythmias.
9. Slow aspiration of pericardial fluid is essential. Occasionally, you will feel the catheter rubbing against the heart; this is of no concern. Towards the end of the procedure the catheter will have a tendency to occlude, instruct the assistant to stop suction and gently reposition the catheter within the pericardial space; this may need to be done several times.

10. The fluid obtained may be serosanguinous, clear or opaque, OR hemorrhagic and dark. The fluid should not clot, unless there is acute hemorrhage from rupture of a cardiac chamber, vessel or neoplasm (or you are in the atrium or ventricle!)

11. With removal of even small volumes of fluid, there is a trend towards reduction in respiratory and heart rates, which return towards acceptable or normal limits as most of the fluid is removed.

Potential complications are:

- Cardiac puncture with aspiration of blood that will clot. Don't worry, retract the catheter slightly.
- Coronary artery laceration is a rare complication and avoided when performed on the right side.
- Lung laceration causing pneumo/hemothorax is also very rare.
- Extension of infection into the pleural space from the pericardial space may occur if infectious etiology is present.

After normalization of cardiac filling and output, a diuresis may occur. Reduced cardiac output during tamponade causes activation of the renin-angiotensin-aldosterone system and ADH to conserve fluid. Once tamponade is resolved there exists a relative hypervolemia resulting in the diuresis. Monitoring weight and urine production and hydration status is advised.

D. After fluid removal and diagnosis made, a definitive treatment plan can be outlined. This may include surgery to remove a heart base, atrial or intracardiac tumor, antibiotics for infectious pericarditis, or corticosteroids for idiopathic pericardial effusion (not proven to be of benefit). For persistent or recurrent pericardial effusion, pericardectomy (via thoracotomy or thoracoscopy) or balloon pericardiotomy remains treatment of choice. About 40% of benign effusions resolve spontaneously following one or two pericardiocenteses. Treatment for congestive heart failure may be required (*see p. 150*).

E. Should a **fungal** etiology be suspected/identified based on physical examination and cytology, commence **itraconozol at 5 mg/kg q24h initially**, especially with lung involvement; this can be increased to q12h after 5 days with a definitive diagnosis. For potential bacterial causes, commence a broad spectrum antibiotic such as **amoxicillin-clavulanate at 15 – 20 mg/kg PO q12h (dogs) or 62.5 mg/cat PO q12h** until culture and sensitivity result are received.

F. Following negative culture results and no evidence of infectious causes, **prednisone 1 – 2 mg/kg/day** for 2 – 4 weeks MAY prevent recurrence of idiopathic pericarditis, however, the efficacy of this treatment is not proven.

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NOTES

INTRODUCTION

Acute, life-threatening congestive heart failure (CHF) can occur in either cats or dogs of any breed. In large breed dogs, especially Doberman pinschers, the underlying problem is usually dilated cardiomyopathy (DCM), whereas the smaller breed dogs, such as toy poodles, tend to develop mitral valve disease. Occasionally, ruptured chordae tendineae is the cause of acute onset CHF. Most commonly in cats, the underlying problem is hypertrophic cardiomyopathy (HCM), however, dilated or restrictive cardiomyopathy may be present. A definitive diagnosis by ultrasonographic examination is required prior to institution of long term therapy. The protocol presented here is for the immediate treatment of life-threatening congestive heart failure, a generic therapy, regardless of the underlying etiology. Initially, IM administration of medications may be indicated to avoid stressing the patient with IV administration, particularly in the cat. The SC route is not acceptable because of poor perfusion.

DIAGNOSIS

History

- While administering oxygen, question the owner with regards to underlying cardiac disease and current medication, recent history of cough, decreased exercise tolerance, orthopnea or dyspnea.
- It is unusual for a dog to present with life-threatening cardiac pulmonary edema without a history of cardiac disease unless ruptured chordae tendineae is the cause. However, cats, and some dogs with DCM, do present with severe congestive heart failure with no previous knowledge of heart disease being present.
- Rarely, dogs with cardiac tamponade may present with signs of CHF. Physical examination and echocardiographic examination will make the definitive diagnosis of cardiac tamponade (*see Pericardial Effusion/Cardiac Tamponade p. 145*).

Clinical Signs/Physical Examination

- Both cats and dogs are weak, dyspneic and anxious. Some animals will present gasping and on the verge of death.
- On auscultation of the chest, determine the location, character and degree of heart murmur. Dogs with CHF should have a murmur, although murmurs associated with DCM are softer and more difficult to hear than most mitral valve disease murmurs and may be missed (consider non-cardiogenic causes). Murmurs are not always heard in cats with CHF. Crackles, wheezes and/or pleural effusion may be present in patients with CHF
- If crackles, wheezes and pulmonary edema are present, but no murmur or abnormal findings of cardiac silhouette are present, consider non-cardiogenic causes of pulmonary edema (*see pulmonary edema p. 556*). Respiratory diseases should also be considered. Non-cardiogenic pulmonary edema and primary respiratory disease can frequently be ruled out on history, physical examination and evaluation of laboratory/diagnostic imaging findings (*see pulmonary edema p. 561*). In patients with florid pulmonary edema of any cause, a frothy, serosanguinous oral or nasal discharge may be present and is usually a poor prognostic sign.
- In heart failure, the mucous membranes are cool and pale or gray with a capillary refill time greater than 2 seconds.
- The dorsal pedal pulses may not be palpable and the femoral pulses are weak in some animals, but may be fairly brisk in dogs with mitral valve disease. If an arrhythmia is present, pulses are irregular.
- With right-sided or bilateral heart failure, jugular veins can be distended with or without pulsation (look for pulsation at least half way up the neck or higher); an enlarged liver and/or ascites, in addition to pleural effusion, may also be detected.
- The rectal temperature may be <38° C (100° F) with a toe-web-to-rectal temperature differential >4° C (39°F).
- Animals with cardiac tamponade (*p. 145*) may present very much like congestive heart failure; weak, severely dyspneic if peracute, distended jugular veins, weak to absent dorsal pedal pulses but may have pulsus paradoxus. With cardiac tamponade, lung sounds are clearly audible unless a moderate to severe degree of pleural effusion is also present, however, heart sounds are muffled to absent.
- Cats with thromboembolic disease may be dyspneic, paretic with no femoral or axillary pulses and some may present with a history of intermittent lameness (*p. 194*).
- With primary respiratory disease, pulses are palpable and the temperature is normal to increased.

Laboratory Evaluation/Imaging Evaluation

Stat

Only obtain the following tests if this does not dangerously stress the patient.

- **ECG** to establish rhythm.
- **Systemic blood pressure**
- **Chest radiographs** (when stable) to identify extent of pulmonary edema and pleural effusion.
- **Echocardiographic examination** – if required for emergency treatment (especially cats) after stabilization (below).
- **PCV/TS** for baseline measurement. May be reduced due to increased water reabsorption as poor perfusion enhances ADH activity and may be an indicator of severity of heart disease. On the other hand a PDA with L-R shunt may result in an increase in PCV.
- **Stick BUN** or creatinine to establish whether renal insufficiency exists as an indicator of poor perfusion.
- **Serum electrolytes.** Low sodium may be present due to poor perfusion and enhanced antidiuretic hormone (ADH) activity and may be an indication of severity of heart disease. A low K^+ may also exist predisposing to arrhythmias.
- **Venous blood gases** (or total CO_2) to assess perfusion and oxygen delivery to tissues

Extended Laboratory/Imaging Evaluation

- **Biochemical profile** for systemic evaluation. Liver, pancreas and renal values may be elevated if cardiac output is poor.
- **CBC** may reveal altered red blood cell count as explained for PCV. Normally WBC unaffected.
- **PT and PTT** if hypercoagulation a concern or for baseline prior to anticoagulation therapy for thromboembolic disease.
- **Echocardiographic examination** (when stable) for definitive diagnosis of underlying cardiac pathology.

MANAGEMENT

DO NOT STRESS UNDULY, HANDLE GENTLY, KEEP QUIET, AVOID A CROWD

SEDATING THE PATIENT IS MUCH SAFER THAN STRUGGLING WITH THEM

A. **Oxygen** by flow-by mask, hood or incubator.

B. Attempt IV catheter placement at any time where this will not unduly stress the patient.

C. **Furosemide 3 – 5 mg/kg IV, or IM (dog), 2 mg/kg (cat).** Dose dependent on severity of edema.

D. If the animal is **very anxious,** give morphine 0.1 – 0.3 mg/kg (dog & cat) IM, butorphanol 0.1 – 0.2 mg/kg IM (dog and cat), or **meperidine at 3 – 5 mg/kg IM.** Combine with midazolam 0.25 mg/kg IM ONLY if necessary as occasional excitement may occur. (*See Sedation in Cardiac Patients p. 105*).

E. **If catastrophic and gasping, intubate.**

1. If sedation is necessary to intubate, administer oxymorphone OR hydromorphone 0.02 – 0.05 mg/kg IV or IM combined with 0.05 – 0.2 mg/kg diazepam IV or midazolam IV, IM. Occasionally, patients are on the verge of death and intubation can be performed without sedation but always spray the larynx with lidocaine. Oxygenate with 100% oxygen and hold patient upside down to 'dump' fluid, follow with suction within the airway. Attach an adapter to the endotracheal tube to allow rapid oxygen delivery between suctions. Use a large suction tip that will pass easily into, and just beyond, the endotracheal tube. Apply suction only when in lower airway and on way out. Suction for no longer than five seconds at the lowest pressure that will gently suction the airway. Repeat procedure as indicated.
2. **Mechanical ventilation** with positive end-expiratory pressure may be indicated. Go to F,G below and treat while suctioning the airway.
3. Perform rapid thoracocentesis if pleural effusion detected on auscultation of the chest (muffled heart and lung sounds), see R below.
4. If airway foaming is present, nebulization with 20% ethanol (20 g/100 mL) may be beneficial, but has never been performed by the author.

F. **Furosemide 3 – 5 mg/kg IV (dog), 2 mg/kg (cat)** if not already given, and repeat if poor/no response to initial dose. Dose dependent on severity of edema. Do not give this dose more than twice in cats with hypertrophic cardiomyopathy. **Administer IV where possible as there will be delayed absorption when given IM.**

    1. The initial dose can be repeated q1–2h until the respiratory rate has decreased by half in dogs. Reassess q1h. The CRI described in (2) below is preferred.

    2. If pulmonary edema is refractory to this regimen, and/or the patient is azotemic, a CRI of furosemide at 0.5 – 1 mg/kg/h, (dog), 0.5 mg/kg/h (cat).

    3. Maintenance furosemide: Dog: 2 – 4 mg/kg/q8–12h and Cat: 1 – 2 mg/kg q12h IM or IV to be tailored to the individuals needs.

G. **Nitroglycerine 2 % ointment** 1/4 – 1" q6 – 8h (dog), 1/4" q6–8h (cat), to carefully clipped skin of thorax (do not apply to abraded skin). Cover area with a pad and mark to indicate treatment site to avoid contact with clinic personnel or animal licking it. Avoid placing in pinna initially as there is usually poor perfusion to the ear. An alternative, effective route is rectal application of nitroglycerine. Using a 1cc tuberculin syringe, nitroglycerin paste can be administered per rectum as follows: Remove the plunger of the syringe and align the 'mouth' of the nitroglycerin paste tube to the back of the syringe, squeeze the required amount of paste into the barrel of the syringe. Then re-introduce the syringe plunger and move the paste forward into the "mouth" of the syringe. Lubricate the exterior of the syringe with vaseline and introduce in the rectum as far as possibe, release the nitroglycerin paste into the rectum and remove syringe (personal communication Dr. Luis Braz-Ruivo).

H. Allow the animal (and you) to relax with supplemental oxygen (incubator, cage, hood, mask, nasal cannula prongs) while making further diagnostic arrangements or preparing drug infusions (CRI).

I. If respiratory rate and effort are not improved go to K (Phlebotomy) below; or M (Dobutamine) ± N (sodium nitroprusside).

J. Place a peripheral IV catheter if not already performed. EMLA cream (Astra) placed over venipuncture site 30 minutes prior to catheterization, may reduce discomfort and facilitate easier catheter placement, in the extremely anxious patient.

    1. If too stressed to do this, sedate. Give butorphanol 0.1 – 0.5 mg/kg IM (cat and dog) or morphine 0.3 mg/kg IM (dog). These opioids can be combined with midazolam 0.05 – 0.1 mg/kg or acepromazine 0.01 – 0.025 mg/kg IM (dog).

    2. When stable, if indicated (i.e., frequent blood sampling and CVP monitoring), place a jugular catheter without stressing the patient. A 12" catheter into the medial saphenous vein in cats and small dogs is an alternative site. **Caution:** CVP may be erroneous if tricuspid regurgitation present.

K. **Phlebotomy** can be life saving if fulminant pulmonary edema cannot be relieved and the patient is dying before your eyes.

    1. Remove 10 mL/kg of blood from a distended jugular vein.

    2. If nitroglycerin and/or furosemide has already been administered, start by removing 5 mL/kg and reassess.

    3. Likewise, if 10 mL/kg appears to be insufficient to relieve signs, remove 15 mL/kg.

L. **Fluids**

NO FLUIDS, if necessary for drug administration, then

    1. Establish CRI with Plasma-Lyte® 56 OR 0.45% saline in 2.5% dextrose solution OR Normosol® M, and deliver at 1/4 maintenance rate (*see Fluid Therapy p. 366*). When congestion is resolved, the total fluid volume should not exceed one-quarter maintenance. (If lactated Ringer's solution is used, verify drug compatibility prior to establishing the CRI). The type of fluid and volume required varies from patient to patient and will need to be adjusted as the patient's condition changes. Always offer water.

OR

    2. Flush catheter with heparinized saline (1 unit/mL) q8h if fluids are to be withheld.

M. **Dobutamine** may be of benefit if patient has known dilated cardiomyopathy or mitral valve insufficiency with known poor contractility.

  1. If in atrial fibrillation start diltiazem to delay conduction through the AV node (*see Supraventricular Tachycardia p. 174*) prior to commencing dobutamine.
  2. Start at 5 μg/kg/min CRI (dog) and titrate up by increasing 25% every 15 minutes until pulses feel stronger or blood pressure is stabilized, up to 15–20 μg/kg/min.
  3. CAUTION IN CATS, can cause vomiting, seizures and sudden death if overdosed. However, don't be afraid to use it if you have to. Start at 1 μg/kg/min to a maximum of 4 μg/kg/min (cat). Do not use in cats with hypertrophic cardiomyopathy.
  4. Monitor closely. Discontinue if heart rate increases consistently above 200 (doesn't usually happen), or if cardiac arrhythmias or vomiting develop. Re-start infusion 30 minutes later and reduce by 20%.
  5. Dobutamine should be administered prior to sodium nitroprusside in DCM cases to improve contractility of the heart and increase cardiac output. This can offset the hypotensive effects of sodium nitroprusside.
  6. Beta receptors likely become refractory to dobutamine after ~ 72h.

N. **Sodium nitroprusside** may be of benefit if fulminant pulmonary edema is present (dogs only).

  1. 1 – 10 μg/kg/min (START AT 2 μg/kg/min and increase by 1 μg/kg/min q15–30min; the average dose is 6 μg/kg/min) CRI and is best monitored by direct arterial pressure monitoring.
  2. In dilated cardiomyopathy administer dobutamine first to help maintain mean arterial pressure above 60 mmHg.
  3. Nitroprusside is light sensitive. Wrap aluminum foil around the bag and line.
  4. Caution: Cyanide toxicity with overdose or when administred for more than 3 days. Monitor urine output q1–4h and urea and/or creatinine q24h.

O. If CRIs of dobutamine or nitroprusside are not possible, or CHF not necessarily requiring intensive care, one may consider initiating **pimobendan orally at 0.5 mg/kg q12h.** This may be administered following furosemide therapy in DCM and mitral regurgitation canine patients treated on an outpatient basis.

P. **Ongoing monitoring**

  1. q15–30min while on various infusions; respiratory rate, heart rate and rhythm, systemic blood pressure and CVP if jugular catheter placed.
  2. q15–30min until stable (when not on various infusions), then q1–2h; respiratory rate, heart rate and rhythm, systemic blood pressure.

Q. Arrange cardiac ultrasound examination, chest radiographs and evaluate ECG. If not obtained, collect blood for CBC and biochemical profile and where indicated, heartworm test, as soon as is safe.

R. If **pleural effusion** evident on auscultation, local block (costochondral junction and the intercostal space)using 1% lidocaine (1:1 2% lidocaine:0.9% saline to diminish pain (*see Local Anesthesia p. 125*), + sedation (*see D previous*), perform thoracocentesis and drain pleural fluid (*see Respiratory Emergencies p. 566*). Measure volume and submit for specific gravity, protein content and cytology (if initial presentation and primary cardiac disease is not confirmed).

S. After stabilisation and when safe, any cat [with non-obstructive HCM (HCM) or obstructive HCM (HOCM)] may be started on a beta blocker (atenolol 12.5 mg/cat PO q12h).

T. Alternatively, cats with confirmed HCM, may be started on diltiazem 7.5 mg/CAT PO q8h, OR 0.1 mg/kg slowly IV, followed by 1 μg/kg/min CRI. It may take 72 h to see improvement. Diuretic therapy should be tapered and possibly discontinued once stabilised on diltiazem.

U. **On-going fluid management.** One-quarter maintenance hourly crystalloid fluid rate (*see Fluid Therapy p. 366*) using Plasma-Lyte® 56 OR Normosol® M OR 0.45% saline in 2.5% dextrose,

  1. Remember, patients can become dehydrated and hypotensive and develop acid-base and electrolyte disorders with the above therapy therefore increasing the volume and changing the fluid type may be necessary.

2. When considering fluid therapy, the kidneys and pancreas can cause a lot of grief if not adequately perfused. Improving cardiac function will improve splanchnic perfusion; as the cardiac problem gets under control, you must consider fluid therapy for the kidneys and pancreas. Fluid rates in excess of maintenance may be required.

3. If renal failure is also present, and patient cannot tolerate higher than maintenance fluids, add pentastarch (or hetastarch) at 5 – 10 mL/kg/24h (dog), 2 – 5 mL/kg/24h (cat). Calculate hourly rate and add to hourly maintenance fluids in a burette after the pulmonary congestion has improved. Do not give more. Monitor carefully for any signs of fluid overload; discontinue immediately.

V. Venous blood gases (or total CO_2) and serum electrolytes should be monitored q24h as furosemide may cause hypokalemia, hyponatremia, hypochloremia and alkalemia.

W. Continue management with protocols for canine dilated cardiomyopathy or mitral valve regurgitation (*see Congestive Heart Failure – Chronic Therapy p. 158*) and specific arrhythmias.

PHARMACOLOGY

1) **Sodium nitroprusside** is predominantly an arteriolar dilator but also has venodilator properties, which produces a rapid reduction in peripheral vascular resistance, arterial blood pressure and pulmonary capillary wedge pressure. There is an associated initial reduction in cardiac output and slight increase in heart rate. These effects are noted upon commencing the infusion and are terminated as soon as the infusion is terminated or reduced. Nitroprusside should only be used where direct arterial pressures can be measured and the patient is constantly monitored. Nitroprusside has to be diluted in 5% dextrose in water and administered as a constant rate infusion. Nitroprusside is metabolized to cyanide and therefore with prolonged use can be toxic.

2) **2% nitroglycerin** relaxes vascular smooth muscle, predominantly venous but, in a dose-related manner, causes dilation of both arterial and venous beds. There is a reduction in both preload (primarily) and afterload which subsequently reduces myocardial work and oxygen demand. When nitroglycerine is placed on the skin, there is a continuous absorption over 3 – 8 hours into the systemic circulation, by-passing the portal circulation. Nitroglycerin causes a slight reduction in blood pressure and possibly a slight increase in heart rate.

3) **Furosemide** is a loop which rapidly removes fluid from the body reducing both intravascular and extravascular volume. Care must be taken not to dehydrate the patient. Hyponatremia, hypochloremia, hypokalemia and alkalemia are common after aggressive furosemide administration.

4) **Morphine**, in addition to its sedative and anxiolytic effects, is a mild venodilator redistributing blood away from the lungs. Morphine should not be used in patients with neurogenic pulmonary edema, where the inciting cause is still present, as it raises intracranial pressure. Morphine in cats may induce vomiting and dysphoria, therefore use low dose IM.

5) **Oxymorphone, midazolam, diazepam, acepromazine** – *see Analgesics and Sedatives p. 81*.

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NOTES

INTRODUCTION

As chronic therapy should be instituted within the first 24 hours of presentation with congestive heart failure (CHF), the treatments suggested in these protocols should be considered while managing the emergent patient.

DOGS

The two most common causes of congestive heart failure (CHF) in the dog are due to either dilated cardiomyopathy (DCM) or chronic mitral valve regurgitation (CMVD). As a rule, DCM occurs mostly in large and giant breeds of dogs (i.e., Doberman, Great Dane, Irish Wolfhound) while CMVD occurs more often in small and toy breeds (i.e., Poodle, Cavalier King Charles Spaniel). Cocker Spaniels are a breed that present with a high incidence of DCM sometimes mixed with CMVD. In some cases, cardiac disease of Cockers is associated with low blood levels of taurine (normal plasma level is 40 – 120 nmol/mL; normal whole blood level is >250 nmol/mL) and can be reversed with taurine supplementation. Special requirements are needed when collecting blood for taurine levels (refer to the end of this chapter). Recently, other breeds have been found to have taurine-responsive DCM. Some examples are the Labrador Retriever, Golden Retriever, Dalmatian, Newfoundland. Taurine evaluation should be done on any patient presented with DCM. Carnitine deficiency has been documented in Boxers in association with DCM, and suspected in other larger breeds as a contributing factor. Unlike taurine, carnitine blood levels are not representative of the myocardial concentration, and therefore not useful in the clinical setting; however, some authors recommend carnitine supplementation in all cases of DCM. The clinical benefit of carnitine supplementation has not been determined. There is no data in veterinary medicine concerning the utility of CoEnzyme Q10 (CoQ10) in patients with heart disease. Human data does not show a benefit when using CoQ10 in people with heart disease.

CATS

The most common causes of CHF in cats are, hypertrophic cardiomyopathy (HCM), restrictive/unclassified cardiomyopathy (RCM) and dilated cardiomyopathy (DCM). Other causes such as congenital heart disease or myocardial infarction are less commonly encountered. The majority of the cases are due to HCM. DCM is rare in cats since the introduction of adequate supplemental levels of taurine in cat food since 1988. Normal plasma levels and whole blood levels in taurine in cats are identical to dogs (see above). When DCM is diagnosed in a cat, obtain a complete diet history and consider evaluation of the plasma taurine level. Recently, the coincidental use of long-acting corticosteroids has been associated with the development of CHF in some cats. However, the precise mechanisms are unclear, and most authors suspect the mineralocorticoid actions to be the major cause, in conjunction with occult heart disease. The author suggests obtaining a lateral view chest radiograph prior to initiation of long-acting corticosteroids in cats older than 5 years of age without physical exam findings suggestive of heart disease. If there is suspicion of heart disease an echocardiogram should be considered prior to initiation of therapy. Uncontrolled hyperthyroid disease may result in high output heart failure. Control of the hyperthyroid disease is crucial for the long-term management of heart failure. In many cases, remodeling of the heart can be achieved once hyperthyroidism is controlled and the discontinuation of cardiac medications is possible.

DIAGNOSIS

History

Dogs
- Exercise intolerance, syncope/collapse, cough, labored breathing, decreased appetite and weight loss are all signs of congestive heart failure.
- Historical presence of a heart murmur is common but not essential in all cases.
- In large breeds, the presence of a new murmur is coincidental in many cases with the presentation of congestive heart failure.
- Cough is usually more pronounced in small breeds, and in some cases may not be a presenting symptom. Syncope/collapse is usually associated with periods of excitement or exertion.

Cats
- Most cats have no signs prior to presentation.
- In some cats a period of lethargy and anorexia precedes development of CHF.
- Historical presence of a heart murmur, third heart sounds or arrhythmia may be found.

- Cough is not usually a historical finding in cats with heart disease, but sometimes is found in cases with very advanced disease. Cough is most commonly the result of small airway disease. In the southern states of America heartworm disease can be a cause of heart failure, and cough can be a historical finding. Some cats with heartworm disease may present in fulminant pulmonary edema that is very difficult to treat.
- Ascites is an uncommon presentation in cats with heart disease, but can be seen in cases with very severe right heart dysfunction.
- Cats with hyperthyroid heart disease have a history consistent with hyperthyroidism (see Hyperthyroidism p. 289). They commonly present extremely tachycardic, and in the author's experience immediate administration of a beta-blocker (atenolol is the drug of choice) can be life saving.

Clinical Signs/Physical Examination
See Congestive Heart Failure (Life-Threatening) p. 149.

Laboratory Evaluation/Diagnostic Imaging
See Congestive Heart Failure (Life-Threatening) p. 150.

Baseline evaluation at initial presentation:
See Congestive Heart Failure (Life-Threatening) p. 150 for interpretation of the following:

- **CBC, complete biochemical profile, and urinalysis.**
- **Taurine plasma levels** in any dog or cat diagnosed with DCM or advanced left ventricular systolic dysfunction.
- **Electrocardiogram**
- **Blood pressure**
- **Thoracic radiography**
- **Echocardiogram**
- **Plasma Cardiac Troponin I** (plasma cTnI concentrations above 0.5 ng/mL are highly suggestive of a diagnosis of HCM in a cat [sensitivity = 95%, specificity = 97%]).

Monitoring parameters for ongoing therapy:

- **Renal (BUN, Creatinine, Phosphorus) and electrolyte status:** Evaluate at 7, 14 and 28 days after initiation of therapy **and** whenever there is a major change in diuretic therapy. Continuing inadequate cardiac output can result in renal insufficiency.
- **Electrolytes** should be monitored as above (renal). Inadequate cardiac output and overzealous diuretic therapy result in hyponatremia, hypochloremia and hypokalemia.
- In **very old patients,** patients that have poor appetite or patients with questionable renal function the re-evaluation should be done in 3 – 5 days after starting diuretic therapy for reasons noted above.
- **PVC/TS** should be assessed every time blood testing is performed as a guide to hydration status or other potential problems.
- **Digoxin serum levels:**
  - Titrate therapy based on serum levels. Measure drug concentration one week after initiation of treatment or earlier if toxicity is suspected.
  - Patients with borderline/mild renal dysfunction should be monitored carefully.
  - Patients with obvious renal dysfunction will most likely develop toxic levels of digoxin; thus, other inotropic therapies may need to be considered.
  - Obtain the sample 8h after the last dose. Do not store serum in plastic tubes. If levels are adequate (see Table 1 p. 163) recheck one week later. If you have to change the dose, further rechecks are needed until you have two consecutive samples at the desired level.
- **Electrocardiogram** if arrhythmias are newly detected or being monitored, or if presented with a major change in the clinical condition of a chronic patient.
- **Blood pressure** whenever vasodilators are titrated to dose effect, or side effects of drug therapy are suspected.
- **Thoracic radiography** to help titrate diuretic therapy by assessing cardiovascular volume.
- **Echocardiogram** if presented with a major change in the clinical condition of a chronic patient.

In large breed of dogs that do not commonly develop DCM, or have evidence of left ventricular systolic dysfunction, assessment of thyroid function should be considered.

Medical therapy for DCM or CMVD is identical. Use the underlying cardiac rhythm presented below, as the criteria to establish a treatment protocol. *If in sinus rhythm go to I; if in atrial fibrillation go to II. See p. 158 for instructions.*

MANAGEMENT OF CONGESTIVE HEART FAILURE

DOGS

Dilated Cardiomyopathy OR Chronic Mitral Valve Disease

I. Sinus Rhythm

II. Atrial Fibrillation

No Arrhythmias OR Occasional Supraventricular Premature Contractions (SVPC's)

A. 1, 2, 3, 4

Several SVPC's

B. 1, 2, 3, 4

Occasional Ventricular Premature Contractions (VPC's)

C. 1, 2, 3, 4

Several VPC's

D. 1, 2, 3

With No or Occasional VPC's

A. 1, 2, 3, 4

With Several VPC's

B. Combined with A. 1, 2, 3, 4

FIGURE 1. Management of Congestive Heart Failure – Dogs

MANAGEMENT OF CONGESTIVE HEART FAILURE

CATS

```
                                    CATS
         ┌──────────────────────────┼──────────────────────────┐
┌─────────────────┐      ┌──────────────────────────┐   ┌─────────────────┐
│ I. Hypertrophic │      │ II. Restrictive/unclassified │ │ III. Dilated   │
│    cardiomyopathy│     │     cardiomyopathy        │   │    cardiomyopathy│
└─────────────────┘      └──────────────────────────┘   └─────────────────┘
```

I. Hypertrophic cardiomyopathy

Sinus rhythm with
no arrhythmia

A. 1, 2, 3, 4

Sinus rhythm
• many SVPCs
• paroxysms SVT
• VPCs
• paroxysms VT

B. 1, 2

Atrial fibrillation

C. 1, 2

II. Restrictive/unclassified cardiomyopathy

Sinus rhythm with
no arrhythmia

A. 1, 2, 3, 4

Sinus rhythm
• many SVPCs
• paroxysms SVT
• VPCs
• paroxysms VT

B. 1, 2

Atrial fibrillation

C. 1, 2

III. Dilated cardiomyopathy

Sinus rhythm

A. 1, 2, 3, 4

Sinus rhythm
• many SVPCs
• paroxysms SVT
• VPCs
• paroxysms VT

B. 1, 2

Atrial fibrillation

C. 1, 2, 3

FIGURE 2. Management of Congestive Heart Failure – Cats

DOG

For the dog, the different protocols presented below use the underlying cardiac rhythm as the criteria to establish treatment. See NOTES TO THERAPY below prior to commencing therapy. **If in sinus rhythm go to I**; if in **atrial fibrillation go to II** below. For management of CHF in the cat go to the **Management – Cat section.**

I   Sinus Rhythm

A. No arrhythmias or occasional **Supraventricular Premature Contractions** (SVPC's); this includes single SVPC's or rare couplets (*see Supraventricular Arrhythmias for rhythm strip p. 172*).

Combine the following:

1. **Furosemide 2 – 3 mg/kg q8h** initially and titrate to the minimal amount needed to control pulmonary edema as determined by follow-up radiographs, renal parameters, physical exam and clinical signs. Some dogs may only need q12h others will need q6h therapy.
2. **Angiotensin converting enzyme inhibitor (ACEI):**
   a. **Enalapril 0.5 mg/kg q12h. OR**
   b. Alternatively, **benazepril, lisinopril,** or **ramipril 0.5 mg/kg q24h.**
3. **Positive inotropes:**
   a. **Digoxin** for dosage *see Table 1* below. In this situation the use of digoxin is OPTIONAL. The author is more likely to use digoxin in cases with documented systolic dysfunction. OR
   b. **Pimobendan 0.25 mg/kg PO q12h** has both vasodilating and positive inotropic properties. It is indicated if DCM or CMVD with moderate to severe systolic dysfunction. It is not required in CMVD with normal systolic function.
4. **Vasodilators:**
   a. **Amlodipine 0.2 – 0.5 mg/kg PO q12h** has been shown to decrease mitral regurgitation fraction. **OR**
   b. **Hydralazine 0.5 – 3 mg/kg PO q12h** can be used as an alternative to amlodipine.
   c. **Titrate vasodilator therapy** based on clinical signs, blood pressure monitoring and side effects (*see Pharmacology below*).

B. Several SVPC's (more than 30% of the total beats) and/or runs of supraventricular tachycardia (SVT) (*see Supraventricular Tachycardia for rhythm strip p. 172*).

1. **Furosemide, ACEI, digoxin** or **pimobendan** as in **I. A** above.
   PLUS
2. **Calcium channel blocker, (Table 3) diltiazem 2 – 3 mg/kg q8h and titrate up as needed,** is the drug of choice. If no response in controlling the arrhythmia try:
3. **Beta-blocker,** *see Table 2* below (be cautious starting beta-blockers in patients with DCM).
   If no response in controlling the arrhythmia try,
4. **Class III antiarrhythmic drug** (*see Table 4*)
   a. If normal systolic function use **sotalol 2 – 3 mg/kg PO q12h.**
   b. If systolic dysfunction is present use **amiodarone 5 – 7.5 mg/kg PO q12h.**

C. Occasional **Ventricular Premature Contractions** (VPC's) or rare couplets.

1. **Furosemide, ACEI** as in **I. A** above.
2. **Digoxin,** for dosage *see Table 1,* or **Pimobendan 0.25 mg/kg PO q12h.** Digoxin can exacerbate ventricular arrhythmias. However, is still a choice, because the arrhythmia may be due to poorly controlled CHF, once CHF resolves this type of arrhythmia has a tendency to improve.
3. **Beta-blocker,** atenolol or metoprolol *see Table 2.*

D. Several VPC's (more than 30% of the total number of beats) and/or runs of ventricular tachycardia.

1. **Furosemide, ACEI, Digoxin or Pimobendan as in I. A above.**

2. Class III antiarrhythmic drug (*see Table 4*)
   - If normal systolic function use sotalol **2 – 3 mg/kg PO q12h.**
   - If systolic dysfunction is present use amiodarone **5 – 7.5 mg/kg PO q12h.**
   - If arrhythmia is still difficult to control change to:
3. **Procainamide** slow release **20 – 30 mg/kg PO q8h.**

II   Atrial Fibrillation

Identification of the true heart rate while in atrial fibrillation can be difficult in some dogs that are very anxious whilst in the clinic. The author prefers to perform a 24 hour Holter ECG to evaluate the heart rate in such cases. The identification of ventricular premature contractions (VPC's) in patients with atrial fibrillation can be difficult due to the variable degree of ventricular conduction aberrancy in dogs with this arrhythmia.

A. **With no or occasional VPC's**
   Combine:
   1. **Furosemide 3 mg/kg PO q8h** initially and titrate to the minimal amount needed to control pulmonary edema. Some dogs may only need q12h; others will need q6h.
   2. **ACEI**
      a. **Enalapril 0.5 mg/kg PO q12h.**
      b. Alternatively, **benazepril, lisinopril** or **ramipril** can be used, at **0.5 mg/kg PO q24h.**
   3. **Positive inotrope:**
      a. If normal systolic function, **digoxin is OPTIONAL.** For dosage *see Table 1*. **Digoxin can exacerbate ventricular arrhythmias.**
      b. If moderate to severe systolic dysfunction, consider using **Pimobendan.**
   4. **Calcium channel blocker (Table 3)** if the diagnosis is DCM.
   5. **Beta-blocker, (Table 2)** if the diagnosis is CMVD.
   6. If unable to reach target heart rate cautiously in 5 – 10 days; discontinue 4 or 5 and commence **amiodarone 5 – 7.5 mg/kg PO q12h. The target heart rate in atrial fibrillation is ~ 150 beats per minute or the lowest the patient can tolerate clinically.**

B. **With several VPC's** (more than 30% of the total beats) and/or runs of ventricular tachycardia, COMBINE IIA ABOVE WITH:
   1. Procainamide (*see Table 4 for other choices*).

MANAGEMENT

CAT

In the cat the management is based on the specific diagnosis of the heart disease and is a continuation of therapy of Life-Threatening CHF.

I   Hypertrophic Cardiomyopathy

A. Sinus rhythm — no arrhythmia.

   Combine:
   1. **Diuretic**
      a. **Furosemide – 1 – 2 mg/kg PO q12–24h** initially and titrate to the minimal amount needed to control pulmonary edema as determined by follow-up radiographs, renal parameters, physical exam and clinical signs (as outlined for the dog above).
      b. **Hydrochlorothiazide at 6.25 – 12.5 PO mg/cat q12h.** The author prefers this diuretic in cases with borderline/mild renal disease. Diuretics in cats may not be needed for long-term management of CHF. Each case needs to be evaluated individually. Over time, try to decrease the dose of diuretic to the lowest possible. Monitoring electrolytes is essential.
   2. **Angiotensin converting enzyme inhibitor (ACEI).**

a. Enalapril – 0.5 mg/kg PO q24h.
  b. Alternatively, **benazepril** or **lisinopril 0.5 mg/kg PO q24h.**
3. Beta-blocker
  a. Atenolol – 6.25 – 12.5 mg/cat PO q12h.
  b. Carvedilol – 3.125 mg/cat PO q12h.
4. Vasodilators (if severe MR and/or concurrent systemic hypertension)
  a. **Amlodipine 0.625 – 1.25 mg/cat** PO q24h. This class is recommend to treat concurrent systemic hypertension, or in cases with moderate to severe mitral regurgitation. This class of drugs is theoretically contraindicated in cats with hypertrophic obstructive cardiomyopathy. The author has used this drug extensively in such cases without noticing any clinical side effects due to decreased afterload. Its primary use is for the treatment of hypertension, or in cases with severe mitral valve regurgitation and HCM.

B. Sinus rhythm with many SVPC's and/or runs of SVT. Also Sinus rhythm with VPC's and/or runs of Ventricular Tachycardia (VT).

  1. Same protocol as in sinus rhythm for the cat, A1–4 but substitute the beta-blocker for:
  2. Class III antiarrhythmic.
    a. **Sotalol – 5 mg/kg PO q12h.**
    Other anti-arrhythmic choices are available, but Sotalol has a broad range of efficacy in cats with both supraventricular and ventricular arrhythmias, therefore is now the drug of choice for the treatment of any arrhythmia in the cat. **Do not use in conjunction with beta-blockers.**

C. Atrial fibrillation

  1. The protocol for sinus rhythm is often enough to control atrial fibrillation ventricular response rate. Our aim is to achieve heart rates in the clinic around 180 beats/minute. If the cat is being treated with a beta-blocker, increase the dose by titrating in 25% increments every 2 – 3 days to effect.
  2. If having difficulty controlling the heart rate to 180 beats/minute, consider changing to sotalol at 5 mg/kg PO q12h.

II Restrictive/Unclassified Cardiomyopathy

A. Sinus rhythm – no arrhythmias:

Combine:
  1. **Diuretic – as in HCM**
  2. **Angiotensin converting enzyme inhibitor – as in HCM**
  3. **Vasodilators – as in HCM**
  4. **Positive Inotropes**
    a. **Digoxin – ¼ of a 0.125 mg tab every other day** for a cat weighing **less than 3 kg** or **¼ of a 0.125 mg tab q24h** for a cat weighing **more than 3 kg.** The elixir preparation is not well tolerated by cats and results in about 50% higher serum concentrations than the tablet formulation.

B. Sinus rhythm with many SVPC's and/or runs of SVT. Also Sinus rhythm with VPC's and/or runs of Ventricular Tachycardia.

  1. Same protocol as in sinus rhythm I, 1 – 4 plus
  2. Class III antiarrhythmic:
    a. **Sotalol – 5 mg/kg PO q12h.**

C. Atrial fibrillation

  1. **Atenolol– 12.5 mg/cat PO q12h** is the best choice.
  2. Alternatively, Sotalol or Diltiazem can be used (*see tables p. 163*).

III Dilated Cardiomyopathy

A. Sinus rhythm – no arrhythmias:

Combine:
1. **Diuretic** – as in HCM and RCM
2. **ACE inhibitor** – as in HCM and RCM
3. **Vasodilators** – as in HCM
4. **Positive Inotropes**
   a. **Digoxin – ¼ of a 0.125 mg tab every other day** for a cat weighing **less than 3 kg** or **¼ of a 0.125 mg tab q24h** for a cat weighing **more than 3 kg.** The elixir preparation is not well tolerated by cats and results in about 50% higher serum concentrations than the tablet formulation.

B. Sinus rhythm with many SVPC's and/or runs of SVT. Also Sinus rhythm with VPC's and/or runs of Ventricular Tachycardia.
1. Same protocol as in sinus rhythm, III 1–4, plus
2. **Class III antiarrhythmic**
   a. **Sotalol – 2.5 – 5 mg/kg PO q12h** (note that this dose is lower than for other types of heart disease in cats).

C. Atrial fibrillation
The protocol for sinus rhythm is often enough to control atrial fibrillation ventricular response rate. Our aim is to achieve heart rates in the clinic around 180 beats/min. If the cat is taking a beta-blocker or calcium channel blocker, increase the dose by titrating the drug to effect. If having difficulty controlling the heart rate to the above value consider changing to **sotalol 2.5 – 5 mg/kg PO q12h (lower dose than for other types of heart disease in cats).**

NOTES TO THERAPY:

- When using **Hydralazine** symptomatic hypotension and reflex tachycardia are less likely to develop if the dose is titrated slowly over 3–4 weeks. If persistent tachycardia is noted, the addition of a beta-blocker drug (if not already included in the protocol) should be considered. If blood pressure monitoring is available the goal is to decrease systolic pressure at least by 20–30 mmHg but no less than a systolic of 100 mmHg, or decreasing mean pressure by 10–20 mmHg but no less than 70 mmHg.
- Optional **digoxin** therapy is based on tolerance. Most patients can benefit. Levels should be assessed at 1 and 3 weeks and ECG performed if necessary. If significant arrhythmia is present, discontinue. If gastrointestinal upset occurs discontinue for 2 days and restart at half dose. If still not tolerated, discontinue. Some dogs or cats may develop intolerance even at sub-therapeutic levels.
- **For dogs,** in **chronic cases,** multiple diuretic therapies may be necessary to control the edematous state. **Hydrochlorothiazide 2–4 mg/kg PO q12h** and/or **spironolactone 2–4 mg/kg PO q12h** may be added. Because of its potency the author prefers to use hydrochlorothiazide as the second diuretic. In recent years the use of spironolactone as a second diuretic has become popular due to the beneficial effects in chronic congestive heart failure. Careful monitoring of renal function is recommended when using multiple diuretics. Cats can be particularly sensitive to the side effects of diuretics, furosemide can induce profound metabolic (alkalosis) and electrolyte changes in some cats, while other tolerate multiple diuretics easily.
- **In the dog,** the use of **amlodipine** at the recommended twice a day doses is standard practice in the author's experience. The author has observed minimal side effects with this dose regimen. One unexpected side effect in 3 dogs was the acute development of polidypsia followed by anasarca-type edematous state. This side effect subsided rapidly (over 24–48 hours) in all cases upon discontinuation of the drug.
- The criteria in classifying the severity of the arrhythmia presented above are established empirically by the author. The true classification of severity of arrhythmias is not established in veterinary medicine, therefore the above criteria are only guidelines and each case should be assessed individually. Consultation with a cardiologist is recommended in most cases, as this will obviate the initiation of potentially dangerous therapy to a specific patient.

PHARMACOLOGY

1) **Furosemide** is a loop diuretic. Can cause metabolic alkalosis and hypokalemia. These side effects are particularly important if the patient is anorexic. Indicated for the treatment of pulmonary edema, pleural effusion and/or ascites due to CHF.

2) **Hydrochlorothiazide** acts primarily in the distal convoluted tubule and it is less potent than furosemide.

3) **Spironolactone** blocks the effects of aldosterone and conserves potassium and magnesium. When using spironolactone in conjunction with ACEI serum potassium levels should be monitored carefully to avoid hyperkalemia.

- Furosemide 1 – 3 mg/kg PO q6–12h
- Hydrochlorothiazide 2 – 4 mg/kg PO q12h
- Spironolactone 2 – 4 mg/kg PO q12h

Overzealous therapy may cause dehydration and exacerbation of pre-existent renal dysfunction.

4) **Enalapril** an **angiotensin converting enzyme inhibitor** (ACEI) is an afterload reducer that also inhibits the production of aldosterone by inhibiting angiotensin II. Inhibition of aldosterone will decrease sodium retention and causes an indirect diuretic effect in CHF. The use of a potassium sparing diuretic (spironolactone) with an ACEI can cause hyperkalemia, monitoring of potassium levels is recommended. Other ACEI such as **benazepril, lisinopril, ramipril** and **captopril,** are available; they all have similar duration of action when compared to enalapril. The use of benazepril in patients with renal dysfunction has been advocated due to its metabolism. In the author's experience the use of ANY drug of this class in patients with renal disease has the potential for adverse effects; therefore, renal parameters should be monitored more frequently in such cases.

5) **Digoxin** is a Na-K ATPase inhibitor, causing calcium overload and a modest increase in contractility. It also has a favorable effect in resetting the baroreceptors in dogs with CHF. Digoxin can cause serious arrhythmias of ANY TYPE. The most common clinical side effects are lethargy and GI signs that indicate overdose, even if blood levels are within normal range. Hypokalemia potentiates the likelihood of intoxication.

6) **Pimobendan** is a benzimidazole-pyridazinone derivative, non-sympathomimetic, non-glycoside inotropic substance with potent vasodilatory effects. Pimobendan increases contractility by increase in calcium sensitivity of the cardiac myofilaments and inhibition of phosphodiesterase (type III). Vasodilatory properties are mediated through inhibition of phosphodiesterase III. Pimobendan is recommended for the treatment of DCM or CMVD with systolic dysfunction. Pimobendan should be used with caution with other positive inotropic agents (digoxin). Pimobendan side effects include GI signs, restlessness, convulsion, polyuria/polydypsia. In the author's experience the side effect profile of this drug is low.

7) **Class I antiarrhythmic** drugs have negative inotropic effects and act by blocking the entry of sodium into the cell. Side effects include GI signs, anorexia, depression, worsening of arrhythmias and with tocainide, corneal edema. Because of the negative reputation that these agents have received from the human literature in the past years, their use is limited to severe cases. The patient should be monitored closely for worsening of the arrhythmia. Procainamide and mexilitine are the most commonly used.
   - Procainamide sustained release: 20 – 30 mg/kg PO q8h
   - Mexilitine: 5 – 10 mg/kg PO q8h

8) **Beta-blockers** (*Class II antiarrhythmic*) are drugs that block the beta-receptors of the adrenergic nervous system. They have negative inotropic properties, protect against the development of serious arrhythmias (especially if sympathetically-mediated), have a beneficial effect in CHF and protect against sudden death. Reports in the human literature show that this class of drugs increases survival in patients with CHF. Side effects include development of hypotension, bradycardia, and heart block. Patients with severe systolic dysfunction, either due to DCM or CMVD, may develop significant side effects with this class of drugs. Careful titration is recommended. Non-selective beta-blockers can cause bronchoconstriction, and are contraindicated in patients with small airway respiratory disease. These drugs are contraindicated if there is evidence of heart block, bradycardia or severe sinus node dysfunction.

9) **Class III antiarrhythmics** are drugs that block the potassium channels resulting in an increase of the repolarization time (increase refractory period), reflected in the surface ECG by a prolongation of the Q-T interval. **Amiodarone** is indicated for the control of ventricular and supraventricular arrhythmias refractory to standard therapy. Amiodarone has slow onset of action and a very prolonged half-life (in man reported to be 25–110 days), therefore an initial loading dose is necessary to achieve faster onset of action. Side effects reported with chronic administration include development of lung fibrosis (not documented in veterinary medicine) thyroid dysfunction and hepatic toxicity amongst others. In dogs it appears that the most serious side effect is liver damage resulting in increase in liver enzymes. Therefore while using amiodarone baseline liver values followed by rechecks every 2–3 months are recommended. The author has seen several cases that developed tremors due to this drug. During chronic therapy it is recommended to assess thyroid function twice a year. **Sotalol** is another Class III agent with strong Class II (beta-blocker) properties. A dose reduction by 50% is recommended in patients in congestive heart failure. Sotalol is quite effective to control atrial fibrillation rate and ventricular arrhythmias. Its side effects are similar to the beta-blockers. In cases with severe left ventricular dysfunction this drug is very poorly tolerated. These drugs are contraindicated if there is evidence of heart block, bradycardia or severe sinus node dysfunction.

10) **Calcium-channel blockers (Class IV antiarrhythmic)** block the entry of calcium into the cell; all types of calcium channels are sensitive to the effects of calcium channel blockers. Calcium channel blockers have negative inotropic properties (not as pronounced as beta-blockers), slow the sinus node rate and slow conduction through the AV node. They also promote vascular smooth muscle relaxation and improve coronary blood flow. Clinically, the most important side effects are reduction of heart rate and contractility. **Diltiazem** and **Verapamil** may increase digoxin blood levels in human patients; therefore caution is advised when using these drugs in combination. This has not been observed in the veterinary medicine. Calcium channel blockers potentiate the negative chronotropic effects of beta-blockers; caution is also advised when these drugs are combined. These drugs are contraindicated if there is evidence of heart block, bradycardia or severe sinus node dysfunction. **Amlodipine** is a calcium channel blocker with primary vascular smooth muscle action, and may be used successfully as a vasodilator. Amlodipine has minimal effects in myocardial electrical potential. It is well tolerated in dogs.

SUGGESTED READING

1. Kienle RD, Kittleson MD. Drugs used in the treatment of cardiac arrhythmias. In: Kittleson MD, Kienle RD. Small Animal Cardiovascular Medicine. St Louis: Mosby, 1998:502–524.
2. Kienle RD, Kittleson MD. Management of Heart Failure. In: Kittleson MD, Kienle RD. Small Animal Cardiovascular Medicine. St Louis: Mosby, 1998:149–194.

DRUG DOSAGE IN CHRONIC CONGESTIVE HEART FAILURE – Dogs

TABLE 1. Digoxin

BODY WEIGHT	TOTAL ORAL DOSE
> 40 kg	0.125 – 0.25 mg q12h
25 – 40 kg	0.125 mg q12h
15 – 25 kg	0.0625 mg q12h
5 – 15 kg	0.0315 mg q12h
< 5 kg	0.03125 mg q24h

Note: Non-selective beta-blockers may have an increased efficacy in preventing sudden death. When starting therapy with these classes of drug choose the low dose and titrate every 1–2 week by increasing the dose 25–33% each time. Dogs with DCM have a higher sensitivity to beta-blockers, therefore be extremely careful.

TABLE 2. Beta-Blocker Drugs

DRUG	ORAL DOSE	BETA 1 SELECTIVITY
Atenolol	6.25 – 50 mg total q12–24h	YES
Metoprolol	5 – 50 mg total q8h	YES
Propranolol	0.25 – 1.0 mg/kg q8h	NO
Carvedilol (CAT ONLY)	0.5 – 0.7 mg/kg PO q12h	NO

Note: The desired digoxin blood level at trough (immediately prior to next dose, exactly 12h after last dose) is 1.0 – 2.0 ng/dl. Dobermans appear to be particularly sensitive to the side effects of digoxin, for them I recommend levels between 0.8 – 1.5 ng/dl. Always titrate the dose based on blood levels and clinical signs.

TABLE 3. Calcium Channel Blockers

DRUG	ORAL DOSE
Diltiazem	1 – 3 mg/kg q8h
Verapamil	0.5 – 1.0 mg/kg q12h–q8h
Amlodipine	0.2 – 0.5 mg/kg q12h

Note: Diltiazem is currently the drug of choice for supraventricular arrhythmias. Start at a low dose and titrate. Verapamil has been associated with adverse, sometimes fatal, reactions in small dogs. Amlodipine (Norvasc®) is a calcium channel blocker with only vascular smooth muscle action. It does not affect velocity of conduction of the action potential in the heart, and therefore has minimal negative chronotropic action. Amlodipine is a vasodilator and it is primarily used for the treatment of systemic hypertension, or to further reduce afterload in cases with advanced mitral valve regurgitation.

TABLE 4. Antiarrhythmics CLASSES I & III

DRUG		ORAL DOSE
Procainamide – SR	Class I	20 – 30 mg/kg PO q8h
Mexilitine	Class I	5 – 10 mg/kg PO q8h
Tocainide	Class I	10 – 20 mg/kg PO q8h
Amiodarone	Class III	5 – 7.5 mg/kg PO q12h
Sotalol (Dog dose)	Class III	2 – 3 mg/kg PO q12h
Sotalol (Cat dose)	Class III	5 mg/kg PO q12h

CAUTION: These drugs have the potential to exacerbate arrhythmias and have been associated with an increased rate of sudden death in human studies. Use only if absolutely necessary.

INTRODUCTION

Bradyarrhythmias may be asymptomatic or may cause weakness or syncope. Sinus rates of 60 (or less) beats per minute (dogs) and 120 (or less) bpm (cats) are frequently quoted as bradycardia. This number alone, particularly in dogs, should be interpreted in light of the patient's condition. If the patient is asleep and in sinus rhythm with good peripheral pulses (blood pressure), then this is normal. Some large breed or athletic dogs will have resting sinus rates <50 bpm. Heart rates measured using Holter ECG monitoring have ranged from 30 – 40 bpm in normal sleeping dogs. Ventricular escape beats may be present in this setting. This should not be treated as the heart rate is appropriate for the patient's condition. If the slow heart rate is inappropriate (patient is symptomatic), then the underlying cause should be elucidated and managed accordingly. Bradyarrhythmias may be due to primary cardiac conduction system disease, secondary to more generalized myocardial or valvular disease, or secondary to extracardiac factors such as high vagal tone (i.e., respiratory disease), metabolic or endocrine disorders.

DIAGNOSIS

History & Signalment

Obtain a complete history, which should include questions related to level of activity, appetite etc., which might relate to primary cardiac disease. Some breeds are predisposed to bradyarrhythmias (i.e., miniature schnauzers with sick sinus syndrome, Springer Spaniels with atrioventricular muscular dystrophy). Include questions investigating non-primary cardiogenic causes of bradycardia listed below:

- Hyperkalemia (*etiology: Renal Failure p. 709 , Urethral Obstruction p. 746, Hypoadrenocorticism p. 275*)
- Administration of opiates (*see Analgesics and Sedatives p. 81*)
- Acepromazine (*see Analgesics and Sedatives p. 93*)
- Digoxin toxicity (*see p. 162*)
- Alpha2 agonists (*see p. 94*)
- Calcium channel blocker or beta-blocker overdose
- Subtherapeutic dose of atropine (transient)
- Substances of abuse i.e., hashish, marijuana (*see p. 653*)
- Hypothyroidism (*see p. 285*)
- Respiratory disease or brachycephalic syndrome
- Gastrointestinal diseases/pain/surgery
- Recent head trauma (*p. 691*) or other intracranial disease (tumour, encephalitis). Elevated intra-cranial pressure can cause a bradyarrhythmia
- Hypothermia (*see p. 291*)
- Severe systemic hypertension (*see p. 205*)
- Severe, late hypoxia (*see p. 555*)
- Vagal stimulation (central or peripheral)
- Hypercalcemia (primary or secondary occult neoplastic disease) may be associated with A-V block

Clinical Signs/Physical Examination

Clinical signs and physical examination will vary depending on the underlying cause of the bradycardia.

- Bradycardia may be an incidental finding in a non-athletic, otherwise normal animal with no clinical signs, yet still be primary cardiac in origin (prodromal phase of cardiac disease below); the femoral pulses are slow but strong.
- Some patients may occasionally appear lethargic or exercise intolerant and have episodes of disorientation, weakness and/or syncope. The syncopal episode may have the appearance of generalized seizure.
- Some dogs with chronic bradyarrhythmias present with ascites.
- With sick sinus syndrome, frequently seen in miniature schnauzers, weakness and syncope and associated sinus arrest, escape rhythms and possible supraventricular tachycardia, may be present.

Laboratory/Imaging Evaluation

This will depend on the history and possible etiologies for bradycardia noted above, but should include:

- **Serum electrolytes** to rule out hyperkalemia (*see p. 396*).
- **Arterial blood gases** where appropriate to assess oxygenation (*see p. 580*).
- **Biochemical profile** to assess organ function and serum calcium concentration (*see Hypercalcemia p. 373*).
- **ECG** diagnosis and monitoring is essential.
    - ECG findings may just be a **slow sinus rhythm or sinus arrhythmia** especially in the athletic or sleeping large breed dog

⇒ **Sick sinus syndrome** ECG findings (Fig. 1) are of a slow, irregular sinus rhythm with short or long pauses of sinus arrest or sinoatrial block, with or without escape beats (⬆). Other findings may include 1st and 2nd degree heart block, ectopic atrial beats or junctional beats/rhythms, or periods of supraventricular tachycardia may follow (bradycardia-tachycardia syndrome).
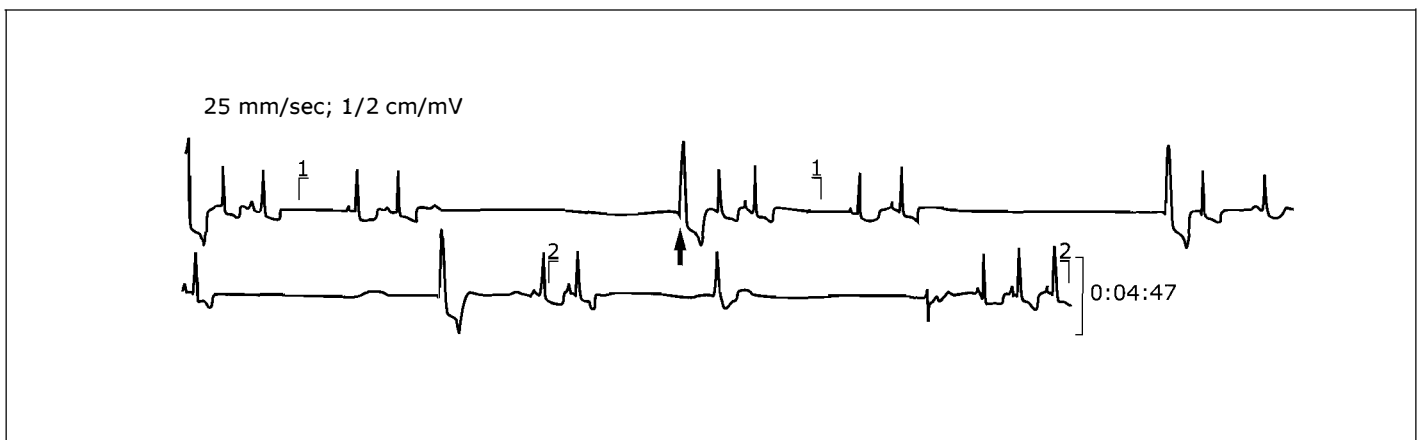
FIGURE 1. Sick Sinus Syndrome.

⇒ **Atrial standstill** is uncommon but is associated with atrioventricular muscular dystrophy. It is seen most commonly in Springer spaniels but may occur in any breed, chronic dilated cardiomyopathies and atrial myocarditis. ECG findings (Fig. 2) are absent P waves with a slow (<60 bpm) and regular ventricular rate. The QRS complexes may be of nearly normal configuration if supra-ventricular in origin or wide and bizarre if ventricular in origin or if a bundle branch block is present.
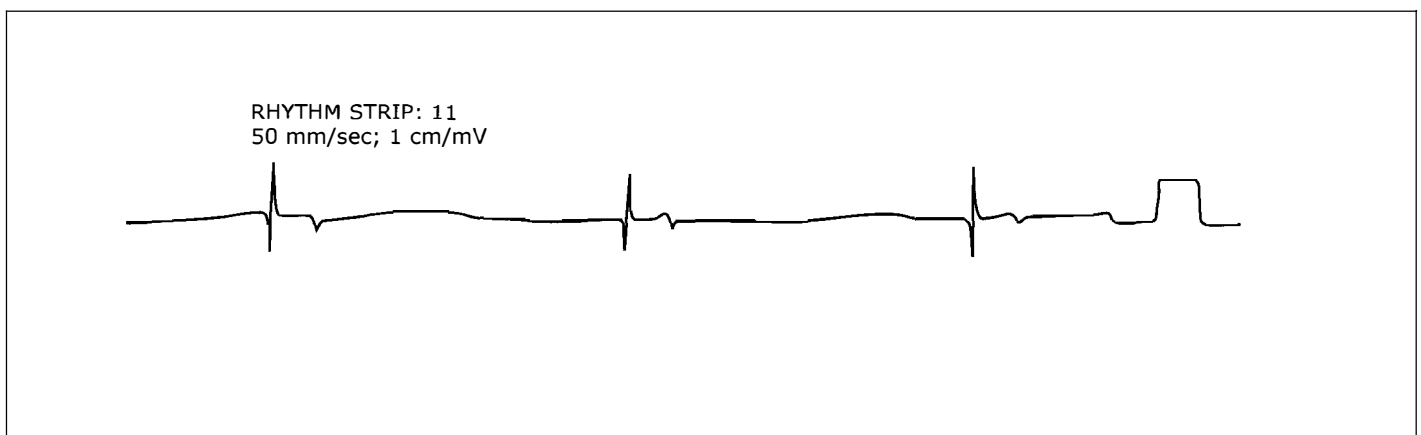
FIGURE 2. Atrial Standstill.

⇒ **First degree A-V block,** is often secondary to non-cardiac causes, and is frequently self-limiting with treatment of the underlying cause (i.e., electrolyte disturbance, high vagal tone). The main ECG finding in 1st degree A-V block is a prolonged PR interval (>0.13 seconds in dogs, >0.09 seconds in cats) similar to that in Fig. 3 (↑). The P-R interval can be variable in dogs with sinus arrhythmia.

⇒ **Second degree (Mobitz Type 1, Wenckebach) A-V block,** may be a normal finding, especially in young dogs, or secondary to non-cardiac causes. It is frequently self-limiting with treatment of the underlying cause (i.e., electrolyte disturbance, high vagal tone, digoxin toxicity). The main ECG findings (Fig. 3) include a P wave not followed by a QRS complex (⇑) (atrial rate faster than the ventricular rate), the QRS complexes are usually of normal duration and morphology and the P-R interval progressively prolongs just prior to the blocked P wave (▲) and this P-R interval is longer than that occurring immediately after the block.
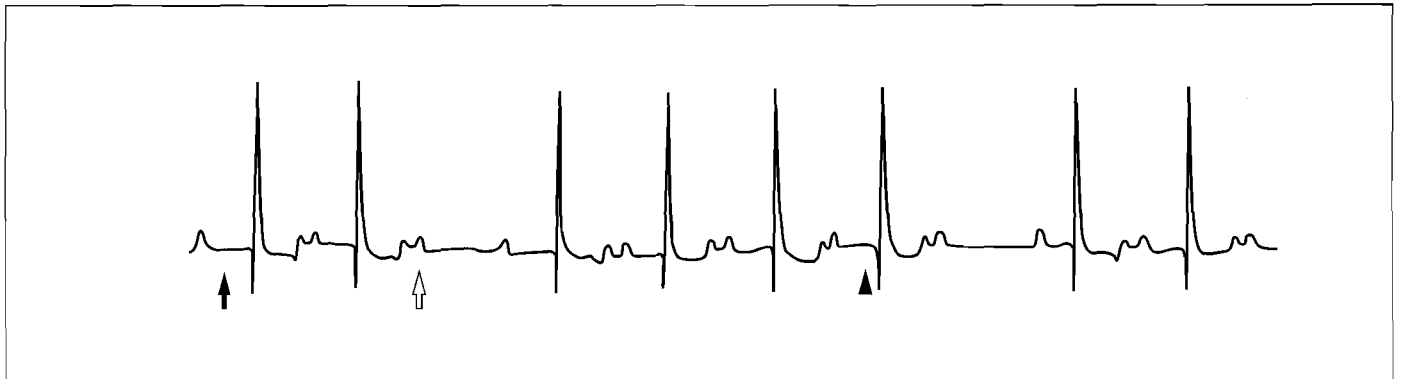
FIGURE 3. Second degree HB Mobitz 1.

⇒ **Second degree (Mobitz Type II) A-V block** is often associated with severe cardiac conduction pathway disease, drug intoxication (low dose atropine, digoxin toxicity, xylaine) or electrolyte disturbance. ECG findings (Fig. 4) include blocked P waves (↑) (atrial rate >ventricular rate), and a constant P-R interval for those beats that are conducted (QRS complexes are associated with the P waves).
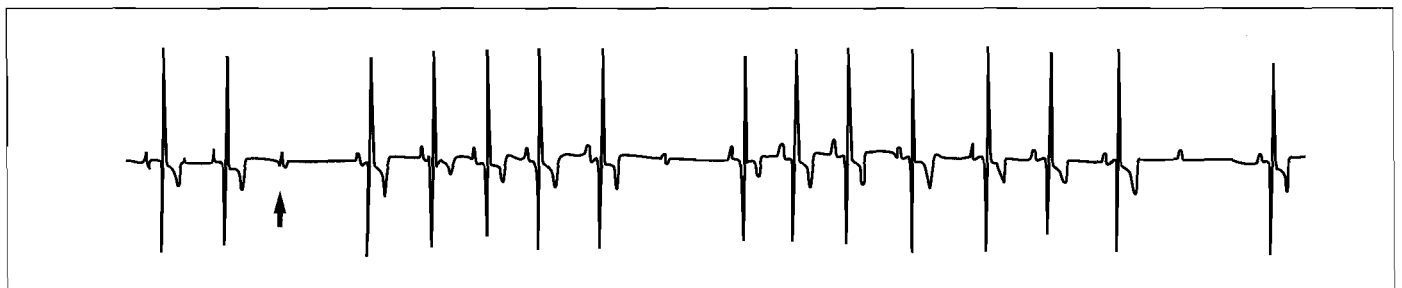
FIGURE 4. Second degree HB Mobitz 2.

⇒ In **high grade 2nd degree A-V block** there are many blocked P waves (i.e., 3 or more P waves to each QRS, **3:1 or 4:1** ↑) in Fig 5. Again, the P-R interval is fairly constant.
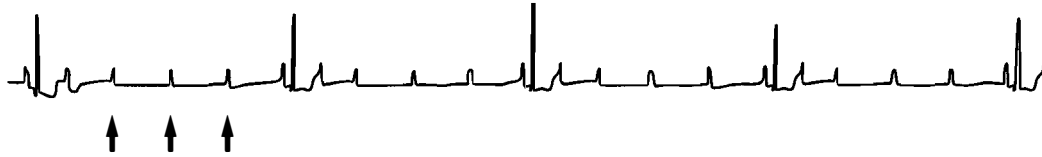
FIGURE 5. High grade Second degree A-V block.

⇒ **Third degree A-V block** is often associated with severe cardiac conduction pathway disease or drug intoxication. ECG findings (Fig. 6) include P waves ↑ that bear no relationship to a slow and regular ventricular rate ⇔ (P waves and QRS complexes are dissociated thus the P-R intervals are highly variable). The QRS configuration is wide and bizarre if the rescue pacemaker is either in the ventricle or the lower A-V junction with bundle branch block, or it is normal when the rescue pacemaker is above the bifurcation of the bundle of His without bundle branch block.
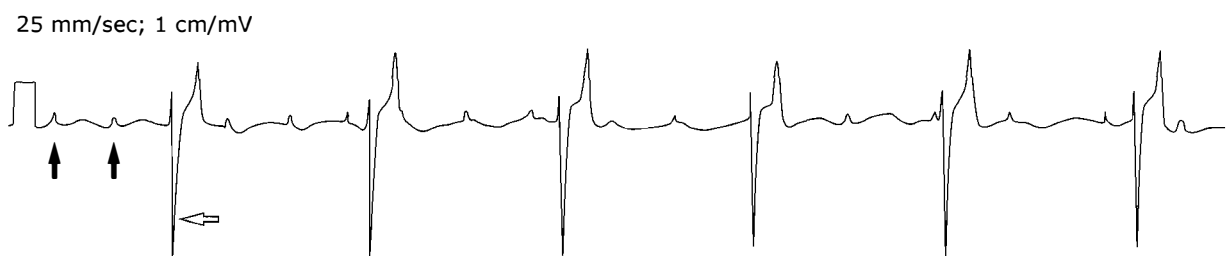
FIGURE 6. Third degree A-V block.

Extended Laboratory/Imaging Data Base

- As indicated based on possible etiologies of bradycardia.

A. In life-threatening situations, (except *hypothermia p. 291, hypothyroidism p. 285, hypoxia p. 581, hyperkalemia p. 396*), treat bradyarrhythmias with atropine **0.04 – 0.06 mg/kg IV** while investigating the underlying cause of the problem. Treat the underlying cause. If hyperkalmic, *see Hyperkalemia p. 397* as management will be dependent on degree of hyperkalemia. If electrolytes cannot be measured to confirm hyperkalemia, atropine treatment can still be instituted; an increase in heart rate with return of P waves may occur.

YOU MUST RULE OUT ALL EXTRA-CARDIAC CAUSES OF BRADYCARDIA PRIOR TO CHRONIC TREATMENT FOR PRIMARY CARDIAC DISEASE.

B. Bradycardia associated with PRIMARY CARDIAC DISEASE. Sustained bradycardia associated with symptoms (i.e., weakness, syncope, collapse), requires treatment **with**

1. **atropine 0.04 – 0.06 mg/kg IV** (if non-responsive to atropine go to (C) below). Most cases of high grade 2nd and 3rd degree A-V block are not responsive to atropine. Some dogs with sick sinus syndrome are partially or totally responsive, others are non-responsive. If responsive to atropine, its continued use is not recommended; the underlying cause of excess vagal tone or cardiac problem should be investigated and treated appropriately.

2. Chronic therapy
   a. Oral **anticholinergics such as propantheline (dogs 7.5 – 30 mg/dog PO q8–12h)** may benefit those responsive to atropine. Alternatively,
   b. **Terbutaline 0.2 mg/kg PO q12h in dogs** OR
   c. **Theophylline 4 – 6 mg/kg PO q8–12h** of regular acting **OR 20 mg/kg PO q12h** of long-acting (**Theo-dur®**).

C. In atropine- refractory bradycardia associated with severe signs (i.e., profound hypotension and collapse) consider

1. **Isoproterenol, 0.01–0.1 μg/kg/min. (dogs and cats). For ease of administration, mix 0.2 mg/mL ampule in 500 mL 5% dextrose and administer at 0.1 – 0.2 mL/kg/min.** Start at the low dose and titrate up in small increments every 5 mins to effect. BEWARE, CAN CAUSE SEVERE HYPOTENSION, VPC's and VENTRICULAR TACHYCARDIA. **If this doesn't work, try**

2. **Dopamine 4 – 6 μg/kg/min initially increasing to 7 – 15 μg/kg/min or to effect.** The high dose, 10 – 15 μg/kg/min may compromise renal function due to alpha effects of vasoconstriction.
   These are all temporary therapies.

3. **Electrical pacing of the ventricle** is the permanent treatment of choice for chronic high grade 2nd degree, or 3rd degree AV block.

D. If the bradycardia is **SECONDARY TO OPIATE USE,**

1. **Glycopyrrolate 0.01 mg/kg** (small and medium dogs or cats) or **0.005 mg/kg** (large dogs), or to effect **max 0.01 mg/kg**. Glycopyrrolate takes a few minutes for full effect to occur but does not result in a potential tachycardia when compared to atropine and lasts longer than atropine. Do not reverse the opiate if the patient is painful. Pain can still be present even with a bradycardia.

2. If bradycardia is life-threatening and/or is accompanied by poor peripheral pulses (establish if the patient is hypotensive) then reverse opiate by titrating with **naloxone 0.1 mL or 0.25 mL (0.4 mg/mL solution) diluted in 10 mL saline, administer at 1 mL increments** until the bradycardia is improved. With this technique, analgesia will not be abolished. Should more naloxone be required, such as to treat an inadvertent overdose, a more rapid but cautious administration should be given (*see Opiate Reversal p. 85*).

   If still painful after reversal, consider giving a different class of analgesic such as a non-steroidal anti-inflammatory analgesic (i.e., **meloxicam 0.1 – 0.2 mg/kg cat and dog; carprofen 4.0 mg/kg dogs; ketoprofen 2.0 mg/kg cat and dog, if not contraindicated** (*see Analgesics and Sedatives p. 87*).

PHARMACOLOGY

1) **Atropine** is a parasympatholytic (vagolytic), anticholinergic agent and is indicated for the treatment of sinus bradycardia, sinus block or arrest. It acts both centrally and peripherally. Duration of action is approximately two hours.

2) **Glycopyrrolate** is an anticholinergic drug which protects the heart against excessive vagal stimulation. Duration of action is similar to atropine.

3) **Isoproterenol** is a sympathomimetic drug producing a $beta_1$ and $beta_2$ adrenergic response increasing the heart rate and atrioventricular conduction. Requires dilution and titration to effect. Hypotension and tachyarrhythmia may occur with use.

4) **Dopamine** in this protocol is a sympathomimetic drug with both dose-dependent alpha and beta effects. An increase in both systolic and diastolic pressure may be noted with high dosage due to alpha stimulation, however, this can be variable.

5) **Terbutaline** is an oral $beta_2$ agonist.

6) **Theophylline** is a phosphodiesterase inhibitor.

SUGGESTED READING

1. Lunney J., Ettinger SJ. Cardiac Arrythmias. In: Ettinger SJ. (ed). Textbook of Veterinary Internal Medicine 4th Edition, Toronto, WB Saunders 1995:959-995.
2. Rishniw M, Thomas WP. Bradyarrhythmias. In: Bonagura JD (ed). Kirk's Current Veterinary Therapy XII: Small Animal Practice. Philadelphia, WB Saunders, 2000:719-725.

NOTES

INTRODUCTION

Supraventricular tachycardia (SVT) includes any tachyarrhythmia originating proximal to the bifurcation of the bundle of His. Ventricular activation occurs via the normal His-Purkinje system and as such, the QRS complex is often normal in appearance. SVT can conduct with aberration, therefore may be manifest as a wide QRS tachycardia as well. SVT can be caused by many pathologic and functional conditions that affect the atria, sinus and atrio-ventricular (AV) nodes. SVT occurs most commonly in the setting of advanced structural heart disease in veterinary patients, however, significant respiratory, inflammatory, neoplastic, endocrine and metabolic disorders, trauma and drug toxicity can also result in SVT. SVT does occur in structurally normal hearts in the absence of systemic disorders as well, such as SVT caused by accessory AV pathways. Increased vagal stimulation, increased catecholamines (pain), physical and emotional stress, and exercise can also result in supraventricular arrhythmias. Dogs present more commonly with SVT than cats. SVT, including atrial fibrillation, can occur in cats with cardiomyopathy and marked atrial dilation. SVT has been noted in cats with structurally normal hearts as well. SVT is less likely to lead to sudden cardiac death than ventricular tachyarrhythmias (VT), however, SVT with rapid ventricular rates can cause hypotension, collapse and death. Rapid SVT may increase the liability to ventricular arrhythmias because of the associated increases in circulating catecholamines and myocardial ischemia. Longstanding paroxysmal or incessant SVT can lead to myocardial failure (tachycardiomyopathy) and ultimately congestive heart failure. In patients with advanced heart disease, the development of atrial fibrillation typically marks the onset of clinical deterioration.

DIAGNOSIS

History/Signalment

- History and physical examination should explore the possibility of underlying structural heart disease (dilated cardiomyopathy, mitral valve insufficiency in dogs, hypertrophic, restrictive or dilated cardiomyopathy in cats, congenital heart defects, tachycardiomyopathy), congestive heart failure or systemic disorders that may predispose the heart to SVT.
- Current medications, especially antiarrhythmic drugs, must be recorded.
- Digoxin toxicity should be ruled out in all cases.
- Clinical signs described by the owner may include weakness, lethargy, exercise intolerance, syncope, collapse and tachypnea/hyperpnea.
- Inappetance, salivation and vomiting are sometimes associated with the initial presentation.

Clinical Signs/Physical Examination

- Heart rates ≥160 bpm in dogs, ≥180 bpm in small dogs, ≥220 bpm in cats are considered "tachycardic".
- Patients presenting with SVT may show mucous membrane pallor, signs of congestive heart failure (tachypnea, pulmonary crackles, jugular venous distension, organomegaly, ascites), weak femoral pulses and signs of underlying heart disease (heart murmur, gallop).
- The presence of "cannon A waves" in the jugular venous pulse (retrograde flow after atrial contraction against a closed tricuspid valve) suggests AV dissociation, as does variable blood pressure and variable intensity of first heart sound (S1) during an otherwise regular rhythm.
- Atrial fibrillation has an irregularly irregular rhythm, described as sounding like "*shoes in a clothes dryer*", although irregular ventricular arrhythmia can sound similar.
- Hypothermia is frequently present due to poor perfusion.

Laboratory Evaluation/Diagnostic Imaging

Stat

These tests are performed to assess the adequacy of peripheral perfusion and to detect the presence of underlying disorders that may cause or exacerbate SVT. Metabolic acidosis (*see Acid-Base p.* 406), reduced venous oxygen tension (<25 mmHg), azotemia, reduced urine production and hypothermia all indicate inadequate perfusion of the peripheral tissues due to reduction of cardiac output and hypotension. These abnormalities are difficult to correct if rapid heart rates can not be controlled.

- **PCV, TP.** Anemia will have a profound effect on oxygen delivery to the myocardium. Polycythemia may be present due to chronic hypoxemia (e.g., congenital right-to-left shunting heart defects, respiratory disease) and substantially impair peripheral perfusion. Decreased TP and PCV may reflect increased total body water due to ADH secretion; ADH secretion occurs in response to a low effective circulating blood volume.
- **Urea, Creatinine** may be increased due to systemic hypotension and peripheral vasoconstriction (pre-renal azotemia) resulting in reduced GFR.
- **Electrolytes** may be altered in heart disease, especially with chronic diuretic use. **Hyponatremia** (*see Hyponatremia p. 386*) is a poor prognostic indicator. Although total body sodium is increased in heart disease, a dilutional effect of ADH may lower serum sodium. Co-morbid conditions such as sepsis, peritonitis and other low effective circulating volume conditions should be investigated if primary heart disease is not evident. **Hypokalemia** (*see Hypokalemia p. 394*) can facilitate atrial and ventricular arrhythmias and should be corrected. Many antiarrhythmic drugs depend on normal serum potassium levels for optimal function. Ectopic rhythms are rare with moderate hyperkalemia (5.5 – 7.5 mEq/L) due to its antiarrhythmic effects. Very high levels of potassium are life-threatening (*see Hyperkalemia p. 396*).
- **Blood gases** are important to assess pH, P_vO_2, SAO_2 or P_aO_2. Arterial hypoxemia and metabolic acidosis can precipitate or exacerbate arrhythmias. Reduced P_vO_2 (<25 mmHg) indicates increased tissue oxygen extraction due to inadequate oxygen delivery or inadequate oxygenation of the blood (decreased P_aO_2).
- **Glucose** Hyperglycemia may be present due to catecholamine release. Hypoglycemia may be associated with sepsis or insulinoma. Weakness, collapse and tachycardia due to insulinoma could mimic the clinical manifestations of SVT.
- **Blood pressure** is usually low due to the arrhythmia. Mean blood pressure ≥60 mmHg is required to maintain renal perfusion.
- **EKG** is required to characterize the arrhythmia and record an accurate heart rate (*see below*). **NOTE: If cardioversion or CPR may be considered due to the condition of the animal, do NOT use alcohol.**

Extended Laboratory/Imaging Data Base

Treatment strategies depend on whether there is evidence for structural heart disease, congestive heart failure (pulmonary edema, pleural effusion, ascites) and/or underlying systemic disorders. Additional diagnostics may be required if systemic disorders are suspected. When these tests are performed will depend on the hemodynamic stability of the patient and the risk of sudden death. Sudden cardiac death is more likely in patients with advanced heart disease and/or rapid heart rates (>300 bpm). In high risk patients thoracic radiographs and echocardiography may have to be performed after initial attempts to stabilize the patient. Treat as if underlying heart disease were present in these cases.

- **CBC** may reflect systemic inflammatory disorders, anemia or polycythemia.
- **Biochemical profile** may show elevated liver parameters due to passive congestion of the liver as well as azotemia, hypoproteinemia.
- **Thoracic radiographs** are helpful to determine if structural heart disease is evident (cardiac enlargement) and if congestive heart failure is present (pulmonary edema, pleural effusion). Other pulmonary infiltrates would imply serious respiratory/systemic disorders that could secondarily result in arrhythmias (e.g., bacterial pneumonia, fungal disease, neoplasia).
- **Echocardiography** is necessary to determine the presence and type of structural heart disease and the adequacy of myocardial function. This may aid in the management the underlying cardiac condition as well as determining prognosis.
- **EKG is required to diagnose SVT!**
EKG should be run in multiple channels (9 leads is ideal) and some segments should be recorded at 50 mm/s to aid in the identification of P waves and to facilitate accurate measurement of the QRS complex duration. It is important to try and differentiate SVT from VT because in the presence of underlying heart disease, the prognosis of a patient with VT is worse than the prognosis of a patient with SVT. In addition, administration of drugs often used in the treatment of SVT (e.g., calcium channel blockers) can cause severe hemodynamic deterioration in patients with VT, resulting in hypotension and ischemia and possibly precipitating ventricular fibrillation. The following criteria should be examined when attempting to differentiate SVT from VT:

Morphology of QRS Complex
1. If the QRS is narrow (≤0.05s in small dogs, ≤0.06s in large dogs, ≤0.04s in cats), then high probability the arrhythmia is SVT. If QRS is wide, see below.
2. If the QRS looks 80 – 90% like the sinus beats then it is most likely SVT.
3. QRS alternans (beat-to-beat oscillation in the amplitude of the QRS) occurs in several types of SVT, probably due to subtle beat-to-beat variation in His-Purkinje refractoriness resulting in subtle beat-to-beat aberration in the QRS. QRS alternans is more commonly associated with pericardial effusion, which should be ruled out (*see Pericardial Effusion/Cardiac Tamponade p. 145*).

Association of P Waves and QRS Complexes

1. Are P waves visible? Look in 9 leads! If so, do they have a fixed association with the QRS complex? If P waves are associated, then the rhythm is supraventricular in origin. P waves are different from "sinus" P waves.
2. If the P wave occurs halfway between the R-R interval, then suspect SVT with 2:1 block (atrial tachycardia, atrial flutter). If there is AV dissociation, then rhythm is most likely ventricular in origin. The atrial rate is typically less than the ventricular rate when AV dissociation occurs during tachycardias.
3. If P waves cannot be identified, they may be buried within the QRS or T wave. This can occur with some SVTs and VT. Altering the heart rate or breaking the tachyarrhythmia with vagal maneuvers can help to reveal the presence of atrial activity and its association with the QRS. While vagal maneuvers rarely affect VT (occasionally they may break VT), they may slow the sinus rate and reveal AV dissociation.

Regularity of the R-R Interval

1. SVTs are often very regular. At rapid heart rates, any irregularity constitutes an "irregular" R-R. Therefore, a regular, narrow complex tachycardia has a very high probability of being supraventricular in origin.
2. Irregular SVTs occur when there is variable conduction through the AV node (atrial fibrillation **AF**, atrial flutter **AFL**, atrial tachycardia **AT**) or multifocal atrial tachycardia (atrial activation from variable sites within the atria).
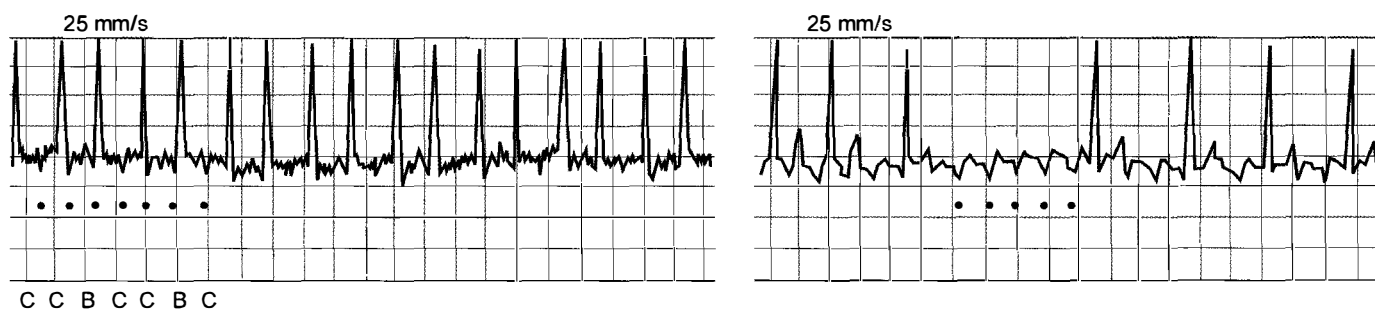
FIGURE 1.   (i) Pretreatment   (ii) Treatment   Diltiazem IV

EKG from a dog with atrial flutter (HR=220 bpm). The pretreatment trace shows a regularly irregular narrow complex tachycardia as a result of 3:2 conduction block. Atrial activity (F waves) are hard to distinguish, however, after increasing AV node block with diltiazem, the atrial activity is easily visualized (atrial rate 330 bpm) and the ventricular response slowed. Each period marks the atrial activity (F wave), C=conducted and B=blocked F wave.
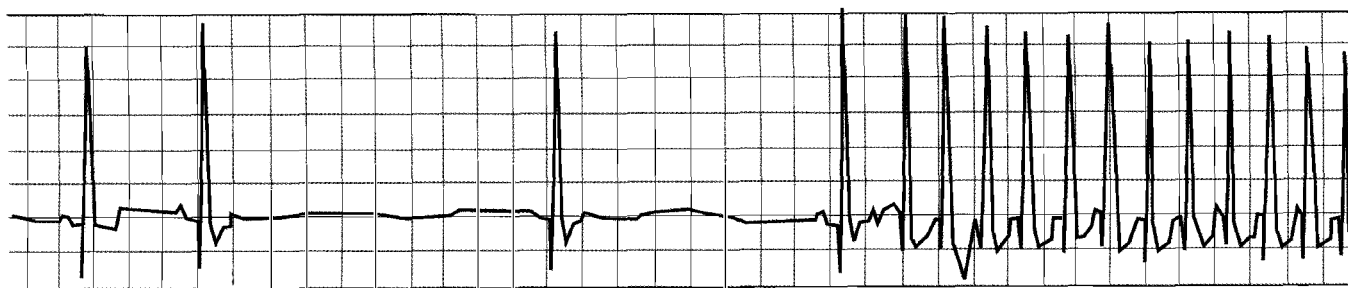
FIGURE 2.

EKG from a dog with a paroxysmal rapid, regular, narrow complex SVT. The 1st four beats represent sinus rhythm resulting from an injection of phenylephrine that broke the SVT, which resumed shortly thereafter. This represents an AV node-dependent arrhythmia, atrio-ventricular reentrant tachycardia (AVRT) caused by an accessory pathway. A negative P wave resulting from retrograde activation of the atria via the accessory pathway is inscribed in the ST segment of the 2nd, 3rd and 4th sinus beats and during the SVT.

Wide QRS tachycardias

Causes of wide QRS tachycardia

1. SVT with functional (rate-related) bundle branch block (BBB).
2. SVT with rate related BBB associated with class Ia and Ic drugs (that have the property of use dependency – prolonged conduction associated with higher heart rates).
3. AVRT (ventricular pre-excitation associated with antegrade conduction over an accessory pathway).
4. Pre-existent BBB.
5. VT.

The following table lists general guidelines that will differentiate SVT from VT in many cases. Exceptions occur for every criterion listed, however. If two of the 1st three criteria (*) are met for SVT or VT, then the probability of that type of arrhythmia is very high. Sustained wide QRS tachycardias in which P waves are not evident cannot be reliably classified as supraventricular or ventricular.

TABLE 1. Differentiation of Supraventricular and Ventricular Arrhythmias

Supraventricular		Ventricular
Narrow	Width of QRS*	Wide
No	A-V dissociation*	Yes
No	Fusion beats*	Yes
No	Intermittent sinus capture	Yes
Termination of SVT or Block	Vagal maneuver	No response
No	Response to lidocaine	Yes
Uniform	Morphology of QRS	Subtle to marked variation
No	ST-T wave variation	Yes
Regular	R-R interval	Slightly irregular

Response to vagal maneuvers

1. Increase in vagal tone may profoundly alter SVT. Vagal maneuvers include applying digital pressure to the eye, carotid sinus massage and deep inspiration that can be achieved with transient occlusion of respiration. Carotid sinus massage is performed by placing the dog in lateral recumbency. The carotid pulse is palpated behind the angle of the jaw on the right and left side of the neck. Firm pressure is applied over the carotid arteries for 5 – 10 seconds by moving the fingertips back and forth in a cranio-caudal direction. Stimulation of the baroreceptors of the carotid sinus should result in increased efferent parasympathetic output to the heart and withdrawal of sympathetic tone, slowing the sinus rate and AV nodal conduction and causing peripheral vasodilation. In dogs with high sympathetic stimulation, these vagal maneuvers are often ineffective.
2. Pharmacologic vagal maneuvers can be achieved with **IV phenylephrine (Neo-Synephrine 10 mg/mL, 1 mL ampoules) given at 0.01 – 0.04 mg/kg IV.** Phenylephrine is an alpha-1 adrenergic agonist that causes transient arterial vasoconstriction and systemic hypertension. Resultant baroreceptor stimulation results in increased vagal tone and sympathetic withdrawal. SVTs that are independent of the AV node (e.g., **AT, AF, AFL**) can be shown to persist in the presence of AV block (Fig. 1). SVTs that are dependent on the AV node will be terminated (e.g., atrio-ventricular reentrant tachycardia **AVRT**) (Fig. 2). The effects of phenylephrine are brief and thus it is used primarily for diagnostic purposes. Occasionally, after termination of the arrhythmia, a profound pause (5 seconds plus) can occur before the resumption of sinus rhythm or the SVT. Use of phenylephrine is not reported in cats.

Treatment goals include

- Correction of the underlying disease if possible. **Note:** Sinus tachycardia is usually an appropriate response to pain, fear, anxiety behaviour *p. 109, Analgesia p. 83/Pain Assessment p. 117* or hypotension (*see Fluid Therapy p. 352*) and should not be treated specifically. Management of the underlying etiology will result in heart rate control, (e.g., sinus tachycardia resulting from cardiac tamponade is appropriate – slowing the heart rate could result in cardiovascular collapse. Resolution of tamponade will result in an almost immediate drop in heart rate (*see Pericardial Effusion/Cardiac Tamponade p. 147*).
- Return of hemodynamic stability (*see Fluid Therapy p. 351*).
- Conversion of SVT to sinus rhythm, with prevention of recurrence.
- Decreasing the ventricular rate response if conversion is unsuccessful or impractical. Target heart rates will depend on the status of myocardial function.

In general, SVTs should be treated

- If the ventricular response rate is elevated >200 bpm (>220 bpm in cats) in sustained paroxysms or incessantly (occurring for greater than 50% of the day).
- If congestive failure is present.
- When the patient displays associated clinical signs.
- When the risk for the arrhythmia to degenerate into a fatal rhythm is high (advanced heart disease, hemodynamic instability, rapid ventricular response >250 bpm).

NOTE: Dogs with hemodynamic instability or ventricular rates >250 bpm should be considered critical and aggressive parenteral drug therapy should be initiated (*see below*). Owners should be warned that beneficial results may not always occur and adverse effects are possible. CPR, including electrical defibrillation, should be readily available prior to initiating therapies. Dosages listed are for dogs. If reported in the literature, dosages for cats will be provided. A description of each drug is given in context of therapy to assist the reader with rapid decision-making.

MANAGEMENT

A. NARROW COMPLEX SVT WITH REGULAR R-R INTERVALS

1. **Calcium Channel Blockers (CCB)**
   a. **Diltiazem** – (0.1 – 0.5 mg/kg) administered in IV boluses of 0.05 – 0.25 mg/kg every 5 minutes to effect, then 1 – 5 μg/kg/min CRI
   Cats: (0.1 – 0.2 mg/kg) IV bolus, then CRI as per dogs

This is the initial drug of choice for SVT. Diltiazem is highly efficacious in terminating SVTs dependent on the AV node and slowing the ventricular response by prolonging AV nodal conduction in AV node independent SVTs. It may also be useful in arrhythmias caused by triggered activity and late after depolarizations. The rhythm should convert in <10 minutes. Diltiazem is less likely to cause hemodynamic collapse than verapamil because of less negative inotropy and less peripheral vasodilation. Reflex stimulation is also, therefore, less than with verapamil. Diltiazem, however, can still cause cardiovascular collapse with excessive doses, particularly if myocardial dysfunction is present.

Warning: Initiation of oral diltiazem while weaning the CRI can also lead to collapse. Oral diltiazem should be initiated under close observation in hospital and ideally once the CRI has been substantially reduced or discontinued. Inotropic support should be considered in conjunction with diltiazem therapy in patients with systolic dysfunction and heart failure (DCM, tachycardiomyopathy). *See dobutamine therapy (Tx of CHF) p. 152.* **Note that diltiazem should be initiated prior to beginning dobutamine,** since the latter facilitates AV node conduction and will induce rapid ventricular response to SVTs if the AV node is not blocked. In the event of cardiovascular collapse (may be a result of excessive bradycardia, negative inotropy and vasodilation), the diltiazem CRI should be discontinued. Add or increase dobutamine CRI. **Calcium gluconate (10%) 1 mL/10 kg will counter the cardiovascular depressant effects** if necessary. Dopamine can be administered if pressor effects are still required.

   OR
   b. **Verapamil** – (0.05 mg/kg) as a slow IV bolus over 3 – 5 minutes, repeated up to 3 times or a maximum of 0.15 mg/kg over a total of 15 – 30 minutes.

   Verapamil is highly efficacious for terminating SVTs. Verapamil should not be used for wide QRS tachycardias, unless they are proven to be supraventricular in origin. Verapamil should also not be used in patients with AF and Wolff-Parkinson-White syndrome as it can facilitate the preexcited ventricular response. Verapamil should not be used in patients with myocardial dysfunction. Cardiovascular collapse should be treated in the same manner as described for diltiazem.

2. **β-Adrenergic Blockers**

   Because of their negative inotropic effects, β-blockers must be used with caution in animals with myocardial dysfunction and heart failure.
   a. **Esmolol** – (0.25 – 0.5 mg/kg) slow IV bolus, then 50 – 200 μg/kg/min CRI.
   Cat: same as for dogs.

Esmolol is advantageous because it is ultra-short acting with a half-life of approximately 9 minutes. Therefore, possible untoward effects associated with negative inotropy are transient and may be rectified by discontinuing the infusion.

b. **Propranolol – (0.02 – 0.05 mg/kg) slow IV bolus in 2 minute increments up to a total dose of 0.1 mg/kg. Cats: same as for dogs.**

Propranolol has membrane-stabilizing effects with mild sodium channel blocking effects. It produces less hypotension than esmolol and is much less expensive. Because it is a non-selective β-blocker, however, it can potentiate bronchoconstriction.

If neither CCBs or β-blockers are effective alone, then combination therapy can be used judiciously. The 2nd agent needs to be administered cautiously in small increments.

3. **Digoxin – 0.01 mg/kg slowly IV given once hourly as needed up to a maximum of 0.04 mg/kg total, then switch to ¼ of the total amount given in 24 hours for maintenance.**

Although digoxin has been used historically for the emergency management of SVTs, its onset of action is slower and the efficacy is less compared to the CCBs. Digoxin is well tolerated in heart failure, however, the risk of toxicity is great with the IV route. Thus, intravenous use of digoxin must be relegated to a 3rd or 4th line drug in animals that cannot tolerate CCB or β-blockers and other treatments are inadequate to control ventricular rate response.

If vagal maneuvers or use of CCB or β-blockers indicate an AV node independent arrhythmia, then drugs affecting the atrial myocardium should be considered such as class Ia drugs (quinidine, procainamide), Ic drugs (propafenone, flecainide) and class III antiarrhythmics (amiodarone, sotalol, ibutilide). These drugs are also useful for refractory AVRT because of their electrophysiologic effects on accessory bypass tracts.

4. **Class Ia Antiarrhythmics**
   a. **Procainamide – (5 – 15 mg/kg) slowly IV followed by 25 – 40 μg/kg/min CRI OR 8 – 20 mg/kg IM q4–6h.**

B. NARROW COMPLEX SVT WITH IRREGULAR R-R

Irregular SVTs are usually caused by variable conduction through the AV node. Only SVTs that don't utilize the AV node as part of the tachycardia circuit can co-exist with AV block. Most irregular SVTs arise from the atria and usually result from significant atrial disease. They include most commonly atrial tachycardia **AT**, atrial flutter **AFL** and atrial fibrillation **AF**. In these patients, pharmacologic conversion to sinus rhythm can be considered with recent onset of the SVT (48 hours or less) in the absence of substantial structural heart disease. Intravenous agents available include class Ia (quinidine and procainamide) or class III agents (amiodarone, ibutilide). Negative inotropy, vasodilation, and hypotension make quinidine poorly tolerated in patients with compromised cardiovascular function or underlying cardiac disease. **Procainamide is the preferred drug for intravenous use.** Chronic (oral) therapy is more common when pharmacologic cardioversion is attempted. Oral procainamide, quinidine, propafenone, flecainide, sotalol and amiodarone have been utilized for pharmacologic cardioversion and prevention of recurrence (*see Pharmacology p. 177*).

If the SVT can't be abolished, which is often the case for automatic atrial tachycardias and atrial fibrillation, control of the ventricular response becomes the goal of therapy. Intravenous diltiazem is the drug of choice:

1. **Diltiazem – 0.05 – 0.25 mg/kg bolus IV, then 1 – 5 μg/kg/min CRI titrated to optimal heart rate.**
   Target heart rates will depend on the individual patient and the underlying cardiovascular status. Heart rates of 150 – 180 bpm may be required initially in patients with advanced heart disease (*see Warning section A*).

C. WIDE QRS TACHYCARDIAS

When it is not possible to differentiate a wide QRS tachycardia as supraventricular or ventricular in origin, it is reasonable to utilize drugs that are useful for both. Intravenous procainamide (A4(a) above) is the safest, if not most efficacious drug to administer for acute treatment of unknown wide QRS tachycardia. Amiodarone (*see D1 below*) can also be considered.

D. REFRACTORY SVT

If all the above measures fail to achieve hemodynamic stability and the patient continues to deteriorate, then consider the following steps:

1. **Amiodarone IV**

   Amiodarone is classified as a class III antiarrhythmic agent, however, it possesses class I, II, III and IV actions. Intravenously, amiodarone slows heart rate and prolongs AV nodal refractoriness. Its acute effects may be partially explained by its sympatholytic and CCB effects. Intravenous amiodarone controls life-threatening ventricular arrhythmias and is also effective in slowing AV nodal conduction in patients with rapid atrial tachyarrhythmias. If amiodarone does not adequately control the ventricular response, then DC cardioversion should be considered. Amiodarone may help to maintain sinus rhythm if cardioversion is successful. Amiodarone is well tolerated hemodynamically with minimal negative inotropic effects. Intravenously, it can induce hypotension. It interacts with digoxin, warfarin, quinidine, procainamide and flecainide, necessitating lower doses of these drugs. Pharmacokinetics are complex. Extrapolating from its use in humans, the following empirical protocol has been utilized in several cases: (*see Pharmacology p. 177 prior to use*).

   a. Premedicate with diphenhydramine (0.5 – 2.0 mg/kg with maximum total dose 50 mg IM) and dexamethasone (0.5 – 1.0 mg/kg IV) as urticaria and angioedema frequently occur.
   b. Amiodarone should be administered in a central line and diluted to 1 mg/mL in D5W
      i.   Bolus 2 – 5 mg/kg over 10 minutes.
      ii. Begin CRI 1.0 mg/kg/h for 6h, then 0.5 mg/kg/h for the remaining 18h.
   c. Repeat boluses (2 – 5 mg/kg) over 10 minutes can be given if inadequate response or if breakthrough arrhythmias occur. Do not exceed 10 mg/kg/h.
   d. EKG should be continuously monitored as the heart rate can drop quite dramatically but the time when this occurs can not be predicted.

2. **DC Cardioversion**

   Electrical (DC) cardioversion refers to the delivery of energy synchronized with the QRS complex. It can be used for the treatment of any tachyarrhythmia during which well-defined QRS complexes can be reliably identified. Defibrillation refers to the delivery of unsynchronized energy. Only personnel trained in the safe use of this equipment should perform the procedure.

   a. **Anesthesia is required.** Use of a benzodiazepine and an opioid analgesic (e.g., midazolam and fentanyl) is useful in achieving transient sedation and amnesia. Only a loss of consciousness justifies shock therapy without sedation.
   b. The animal should be placed in **sternal position.** The chest should be **clipped on both lateral thoracic walls at the 5ᵗʰ to 6ᵗʰ intercostal spaces**, midway between the thoracic spine and sternum. Lower placement may result in a lower success rate.
   c. **Conductive gel** should be applied to the electrodes to reduce transthoracic impedance and avoid skin trauma. **NEVER USE ALCOHOL AS THIS WILL IGNITE.** Electrodes should not be rubbed together. Close attention should be paid when applying a conductive gel, particularly between subsequent shocks; **DO NOT** smear the gel over the chest wall as this will shunt the current between the electrodes, thus decreasing the energy delivered to the heart. Applying firm pressure over the electrodes will also improve conduction across the electrode-skin interface. The delivery of the shock during expiration has been noted to marginally decrease the atrial defibrillation threshold (DFT). Note that EKG leads often become disconnected during the shock due to the tetanic contraction of the limbs. These should be securely placed and monitored during and immediately after delivery of the shock.
   d. **Defibrillation** is achieved over a range of delivered energies. Biphasic waveforms may be more effective for defibrillation than monophasic waveforms with lower defibrillation threshold i.e. the energy values associated with successful defibrillation. Shocks of equal energy will not always result in the same outcome, therefore, energies used are a guideline only. Energies for cardioversion are not well established. It would be reasonable to **start with 50 J in dogs < 15 kg and 100 J in dogs over 15 kg then increase by 50 – 100 J increments until conversion occurs.** Lower energy is usually required to convert atrial flutter (vs atrial fibrillation). In human cardiology, the use of higher energy shocks initially (200 – 360 J) was reportedly more successful and as safe as lower energy (100 J) shocks with no increase in adverse affects (sinus bradycardia, AV block, troponin I enzyme elevation). **For ventricular fibrillation in veterinary patients, 7 (<15 kg) – 10 (>15 kg) J/kg is recommended.**
   e. **Complications** could include bradycardia and rarely ventricular arrhythmias including ventricular fibrillation, pulmonary edema and hypotension.

E. **Oral therapy** (see individual drugs in Pharmacology below) is indicated for maintenance of sinus rhythm or chronic heart rate control in rhythms that cannot be converted to sinus. It is reasonable to initiate oral therapy in

patients with SVT who are hemodynamically stable. These patients usually are not in congestive heart failure and have heart rates <250 bpm. Oral therapy is selected based on the criteria above, or as a continuation of the successful intravenous therapy. As some antiarrhythmics may not be available in a parenteral formulation in various countries, the therapeutic benefit of oral formulations in an emergency situation is very limited. However, if a case fails to respond to parenteral drugs and/or these drugs or electrical cardioversion are unavailable, oral medication should be tried.

PHARMACOLOGY

1) **Procainamide** 10 – 20 mg/kg PO q6h or q8h if sustained-release (S-R); cats: 2 – 5 mg/kg PO q12h–q8h, and **quinidine 10 – 20 mg/kg** PO q8h–q6h dogs: are class Ia drugs but depress conduction in all cardiac tissues and prolong refractoriness in the atria, ventricles, accessory bypass tract and the His-Purkinje system. They are useful in chemically converting and treating patients with ectopic atrial tachycardia, atrial flutter, atrial fibrillation and SVT. Quinidine can facilitate AV node conduction and can cause significant hypotension because of its alpha-adrenergic receptor blocking effects. Procainamide has no effect or may cause slight shortening of the AV node refractory period. It should be administered with drugs that slow A-V node conduction. Hypotension can occur with the intravenous route due to mild ganglionic blocking action that impairs cardiovascular reflexes. Prolonged oral use can result in a systemic lupus-like reaction in 10-20% of patients.

2) **Lidocaine** is a class Ib drug with more conduction-slowing properties in ischemic tissue. This agent is useful in the acute management of ventricular arrhythmias. Lidocaine has little to no effect on atrial , AV nodal, or accessory pathway tissue; thus, it is ineffective in treating SVT. Response to lidocaine can strongly suggest ventricular origin in wide QRS tachycardias. The increased potency of lidocaine during the relative refractory period explains why this drug is not particularly effective in treating atrial arrhythmias. Because atrial action potentials are shorter than those in the ventricles and His-Purkinje system, at rapid heart rates, the time-dependent potentiation of the effects of lidocaine is greater in the ventricle than in the atria. The response of the ventricles to lidocaine is heightened because their longer action potential maintains a larger fraction of the sodium channels in the lidocaine-sensitive closed (inactivated) state.

3) **Flecainide** 1 – 5 mg/kg PO q8h–q6h is a Class Ic antiarrhythmic. It prolongs refractoriness and slows conduction in the atria, AV node, His-Purkinje system, ventricles, and accessory pathways. It predominantly blocks sodium channels in the activated state with rate-dependent block occurring slowly. In humans, it has been demonstrated to be a very effective agent in the treatment of reentrant SVT, atrial origin arrhythmias and atrial fibrillation. Most often used in patients without concomitant organic heart disease because of depression of left ventricular function and its proarrhythmic potential (CAST study showed increased mortality in patients with ventricular arrhythmias post-myocardial infarction). In patients without significant structural heart disease and SVT, there is no risk of worsening survival. Experience with class Ic drugs is limited in veterinary medicine.

4) **Propranolol** 0.3 – 1.5 mg/kg PO q8h; cats: 2.5 – 10 mg/cat PO q12h–q8h, **atenolol** 0.5 – 1 mg/kg PO q24h–q12h PO; cats: 6.25 – 12.5 mg/cat PO q24h–q12h: β-blockers inhibit many of the effects of β-receptor stimulation, such as blocking enhanced automaticity, enhanced conduction and shortened refractory periods. They also block adrenergic activation of calcium channels. Resting heart rates are slowed. Refractoriness of the AV node is prolonged with little effect on refractoriness of other cardiac tissues. Significant negative inotropic effects can result in dose-related worsening of CHF. If used in CHF, β-blockers must be started at a low dose and titrated upwards very carefully.

5) **Sotalol** 0.5 – 2.0 mg/kg PO q8–12h dogs and cats [anecdotal reports of 10 – 20 mg/CAT q12h] (can be made in a suspension) is a unique, noncardioselective β-blocker with class III properties. Sotalol has 1/3 the β-blocking potency of propranolol. It's β-blocking effects predominate at lower doses and its Class III effects predominate at higher doses. Sotalol prolongs repolarization in a concentration-dependent fashion, resulting in prolongation of the QT interval and action potential duration. Sotalol slows the sinus node cycle length and lengthens AV nodal conduction and effective refractory period of the atria, AV node, ventricle and accessory pathway. Sotalol is well tolerated with less negative inotropy than pure β-blockers. Reverse use-dependence means it is less efficacious at high heart rates. Proarrhythmia in the form of torsades de pointes is possible.

6) **Amiodarone** loading dose 10 mg/kg for 7 days, then 5 mg/kg PO q24–48h is a Class III antiarrhythmic however, it also possesses class I, II and IV actions. Amiodarone prolongs refractoriness and slow conduction in the atria, AV node, His-Purkinje system, ventricles and accessory pathways and slows sinus node automaticity. Oral amiodarone, even at low doses, can be effective in controlling 2/3 of the human patients with otherwise drug-refractory atrial fibrillation or paroxysmal SVT. Because of its AV node effects, amiodarone is effective in slowing the ventricular response in chronic or recurrent atrial fibrillation. Electrophysiologic effects when given intravenously (IV) are different, with little acute effect on atrial or ventricular refractoriness and little use-dependent sodium channel blockade (Class I effect). Its acute effects may be partially explained by its sympatholytic and calcium channel-blocking effects. The clinical pharmacology of amiodarone is not well understood with a large volume of distribution and long half-life (53 days). Amiodarone is well tolerated hemodynamically with minimal negative inotropic effects. It can be used in patients with CHF. IV amiodarone can cause drug-induced hypotension. The main concern with its use is cost, slower onset of action and noncardiac side effects (e.g., corneal microdeposits, elevated liver

enzymes, thyroid dysfunction, neutropenia, thrombocytopenia). The most serious adverse effect requiring discontinuation is interstitial pneumonitis and fibrosis. This is a dose-related effect. Most adverse effects are reversible and less likely at lower doses. Close monitoring of the CBC, liver enzymes, thyroid function and thoracic radiographs is necessary with prolonged therapy. Potentially, critically unwell patients, fully dependant on sympathetic drive can decompensate when recieving the added insult of Polysorbate 80 (vehicle), in addition to that of amiodarone itself. The vehicle for intravenous amiodarone (Cordarone X) is polysorbate 80 (polyethylene sorbitan monooleate) which is used for solubilising, emulsifying and wetting medicinal products. The intravenous form of amiodarone contains 150 mg amiodarone and 300 mg polysorbate 80. Polysorbate 80 is known to have vasodilatory and negative inotropic effects. In addition to haemodynamic effects, Polysorbate 80 has been suggested as a cause for the acute hepatotoxicity of Amiodarone.

7) **Diltiazem** 1 – 3 mg/kg PO q8h; cats: 7.5 – 15 mg/cat PO q12h–q8h, Cardizem CD 10 mg/kg PO q24h is a Class IV antiarrhythmic drugs that depresses the slow inward Ca^{++} current by blocking the slow L-type calcium channel. It has "use-dependent" action on AV nodal conduction that leads to greater therapeutic effects at faster heart rates.

8) **Digoxin** 0.005 – 0.01 mg/kg q12h exerts its major antiarrhythmic effect by way of an indirect action mediated by the autonomic nervous system producing enhancement of vagal activity. Thus, digoxin may slow sinus node automaticity and slow AV node conduction, prolonging AV node refractoriness. Oral digoxin is frequently added as a 2nd agent for ventricular rate control in dogs with significant myocardial dysfunction or congestive heart failure. Because of its propensity for toxicity including arrhythmia, however, low dose digoxin is currently recommended in heart failure, with steady state levels in the subtherapeutic range (<1ng/mL). This may limit its efficacy in heart rate control.

TABLE 2. Antiarrhythmic Drugs for Atrial Fibrillation

CLASS	DRUG	ATRIAL STABILIZATION	A-V NODE BLOCKADE
IA	quinidine	+ +	-
IC	flecainide	+ +	0
	propafenone	+ +	(+)
II	β-blockers	(+)	+ +
III	sotalol	+	+ +
	amiodarone	+ +	+ +
IV	verapamil/diltiazem	(-)	+ + +
other	digoxin	(-)	+ +

*()= borderline, +=beneficial effect, -=adverse effect, 0=no effect

SUGGESTED READING

1. Fox PR, Sisson D, Moise NS. Textbook of Canine and Feline Cardiology: Principles and Clinical Practice, 2nd ed. Toronto, ON, WB Saunders, 1999:331-385.
2. Kittleson MD, Kienle RD. Small Animal Cardiovascular Medicine, 1st ed. Toronto, ON, Mosby Inc., 1998:461-475.
3. Podrid PJ, Kowey PR. Cardiac Arrhythmia: Mechanisms, Diagnosis & Management, 2nd ed. New York, NY: Blackwell Publishing, 2001:127-164.

NOTES

INTRODUCTION

Ventricular premature contractions (VPCs) and ventricular tachycardia (VT) are associated with primary cardiac disease and non-cardiac causes. Non-cardiac causes include the gastric dilation-volvulus complex (GDV), trauma, sepsis, hypoxia, pancreatitis, splenic, hepatic or atrial hemangiosarcoma, **pain**, electrolyte and acid-base disturbances, and drugs. When considering treatment of VT, elucidate and treat the underlying cause. VT secondary to traumatic myocarditis is difficult to treat, and supportive care in this, as in all situations, is important in preventing worsening of the VT. VT, by definition, is a series of more than three consecutive beats (VPCs) that originate in the ventricular conduction system distal to the bundle of His or the ventricular muscle (*Fig. 1*). The morphology is typically different from sinus beats, and QRS complexes are frequently wider and bizarre; however sinus beats superimposed on the VPC, a fusion beat, will be smaller and of different morphology (*Fig 2* ⇧). There is no relationship between the P wave, which has a normal configuration, and the QRS complex. The P wave may occur before or after, or can be hidden within the QRS complex. The T wave is typically directed opposite the QRS. The complexes may all appear the same (unifocal) or variable (multiform). Of major concern is the 'R on T' where there is no isoelectric shelf after the T wave and onset of the next QRS complex, or no isoelectric shelf between upward and downward deflection (*Fig. 2* ↑), which may progress from two to several beats and continue as ventricular 'flutter'; and Torsades-de-pointe. Torsades-de-pointe, in veterinary patients, is usually associated with a pre-existing v-tach where bursts of polymorphic v-tach occurs, during which there is changing QRST morphology and axis (180° twist). These are especially worrisome as they may preceed ventricular fibrillation. Ventricular tachycardia is rare in the cat. The protocol outlined in this section is restricted to the treatment of non-cardiac causes of VT. VT associated with cardiac disease requires specific treatment (*see Congestive Heart Failure Life-Threatening p. 149/150, or Chronic Therapy p. 158, Supraventricular Tachycardia p. 174*). This chapter will deal with the emergency situation only, as the reader is referred elsewhere for chronic treatment.

FIGURE 1.

50 mm/sec; 1 cm/mV
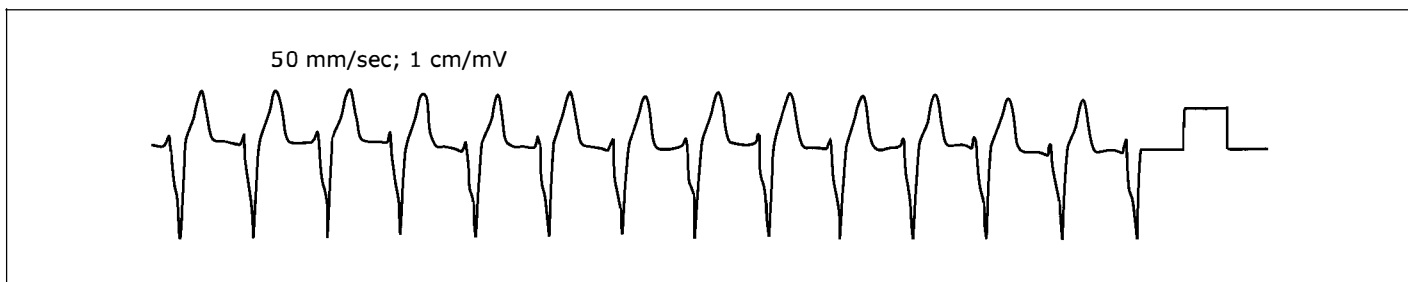
FIGURE 2.
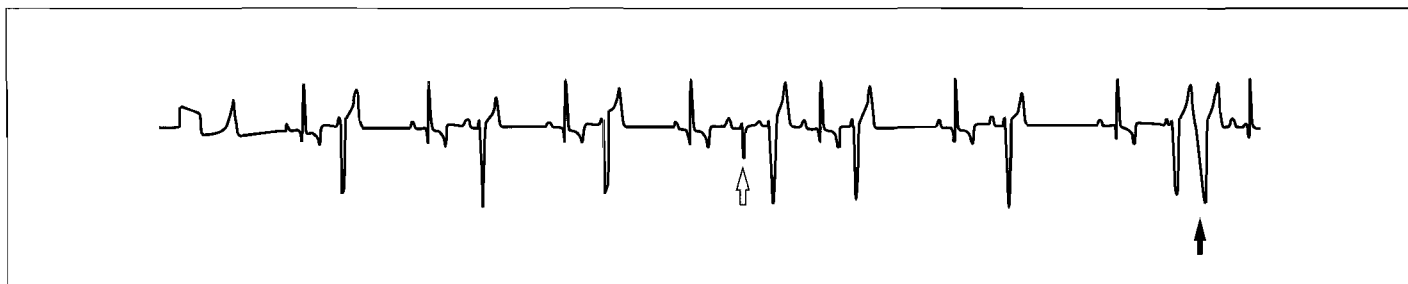
DIAGNOSIS

History

The history will depend on the underlying cause of the arrhythmia. If none of the above conditions are obvious, question the owner with regard to recent trauma, illness (sepsis), abdominal pain (i.e., splenic pathology, pancreatitis), decreased exercise tolerance or appetite, and medication.

Clinical Signs/Physical Examination

- Patients may be asymptomatic with the arrhythmia being discovered on physical examination, or associated with any of the above conditions.
- When symptomatic, the patient may be weak, depressed, syncopal, or in shock.
- The heart rate will be variable, with a range of 60 to >250 beats/min. Peripheral pulses may be normal, or weak and irregular.
- Pulse deficits may be present, alerting the examiner to the abnormal rhythm. However, in sustained VT with a normal heart rate, pulse deficits may not be present and the arrhythmia is difficult to detect.
- Synchronized cardiac murmurs are associated with specific cardiac pathology, and not present in non-cardiac associated VT. Heart sounds are variable in intensity.
- Canon "A" waves (retrograde jugular flow from the atrium after an atrial contraction against a closed A-V valve) may be seen in the jugular vein.
- Mucous membranes may be pale with a capillary refill time greater than 2 seconds, especially when associated with splenic, hepatobiliary, GI injuries/pathology or trauma.
- General physical findings will depend on the underlying cause of the arrhythmia. Therefore a **thorough examination is necessary.**

Laboratory Evaluation/Diagnostic Imaging

Stat

- An **ECG** is necessary to confirm the VT. VT is a wide-complex tachycardia (>0.06 seconds in the dog, >0.04 seconds in the cat). A wide-complex tachycardia can occasionally be the result of supra-ventricular tachycardia (SVT) in a patient with pre-existing or rate-related aberrant ventricular conduction. (*see p. 170*). In cats, where pre-existing conduction blocks (left anterior fascicular block, right bundle branch block) are more common, SVT should be more strongly considered. Vagal maneuvers (pressing on the globes or carotid sinus massage) may slow down or terminate an SVT, making a definitive diagnosis possible. If it is not possible to determine whether the rhythm is a VT or an SVT with aberrancy, treat a wide-complex tachycardia as VT, as the therapy is safer (*see Supraventricular Tachycardia p. 174*).
- **Indirect or direct blood pressure** measurements are important, because hypotension may be a result of severe arrhythmia, or indicative of severe fluid loss or distributive shock.
- **PCV, TS** may be below normal in trauma and other blood loss settings (*see Hemorrhage p.* 619).
- **Stick BUN** or serum creatinine to identify pre-renal, renal or post-renal azotemia as a potential cause.
- **Blood glucose** to rule out hyper- or hypoglycemia, which may be associated with underlying illness.
- **Blood or serum electrolytes** to identify potential causes (*see Hypokalemia p. 394 or Hyperkalemia p. 396, Hypomagnesemia p. 403*) or associations with underlying illness.
- **Serum ALT** to rule out potential hepatic disease as primary cause (*see Acute Liver/Dysfunction p. 37, Icterus p. 70*).
- **Urine specific gravity** as an assessment of renal failure or dehydration.

Extended Data Base

The extended data base will depend on the above findings but should include:
- **CBC** to identify sepsis, anemia, polycythemia etc, as potential causes.
- **Biochemical profile** is required to rule out any organ dysfunction as potential causes.
- **Blood/Serum electrolytes** (*see above*).
- **Chest radiographs** may reveal primary abnormalities in cardiac (e.g., enlargement, mass), or pulmonary (i.e., parenchymal, pleural, vascular) structures.
- **Abdominal radiographs** may identify GI, splenic, renal, hepatobiliary abnormalities.
- **Ultrasonographic examination of abdomen** may identify splenic lesions which are commonly associated with VPCs.
- **Echocardiographic** examination may identify cardiac mass (e.g., right atrial hemangiosarcoma) or primary cardiac disease.

MANAGEMENT

A. **Treat the underlying cause** (i.e., GDV, splenic involvmenet, septic focus). Traumatic myocarditis is self-limiting; however attempt to treat if criteria (*see D below*) are present.

B. **Supportive Care.** To reduce myocardial work by optimizing oxygen delivery to the tissues (and to optimize myocardial perfusion and oxygen delivery), oxygen supplementation, analgesia, fluid therapy, colloids, blood products, etc., should be administered based on presenting complaint and physical examination. *See Magnesium J below* as a potential addition to supportive care.

C. **Potassium** measurements must be obtained. **Supplementation** may be required to maintain serum potassium at 4.5 – 5.0 mmol/L. (*see Hypokalemia p. 394*). **Initially, hyperkalemia** may rarely cause VT (*see Hyperkalemia p. 396*). Potentiation of arrhythmias may occur with abnormally high or low serum potassium levels. If magnesium is administered, the serum potassium may increase; therefore monitor potassium levels q8h and reduce potassium supplementation accordingly. Worthy of note is that many antiarrhythmic drugs (should this be required) depend on normal serum potassium levels for their optimal function i.e., the effectiveness of lidocaine is reduced in the presence of hypokalemia.

D. **Criteria for treatment of ventricular tachycardia**

    1. Sustained paroxysmal or polymorphic VT at an instantaneous rate of >170/min (Fig. 1); >140/min with R on T (no isoelectric shelf after T wave and onset of next QRS complex, or no isoelectric shelf between upward and downward deflection – Fig. 2 ↑) or with Torsades-de-Pointe.

    2. Sustained, paroxysmal or polymorphic VT (with or without R on T, with or without Torsades de Pointe) at an instantaneous rate of >140/min with a mean blood pressure <75 mmHg.

    3. Sustained, paroxysmal or polymorphic VT, or VPC's > 15/min while under anesthesia. However, this should be considered on an individual basis, after ruling out intraoperative complications, based on blood pressure (pulse deficits if monitoring equipment not available) and underlying problem.

    4. In general, lidocaine need not be administered with heart rates lower than 140/min, as a further reduction in heart rate may reduce cardiac output. However, this should be considered on an individual basis if there are paroxysms of a faster rate.

    5. **NOTE:** Ventricular tachycardia due to non-cardiac causes is usually self-limiting lasting up to 72 – 96 hours providing the patient is managed appropriately for the underlying problem and supportive care is administered. Once the VT is controlled the patient should be weaned off the anti-arrhythmic medication.

E. **Lidocaine**: Precautions: *See Pharmacology below*.

Lidocaine bolus 0.25- 1 mg/kg CAT (over 5 mins), or 2 mg/kg DOG (over 30 seconds): initially, this can be repeated if no effect is seen within 2 minutes. If not lidocaine responsive go to *F, G or H below*. In dogs, if lidocaine responsive, establish a CRI of 30 – 50 μg/kg/min (*see Lidocaine Infusion Chart p. 247*). Rarely, the infusion can be increased to 60 μg/kg/min (multiply the lower range [mg/kg] by 2 on the chart, for dose) or 80 μg/kg/min (add the lower + upper range [mg/kg] on the chart, for dose). Do not expect to always eradicate the VT. The aim is to reduce the high rate to a lower rate (<150) thereby enabling adequate filling of the ventricles and improved cardiac output. Titrate the lidocaine infusion accordingly.

Lidocaine infusion (*see Preparation and Chart p. 247*):

    1. If nausea (excessive swallowing, drooling, depression) or vomiting develops this may be an indication of lidocaine toxicity. Stop the infusion for 2 – 4 hours and check the rate of delivery. If overdosed, re-start at appropriate dose. If the dose is appropriate, reduce 50% (*see Pharmacology: Lidocaine: toxicity below*). Usually nausea precedes CNS adverse effects.

    2. If lidocaine at the higher dose does not reduce the VT to <150 but slows the rate somewhat, add procainamide (*see F below*).

    3. If VT worsens, stop infusion. Lidocaine pro-arrhythmic effects may be occurring (*see Lidocaine toxicity under Pharmacology below*).

    4. If the patient cannot tolerate lidocaine, then use procainamide alone.

F. Procainamide

   1. Dog:

      a. **6 – 20 (usually start at 10) mg/kg IV over 10-20 (higher dosages) mins** (CAUTION, can cause hypotension if given rapidly), **then 25 – 50 μg/kg/min. CRI** Calculate: total required μg x 60 (=μg/h), divide by 1000 (=mg/h), divide by 100 (100 mg/mL concentration of procainamide) for a final dose of mL/h.

         OR

      b. **6 – 20 mg/kg q6h IM.**

         OR

      c. **8 – 20 mg/kg q6h PO regular tabs or caps.**

         OR

      d. **25 – 50 mg/kg sustained release (S-R) q8h.**

   2. **Cat: 5 – 10 mg/kg** IV over 10 mins. q8h is the recommended treatment while treating the underlying cause. Monitor for hypotension. **Cats rarely get VT.** Treatment is not advised unless the rate is >240/min.

   3. In **dogs,** if a slight reduction in heart rate is noted with procainamide therapy, but a further reduction is required, **procainamide combined with lidocaine** may be synergistic. Determining the effective dose of each drug may be difficult. A mid-range dose of both drugs should be used initially. Should high dosages of both be required, adverse effects should be expected, and discontinuation will be necessary. Nausea precedes CNS adverse effects associated with lidocaine.

Alternatively, if procainamide does not reduce the VT, administration of a beta blocker (*see G below*) is suggested.

G. Beta blockers

   1. Dog:

      a. **propranolol 0.02 – 0.06 mg/kg IV** over 5 min, or IM q8h or **0.2 mg/kg PO q8h.**

         OR

      b. **metoprolol 0.5 – 1.0 mg/kg PO q8h** (start at low dose, Dobermans are very sensitive therefore start with 5 mg/dog q8h).

   2. Cat:

      a. **propranolol 0.25 – 0.5 mg/cat IV over 10 mins or IM, followed by 2.5 – 5.0 mg/cat PO q8h. Start at the low dose.**

H. **Sotalol 1 – 2 mg/kg PO q12h (dogs and cats)** may be instituted should the above fail. **Anecdotal reports of 4 – 5 mg/kg PO q12h (cats), max 20 mg/CAT have been reported** but not used by the author.

I. **Amiodarone IV when all else fails to manage severe life-threatening arrhythmia.**

Amiodarone (*see Supraventricular Tachycardia for details p. 176*) is classified as a class III antiarrhythmic agent, however, it possesses class I, II, III and IV actions. Intravenous amiodarone controls life-threatening ventricular arrhythmias and is also effective in slowing AV nodal conduction in patients with rapid atrial tachyarrhythmias. If amiodarone does not adequately control the ventricular response, then DC cardioversion should be considered (*see Supraventricular arrhythmias p. 176*). Amiodarone may help to maintain sinus rhythm if cardioversion is successful. Amiodarone is well tolerated hemodynamically with minimal negative inotropic effects. Intravenously, it can induce hypotension. It interacts with digoxin, warfarin, quinidine, procainamide and flecainide, necessitating lower doses of these drugs. Pharmacokinetics are complex. Extrapolating from its use in humans, the following empirical protocol has been utilized in several cases:

   1. Premedicate with:

      a. **diphenhydramine (0.5 – 2.0 mg/kg with max total dose 50 mg IM) and**

      b. dexamethasone (0.5 – 1.0 mg/kg IV) as urticaria and angioedema frequently occur.

   2. **Amiodarone** should be administered in a central line and diluted to 1mg/mL in D5W

      a. **Bolus 2 – 5 mg/kg over 10 minutes.**

      b. **Begin CRI 1.0 mg/kg/h for 6 hours, then 0.5 mg/kg/h for the remaining 18 hours.**

      c. **Repeat boluses (2 – 5 mg/kg) over 10 minutes** can be given if inadequate response or if breakthrough arrhythmias occur. Do not exceed 10 mg/kg/h.

   3. EKG should be continuously monitored as the heart rate can drop quite dramatically but the time when this occurs cannot be predicted.

J. **Magnesium sulfate** can be administered to cats or dogs if VPCs are present at any rate. Magnesium should be given prior to lidocaine, because early administration may prevent VT. The dose is empirical, but current recommendations are **30 – 40 mg/kg (0.15 – 0.3 mEq/kg) diluted to at least 20% (200 mg/mL, administered over 2 – 4 hours in a burette with the hourly fluids** (*see Magnesium p. 404 for dosing clarification*)**.** More rapid administration may be necessary, but could result in severe hypocalcemia in a calcium-depleted patient. Serum calcium levels should be monitored in this setting. Magnesium may be repeated to a maximum of 125 mg/kg/day [1 mEq/kg/day] as a CRI. Do not expect to eliminate the VT. A satisfactory reduction in heart rate is <150/min. (lower if multiform VT or continued poor pulse pressure). Magnesium sulfate should be reduced by 50% – 75% if patient is azotemic after fluid resuscitation, as primary renal disease is likely present and magnesium is cleared by the kidneys. Excessive magnesium administration will cause a diuresis and potential dehydration. If non-responsive to magnesium sulfate, try lidocaine (*see Lidocaine Infusion Chart p. 247*).

PHARMACOLOGY

1) **Magnesium** is an essential cation required in the production and use of adenosine triphosphate (ATP). It is necessary for normal function of the sodium-potassium ATPase pump, which regulates intracellular potassium balance. Magnesium is also required for many other cellular functions.

2) **Lidocaine** is a class 1B antiarrhythmic drug which acts as a membrane stabilizer through inhibition of sodium channels which depresses automaticity in NORMAL and abnormal (i.e.,ischemic) Purkinje fibres. However, the decrease in conduction velocity in ischemic or hypoxic cardiac tissue is much more pronounced than through normal tissue. It is the decrease in automaticity of normal as well as that of abnormal tissue that is of concern with lidocaine administration when the heart rate is <140/min with VPCs, sustained or paroxysms of VT.

   Precautions: The dose of lidocaine should be decreased by 50% in the presence of impaired hepatic blood flow (acute myocardial infarction, congestive heart failure or shock) as total body clearance of lidocaine is reduced. Human geriatric patients have a reduced volume of distribution, and in such patients the dose is also reduced by 50%. Large breed dogs should receive the lower to mid-range, because dosing on a weight, rather than a mass, basis may result in overdose. Careful monitoring should be the guide to increasing or decreasing the dose.

   Toxicity: Excessive doses of lidocaine are capable of producing myocardial and circulatory depression and arrhythmias. Clinical indicators of lidocaine toxicity include drowsiness, disorientation, decreased hearing ability, paresthesia, and muscle twitching. Some patients may become agitated or nauseated, and vomit. With serious toxicity, seizures may occur. The drug should be withdrawn and diazepam administered. Lidocaine undergoes hepatic degradation therefore the dose should be reduced with impaired liver function. In patients with renal disease, excretion of metabolites may be abnormal and these may have pharmacologic activity. In therapeutic doses, lidocaine can be used safely in patients with conduction disturbances. However, large doses may infrequently induce heart block, depress spontaneous discharge from the sinus node, or alter AV conduction. Lidocaine toxicity in cats has been reported and a recommended dose for CRI has not been established.

   Advantages of lidocaine are its analgesic, anti-inflammatory and oxygen radical scavenging properties.

3) **Procainamide** is a class 1A antiarrhythmic which prolongs the effective refractory period throughout the heart with little effect on sinus node or atrioventricular node automaticity. Procainamide's effect on sodium channels is ineffective during hypokalemia and produces myocardial depression in hyperkalemic states. Ventricular arrhythmias are often successfully managed with procainamide. If given rapidly, procainamide can cause severe hypotension. Toxic concentrations can produce fever, anorexia, depression, vomiting and cardiac arrhythmias.

4) **Propranolol** is a class II antiarrhythmic, short-acting, non-selective beta-blocker. It is a membrane stabilizer and is capable of decreasing spontaneous frequency, depressing conduction velocity and increasing the electrical threshold for excitability. The greatest effect is catecholamine antagonism. Hemodynamic instability (decreased cardiac output, cardiac contractility and arterial blood pressure) may occur with inappropriate dosing.

5) **Sotalol** is a Class III anti-arrhythmic agent with strong Class II (beta-blocker) properties. Class III anti-arrhythmics are drugs that block the potassium channels resulting in an increase of the repolarization time (increase refractory period), reflected in the surface ECG by a prolongation of the Q-T interval. A dose reduction by 50% is recommended in patients in congestive heart failure. Sotalol is quite effective in controlling atrial fibrillation rate and ventricular arrhythmias. Its side effects are similar to the beta-blockers. In cases with severe left ventricular dysfunction this drug is very poorly tolerated. Sotalol is contraindicated if there is evidence of heart block, bradycardia or severe sinus node dysfunction.

6) **Amiodarone** (Class III agent) is indicated for the control of ventricular and supraventricular arrhythmias refractory to standard therapy. Amiodarone has slow onset of action and a very prolonged half-life (in humans reported to be 25-110 days), therefore an initial loading dose is necessary to achieve faster onset of action. Side effects reported with chronic administration include development of lung fibrosis (not documented in veterinary medicine) thyroid dysfunction and hepatic toxicity amongst others. In dogs it appears that the most serious side effect is liver damage resulting in increase in liver enzymes. Therefore while using amiodarone baseline liver values followed by rechecks every 2-3 months are recommended. Several patients developed tremors during administration of this drug (personal communication Dr. Braz-Ruivo). During chronic therapy it is recommended to assess thyroid function twice a year.

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NOTES

INTRODUCTION

Caval syndrome is an acute, life-threatening complication of chronic heartworm disease (HWD) associated with movement of a large number of worms from the pulmonary arteries into the right ventricle (RV), the right atrium (RA), +/- the vena cavae. The mass of worms disrupts the tricuspid valve (TV) apparatus and causes severe tricuspid regurgitation. Coupled with pulmonary artery hypertension (PAH) from chronic HWD, acute right heart failure and cardiogenic shock (from poor cardiac output) result. The syndrome is also characterized by intravascular hemolysis due to shear forces on the RBC's flowing between the worms at high velocity and due to increased RBC fragility. Renal and hepatic failure, and disseminated intravascular coagulation (DIC) are also common features. The precise mechanism by which worms appear in the RV, RA, and vena cavae is unknown, however transient or sustained reduction in right ventricular outflow may result in worms falling back into the RV, entwining in the TV, then migrating into the RA and vena cavae. Precipitating factors may include moderate to severe pulmonary artery hypertension (PAH), new thromboembolic events, and large worm burdens. It appears that male dogs may be predisposed. Caval syndrome has also been identified in cats. This acute syndrome may be the first indication that HWD is present (no previous clinical signs).

DIAGNOSIS

History/Signalment

- The most common historical findings reported by owners include acute onset of inappetance or anorexia, lethargy, weakness, respiratory distress, and dark, red-colored urine.
- Many animals have no history suggestive of HWD prior to the acute signs above.
- Inquire about heartworm status and prevention history.

Clinical Signs/Physical Examination

- Patients show acute clinical signs and physical exam findings associated with cardiogenic shock, intravascular hemolysis, and right heart failure. Table 1 lists potential clinical findings and physical exam findings according to underlying pathology.

TABLE 1. Clinical Signs/Physical Examination Findings

Cardiogenic shock (poor cardiac output and poor perfusion)	Intravascular hemolysis and anemia	Tricuspid regurgitation and PAH causing right heart failure	Other signs associated with HWD
Weakness or collapse	Lethargy or weakness	Jugular venous distension/pulsation	Cough (rare)
Pale or cyanotic mucous membranes	Pale mucous membranes	Right-sided systolic murmur	Hemoptysis (rare)
Slow capillary refill time	Dark red discoloured urine	Extra heart sounds including gallop or split S2 (latter due to PAH)	Tachypnea/dyspnea and increased bronchovesicular sounds if pulmonary parenchymal disease present
Weak femoral pulses	Rarely icterus	Arrhythmias (typically premature beats)	
Tachycardia		Tachypnea/dyspnea and reduced breath sounds if pleural effusion present	
Tachypnea		Abdominal distension and fluid wave if ascites present	
		Hepatomegaly and/or splenomegaly	
		Peripheral edema (rare)	

Laboratory Evaluation/Diagnostic Imaging

- **PCV** is decreased due to intravascular hemolysis.
- **Total solids** may be decreased due to protein loss in urine and/or right heart failure (dilutional).
- **Stick BUN** is elevated due to poor renal perfusion +/- renal failure.
- **ACT** may be prolonged if DIC present; baseline useful for heparin therapy.
- **Blood smear.** Agglutination absent as hemolysis is not immune-mediated; microfilariae may be observed.
- **Blood gas and electrolytes**
    - Metabolic acidosis (in part due to due lactic acidosis from poor perfusion).
    - Hypoxemia (PaO_2 <60 mmHg in 30 – 40%, PvO_2 <30 mmHg in 60%).
    - Hypocarbia ($PaCO_2$ <25 mmHg in 20 – 30%) due to compensatory hyperventilation.
    - Hyponatremia and hyperkalemia, particularly if renal failure present.
- **Urine dipstick**
    - Positive for blood due to hemoglobinuria (intravascular hemolysis at a rate exceeding liver's capacity for conversion of hemoglobin to bilirubin).
    - Bilirubinuria (due to intravascular hemolysis).
    - Proteinuria (common in HWD in general due to immune complex glomerulonephritis).
- **Systemic blood pressure.** Hypotension due to poor cardiac output and right heart failure.
- Diagnostic **abdominocentesis** is indicated if abdominal distension and a fluid wave are present – rules out hemoabdomen as abdominal fluid will be a transudate or modified transudate.

Extended Laboratory Data Base

- **CBC.** The erythron findings may include a regenerative anemia, hemoglobinemia, polychromasia, reticulocytosis, nucleated RBC's, schistocytes, and thrombocytopenia. The leukogram findings may include an inflammatory leukogram, eosinophilia, and basophilia.
- **Biochemistry profile** findings reflect renal and hepatic dysfunction with elevations in urea, creatinine, ALT, AST, ALP, and bilirubin, and decreased albumin.
- **Urinalysis.** Hemoglobinuria, bilirubinuria, and proteinuria are common; casts may be seen indicating renal tubular damage.
- **Coagulation profile** may have prolonged PT and PTT and elevated fibrin degradation products (FDPs) if DIC present.
- **Heartworm antigen test** is positive.
- **Modified Knott's test** may be positive or negative.
- **Electrocardiogram** is indicated if an arrhythmia is heard on auscultation. Supraventricular and ventricular premature beats are most common. Evidence of RV enlargement may be seen in sinus beats (S waves in leads I, II, and III; MEA shifted to right [> 100° in dogs, >160° in cats]; S wave > 0.7 mV in lead V3; S wave > R wave in lead V3).
- **Central venous pressure (CVP)** is elevated. Placement of a short jugular catheter in the left jugular vein allows measurement of CVP (right jugular vein is needed for worm removal as described later). *See Fluid Therapy p. 371* for catheter placement and CVP measurement technique. Normal CVP is 0 – 5 cmH$_2$O. In a series of 19 caval syndrome dogs, CVP averaged 10.2 cmH$_2$O (range 3.2 – 18.7 cmH$_2$O).

Imaging

- **Thoracic radiographic** findings may include right-sided cardiomegaly, enlarged main pulmonary artery (MPA), dilated and tortuous lobar pulmonary arteries, blunting of pulmonary arteries, enlarged caudal vena cava, and patchy interstitial/alveolar pulmonary infiltrates.
- **Echocardiography** is the most important diagnostic test, as visualization of the mass of worms in the RV and RA is pathognomonic for caval syndrome. Worms appear as a mass of short parallel lines, typically seen to flow across the tricuspid valve in diastole. Other two-dimensional findings include RV dilation and hypertrophy, paradoxic septal motion, enlargement of the RA and vena cavae, enlargement of the MPA and PA branches, and small left-sided structures (underfilling). Colour Doppler shows severe tricuspid regurgitation (TR), and pulmonic insufficiency (PI) may also be noted. Doppler evidence of PAH is found by measuring a peak TR velocity >3m/s in the absence of pulmonic stenosis (*see Pulmonary Artery Hypertension p. 189*).

MANAGEMENT

Treatment of cardiogenic shock and prompt surgical worm removal are the mainstays of acute therapy, however the prognosis is guarded to poor with a mortality rate of 30 – 40%. Multi-organ failure and DIC can develop before or after treatment.

ACUTE THERAPY

A. **Oxygen** administration by nasal cannula, prongs, or mask is indicated as many patients are hypoxemic due to ventilation/perfusion mismatch, poor cardiac output and increased peripheral extraction, increased intrapulmonary shunting, and diffusion impairment (if pulmonary parenchymal disease due to HWD present). Oxygen also relieves hypoxic vasoconstriction which contributes significantly to PAH.

B. **Intravenous fluids** are necessary to support circulation (increase cardiac output and blood pressure), prevent hemoglobin nephropathy, reverse lactic acidosis, and help treat DIC. However many patients have elevated CVP and right heart failure, therefore fluid administration must be performed cautiously. Placement of a short **jugular catheter** in the **left** jugular vein to serially measure CVP will facilitate monitoring of fluid therapy. Alkalinizing crystalloids (e.g., Plasma-Lyte® 148 or Lactated Ringer's) are a reasonable first choice. Shock dose fluid therapy (up to 90 mL/kg/h in dogs; 60 mL/kg/h in cats) may be required initially if the patient is hypotensive and collapsed (*see Fluid Therapy p. 351*). Reassessment at frequent (i.e., 10 min) intervals is necessary if such large volumes are to be administered, and shock doses are contraindicated if CVP is >10 – 20 cmH$_2$O. Otherwise, calculation of deficits and replacement over 24 hours with CVP monitoring is indicated.

C. **Corticosteroids** (**methylprednisolone** or **prednisolone sodium succinate 2 mg/kg IM or IV over 15 min,** repeat once if needed) and **heparin 100 – 200 U/kg SC** may be administered prior to worm removal due to the risks of massive antigen release and anaphylactic reaction (with worm maceration) and thromboembolism.

D. **Other therapy** necessary to stabilize the patient prior to surgical worm removal may include whole **blood transfusion** only for severe anemia (PCV <10 – 15%), fresh frozen plasma if ACT is very short or prolonged (<70 or >120 secs) and **sodium bicarbonate** only for severe metabolic acidosis (*see Acid-Base Disorders p. 406*).

E. **Surgical worm removal** must be performed as soon as possible. Worm removal is performed via jugular venotomy with the use of a retrieval instrument such as long (20 – 40 cm), small-diameter, flexible alligator forceps (Fujinon Inc., Japan), an endoscopic basket retrieval device, or string brush in cats. It is ideally performed with the use of fluoroscopic or echocardiographic guidance (or both). If neither is available, the distance of the right atrium from the neck may be estimated and pre-measured on the instrument as the distance from the venotomy site to the level of the 4th intercostal space. Sedation +/- general anesthesia may be necessary in patients that are not severely debilitated. Cats generally require general anesthesia. In left lateral recumbency, an area of the right lateral neck over the right jugular vein is clipped and surgically prepared. Local anesthesia is applied in the skin over the jugular vein using 0.5 – 1 mL 2% lidocaine. A jugular vein cutdown is performed to isolate the right jugular vein. The jugular vein proximal to the planned venotomy site (toward the head) is ligated, while umbilical tape or an elastic band is applied around the vein distally to control bleeding. Venotomy is performed by a stab incision into the jugular vein. The retrieval instrument is advanced slowly and gently to the level of the right atrium. The instrument is opened, advanced slightly, closed, and retracted. Typically 1 – 4 worms are removed at a time, and this procedure is continued until 5 – 6 consecutive attempts yield no worms. Care must be taken to avoid perforation of the RA or cranial vena cava, and to avoid maceration of the worms, which can result in massive antigen release with pulmonary vasoconstriction and/or DIC.

ONGOING THERAPY

Signs of shock, right heart failure, and intravascular hemolysis tend to resolve rapidly after successful worm removal. Post-op monitoring of temperature, PCV/TS, BUN, arterial blood gas, urinalysis, CVP, murmur intensity, and recheck echocardiography help guide therapy and assess prognosis. Management of complicating factors (ongoing PAH +/- right heart failure, renal or hepatic failure, DIC) and therapy for HWD constitute ongoing therapy. Poor prognosis is indicated by persistent hypoxemia, reduced cardiac output, severe PAH, hypothermia, ongoing ascites, and elevated CVP.

A. Oxygen therapy is often needed post-op. Persistence of low PaO_2 and low PvO_2 are poor prognostic signs.

B. Intravenous fluids may be administered more aggressively following worm removal as elevated CVP and right heart failure tend to resolve rapidly.

C. Steroids and **heparin** (100 – 200 U/kg SC q8h to maintain ACT 1.5 – 2 X normal) may be continued. Steroids are administered in tapering doses upon discharge.

D. Strict rest must be enforced

E. Other post-op considerations include:
   1. Broad-spectrum **antibiotics (clavamox 10 mg/kg q12h)**
   2. **Vasodilator** therapy for moderate to severe PAH (typically **amlodipine 0.1 mg/kg PO q24h**) (*see Pulmonary Artery Hypertension, p. 193*).
   3. **Therapy for right heart failure** with angiotensin converting enzyme (ACE) inhibitors, furosemide, +/- pimobendan, and abdominocentesis as needed (*see Pulmonary Artery Hypertension, p. 193*).

F. Adulticide therapy is administered 2 – 3 weeks post-worm removal in dogs (once appetite, respiration, PCV, and urea are normalized) to kill remaining heartworms, and is generally not recommended in cats. **Microfilaricide therapy** is administered 4 – 6 weeks following the completion of adulticide therapy, followed by **ongoing preventative therapy**. See references 1, 2, 6, and 7 in **Suggested Reading** for details.

PHARMACOLOGY

1) **Heparin** is an anticoagulant that binds to antithrombin III and facilitates the inhibition of clotting factors II, IX, X, XI, and XII. Side effects include a sometimes unpredictable dose response, hemorrhage, and thrombocytopenia.

2) **Corticosteroids** are used for their anti-inflammatory actions. When administered intravenously, they must be administered very slowly to avoid hypotension.

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NOTES

INTRODUCTION

The pulmonary circulation is normally a low-pressure and low-resistance vascular bed. Normal pulmonary artery pressures (PAP) in an awake dog are:

Peak systolic PAP	15 – 25 mmHg
End-diastolic PAP	5 – 10 mmHg
Mean PAP	10 – 15 mmHg

Definitive measurement of PAP involves catheterization of the pulmonary artery. Pulmonary artery hypertension (PAH) is typically defined as systolic PAP exceeding 30 mmHg or mean PAP exceeding 20 mmHg at cardiac catheterization. However, PAP can be estimated non-invasively with the use of Doppler echocardiography (*see Echocardiography* below). PAH may be primary (idiopathic) or secondary to a number of other diseases. The main mechanisms responsible for PAH include increased pulmonary vascular resistance, increased pulmonary blood flow, and increased blood viscosity. More than one mechanism is often involved. Table 1 provides a summary of mechanisms and etiologies of PAH.

TABLE 1. Mechanisms and Etiologies of PAH

MECHANISM	ETIOLOGY
Increased left atrial and/or pulmonary venous pressures	Left-sided cardiac disease, e.g., mitral valve disease (MVD), dilated cardiomyopathy (DCM), mitral stenosis Obstruction of pulmonary veins
Histopathologic narrowing of pulmonary vessels (intimal proliferation and medial hypertrophy)	Heartworm disease Primary (idiopathic) PAH Eisenmenger's syndrome
Hypoxic vasoconstriction	Pulmonary parenchymal disease (cor pulmonale) High altitude Hypoventilation
Obstruction of pulmonary vessels	Pulmonary thromboembolism (heartworm disease, IMHA, sepsis, DIC, Cushing's disease, nephrotic syndrome, pancreatitis, neoplasia)
Destruction of pulmonary vessels	Pulmonary parenchymal disease (cor pulmonale)
Increased pulmonary blood flow	Large left-to-right shunts (e.g., PDA, VSD) High cardiac output states (e.g., anemia, pyrexia)
Increased blood viscosity	Polycythemia Hyperproteinemia

DIAGNOSIS

History/Signalment

- Collect a thorough history, checking for signs of chronic respiratory disease, cardiac disease, and causes of pulmonary thromboembolism (PTE) (*see Table 1*).
- Ask about heartworm status and heartworm prevention history.

Clinical Signs/Physical Examination

Clinical signs may be a direct result of severe PAH or may reflect the underlying disease (often respiratory or cardiac disease), and include:

- **Exercise intolerance/lethargy** due to poor cardiac output, hypoxia, and right heart failure.
- **Syncope** due to reduced cardiac output and hypoxia.
- **Dyspnea/tachypnea** direct result of severe PAH or due to primary pulmonary disease; may also be due to pleural effusion from right heart failure.
- **Cough** due to pulmonary disease.
- **Hemoptysis** due to pulmonary disease or heartworm disease.
- **Abdominal distension** due to ascites from right heart failure.

Physical examination findings may include:

- **Pale mucous membranes** due to poor perfusion as a result of poor cardiac output or anemia.
- **Cyanosis. Peripheral** cyanosis due to poor cardiac output and peripheral vasoconstriction. **Central** cyanosis if right-to-left shunt present (Eisenmenger's syndrome).
- **Jugular venous distension/pulsation** as a result of high central venous pressures.
- **Abnormal lung sounds**
    - Increased bronchovesicular sounds, coarse crackles, or wheezes – due to pulmonary disease.
    - Fine crackles due to pulmonary edema with left-sided heart diseases.
    - Decreased breath sounds due to pleural effusion from right heart failure.
- **Abnormal cardiac auscultation**
    - Sinus tachycardia due to systemic hypotension or right heart failure.
    - Arrhythmias may be present; tachyarrhythmias (typically premature beats) if left sided heart disease or right heart failure present; bradyarrhythmias reported in some cases of severe respiratory disease.
    - Right sided systolic murmur due to tricuspid regurgitation.
    - Left sided systolic murmur if PAH is due to MVD or DCM
    - Gallop rhythm due to increased diastolic pressure in a dilated and/or hypertrophied right ventricle (RV).
    - Loud and/or split second heart sound due to increased RV afterload and delayed pulmonic valve closure, respectively.
- **Abdominal distension +/- fluid wave** due to ascites from right heart failure.
- **Peripheral subcutaneous edema** from right heart failure (uncommon).
- **Cachexia** due to chronic disease.

PATIENT EVALUATION

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV** may be normal; increased if polycythemic secondary to chronic hypoxia; or decreased if IMHA, DIC, heartworm disease or CHF.
- **TS** is decreased with severe heartworm disease, nephrotic syndrome, or CHF.
- **Stick BUN** may be increased due to poor perfusion.
- **ACT** may be prolonged if DIC present.
- **Arterial blood gas** hypoxemia is common (PaO_2 ranged from 35 – 76 mmHg, mean 53.5 +/- 13 mmHg, in one case series) due to pulmonary parenchymal disease or PTE with ventilation-perfusion mismatch, and right heart failure with increased extraction, but hypoxemia is not always present.
- **Systemic blood pressure**. Systemic hypotension due to poor cardiac output, right heart failure; exception: systemic hypertension could be present if Cushing's disease is responsible for PTE.
- Diagnostic **abdominocentesis** is indicated if abdominal distension and fluid wave present; rules out hemoabdomen as abdominal fluid is a transudate, or modified transudate.

Extended Laboratory Data Base

- Clinical pathology findings are non-specific and reflect the underlying disease.
- **CBC.** Mild nonregenerative anemia and eosinophilia common with heartworm disease; basophilia possible as well. Severe regenerative anemia may be present with IMHA and PTE. Nucleated RBC's secondary to hypoxia.
- **Biochemistry profile.** Urea +/- creatinine may be elevated due to poor perfusion. Hepatic enzymes (ALT, AST, ALP) may be elevated with right heart failure.
- **Urinalysis.** Proteinuria common in heartworm disease, nephrotic syndrome.
- **Heartworm antigen test** is positive in heartworm disease.
- **Electrocardiogram** if severe PAH, there may be:
  - Evidence of RV enlargement (mean electrical axis shifted to right; S waves in leads I, II, and III; S wave in V3 > R wave in V3).
  - Evidence of right atrial (RA) enlargement (P wave amplitude > 0.4 mV).
  - Use to confirm any arrhythmias heard on auscultation.
- **Central venous pressure (CVP)** may be elevated. *See Fluid Therapy p. 371* for catheter placement and CVP measurement technique.

Imaging and Other Diagnostics

- **Thoracic radiographs**
  Abnormal findings may include enlargement of the main pulmonary artery (MPA) and branches, tortuous or blunted pulmonary arteries, right-sided cardiomegaly, pulmonary infiltrates, left-sided cardiomegaly and enlarged pulmonary veins in the case of left-sided heart disease, enlarged caudal vena cava, and pleural effusion with right heart failure. Absence of pulmonary changes in the face of dyspnea is suggestive of acute PTE, but may also be found in primary PAH.

- **Echocardiography**
  - Doppler echocardiography is used to non-invasively estimate PAP. In the absence of pulmonic stenosis, peak velocity of tricuspid regurgitation (TR) is used to estimate peak systolic PAP. Velocity is translated into pressure gradient using the modified Bernoulli equation $\Delta P = 4V^2$, where ΔP is the pressure gradient between the RV and RA, and V is the peak TR velocity. Estimated RA pressure is then added to the pressure gradient to estimate PAP. In this manner, peak TR velocity >3 m/s is abnormal and indicative of PAH.
  - Structural changes may include RV concentric and eccentric hypertrophy, RA enlargement, paradoxic septal motion, caudal vena caval enlargement, and a small left heart.
  - However, if PAH is due to left-sided heart disease, LV eccentric hypertrophy, left atrial enlargement, mitral regurgitation, reduced LV contractility (in DCM), and abnormal mitral valve morphology (in MVD) will be present.

- **Nuclear scintigraphy** (available only at specialty referral centres). A pulmonary perfusion scan is indicated to try to differentiate PTE from primary PAH (both may produce normal lungs radiographically in the face of PAH). The characteristic finding in PTE is a segmental or lobar defect in pulmonary perfusion, and a normal perfusion scan rules out major PTE. Diffuse, non-segmental perfusion defects may be found in primary PAH.

- **Cardiac catheterization and angiography** (available only at specialty referral centres). While cardiac catheterization remains the definitive means of diagnosing PAH, it is rarely performed because of the high-risk nature of the patients, and the information derived from Doppler echocardiography is usually diagnostic. Cardiac catheterization may be performed in cases of PAH with complex congenital cardiac disease or PTE to measure pressures and perform angiographic studies.

- PAH can be very difficult to treat.
- Underlying disorders must be sought and treated appropriately, particularly to avoid permanent pulmonary vascular damage.
- If the underlying cause is unknown or untreatable, therapy is directed at reducing pulmonary vascular resistance, controlling RV pressure overload, and treating right heart failure.

General Therapy – Acute

A. **Oxygen.** Hypoxic vasoconstriction is a primary or secondary feature of PAH. Oxygen by nasal cannula, prongs, or mask is indicated in hypoxemic patients (PaO_2 < 70 mmHg) [*see Supplemental Oxygen, p. 577*].

B. **Intravenous fluids** are indicated to support circulation in dehydrated or hypotensive patients. Initial choice is typically a replacement-type alkalinizing crystalloid (e.g., Plasma-Lyte® 148 or Lactated Ringer's) [*see Fluid Therapy, p. 362*]. Fluids may need to be administered more slowly to patients in right heart failure. Monitor fluid therapy using CVP and signs of fluid overload (*see Fluid Therapy, p. 371*).

C. **Thoracocentesis** is indicated if there is physical examination or radiographic evidence of pleural effusion and the patient is dyspneic. *See Respiratory Emergencies p. 574* for thoracocentesis technique.

D. **Vasodilators** are administered to reduce pulmonary vascular resistance. The systemic vasculature is affected as well, often more profoundly, potentially causing or exacerbating systemic hypotension and necessitating periodic blood pressure monitoring. Diseases in which the pulmonary vasculature is markedly abnormal may not be responsive to vasodilator therapy.

   1. **Amlodipine** (calcium channel blocker) at 0.1 mg/kg PO q24h is typically the vasodilator of choice. A 1 mg/mL suspension may be specially prepared by a pharmacy for small dogs and cats.

   2. **Pimobendan** is a drug with vasodilating and positive inotropic properties. It is administered at 0.25 mg/kg PO q12h. This therapy is also useful in the presence of RV or LV failure. Pimobendan may be used in conjunction with amlodipine, however careful monitoring of systemic blood pressure is recommended.

E. **Therapy for right heart failure** is indicated in the presence of ascites, pleural effusion, or peripheral edema.

   1. **Angiotensin-converting enzyme (ACE) inhibitors.** (Enalapril or benazepril at 0.5 mg/kg PO q12h as a mixed vasodilator and neurohormonal modulator (reduce angiotensin II and aldosterone production).

   2. **Diuretics.** Furosemide at 2 – 4 mg/kg PO q8–12h to control effusions. Caution must be exercised with the use of diuretics in the face of severe PAH as reduction in blood volume may significantly reduce cardiac output. High doses of diuretics should thus be avoided.

   3. **Abdominocentesis** is indicated if ascites is severe and compromising breathing. It should be performed slowly, and as such, a blunt instrument like a teat cannula or a catheter should be used rather than a needle. An area to the right of the umbilicus is shaved and surgically prepared. The skin, subcutaneous tissues, and abdominal musculature are infiltrated with 1.0 mL of 1% lidocaine solution. A 2 mm stab incision is made through the skin using a scalpel blade, and the teat cannula or catheter is advanced through the incision. A teat cannula is more efficient for abdominal drainage than a catheter as the latter tends to kink and clog, however a catheter may need to be used for small dogs. Extension tubing, a three-way stopcock, and a syringe are attached to the cannula/catheter, and slow, gentle suction is applied. When suction yields no fluid, it is helpful to change the position of the cannula/catheter or change the patient's position. A light abdominal wrap may be applied afterwards for cleanliness as leakage tends to continue from the incision site.

F. **Monitoring**

   1. Respiratory rate and effort.
   2. Systemic blood pressure (maintain systolic BP >100 mmHg).
   3. Renal parameters (urea, creatinine) and electrolytes to monitor renal perfusion, particularly in the face of therapy with ACE inhibitors and diuretics.
   4. PAP may be monitored using Doppler echocardiography.
   5. Abdominal girth may be periodically measured to monitor ascites production.

General Therapy – Ongoing

A. **Vasodilators** are adjusted on the basis of clinical signs, systemic blood pressure, and Doppler echo PAP estimates. Amlodipine may be increased in small increments, sometimes up to 0.2 – 0.3 mg/kg PO q24h. The limitation is systemic blood pressure, which should be monitored closely during therapeutic adjustments.

B. **Therapy for right heart failure**
   1. **ACE-inhibitor** dose is typically kept at 0.5 mg/kg PO q12h, unless renal insufficiency develops in which case the dose may have to be reduced.
   2. **Diuretic** doses are adjusted as needed to control effusions yet maintain renal function. The goal is to use the lowest dose that reasonably controls effusions since diuretic use can significantly lower cardiac output in PAH patients.
   3. **Abdominocentesis** and **thoracocentesis** as needed.
   4. **Strict rest** is necessary. Even mild physical activity can dramatically increase PAP in the presence of abnormal pulmonary vasculature, thus rest should be enforced.
   5. **Moderate dietary Na⁺ restriction** – Diets moderately restricted in Na⁺ such as the renal diets (e.g., Hill's K/D, Purina NF) are ideal in the heart failure setting, however it is more important to keep the patient eating.

C. **Monitoring.** Same as **F** above. Rechecks may be required q1–2 weeks initially. The frequency may be decreased to q1–2 months once stabilized on therapy.

Specific Therapy for Underlying Causes

A. Heartworm disease (*see Ongoing therapy section of Caval Syndrome, p. 187*).

B. Small airway/pulmonary disease (*see Respiratory Emergencies, p. 567*).

C. Left-sided heart failure (*see Chronic Congestive Heart Failure, p. 158*).

D. PTE (*see Thromboembolic Disease in Cats p. 195, Thromboembolic Disease in Dogs p. 201*).

PHARMACOLOGY

1) **Amlodipine** is a dihydropyridine calcium channel blocker acting on vascular smooth muscle to cause vasodilation. It has little effect on cardiac calcium channels and thus does not have noticeable negative inotropic or negative chronotropic properties. It has a long half-life and may take 1 – 2 days to reach maximum effect. Its main side effect is systemic hypotension.

2) **Pimobendan** is a phosphodiesterase inhibitor and calcium sensitizing agent with vasodilating and positive inotropic properties. It is newly licensed in Canada for the treatment of congestive heart failure in dogs, thus its use for PAH is not a labelled use. Pimobendan has been useful in the treatment of PAH in people. In theory, positive inotropes may be associated with increased ventricular arrhythmias, however this may not be the case with calcium sensitizers.

3) **Enalapril** and **benazepril** are both ACE-inhibitors. They reduce sodium and water retention and have venous and arterial vasodilating properties. Within the renal vasculature, they preferentially dilate the efferent arteriole, reducing glomerular filtration pressure and potentially reducing GFR if renal blood flow is not adequate. Hypotension is rarely recognized in dogs.

4) **Furosemide** is a loop diuretic, inhibiting the Na⁺-K⁺-2Cl⁻ cotransporter in the thick ascending limb of the loop of Henle in the nephron, thereby increasing excretion of Na⁺, K⁺, Cl⁻, and water. Ca²⁺ and Mg²⁺ excretion and H⁺ secretion are also indirectly increased. Side effects include dehydration, hypokalemia, hyponatremia, metabolic alkalosis, and activation of the renin-angiotensin-aldosterone system.

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INTRODUCTION

Thromboembolism in cats is most commonly localised at the level of the aorto-iliac bifurcation. In some cases, the front limbs may be affected. More rarely thromboembolic disease may affect the central nervous system, lungs, or abdominal organs. The most common etiology is underlying cardiac disease, and any cat that presents with thromboembolism should be evaluated for the presence of heart disease. Thrombus formation can occur in all types of cardiomyopathies, and results from one or more factors such as exposed subendothelial tissue, abnormal stagnant blood flow (commonly due to left atrial enlargement), increased blood coagulability and feline platelets are highly reactive. Other causes of thromboembolism include dysproteinemias, DIC, liver disease, neoplasia, paradoxic heartworm embolization, nephropathies, endothelial injury, hyperadrenocorticism and bacterial endocarditis.

DIAGNOSIS

History/Signalment

The diagnosis is based mainly on the history and physical exam findings. A prior history of heart disease may not be established. The most common presenting complaint in cats is acute paresis or paralysis of the hindlimbs. The presenting signs are dependent on the localization of the thrombus. Acute onset of hindlimb paresis or paralysis is the most common presentation. Occasionally cats present with paresis or paralysis of a forelimb. Partial thromboembolism can result in decreased blood flow to a specific muscular region and present as lameness. Other less common presentations of thromboembolic events can be associated with the central nervous system (e.g., seizures, vestibular signs, change in mentation), gastrointestinal system (acute vomiting, diarrhea, acute abdomen), and acute renal failure (bilateral renal thrombosis) usually accompanied by bilateral hindlimb paralysis. Differential diagnoses include, intervertebral disk extrusion (diagnosed more frequently than expected), trauma, peripheral neuropathy and myasthenia gravis.

Clinical Signs/Physical Examination

Physical exam findings resulting directly from **aorto-iliac thromboembolism** include:
- Paresis or paralysis of the hindlimb(s).
- Lack of or decreased femoral arterial pulses.
- Blanching of the footpads and/or cyanosis of the nail bed of the affected limb(s).
- Cool extremities of the affected limb(s).
- Firm and painful gastrocnemius muscle(s).
- Severe pain resulting in tachypnea ± vocalization localized to limbs or lumbar area if kidneys involved.

Physical exam findings resulting from **underlying heart disease** include:
- Respiratory distress either due to pulmonary edema or pleural effusion.
- Reduced lung sounds due to pleural effusion, or crackles and wheezes if congestive heart failure is also present.
- Cardiac arrhythmias, murmur or gallop rhythm are usually detected due to underlying cardiomyopathy and stress.

LaboratoryEvaluation/Diagnostic Imaging

Stat
- Only attempt blood collection and radiographic imaging if the cat does not have significant respiratory compromise, or is unduly stressed with handling. Pain should be treated immediately.
- **PCV, TS** in most cases are normal, elevations can be seen due to dehydration.
- **BUN, Creatinine** may be increased due to chronic or acute renal disease, or embolism of the renal arteries.
- **Blood glucose** levels obtained from venipuncture of the affected region is usually lower than that obtained from a normal area (e.g., jugular v).
- ACT are usually normal but may be abnormal if DIC or other coagulation abnormality is present.
- Blood gas (venous) frequently reveals a metabolic acidosis.
- Lactate levels from the affected limb are much higher than a normal area.
- Electrolytes are usually within normal limits; however potassium may be markedly increased with re-perfusion.

Extended Laboratory Data Base

Definitive diagnosis can only be made by aortic angiography or nuclear scintigraphy, but this is usually unnecessary. Diagnosis can also be established by means of vascular ultrasonography.

- **CBC** is frequently within normal limits.
- **Biochemical profile.** Creatinine kinase is greatly increased with values usually in the tens of thousands. Renal parameters are abnormal if there is underlying renal disease or the renal arteries are thrombosed.
- PT, PTT are usually within normal limits but should be obtained for baseline.
- Urinalysis for baseline assessment and completeness in assessing renal function.
- **Chest radiographs** to identify pulmonary edema or pleural effusion, and evaluate the cardiac silhouette.
- **Echocardiographic examination** is not usually necessary at the time of presentation with thrombo-embolic disease unless pulmonary edema is present with poor response to therapy (*see Congestive Heart Failure – Life-Threatening p. 150*). As soon as the patient is stable, an echocardiogram should be performed as this may aid in establishing prognosis.
- To verify if blood flow is present in the femoral or brachial artery:
  - Use the Doppler blood pressure device.
  - Expose the vascular ungual process by clipping the nailbed and assess the colour; this should be bright red oxygenated blood if blood flow is present.
- Compare the serum glucose level obtained from the affected limb with a sample obtained from a well perfused area (i.e., compare the medial saphenous glucose level with jugular glucose level). The serum glucose level in the affected limb(s) should be well below normal.

MANAGEMENT

I. Emergency Therapy

A. If in respiratory distress *see Congestive Heart Failure – Life-Threatening p. 150*. After stabilization proceed below to **B or D (not both).**

B. After collecting baseline coagulation parameters, initiate acute antithrombotic therapy with **heparin sulfate.**

1. **200 Units/kg IV loading dose, followed by:**
   a. **150 – 200 Units/kg SC, 4 hours later after obtaining ACT or PTT★, then at 8 h,** until ACT or PTT are prolonged to twice above baseline. OR
   b. **10 – 25 Units/Kg/h in D5W** CRI can be used instead of (a).
2. Obtain ACT or PTT 4 hours after loading dose and 6 hours after starting CRI. **★Adjust heparin dose as needed** based on coagulation times. When ACT or PTT are twice baseline (usually within 12 – 24 hours), **reduce dose to minimum needed to maintain this level of anticoagulation; usually 100 – 150 Units/kg q8h.** If using the constant rate infusion, reduce or increase infusion by 1/3 as needed to maintain target anticoagulation level. Monitor ACT or PTT 4 hours after each change and titrate subsequent dose accordingly.

C. **Protamine 0.5 – 1.0 mg IV per 100 U of heparin** should be administered slowly as **antidote for** inadvertent overdose of heparin sulfate, If heparin was administered 1 hour prior to treatment with protamine reduce the protamine dose by one-half. Protamine overdose may result in excessive bleeding.

D. **Low Molecular Weight Heparins (LMWHs)** can be used for chronic treatment and prevention of thromboembolism.

1. **Enoxaparin (Lovenox) at 1 mg/kg SC q12h,** OR
2. **Dalteparin (Fragmin) at 100 units/kg SC q24h.**
3. LMWH administration does not require monitoring of coagulation times.

E. **Analgesia** is absolutely necessary as the thromboembolic event is very painful.

1. **Oxymorphone or hydromorphone 0.02 – 0.05 mg/kg, or to effect, q2–4h for severe pain.** There is no concern for hypotension with these analgesics.
2. **Butorphanol 0.4 – 0.8 mg/kg q2–4h, or to effect, for mild to moderate pain.**

F. **Keep limb(s) warm.** Do not apply any heat source greater than you can tolerate on the ventral surface of your wrist otherwise thermal injury may occur.

G. Collateral circulation may be promoted by the use of vasodilators such as:

1. **Acepromazine 0.01 – 0.02 mg/kg SC q8h** Avoid excessive hypotension by using the low end of the dose initially. OR
2. **Hydralazine at 0.5 – 1 mg/kg PO q8h.**
3. Do not administer these drugs if hypotensive.

H. The use of **thrombolytic agents such as streptokinase or tissue plasminogen activator (t-PA)** are advocated. In the author's experience **t-PA** results in effective thrombolysis but with **devastating reperfusion complications** (acidosis, hyperkalemia followed by death), and it is not recommended. **Streptokinase can be used as follows:**

   a. Its use is only recommended for cases presented in the first 8 hours of embolization.
   b. Initiate intravenous infusion of **90,000 IU over 30** minutes followed by a 45,000 IU/h CRI for up to 8 hours.
   c. **Stop infusion after 8 hours** or whenever reperfusion is established – whichever occurs first.
   d. **Monitor serum K$^+$ every 2 hours** during the infusion. Consider placing a jugular catheter for ease of sampling. To reduce stress apply EMLA® cream (local anesthetic cream) to the venipuncture area 30 mins prior to catheter placement. Although insensitive, continuous ECG monitoring can indirectly monitor potassium levels. Increasing tachycardia or bradycardia, lack of P waves in any lead, and peaked T waves may be an indication of hyperkalemia. If potassium levels rise above 7 mEq/L initiate treatment for hyperkalemia (*see Hyperkalemia p. 397*).
   e. If reperfusion is not established after 8 hours of Streptokinase CR, stop the infusion.
   f. Concurrent treatment with heparin can be performed or initiated after treatment with Streptokinase.

II. Chronic Therapy

Chronic therapy relies on the treatment of the underlying disease predisposing to thromboembolism and the prevention of further episodes. Although aspirin has been used to prevent thromboembolism, its effectiveness is questionable. The only effective way of preventing further episodes is by use of specific anticoagulants.

A. **Warfarin** is a first line anticoagulant.

   1. **Warning:** Warfarin therapy should only be started after achieving the recommended level of anticoagulation with heparin (IB above). Otherwise, initial warfarin therapy promotes a prothrombotic state, due to rapid reduction in protein C (antithrombotic protein) levels, leading to the development of a thrombus. Usually, warfarin and heparin therapy are overlapped for 3 days. In the author's experience, the need for overlapping heparin and warfarin therapy is questionable and, therefore, no longer follows this protocol. After initial therapy with heparin, the author starts the patient on coumadin without significant overlap.
   2. **Warfarin should be started at a dose of 0.25 – 0.5 PO mg/cat once a day and titrated to obtain a PT level twice above baseline.** The use of a suspension (1 mg/mL) may provide less variability in the levels of anticoagulation.
   3. The first recheck PT should be done on day 3 then repeated on day 7 and then weekly until the adequate dose is found.
   4. A cat on chronic warfarin therapy should have a recheck PT every 6 – 8 weeks. Consult with a cardiologist for titration of therapy.
   5. Adjustments to therapy are made in increments of 25 – 30%. Recheck patient one week after drug adjustment.

B. **Chronic heparin sulfate** administration (subcutaneously) is an alternative. Adjust dose to maintain desired anticoagulation. Some authors advocate this method because the level of anticoagulation is more stable, and experience is favourable.

C. **Chronic LMWH.** The author has limited experience with this method of therapy. The major advantage is the lack of need for monitoring of clotting times. The margin of safety is apparently larger. The major drawback is expense, this may be offset however by the reduced recheck visits.

D. **Aspirin 81 mg/cat q72h.** The efficacy of aspirin is questionable for long-term management.

E. **Physiotherapy** is required several times daily until paralysis is resolved.

NOTE: Chronic anti-thrombotic therapy may not be feasible for every owner or for every cat. Fractious cats and poorly compliant owners increase the risk of complications with this therapy. The lifestyle of the cat should also be considered: outdoor cats may be at higher risk of bleeding from injury or "missing" doses. This can de-stabilize the coagulation equilibrium and increase the risk of potential complications.

PHARMACOLOGY

1) **Heparin sulfate** (unfractionated heparin- UFH) is a potent anticoagulant. Promotes anticoagulation indirectly by increasing antithrombin activity. It is destroyed in the gastrointestinal tract; therefore it is only available for IV or SC use. The most important side effect is uncontrollable bleeding. This can be controlled with the antidote protamine sulfate (1% solution). Each 1 mg of protamine neutralizes 90 U of heparin. A maximum dose of 50 mg of protamine is recommended in humans. Chronic administration of heparin in humans (>5 days) has been shown to cause thrombocytopenia in some patients, however this is felt to be species specific.

2) **Acepromazine** is a phenothiazine tranquilizer. Causes alpha adrenergic receptor blockade, thereby lowering systemic vascular resistance and blood pressure. This action may promote the development of collateral circulation. Side effects are excessive sedation and/or hypothermia. Extreme hypotension can cause collapse, renal failure or hepatic failure.

3) **Hydralazine** is a direct-acting arteriolar dilator. The mechanism of action is not completely understood. It is thought to be dependent on nitric oxide release. The most important side effect is the development of severe hypotension and reflex tachycardia.

4) **Aspirin** is a non-steroidal anti-inflammatory drug that irreversibly inhibits cyclo-oxygenase. This drug inhibits conversion of thromboxane A2 in platelets. Thromboxane A2 has vasoconstrictor effects. Its inhibition is thought to promote collateral circulation. Aspirin also inhibits the production of prostacyclin, a prostaglandin that inhibits platelet aggregation. Cats tolerate aspirin only in small doses due to very slow hepatic metabolism. Toxic reactions include anorexia, vomiting, lethargy and death.

5) **Warfarin** is an anticoagulant. Its action is due to inhibition of vitamin K dependent clotting factors (II, VII, IX, X) and inhibition of the anticoagulant proteins C and S. Its major side effect is uncontrollable bleeding that can be reversed by administration of vitamin K and blood transfusion if needed. There are numerous drug interactions with warfarin, *see reference 1, page 869 below.*

6) **Streptokinase** is a thrombolytic agent. Thrombolytics act by promoting the conversion of plasminogen to plasmin. Plasmin has fibrinolytic activity. When streptokinase binds to plasminogen it becomes an active enzyme to convert plasminogen to plasmin. In addition, it may increase circulating levels of activated protein C enhancing clot lysis. Side effects are mainly related to bleeding tendencies, especially when combined with heparin therapy. If major bleeding develops during therapy, administration of fresh frozen plasma or fresh blood is indicated to stop the fibrinolytic state. Hypersensitivity reactions have been reported in people. Streptokinase is contraindicated if there are pre-existing bleeding tendencies. The presence of bacterial toxins due to recent streptococcal infection induce resistance to streptokinase. Previous treatment may induce the development of antibodies; therefore subsequent treatments are shown not be as effective and can be followed by hypersensitivity. The experience with this agent in veterinary medicine is limited and should be used with a full understanding of potential complications and owner consent.

7) **Low molecular weight heparins (LMWH)** are short heparin polymers obtained by chemical or enzymatic cleavage of standard UFH (regular heparin). Similar to UFH, LMWHs exert their effect by interaction of their pentasaccharide sequence with antithrombin, thus inhibiting factor Xa. Unlike UFH, LMWHs are not efficient at inactivating thrombin. LMWHs have greater activity against factor Xa. LMWH also has a longer half-life and more predictable pharmacokinetics than UFH. It is administered subcutaneously once or twice a day, often without laboratory monitoring. LMWH appears to be at least as safe and as effective as UFH, with greater ease of dosing according to human studies. Enoxaparin and Dalteparin are two preparations of LMWH that are in frequent use in the United States and Canada. One initial study in cats suggested that 100 IU/kg SC of dalteparin (Fragmin®) once daily had an effect on anti-Xa activity. Enoxaparin (Lovenox®) has been used clinically in dogs and cats at a dosage of 1 mg/kg SC q12–24h.

SUGGESTED READING

1. Harpster NK, Baty CJ. Warfarin therapy of the cat at risk of thromboembolism. In: Bonagura JD (Ed) Current Veterinary Therapy XII, Toronto: Saunders, 1995:868-873.
2. Mark D. Kittleson. Thromboembolic disease. In Mark D. Kttleson and Richard D. Kienle (Ed) Small Animal Cardiovascular Medicine, Mosby, 1998:540-551.
3. Pion PD, Kittleson MD. Therapy for feline aortic thromboembolism. In: Kirk RW (Ed) Current Veterinary Therapy X, Toronto: Saunders, 1989:295-302.

NOTES

INTRODUCTION

Thromboembolic disease is extremely complex with many and varied etiologies affecting both the arterial and venous circulation. **Systemic arterial thromboembolism** (SAT) is rare in dogs and is usually indicative of systemic, metabolic or cardiac disease (e.g., infective endocarditis). Arterial thrombosis is predisposed by conditions resulting in vascular endothelial damage, sluggish blood flow and changes in blood constituents resulting in a hypercoaguable state (Table 1). In dogs, a common location for obstruction is the aortic trifurcation, iliac, renal and femoral arteries. Approximately 50% of dogs with SAT present with acute clinical signs, and the remaining 50% present with sub-acute to chronic signs such as a progressive lameness. As SAT may occur in any part of the body, the clinical signs will vary depending on the location of the obstruction. In some instances, a careful history, physical examination, high level of suspicion and laboratory investigation is required to identify SAT.

Thromboembolic disease involving the **venous system** frequently results in minor clinical consequences, however, major consequences may occur. Infectious thrombophlebitis secondary to intravenous catheter, or other contamination, may result in bacterial emboli to the lungs, heart valves and dissemination through the arterial system. Catheter-related obstruction of the cranial vena cava results in edema of the forelimbs causing pain; and edema of the head and neck, as well as pleural effusion, both causing dyspnea. Other causes of head, neck and forelimb swelling are mentioned in the Physical Examination/Clinical Signs section below.

Pulmonary thromboembolism occurs when the thrombus in the venous system or right side of the heart breaks away and is carried with the blood into the pulmonary arteries. Lung involvement is dependent on the size and number of thromboemboli obstructing the pulmonary vasculature and the degree of associated serotonin and thromboxane A2 vasoconstriction. In addition to a thrombus, air, fat, catheter fragments or heartworm may embolize to the lung. Heartworm is discussed elsewhere (*see Caval Syndrome p. 185*). The predisposition to forming PTE is similar to etiologies for SAT (Table 1) and venous thrombosis.

Approximately 50% of dogs with PTE have multiple underlying disease processes, which must be identified and treated along with prophylactic therapy for PTE. Common situations where thromboembolic disease will present itself in veterinary practice are in patients with protein-losing nephropathy (PLN) or enteropathy (PLE) due to the loss of antithrombin through the kidney or bowel; immune-mediated hemolytic anemia (*IMHA p. 411*) where endothelial damage by the erythrocyte antibody reaction triggers thrombosis (*see p. 412*); hyperadrenocorticism (*p. 270*) where concentrations of clotting factors II, V, VII, IX, X, XII and fibrinogen are increased, and antithrombin decreased; prolonged use of exogenous corticosteroids; pancreatitis (*p. 45*) where proteolytic enzymes released into the circulation injure the endothelium and activate the coagulation cascade, antithrombin and plasminogen are also reduced; atherosclerosis (*Hypothyroid p. 285*) and neoplasia due to endothelial damage or venous stasis.

TABLE 1. Predisposing Factors of Thromboembolism

Endothelial Damage	Abnormal Blood Flow	Hypercoaguable State
IMHA	Polycythemia	Hyperadrenocorticism
Pancreatitis	Dehydration	Pancreatitis
Arteriosclerosis	Shock	DIC
Atherosclerosis	Cardiac Disease	PLE and PLN
Heartworm	Neoplasia	Neoplasia
Vasculitis	Hyperviscosity	Thrombocytosis
Catheterization	Hypovolemia	Platelet hyperreactivity
Vascular incarceration/Compression	Endocarditis	Infection/sepsis/abscess
	Hyperthermia	IMHA
Hyperosmolar/irritating Substances IV		Parvovirus infection
		Acidosis

Modified after Fox PR, Petrie J-P, Hohenhaus AE. Peripheral vascular disease.In:Textbook of Veterinary Internal Medicine Sixth edition. Ettinger SJ, Feldman EC (eds). St. Louis, MO, Elsevier Saunders. 2005:1145-1165.

History/Signalment

The history and questions to the owner are directed towards the potential underlying causes. Differential diagnoses to be considered with limb involvement include intervertebral disk extrusion (*p. 473*), trauma (*p. 691*), peripheral neuropathy (*p. 491*) and myasthenia gravis (*p. 496*). Differential diagnosis for respiratory distress are pneumonia, (*p. 568*), acute congestive heart failure (*p. 149*), airway obstruction (*p. 565*), pericardial tamponade (*p. 145*), non-cardiogenic pulmonary edema (*p. 569*), or pleural effusion (*p. 566*).

- Breeds predisposed to PLN are soft-coated Wheaton Terriers and Shar Pei (amyloid); and PLE are the soft-coated Wheaton Terrier, Yorkshire Terrier, Irish Setter, Basenji, Rottweiler.
- There may be no previous clinical signs prior to acute dyspnea. Occasionally, dogs are playing vigorously prior to acute onset dyspnea.
- A history of leptospirosis, Lyme disease, or other renal pathology can be associated with glomerulonephritis.
- A history of heart disease is also a pre-disposing cause of SAT and occasionally results in sudden death with thrombosis in the heart or brain.
- Question the owner regarding heartworm prevention program.
- Diarrhea and weight loss are noted with PLE, although ascites may be mistaken for weight gain.
- Occasionally, reduced exercise tolerance or respiratory signs are noted due to pleural effusion in PLE.
- Acute onset of hindlimb paresis or paralysis is the most common presentation of arterial occlusion.
- Partial thromboembolism can result in decreased blood flow to a specific muscular region and present as lameness. A relatively high incidence of femoral artery thrombosis is reported in Cavalier King Charles spaniels
- Other less common presentations can be associated with the central nervous system (brain or spinal cord), gastrointestinal system (i.e., acute abdomen), acute renal failure (due to bilateral renal thrombosis).
- Further questions to the owner should be directed towards those associated with predisposing causes for thromboembolic disease.
- PTE may gradually occur in hospitalized patients with illnesses that predispose to PTE, such as immune-mediated hemolytic anemia, pancreatitis etc.
- PTE may be associated with presence of a cardiac pacemaker. These tend to develop chronically and are well organized.
- Aortic thromboembolism has been associated with a history of gastric-dilation-volvulus.
- Cranial vena caval thrombosis is also strongly correlated with the presence of a jugular catheter.

Clinical Signs/Physical Examination

Pain should be treated immediately. Go to MANAGEMENT E below (*p. 202*).

- Acute arterial occlusion of the aortic trifurcation or limbs is described by the seven P's: Pain (gentle touch elicits pain), pallor (expose the vascular ungual process by clipping the nailbed and examine for colour), paresthesia, polar (cold), paresis or paralysis, prostration and pulselessness. Spinal cord injury (*p. 473*) must also be considered, however, these lesions tend to result in warm, rather than cold limbs. Orthopedic injuries are readily distinguished from SAT.
- Severe dyspnea is noted with acute massive pulmonary arterial occlusion. Usually breath sounds are increased but no other abnormalities are noted on auscultation. Mucous membranes are cyanotic or grey.
- Signs of right heart failure secondary to severe pulmonary hypertension and myocardial hypoxemia may be present.
- Tachycardia is frequently present due to pain, hypoxemia and hypotension with PTE.
- Various neurological disorders are evident when associated with CNS thrombosis.
- Pain, arched back and anuria are associated with renal embolization.
- Signs of acute abdomen are associated with mesenteric embolization and infarction. If presented several hours after the event hematochezia, severe depression, and distended abdomen are noted.
- Heart murmur of mitral or aortic insufficiency secondary to endocarditis may be noted.
- **Jugular venous distension** may be present.
- Engorgement of conjunctival and scleral vessels may be present with cranial vena cava obstruction.
- **Swelling of head and neck, ± forelimb** associated with PTE, is identified as pitting edema, is symmetrical, non-painful and cool to the touch.
- **Myxedema of hypothyroidism** (*p. 285*) has a firm thickening of facial skin which is non-pitting. However, atherosclerosis due to hypothyroidism is a pre-disposing factor in thromboembolic disease.
- Other causes of facial swelling include salivary mucocele, abscessation/cellulitis both tend to be assymetrical with characteristic findings on examination.

- Subcutaneous emphysema from upper or lower airway pathololgy and esophageal injury may present with enlargement of the head and neck, however, this has a characteristic 'crepitus' on palpation.
- Other differentials include angioedema (*p. 212*), and rattlesnake bite (*p. 304*).

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, TS** are frequently normal unless the patient is dehydrated in which case they will be increased. With PLE or PLN, the TS is decreased.
- **BUN, Urea or Creatinine** may be increased due to underlying renal disease, dehydration or embolism of the renal arteries.
- **Blood glucose** may be altered based on the underlying disease. Blood glucose obtained from the jugular vein or non-affected limb, is higher than that of the affected limb (e.g., medial or lateral saphenous).
- **ACT, and/or baseline coagulation panel (PT, PTT)** may be normal, or abnormal as a result of DIC or an abnormality in the coagulation system. Thrombosis has not been correlated with shortened times.
- **Venous blood gases** reveal a non-respiratory acidosis due to hypoxemia or lactatemia. Hypoxemia and acidosis can contribute to worsening pulmonary hypertension in PTE.
- **Blood lactate** levels are markedly higher when obtained from the affected limb when compared to that obtained from a jugular venous, or non-affected limb, sample. This comparison can be used during the recovery phase to monitor reperfusion. Lactate levels will likely also be increased in SAT due to ischemia.
- **Arterial blood gas** analysis is a sensitive test for hypoxemia due to PTE but is not specific for this. In milder cases, blood gases are within normal limits. Hypocapnea may be associated with hypoxemia.
- **Electrolytes** are usually normal or altered by the predisposing cause. Potassium may be markedly increased with reperfusion.
- **Hematuria** may be present where renal infarction has occurred.
- **Systemic blood pressure** should be measured as hypotension frequently exists with severe PTE. Hypertension may be associated with urine protein losses, including antithrombin loss.
- The presence or absence of **blood flow** in the femoral or brachial artery can be verified using an ultrasonic blood flow detector (the common Doppler blood pressure device).

Extended Laboratory Data Base

- **CBC.** Severe leukocytosis, left shift and toxic changes in neutrophils may support systemic thrombosis. Schistocytes and thrombocytopenia may be present if there is an underlying problem causing DIC. Spherocytosis and/or agglutination are frequently observed in IMHA (*p. 411*). Polycythemia may be present in dogs with hyperadrenocorticism.
- **Biochemical profile.** Where SAT affecting the limbs is the presenting problem, creatinine kinase is greatly increased with values usually in the tens of thousands. Renal parameters are abnormal if there is underlying renal disease or the renal arteries are thrombosed. Metabolic abnormalities resulting in increased bilirubin and ALP have been associated with development of thrombosis. Increased cholesterol may indicate hypothyroidism, Cushing's disease or PLN as a cause for SAT. Hyperglycemia associated with diabetes mellitus as a pre-disposing cause may be present.
- **Serum electrolytes** as potassium (as above) and phosphorous may be increased due to cell lysis.
- **ACT and PT, PTT** results vary according to the underlying disease. These parameters should be measured as baseline and monitored throughout therapy.
- **Blood and urine** cultures should be obtained if sepsis is suspected.
- **Antithrombin levels** if low are highly suggestive of the underlying cause of thromboembolic disease; however, these may be normal if not the cause of the problem.
- Levels of **fibrinogen and fibrin degradation products** may be increased but this is not specific for thromboembolic disease. D-dimers are more specific to fibrinolysis, however, interpretation of abnormal values in thromboembolic disease in veterinary medicine is not determined. A negative test might be useful in ruling out thromboembolic disease.
- **Urinalysis** to identify proteinuria, and for baseline assessment and completeness in assessing renal function.
- **Chest radiographs** that are normal in dogs with severe respiratory distress are highly suspicious for a diagnosis of PTE. Other findings are interstitial, alveolar and lobar infiltrates. Vascular abnormalities include enlarged central pulmonary arteries, disproportionate vascular tapering, and oligemia. Cardiomegaly and mild pleural effusion may also be present. Pleural effusion may occur with cranial vena caval heartworm disease, severe

hypoalbuminemia associated with PLN or PLE. Thoracic neoplasia, abscess or granuloma (cryptococcosis, blastomycosis) may be an underlying cause of thromboembolism, or cause of edema of head, neck and the forelimbs.

- **Central venous pressure** is frequently increased above normal with PTE.
- **Two-dimensional echocardiography and Doppler examination** may identify large thrombi and pulmonary hypertension respectively (*see Pulmonary Hypertension p. 189*) for details.
- **Selective angiography,** using nonionic contrast media, is the gold standard for diagnosing peripheral and central vascular disease as the filling defect can be visualized. **Dogs with PTE and severe pulmonary hypertension may die acutely following contrast media injection directly into the pulmonary artery.**
- **Contrast-enhanced MRI** may also identify the occluded vessel but as general anesthesia is required this is reserved for stable patients with limb involvement.
- **Spiral CT** is being used more frequently in humans to diagnose PTE, however, general anesthesia risks in veterinary patients are a concern.
- **Ventilation-perfusion scans** using nuclear scintigraphy (technetium macroaggregated albumin) are sensitive and specific for PTE as areas of lung parenchyma which are aerated but not perfused can be identified.
- **Thyroid panel** where hypothyroidism is suspected (*p. 285*).
- **For non-thrombotic causes** of facial, neck and forelimb swelling consider:
  - **Fungal titres** are indicated if intra-thoracic fungal granulomas are suspected.
  - **Fine needle aspirates** of thoracic masses for cytology, culture and sensitivity to identify neoplasia or abscess.

MANAGEMENT

Treatment for identified underlying disease responsible for the thromboembolic event is essential. Management of the thromboembolic event requires general supportive care and anti-coagulation. Complete occlusion of renal, mesenteric and pulmonary arteries are frequently fatal due to irreversible organ injury. In general, dogs lyse thromboemboli rapidly and resolution of clinical signs may occur.

A. Oxygen therapy (*p. 577*) if in respiratory distress. After stabilization and definitive, or highly suspect diagnosis proceed below to **B or D (not both).**

B. **Anticoagulation** is initiated to prevent further thrombus formation. Anticoagulants do not have thrombolytic effect (*see H below*). CAUTION when performing venipuncture or inserting IV catheters if thrombolytic therapy is to be considered. The clot associated with the venipuncture site will be dissolved and hemorrhage will be observed. This is especially a concern with jugular venipuncture sites when attempting placement of a catheter directly to the thrombus in the anterior vena cava.

   1. Collect baseline ACT, PTT. The goal is to increase to twice baseline if not already above normal values for your laboratory. Normal ACT at the OVC is 75 – 120 (outlyer 125 secs) performed using grey top silica tubes incubated with a heat source (i.e., block heater or pushed tightly into the axilla, over a shirt or blouse but under the white coat!) Initiate antithrombotic therapy with **heparin sulfate at a loading dose of 100 Units/kg IV, followed by:**

      a. **Subsequent doses of 150 – 200 Units/kg SC,** at 4h, and then q8h. Measure ACT or PTT prior to each dose (*see c below*). **OR**

      b. A **constant rate infusion of heparin sulfate at a rate of 15 – 25 Units/kg/h in 0.9% saline** as a separate infusion from maintenance fluids to allow for adjustment. Obtain ACT or PTT 4 hours after loading dose and 6h after starting heparin CRI. Monitor q8–12h (*see c below*).

      c. **Adjust heparin dose as needed** based on coagulation times. When ACT or PTT are twice baseline (usually within 12–24h), **reduce dose to minimum needed to maintain this level of anticoagulation; usually 100 – 150 Units/kg q8h.** Increasing to 300 Units/kg or to q6h may be required. If using the constant rate infusion, reduce or increase infusion by 1/3 as needed to maintain target anticoagulation level. Monitor ACT or PTT 4h after each change and titrate dose accordingly.

      d. Should hemorrhage occur go to C below.

C. **Protamine 0.5 – 1.0 mg IV per 100 U of heparin should be administered slowly as antidote for inadvertent overdose of heparin sulfate.** If heparin was administered 1 hour prior to treatment with protamine, reduce the protamine dose by one-half. Protamine overdose may result in excessive bleeding.

D. **Low Molecular Weight Heparins (LMWHs)** can be used in place of heparin. LMWHs are expensive and superiority to heparin has not been confirmed in veterinary medicine. However, they are considered safer than heparin and do not require extensive monitoring.

    1. **Enoxaparin (Lovenox) at 1 mg/kg SC q12h,** OR

    2. **Dalteparin (Fragmin) at 100 – 150 Units/kg SC q12–24h**

E. **Analgesia** is absolutely necessary as the thromboembolic event is very painful.

    1. **Oxymorphone or hydromorphone at 0.02 – 0.05 mg/kg, or to effect, q2–4h for severe pain.** There is no concern for hypotension with these analgesics.

    2. **Butorphanol 0.4 mg/kg q2–4h, or to effect, for mild to moderate pain.**

    3. Diazepam or acepromazine 0.01 mg/kg (*see G*) combined with an opioid is recommended for anxious, painful animals.

F. **Keep limb(s) warm.** Do not apply any heat source greater than you can tolerate on the ventral surface of your wrist otherwise thermal injury may occur.

G. Previous recommendations to enhance collateral circulation of the limbs by the use of **vasodilators** such as in 1 and 2 below, have come into question as there is no support for their use. However, if hypotension is not a concern, there may be an individual benefit (personal communication Dr. Luis Braz-Rivo).

    1. **Acepromazine 0.01 – 0.02 mg/kg SC q8h,** OR

    2. **Hydralazine at 0.5 – 1 mg/kg PO q8h.**

    3. Do not administer these drugs if hypotensive or dehydrated.

H. **Thrombolytic agents such as streptokinase or tissue plasminogen activator** (t-PA) have been used infrequently in dogs. Effective thrombolysis is associated with reperfusion complications such as acidosis (especially with SAT) and hyperkalemia, and hemorrhage can be serious.

    1. **Streptokinase can be used as follows and is only recommended for cases presented in the first 8 hours of embolization:**

        a. Initiate intravenous infusion of **90,000 IU over 30** minutes [see (c) below] followed by a **constant rate infusion at 45,000 IU/h for 3 hours (may require up to 8 hours).**

        b. **Stop infusion** whenever reperfusion is established.

        c. If after 8 hours of constant rate infusion with Streptokinase, reperfusion is not established, stop infusion.

        d. Concurrent treatment with heparin can be performed or initiated after treatment with Streptokinase.

    2. **t-PA 1 mg/kg/h** for 45 minutes followed by 0.25 – 1 mg/kg/h until re-perfusion is established (or 1 – 2 hours). Lower dosages may be used for venous thrombi, especially if an IV catheter can be placed to the level of the thrombus allowing direct injection into it. Heparin (*see B 1a above*) is also administered. As there is very little information on this procedure, the clinician will have to decide how to manage these cases. In experimental PTE in dogs, rapid resolution with the first dose occurred. Reperfusion complications such as acidosis and hyperkalemia which may cause death may occur.

    3. **Reperfusion Syndrome will occur.**

        a. **Monitor serum K^+ every 2 hours** during the infusion (consider placing a jugular catheter for ease of sampling). Continuous ECG monitoring is essential in monitoring K^+ levels. Presence of bradycardia, lack of P waves in any lead, and peaked T waves may be an indication of hyperkalemia, although tachycardia may be an initial change. If potassium levels rise above 7 mEq/L consider initiating treatment for hyperkalemia (*see Hyperkalemia p. 397*).

        b. **Monitor acid-base and lactate levels q2h.** Appropriate fluid and adjunctive therapy is based on findings (*see Acid-Base Assessment p. 406*).

        c. **General patient monitoring** such as HR, RR, mucous membrane colour and capillary refill time, systemic blood pressure, urine (hematuria), bowel movements (hematochezie), venipuncture and IV catheter sites, and mentation should be conducted throughout as hemorrhage may occur at any time, from anywhere. PCV and TS should be measured if indicated.

I. **Cage rest** and gentle handling is recommended to avoid injury and hemorrhage. Restricted exercise is also recommended when discharged from hospital.

J. **Chronic therapy** relies on treating the underlying disease predisposing to thromboembolism and preventing further episodes. Although aspirin has been used to prevent thromboembolism, its effectiveness is questionable. Specific anticoagulant therapy is recommended.

1. **Warfarin** may be used for longterm anticoagulant therapy and takes approximately 2 – 7 days for effect. Warfarin should only be started after achieving the recommended level of anticoagulation with heparin. Otherwise, initial warfarin therapy may enhance thrombus formation. Usually, warfarin and heparin therapy are overlapped for 3 days. **Warfarin should be started at a dose of 0.1 – 0.2 mg/kg PO q24h to obtain a PT level twice baseline.** The use of a suspension (1 mg/mL) may provide less variability in the levels of anticoagulation. The first recheck PT should be done on day 3 then repeated on day 7 and then weekly until the adequate dose is found. Dogs on chronic warfarin therapy should have the PT checked every 6 – 8 weeks.

2. **Heparin sulfate 10 – 75 Units/kg SC q8h** may also be effective in prevention. Adjust dose to maintain desired anticoagulation. This method is advocated by some, as the level of anticoagulation is more stable (personal communication Dr. Luis Braz-Ruivo).

3. **Chronic LMWH (dalteparin at 100 Units/kg SC q12h)** may also be effective for chronic use but no veterinary studies on efficacy of prevention have been reported. Low molecular weight heparin may have a more predictable anticoagulant effect as it only inhbits factor Xa. Anecdotally in a small number of cases, it appears effective. The major advantage is the lack of requirement for monitoring of coagulation status as occurrence of coagulopathy is minimal. The major drawback is expense, however, this may be offset by less recheck visits required.

4. **Physiotherapy** is required several times daily until paralysis is resolved.

5. **Supervised activity** only to prevent the risk of bleeding.

PHARMACOLOGY

1. **Heparin sulfate** (unfractionated heparin- UFH) is a potent anticoagulant. Promotes anticoagulation indirectly by increasing antithrombin III activity. It is destroyed in the gastrointestinal tract, therefore it is only available for IV or SC use. The most important side effect is uncontrollable bleeding, this can be controlled with the antidote protamine sulfate (1% solution). Each 1 mg of protamine neutralizes 90 U of heparin. A maximum dose of 50 mg of protamine is recommended in humans. Chronic administration of heparin in humans (> 5 days) has been shown to cause thrombocytopenia in some patients, however this is felt to be species specific.

2. **Acepromazine** is a phenothiazine tranquilizer. It causes alpha adrenergic receptor blockade lowering systemic vascular resistance and blood pressure. This action may promote the development of collateral circulation. Side effects are excessive sedation and/or hypothermia. Extreme hypotension can cause collapse, renal failure or hepatic failure.

3. **Hydralazine** is a direct-acting arteriolar dilator. The mechanism of action is not completely understood. It is thought to be dependent on nitric oxide release. The most important side effect is the development of severe hypotension and reflex tachycardia.

4. **Acetylicylic acid (ASA)** is a NSAID that irreversibly inhibits cyclo-oxygenase in platelets. This drug inhibits conversion of thromboxane A2 in platelets resulting in reduced platelet aggregation. Thromboxane A2 also has vasoconstrictor effects and its inhibition is thought to promote collateral circulation. However, aspirin also inhibits the production of prostacyclin, a prostaglandin that inhibits platelet aggregation, which is produced by the endothelial cells. At recommended dosages, however, this prostacyclin inhibition is short-lived as the endothelial cell is reversibly altered and can synthesize additional cyclooxygenase

5. **Warfarin** is an anticoagulant. Its action is due to inhibition of vitamin K dependent clotting factors (II, VII, IX, X) and it also inhibits the anticoagulant proteins C and S. Its major side effect is uncontrollable bleeding that can be reversed by administration of vitamin K and blood transfusion if needed. There are numerous drug interactions with warfarin, see reference 1, page 869 below.

6. **Streptokinase** is a thrombolytic agent. Thrombolytics act by promoting the conversion of plasminogen to plasmin. Plasmin has fibrinolytic activity. When streptokinase binds to plasminogen it becomes an active enzyme to convert plasminogen to plasmin, in addition it may increase circulating levels of activated protein C enhancing clot lysis. Side effects are mainly related to bleeding tendencies especially when combined with heparin therapy. If major bleeding develops during therapy, administration of fresh frozen plasma or fresh blood is indicated to stop the fibrinolytic state. Hypersensitivity reactions have been reported in people. Streptokinase is contraindicated if there are pre-existing bleeding tendencies. The presence of bacterial toxins due to recent streptococcal infection induce resistance to streptokinase. Previous treatment may induce the development of antibodies, therefore subsequent treatments are shown not be as effective and can be followed by hypersensitivity. The experience with this agent in veterinary medicine is limited and should be used with a full understanding of potential complications and owner consent.

7. **Tissue plasminogen activator** (t-PA) is a thrombolytic agent (alteplase). T-PA is an intrinsic protein present in all mammals. When introduced into the systemic circulation, alteplase binds to fibrin in a thrombus and converts the entrapped plasminogen

to plasmin. This initiates local fibrinolysis with minimal systemic effects. There is a decrease, 20%-30%, in circulating fibrinogen, and some decrease in plasminogen and alpha$_2$ –antiplasmin. The activity of genetically engineerd t-PA in feline plasma (not known for canine) is 90%-100% of that seen in human plasma. The half-life is quite short ~ 5 minutes in humans. Clearance is mediated through the liver. Heparin must be administered concomitantly to prevent acute re-thrombosis. Fatalities associated with its use in cats were reperfusion syndrome (70%), CHF (15%), sudden arrhythmic death, presumed due to embolization of coronary artery (15%). Severe hemorrhage also occurred.

8. **Low molecular weight heparins** (LMWH) are short heparin polymers obtained by chemical or enzymatic cleavage of standard unfractionated heparin (UFH) (regular heparin). Similar to UFH, LMWHs exert their effect by interaction of their pentasaccharide sequence with antithrombin, thus inhibiting factor Xa, hence their lack of effect on PTT. Unlike UFH, LMWHs are not efficient at inactivating thrombin. LMWHs have greater activity against factor Xa. LMWH also has a longer half- life and more predictable pharmacokinetics than UFH. It is administered subcutaneously once or twice a day, often without laboratory monitoring. LMWH appears to be at least as safe and as effective as UFH, with greater ease of dosing according to human studies. enoxaparin and dalteparin are two preparations of LMWH that are in frequent use in the United States and Canada. One initial study in cats suggested that 100 IU/kg SC of dalteparin (Fragmin®) once daily had an effect on anti-Xa activity. Enoxaparin (Lovenox®) has been used clinically in dogs and cats at a dosage of 1 mg/kg SC q12-24h.

SUGGESTED READING

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NOTES

INTRODUCTION

Systemic hypertension denotes an increase in systemic arterial blood pressure. Systemic arterial hypertension is often recognized after the development of clinical signs. Hypertension is defined as either primary (essential) or secondary. Primary or essential hypertension is by definition idiopathic, and the diagnosis is established by exclusion. Secondary hypertension is the result of an underlying systemic disease and is the most common cause of hypertension in veterinary patients. In the cat, the most common causes of hypertension are hyperthyroidism, chronic renal disease, and diabetes mellitus. Systemic hypertension in hyperthyroidism (*p. 288*) is usually reversible with adequate control of the disease. Hypertension secondary to chronic renal failure requires long-term management with anti-hypertensive therapy. The presence of systemic hypertension does not correlate with the severity of the renal disease. It is common for cats with mild subclinical renal disease to present with clinical signs of systemic hypertension. In the dog, hypertension is most commonly associated with chronic renal disease, hyperadrenocorticism (*p. 270*), and diabetes mellitus (*p. 263/280*). Protein losing nephropathies (glomerulonephritis or amyloidosis) are commonly associated with systemic hypertension. Pheochromocytoma is a rare tumor of the adrenal gland, which can cause episodic or sustained hypertension, collapse, and sudden death. Rarely, these signs may be seen with tumors other than pheochromocytoma.

Systemic blood pressure can be obtained either by direct or indirect methods. The direct method is limited by the skill and experience of the examiner with smaller patients being the most difficult to obtain arterial access. Direct blood pressure is the gold standard. The indirect blood pressure method is most commonly used in clinical practice. Indirect blood pressure measurement in the cat is most accurate using the Doppler system. This system consists of a cuff and an ultrasound transducer. The width of the cuff should be approximately 40 – 50% the circumference of the limb. Cuffs too large give falsely low pressures, and cuffs too small give falsely high pressures. The site selected should be approximately at the level of the heart; therefore the animal should not be standing if the distal limb site is used for measurement. Different sites for acquiring blood pressure in the **cat** include the metacarpal or metatarsal (sternal or lateral recumbency), and tail artery (standing, sternal or lateral). Usually a size #2 – 4 or appropriately sized cuff is needed for the blood pressure measurement, and in the author's opinion, the tail gives the most reproducible values with minimal amount of stress. The cuff is usually taped in place with an attached gauge to read the pressure. The ultrasound transducer is applied to a large palmar. plantar or medial caudal artery at the root of the tail after the hair is clipped and ultrasound gel applied. The transducer is taped in place when an audible 'swoosh' (Doppler signal) is detected. The cuff is inflated until the signal disappears. The systolic pressure is the first audible sound heard with the Doppler, and occasionally the diastolic pressure, which is the muffling of the Doppler signal, can be heard. Four to six measurements are taken, and the pressures should be consistent or show a downward trend. Inconsistent measurements with variability over 20 mm Hg should be ignored. Usually systemic blood pressures decrease as repeated blood pressures are taken, and stabilize at a repeatable level. Systolic blood pressure above 180 mmHg, especially with clinical signs, is consistent with systemic hypertension. Follow-up blood pressures should always be taken with the cat in the same position, and by using the same site. Cats should be as stress-free as possible. As hypertension may be due to the stress of being in the clinic ('white coat phenomenon'), the author recommends the owner be present during repeated blood pressure measurements after a 15 – 20 minute rest period where hypertension is detected to rule out false positive results.

Indirect blood pressure in **dogs less than 10 kg,** appears to be most accurate using the Doppler method. Systemic arterial blood pressures in **larger dogs** are most accurate using the oscillometric technique. The metatarsal and metacarpal arteries are commonly used sites, but the tail site is also effective, reproducible, and may be preferred. Systolic arterial blood pressures above 180 mmHg and diastolic pressure above 100 mmHg, especially with clinical signs, is consistent with hypertension. Serial blood pressures are needed if stress, rather than a pathological process, is suspected to result in the increased blood pressures.

This chapter will focus on therapy for the initial management of hypertension.

History – Cats

The history will vary depending on the underlying etiology of the hypertension.

- Cats may present initially for blindness or neurological signs (*see Weakness p. 491, Seizures in Cats p. 456*).
  - Weakness, nyastagmus, ataxia, seizures, neurological deficits, vocalizing.
- Chronic renal disease
  - Polyuria, polydipsia, weight loss, and vomiting. Cats with early renal insufficiency have mild clinical signs of polyuria and polydipsia with minimum weight loss.
- Hyperthyroidism (*p. 288*)
  - Good appetite with weight loss, vomiting, diarrhea, polyuria, and polydipsia.
- Uncomplicated diabetes mellitus
  - Good appetites with weight loss, polyuria, polydipsia, and vomiting.
- Acromegaly
  - Usually diagnosed with diabetes mellitus, with insulin resistance requiring large amount of insulin for control of the diabetes mellitus.
  - In cats with acromegaly, the most common presenting symptom is unregulated diabetes mellitus with polyphagia, initial weight loss followed by weight gain, polyuria, polydipsia and clinical signs of underlying heart disease.

History – Dogs

The history will vary depending on the underlying etiology of the hypertension.

- Some dogs present for **blindness.**
- **Acute renal disease** (*p. 709*)
  - Anorexia, mild weight loss, vomiting, and lethargy.
- **Chronic renal disease**
  - Polyuria, polydipsia, vomiting, anorexia with weight loss.
- **Hyperadrenocorticism** (*p. 270*)
  - Ravenous appetite with weight gain, distended abdomen, polyuria, polydipsia, panting, and skin problems with thinning of the hair coat and secondary pyoderma.
- **Uncomplicated diabetes mellitus**
  - Good appetites with progressive weight loss, polyuria, and polydipsia.
- **Pheochromocytoma**
  - Vague history of weakness, lethargy, collapse, polyuria, polydipsia, tremors, restlessness and panting. This may be episodic due to intermittent secretion of catecholamines, or sustained with continuous secretion.

Clinical Signs/Physical Examination

I. **Mild** hypertension **(blood pressure [BP] 150/95 – 160/100).** Blood pressure in this range requires monitoring. Treatment is recommended when there is evidence of renal failure (azotemia) or end organ damage (e.g., retinal hemorrhages). Intermittent blood pressure rechecks should be performed over time.

   #### CATS
   - With **renal disease** (*p. 709*), presentation is dependent on the severity of the azotemia, but is usually indicated by poor body condition (thinness, with poor and hair coat, and small palpable kidneys, bilaterally.
   - With **hyperthyroidism** (*p. 288*) are thin, have an increased heart rate, intermittent gallop rhythm and murmur and palpable thyroid nodule(s).
   - With **diabetes mellitus** have clinical signs depending on the severity and type of diabetes mellitus, Type I or II. Cats with type I diabetes mellitus are thin with a poor hair coat andcats with type II diabetes mellitus are obese.
   - With **acromegaly,** have overgrowth of connective tissue, viscera, and bone with increased tissue mass, and present with inspiratory stridor, increase in mandibular bone mass, and a plump appearance to the head and neck region An intermittent gallop rhythm and murmur may be detected.

DOGS

- With **renal disease** (*p. 709*), depending on the acuteness or severity of the azotemia, are usually thin with weight loss. Dogs with acute renal disease may present with anorexia, vomiting, lethargy but no, or only mild, weight loss.
- With **protein-losing nephropathy** may present with clinical signs of the underlying disease i.e., fever, uveititis, enlarged lymph nodes.
- With **hyperadrenocorticism** (*p. 270*) have, increased respiratory rates, hepatomegaly, distended abdomen, poor hair coat with alopecia, thin skin, comedones, and pyoderma.
- With **diabetes mellitus,** depending on the severity of the disease, present with polyphagia, weight loss, polyuria and polydipsia; whereas dogs with ketoacidosis (*p. 263*) may present with lethargy, severe weight loss, dehydration, and increased respiratory rate and depth.

II. **Moderate to severe** hypertension **(moderate: BP >160/100, severe: BP >180/120).** A systolic blood pressure **>200 mmHg, or 170 – 200 mmHg with renal failure (azotemia) and end organ damage, or with clinical signs of hypertension,** must be treated. Close monitoring only is recommended with **systolic BP 170 – 200 mmHg where renal function is normal and there is no evidence of end-organ damage.** Renal insufficiency may not be evident in its early stages but may be more obvious with follow-up rechecks.

- **High risk requiring immediate treatment (see MANAGEMENT below) include those with ocular and neurological signs:**
- The most common presenting signs for cats and dogs with severe hypertension are ocular changes:
    - Cats present with acute onset of blindness with bilateral mydriasis, retinal detachment, retinal edema, retinal hemorrhage and retinal artery tortuosity, hyphema, and vitreal hemorrhage. Blindness is more common in cats than dogs.
    - Dogs present with acute onset of blindness with bilateral mydriasis, retinal detachment, retinal edema, retinal hemorrhage and retinal artery tortuosity, hyphema, and vitreal hemorrhage.

Laboratory Evaluation/Diagnostic Imaging

The goal of the work up is to determine an underlying etiology for the hypertension:

- **CBC** may show a decreased hematocrit due to a non-regenerative anemia of renal disease or chronic illness; fluid loss may result in increased hematocrit and blood viscosity; leukocytosis, monocytosis, eosinopenia with hyperadrenocorticism; a leukocytosis with a left shift or monocytosis may indicate infectious disease and chronic disease. There are no consistent findings on CBC in animals with pheochromocytoma.
- **Urea and creatinine** to rule out renal disease.
- **ALT and alkaline phosphatase** are increased in hyperthyroidism in cats; hyperadrenotcorticism and may be present in pheochromocytoma in dogs.
- **Glucose** is elevated in diabetes mellitus.
- **Serum albumin** is decreased in protein-losing nephropathy.
- **Urinalysis** shows low urine specific gravity, casts, white and red cells, and increased protein in renal disease. Glucosuria is present in diabetes mellitus.
- **Urine Culture** should be obtained to rule out an occult urinary tract infection and pyelonephritis in renal disease, hyperadrenocorticism, and diabetes mellitus.
- **Thoracic radiographs** may reveal support for secondary heart disease as a result of hypertension, which may include any of the following: loss of cranial waste from a dilated aorta, an enlarged descending aorta, an undulating aorta, and a tall heart secondary to left heart enlargement (hypertrophy), enlarged pulmonary veins (venous congestion) and increased interstitial pattern or alveolar pattern (heart failure). Evaluation of the lung patterns for interstitial changes, nodules, or masses may support an underlying systemic disease leading to systemic hypertension.
- **Abdominal radiographs** may identify small kidneys associated with chronic renal disease, or normal or enlarged kidneys (e.g., lymphoma, leptospirosis) when associated with acute renal failure. Calcification of adrenal tumours, may be seen with cortico-adrenal tumours but rarely (~ 7%) pheochromocytoma. Hepatomegaly is usually associated with hyperadrenocorticism.

Extended Laboratory/Imaging Data Base

- **T4** is increased in cats with hyperthyroidism. A free T4 or TSH suppression test may be required where hyperthyroidism is suspected in a cat but is not confirmed with a baseline T4.
- **Echocardiogram** is recommended to confirm hypertrophy. A dilated aorta, hypertrophy of the septum and left posterior free wall may be present resulting in diastolic dysfunction. Diastolic dysfunction is seen with an inverted mitral inflow pattern with a reversal of the E wave to A wave (E<A). The severity of left ventricular hypertrophy does not correlate with the systemic hypertension.
- **Adrenal function tests** are to be used where hyperadrenocorticism is suspected based on history, clinical signs, and physical examination (*p. 270*). Obtain screening tests (ACTH stimulation test and urine cortisol creatinine ratio) for hyperadrenocorticism, and low-dose dexamethasone suppression (pituitary dependent hyperadrenocorticism) and high-dose dexamethasone suppression test (to distinguish between adrenocortical tumors and pituitary hyperadrenocorticism).
- **Catecholamines and their metabolites** can be detected in a 24-hour urine sample in pheochromocytomas.
- **Abdominal ultrasonographic examination** is effective in identifying adrenal tumours (pheochromocytoma and adrenocortical). To differentiate a pheochromocytoma from a cortisol-secreting tumour, the contra-latereral adrenal gland with pheochromocytoma is usually normal sized, whereas with the adrenal tumour the contralateral adrenal gland is atrophied. Ultrasonographic examination is useful in assessing metastases and invasion of the caudal vena cava of a potential tumor; however in one study invasion of adjacent tissue was missed in 75% of affected animals examined. Hepatomegaly can be seen with hyperadrenocorticism. Renal size and architecture can differentiate the various etiologies of renal failure. Occasionally, adrenal tumors other than pheochromocytomas may produce clinical signs of pheochromocytoma.
- **Non-selective angiography** is effective in identifying invasion of the caudal vena cava, which is most commonly seen with right adrenal tumors.
- **MRI & CT** are the most sensitive diagnostic tools to assess the extent of invasion of the tumor and thrombosis of the caudal vena cava, and metastases. This is useful information when adrenalectomy is being considered.
- **Serum fructosamine** levels should be obtained, especially in cats, to evaluate for **early or Type II diabetes mellitus,** or in both dogs and cats to evaluate for adequate glycemic control. These measurements reflect the average blood glucose concentration over the preceding one to two weeks. Fructosamine levels <400 mmol/L indicates good glycemic control whereas levels >500 mmol/L are found in newly diagnosed or poorly controlled diabetics.
- **Glycosylated Hgb** may also be measured to **assess response to treatment** over the preceding one to two months and is 4% – 6% in well controlled diabetic dogs and >7% if poorly controlled.
- **Urine protein to creatinine ratio** is required for evaluation of **protein-losing nephropathy** if urinalysis shows absence of inflammatory cells, the urine culture is negative, and proteinuria is present.
- **Serology** is required to identify potential underlying causes of the protein-losing nephropathy (if urine protein to creatinine ratio is greater than 3). If these illnesses are suspected, obtain samples for Rickettsial, Leptospirosis and fungal titers, a heartworm test, and ANA in both dogs and cats.
- **Insulin-like growth factor:** Obtain an IGF-1 in cats with **insulin resistance** and clinical manifestations consistent with acromegaly (Commercial growth hormone assays for cats are not available).

MANAGEMENT

CATS

- With chronic renal failure, long-term treatment with anti-hypertensives is needed. Adequate control of the hypertension helps sustain renal function.
- With other diseases resulting in hypertension such as hyperthyroidism and insulin resistant diabetes, control of the disease will also control the hypertension, and long-term anti-hypertensives may or may not be needed.

DOGS

- With chronic renal failure, diabetes mellitus and hyperadrenocorticism need long-term management with anti-hypertensives to control blood pressure.

  Single drug therapy is recommended initially. Combination drug therapy may be needed to control hypertension in resistant patients. Too rapid reduction of blood pressure may occur if a dose is excessive or when combined with similar classes of drug (i.e., two vasodilators). In the author's opinion, **amlodipine** is the most effective drug to control hypertension in both the cat and dog.

  Overdose symptoms: lethargy, weakness, reduced renal function (reduced renal blood flow), reduced coronary blood flow. Drug dosages should be reduced in this setting. **In general,** however, anti-hyptertensive drugs should be reduced or withdrawn gradually with appropriate monitoring.

A. **Emergency management of a HYPERTENSIVE CRISIS:**
The criteria for the use of aggressive anti-hypertensive therapy in veterinary medicine are poorly defined. Even in severe cases, a rather conservative approach (management above) is used. Often, the secondary effects of hypertension, i.e., retinal detachment and bleeding, are already chronic at the time of presentation, and emergency therapy does not seem to improve outcome. A systolic blood pressure higher than **250 mmHg, if associated with the situations listed below,** may require emergency intervention. The target of emergency therapy is to reach a systolic BP <200 mmHg and then institute oral therapy as above.

Indications for emergency therapy are:
- Unstable neurologic disease where cerebral hemorrhage is suspected
- Uncontrolled epistaxis
- Acute renal disease
- Pheochromocytoma
- Hyperthyroidism

1. **Sodium nitroprusside** (given as a constant rate infusion in D5W or 0.9% NaCl) for no longer than 72h (most commonly 12–24h) WITH CONSTANT OBSERVATION AND BLOOD PRESSURE MONITORING:
   - **Cat:** start at **1 μg/kg/min** and titrate to effect. Monitor blood pressure initially every 15 minutes and adjust **CRI by 0.5 μg/kg/min** until the target BP is achieved.
   - **Dog:** start at **2 – 3 μg/kg/min** and titrate to effect. Monitor blood pressure continuously if possible or every 15 minutes and **adjust CRI by 1 – 2 μg/kg/min** until reaching target BP.

   OR

2. **Phentolamine 0.02 – 0.1 mg/kg IV bolus** as needed to control blood pressure (dog only).

   OR

3. **Diltiazem**
   - **Dogs: 0.1 – 0.5 mg/kg** administered in IV boluses of **0.05 – 0.25 mg/kg** every 5 minutes to effect, then **1 – 5 μg/kg/min CRI**
   - **Cats: 0.1 – 0.2 mg/kg IV bolus, then CRI as per dogs**

   OR, if no infusion pump, or 1, 2, 3 above are not available, go to 4

4. **Hydralazine**
   - **Dog: 0.2 – 0.4 mg/kg IV,** titrate up if no change in 1 – 2h
     0.5 – 2 mg/kg PO q12h
   - **Cat: 2.5 – 10 mg/CAT PO**

   Once the blood pressure is reduced to <170/110, treatment is continued using oral medication

B. **First line drug therapy:** initial therapy for systolic blood pressures **>180 mmHg.**

1. **Amlodipine**
   CATS
   a. **Amlodipine (Norvasc®) 0.625 mg** once a day in **cats less than 5 kg,** OR **1.25 mg** once a day in cats **greater than 5 kg.**
   b. Recheck in 3 – 7 days and titrate dose until systolic blood pressure is less than 150 – 160 mmHg. For titration the author uses the following schedule:
      i. If starting at **0.625 mg once a day,** increase in increments of 0.625 mg until reaching acceptable control or side-effects.
      ii. If starting at **1.25 mg once a day,** increase in increments of 0.625 mg until reaching acceptable control or side-effects.
      iii. In some cases, a 1 mg/mL suspension can be made to titrate dose in smaller increments.

DOGS

Amlodipine 0.25 – 0.5 mg/kg q12h. Note: this higher dosage is required for dogs.

OR

2. **Prazosin 0.5 – 2 mg/kg q12h–q8h (dogs only)**

OR

3. **Hydralazine 1 – 3 mg/kg q12h for dogs and cats**

C. **Second line drug therapy:**
These drugs can be used in conjunction with first-line drugs in two settings: (1) once stable, allowing for a decrease of the amount of either drug needed (i.e., amlodipine can become expensive is large dogs, reduction of potential adverse effects); (2) where the single drug does not sufficiently lower blood pressure.

1. **Beta-blockers:**
   a. **Atenolol**
      i. **Cat: 6.25 – 25 mg/CAT PO q12–24h**
      ii. **Dog: 1 – 2 mg/kg PO q12–24h**

      OR

2. **ACE inhibitors:**
   a. **Enalapril 0.5 mg/kg PO q12h**
   b. **Benazepril 0.5 mg/kg PO once daily.**
   Titrate up as needed. ACE inhibitors should be used with caution in patients with renal disease. **ACE inhibitors are contraindicated if creatinine is > 250 μmol/L (3 mg/dl).**

D. **Third line drug therapy:**
These drugs can be used in addition to combination drug therapy with first and second line drug therapy in selected cases where it is difficult to control blood pressure with the above drugs.

1. **Diuretics:**
   a. **Furosemide 0.25 – 1 mg/kg q12h**
   b. **Hydrochlorothiazide 1 – 2 mg/kg q12h**

2. **Low salt diet**

E. **Pheochromotytoma**
Management will depend on presentation.

1. Approach as outlined in **A1 – 4** above as required.

2. **OR** if not emergent

   a. **Phenoxybenazmine 0.2 – 0.4 mg/kg PO q12h,** gradually increase until BP within normal range Pre-surgical management is **required 10 – 14 days prior to surgical excision of the tumor.**
   b. **Beta blockade** maybe required to treat tachycardia but only after adequate alpha blockade has been established to avoid severe hypertension.
      i. **atenalol 0.2 – 1.0 mg/kg q12h OR**
      ii. **propranolol 0.2 – 1.0 mg/kg PO q8h**

PHARMACOLOGY

1) **Amlodipine besylate (Norvasc)** is a calcium channel blocking agent of the dihydropyridine class which inhibits calcium reflux across cell membranes in cardiac and vascular smooth muscles. It has a greater effect on vascular smooth muscle and acts as a peripheral arteriolar vasodilator by reducing afterload. Amlodipine is almost completely absorbed after oral administration and peak plasma concentrations occurs 6 to 8 hours post dose. **Missed dosages may cause rapid redevelopment of hypertension.** Amlodipine rarely causes adverse effects because of its slow onset of action, but can cause lethargy, hypotension, reflex tachycardia, and inappetence. Amlodipdine is considered first line therapy in cats with hypertension unless the hypertension is secondary to hyperthyroidism, where a beta-blocker should be used. In the author's opinion, the drug also is the first line choice for dogs with hypertension, but usually requires q12h dosing rather than q24h.

2) **Prazosin HCL** (Minipress) is an alphal blocker and reduces blood pressure and peripheral vascular resistance with its selective competitive inhibition of alpha1 adrenergic receptors. Prazosin reduces systemic and venous pressures, right atrial pressures, and increases cardiac output. Prazosin can cause reflex tachycardia. Tachyphylaxis (drug tolerance) is reported in humans, but dosage adjustment, temporarily withdrawing the drug, or adding an aldosterone antagonist usually corrects the problems. It is variably absorbed after oral administration, and peak levels occur in 2 to 3 hours.

3) **Hydralazine HCL** (Apresoline) has a direct action on vascular smooth muscle and reduces peripheral resistance and blood pressure. It is thought Hydralazine's mechanism of action is alteration of the calcium metabolism in smooth muscle interfering with calcium movement and preventing the initiation and maintenance of the contractile state. Hydralazine has more effect on arterioles than veins. Hydralazine is an effective drug in CHF because it increases cardiac output and decreases systemic vascular resistance. Hydralazine can activate the renin-angiotension system with an increase in sodium and water retention if hydralazine is not given in conjunction with diuretics or sympathetic blocking drugs. The primary use of hydralazine in dogs is as an afterload reducer in treatment of CHF. Hydralazine is rapidly absorbed after oral administration. Adverse effects in small animals included hypotension, reflex tachycardia, sodium/water retention and GI signs (vomiting and diarrhea).

4) **Enalapril** is a pro drug that is converted in the liver to the active compound enalaprilat, which prevents the formation of angiotensin II (a potent vasoconstrictor) by competing with angiotensin I for angiotensin converting enzyme (ACE). The angiotension II concentrations are decreased, therefore aldosterone secretion is reduced and plasma renin activity is increased. The primary use of Enalapril is a vasodilator in the treatment of heart failure. It causes venous and arterial vasodilation and reduces preload and afterload. It has been shown to be effective in reducing protein loss in the urine in protein-losing nephropathy. Enalapril's onset of action is 4 to 6 hours with a duration of 12 hours. Adverse effects can include hypotension, renal dysfunction, hyperkalemia, and GI signs with anorexia, vomiting, or diarrhea. Enalapril's primary toxicity affects the proximal tubular epithelium of the kidney, and is potentiated by high doses and hypotension.

5) **Benazapril** is a pro drug that is converted to benazeprilat primarily in the liver. Peak plasma concentrations are reached within 1 to 3 hours. It is excreted equally in the bile and urine in dogs, and is less dependent on renal excretion.Benazapril has a similar duration of action when compared to enalapril. The use of benazepril in patients with renal dysfunction has been advocated due to its metabolism. In the author's experience the use of ANY drug of this class in patients with renal disease has the potential for adverse effects; therefore, renal parameters should be monitored more frequently in such cases.

6) **Atenolol** is a Class II anti arrhythmic drug (beta-blocker) that competitively binds with B adrenergic receptors and inhibits the effects of the adrenergic system on the heart. Atenolol is a cardioselective B1 blocker, which avoids B2 receptor- mediated bronchoconstriction and hypoglycemia. Atenolol decreases heart rate, myocardial contractility, atrioventricular conduction velocity, and automaticity.

7) **Furosemide** is a sulfonamide-type of loop diuretic which inhibits the reabsorption of electrolytes in the thick ascending loop of Henle, and decreases the reabsorption of sodium and chloride in the distal renal tubule. The diuresis results in excretion of sodium, chloride, potassium, hydrogen, calcium, and magnesium. The potassium excretion is much less affected in dogs. As electrolyte disturbances may be severe, routine follow-up measurements are advised.

SUGGESTED READING

1. Acierno MJ, Labato MA. Hypertension in Dogs and Cats. Comp on Cont Edu. 2004 Vol 26;5.
2. Egner, Beate, Carr, Anthony, and Brown, Scott, Essential Facts of Blood Pressure in Dogs and Cats. Beate Egner Vet Verlag. 2003.
3. Ettinger, Stephen and Feldman, Edward. Textbook of Veterinary Internal Medicine, Diseases of the Dog and Cat. Sixth Edition, Elsevier Saunders 2005:1731-1752.
4. Feldman EC, Nelson RW. Canine and Feline Endocrinology and Reproduction, 3rd ed. St Louis MO. Saunders. 2004:157-159, 162, 267, 300-318.
5. Kittleson MD, Kienle RD. Small Animal Cardiovascular Medicine. St Louis MO. Mosby. 1998:439-446.

INTRODUCTION

After contact with the inciting allergen, facial swelling or urticaria usually occurs in about 20 minutes. The animal frequently rubs the face along the ground to relieve irritation. Causes are insect bites, ingestion of toads, food allergies and rotten foods, transfusion of blood products and contact with certain chemicals. Ingestion of rotten food and food allergies may also result in gastroenteritis.

DIAGNOSIS

History/Signalment

While examining the patient, obtain a history with regard to exposure to any of the above, or other potential allergens.

Clinical Signs/Physical Examination

- Facial swelling, occurs especially around the eyes, mouth and ears.
- Trauma to the skin may be evident due to rubbing the face on the ground.
- Examine the patient for ticks or bee stings etc.
- Acute hemorrhagic gastroenteritis may be associated with ingestion of various proteins (allergens) or garbage. Physical findings will vary depending on the presentation. If hemorrhagic gastroenteritis is a problem and fluid loss is extensive, the patient may be dehydrated, tachycardic with poor peripheral perfusion (*see Acute Diarrhea p. 32*).

Laboratory Evaluation and Diagnostic Imaging

Stat
- **PCV, TS, Stick BUN** and **glucose** (especially if hemorrhagic gastroenteritis – *see Acute Diarrhea for more detail p. 32*).
- Further laboratory investigation will depend on history and physical findings.

MANAGEMENT

A. Ascertain the cause of the reaction and remove it if possible. Stop blood or plasma transfusion, wash off any chemical residues. Laxatives and 37°C (101°F) high colonic enemas may be beneficial if condition is serious and due to food allergies. .

B. If facial edema is present, administer
   1. **Methylprednisolone sodium succinate or prednisolone sodium succinate at 2.0 mg/kg IV** over 15 – 20 minutes; no faster as you may precipitate hypotension. Always ensure normotension prior to steroid use. OR
   2. **Dexamethasone sodium phosphate 0.25 mg/kg SC, IM** can be used as an alternative.
   3. It is not necessary to administer corticosteroids if a blood, or blood product, reaction has occurred as this will subside after stopping the transfusion. However, if facial edema is severe, then corticosteroids may be indicated. The author rarely administers corticosteroids with blood transfusion reactions and never with hemorrhagic gastroenteritis.

C. Antihistamine –
   1. **Diphenhydramine 0.5 – 2.0 mg/kg** (max total dose 50 mg) IM, PO q8h (do **not** give IV, can cause hypotension and vomiting) or
   2. **Tripelennamine HCl at 1 mg/kg IV or IM q12h** .
   3. Only use epinephrine if angioedema is severe and the swelling interferes with normal respirations (*see Anaphylactic Shock p. 616*).

D. If on initial examination a cause is not found, continue at this stage with a thorough search through the hair coat for arthropods (e.g., ticks).

E. The animal should be hospitalized, with constant observation, until signs of improvement are evident (up to 24 hours). Alternatively, send the patient home and advise the owners to observe closely for 24 hours. Continue with antihistamine treatment (C above).

PHARMACOLOGY

1) **Methylprednisolone or prednisolone** sodium succinate, inhibits the normal immune cascade at almost all levels from macrophage processing to effector cell function. There is a decrease in IgE receptor binding and inhibition of phospholipase A2 activity, which cleaves arachidonic acid from cell membrane phospholipids, thereby stabilizing cell membranes.

2) **Diphenhydramine or tripelennamine** HCl compete for H1 or H2 histamine receptor sites.

SUGGESTED READING

1. Angioneurotic Edema (urticaria). In: Kirk RW, Bistner SI and Ford RB (eds). Handbook of Veterinary Procedures and Emergency Treatment 5th Edition, Philadelphia: Saunders; 1990:28-29.

NOTES

INTRODUCTION

Aural hematoma refers to the collection of blood within the cartilage of the pinna. It typically results from hemorrhage of the great auricular artery when the ear cartilage is fractured. Trauma and coagulopathy are the two most common etiologies of this condition.

DIAGNOSIS

History/Signalment

- Dogs usually present with a history of head shaking and/or chronic ear problems (otitis media/externa).
- Shaking and scratching at their ears result in traumatic fracture of the cartilage and subsequent hematoma formation.
- Any other recent episodes of bleeding or bruising may indicate a coagulopathy.
- May have a history of aural hematomas. These often recur if not treated appropriately or if an underlying ear disease remains unaddressed.

Clinical Signs/Physical Examination

- Head tilted toward the affected ear
- Head shaking
- Scratching of affected ear
- Pinnal erythema
- Swelling involving the concave aspect of the pinna
- Multifocal areas (e.g., sclera) of petechiation, ecchymoses or hemorrhage may be present in the case of a coagulopathy.
- Otoscopic examination – this should always be performed, since most aural hematomas result from underlying ear problems (i.e., otitis media/externa from allergies, foreign bodies, neoplasia, etc.) (*see p. 225*).

Laboratory Evaluation/Diagnostic Imaging

Stat

- **ACT and/or PT/PTT** are indicated if a coagulopathy is suspected. Times will be prolonged.
- **Platelet count** is indicated if a coagulopathy is suspected. Thrombocytopenia will be present if the hematoma is from a disorder of platelet numbers (count may be normal if due to a disorder of platelet function).
- **PCV & TS** may be required if hemorrhage elsewhere is reported
- **Stick BUN** prior to anesthesia to rule out azotemia

Extended Laboratory Data Base

- **Ear canal cytology/microbial examination** should be performed to identify causative agents (*see p. 227/228*).

MANAGEMENT

A. ACUTE
Aural hematomas should be treated soon after occurrence, to minimize the development of fibrous tissue and secondary deformation of the pinna. While various techniques have been utilized, the objectives of all surgical treatments are to remove the accumulated blood, eliminate the dead space, and maintain a cosmetic appearance to the pinna.

1. The patient is placed under general anesthesia (*see Anesthesia p. 114*) and the affected pinna clipped and surgically prepared.
2. A vertical incision is made through the tissues overlying the hematoma, on the concave surface of the pinna.
3. The hematoma is evacuated and tissues are maintained apposed with one of the following techniques:

FIGURE 1. Staggered full-thickness stents in a vertical plane.

FIGURE 2. Teat cannula through a stab incision into the hematoma.

FIGURE 3. Closed or open drain through a stab incision into the hematoma.

Note: Single needle-drainage of the hematoma, or infusion of cortisone are usually ineffective at preventing recurrence.

B. **CHRONIC**

Long-term management of aural hematomas involves identifying and treating the underlying ear disease (*see p. 225*) or coagulopathy.

Prognosis is good, with recurrence unlikely, if the aural hematoma is treated appropriately within a few days of occurrence; and the underlying disease is controlled.

SUGGESTED READING

1. Fossum TW. Surgery of the Ear. In: Fossum TW. Small Animal Surgery, St. Louis, Mosby 2002:229-253.

INTRODUCTION

Dermatological emergencies are not common, but do occur with a greater degree of frequency than most people realize. Burn wounds (*see Burn Injury p. 682*) and topical toxins (*see Toxicological Emergencies p. 630*) will be covered separately. Neoplasia, metabolic diseases, immunological diseases and bacterial skin disease can, and often do, present as emergency situations. The following is a list of skin diseases that could present as emergencies. For ease of clinical assessment and treatment, approaches will be based on clinical presentation.

Canine Diseases	Feline Diseases
Deep Pyoderma	Paraneoplastic alopecia
Pemphigus complex	Feline Plasma Cell Pododermatitis
Bullous pemphigoid	
Systemic Lupus Erythematosus	
Vasculitis	
Erythema Multiforme	
Toxic Epidermal Necrolysis	
Urticaria and Angioedema	
Juvenile Cellulitis	
Superficial Necrolytic Migratory Erythema	
Epitheliotropic Lymphoma	

DIAGNOSIS

- **Characteristic** features of most of these diseases are involvement of the pinnae, planum nasale, foot pads, or muco-cutaneous junctions and oral cavities as well as generalized distribution. The exception to this rule is pyoderma.
- **Cytology** can be a very helpful test especially when searching for acantholytic or neoplastic cells. Tape, aspirates and impression smears are all useful techniques.
- **Skin biopsy** is the single most useful diagnostic test. Send as many samples as is practical. The standard size is 6 mm with 3 mm being more appropriate for pinnae, nasal planum and foot pads. Select intact pustules and/or vesicles if possible (may be very small and a sharp eye is required). Areas of fading pigment (pewter grey colour), very new erythematous macules, and areas adjacent to ulcers are also appropriate sites. Send crust as well, if present. Generally the most horrific lesions are the least diagnostic.

DEEP PYODERMA – DIAGNOSIS

Clinical Signs/Physical Examination

- Pressure points such as face and legs are usually involved but may be generalized. Planum nasale and foot pads are NOT affected.
- Patchy alopecia, papules, pustules, nodules, haemorrhagic bullae, bloody crusts and cellulitis typify these follicularly oriented lesions..
- Lethargy, anorexia and fever may be present in severe cases.

Laboratory Evaluation

- **Hair plucks** or **skin scrapings** to rule out demodicosis.
- **Skin cytology** and **biopsy** to rule out actinomycosis, nocardiosis, mycobacteriosis, blastomycosis and neoplasia.
- **Culture** and **sensitivity** to identify presence of bacteria. Remove crust and squeeze skin to obtain deep sample. Do not touch area of culture without sterile gloves.
- **CBC** and **biochemical profile** may be warranted if patient systemically ill to assess renal function (pre-renal azotemia). Sepsis may result in low total protein, low glucose and increased liver enzymes and bilirubin.

MANAGEMENT

A. Intravenous fluids if systemically ill.

B. Begin systemic antibiotic therapy with **Cephalexin 20 mg/kg IV q6h (if on IV fluids) or 30 mg/kg PO q12h** until culture results are available.

C. *Staph. Intermedius* is generally cultured but if other organisms are identified then antibiotic choice should be based on sensitivity. Fluoroquinolones are suitable.

D. Treat for 6 – 12 weeks or longer if necessary.

E. Tub soaks with antibacterial solutions may be helpful.

CORTICOSTEROIDS ARE CONTRAINDICATED!

URTICARIA AND ANGIODEMA (see p. 212) – DIAGNOSIS

Clinical Signs/Physical Examination
- Hypersensitivity reaction to insect bites, food, plants, heat, cold or drugs etc.
- Pruritic, often erythematous wheals (urticaria) or large areas of edema, especially, muzzle, vulva, prepuce and pinnae (angioedema).
- Respiratory distress if there is laryngeal or pharyngeal edema.
- Appearance is typical but cytology will help confirm the absence of pathogens.

Laboratory Evaluation
- Skin cytology, biopsy and culture if diagnosis is in doubt.

MANAGEMENT

A. Corticosteroid therapy with **prednisone or prednisolone** at a dose of **1 – 2 mg/kg q24h.**

B. Actual dose and route of administration depend on the severity of the lesions.

C. Epinephrine may be necessary if condition is life threatening (*see p. 212*).

JUVENILE CELLULITIS – DIAGNOSIS

Clinical Signs/Physical Examination
- Immune mediated, NON-SEPTIC, cellulitis affecting mainly the muzzle, pinnae, anus, vulva or prepuce and lymph nodes of 3 – 6 month old puppies.
- Swollen areas ooze serous to purulent exudate.
- Enlarged lymph nodes may also drain purulent material.
- Usually accompanied by fever and inappetance.

Laboratory Evaluation
- Cytology of lesions reveals absence of pathogens and toxic neutrophils.

MANAGEMENT

A. **Prednisone** administered at **1 – 2 mg/kg daily** for 1 – 2 weeks is usually curative.

B. For comfort, very gently wash or use compresses, especially eyes, nose and mouth.

C. Encourage food and water intake.

THE PEMPHIGUS COMPLEX – DIAGNOSIS

Clinical Signs/Physical Examination
- An autoimmune group of epidermal diseases that result in separation of various layers of the epidermis.
- Characterized by sudden onset of pustules, vesicles and/or bullae whose delicacy leads to rapid rupture with crust formation.
- A generalized truncal distribution is typical with one or more of the following always involved: **pinnae, planum nasale, foot pads, and/or mucocutaneous junctions and oral mucosa.**
- *Pemphigus foliaceous* is by far the most common form both in dogs and cats with very superficial (sub corneal) clefts filled with non-toxic neutrophils and acantholytic epidermal cells. These pustules form a crumbly crust when broken and have a truncal and "**pinnae, planum and pad**" distribution.
- *Pemphigus erythematosus*, a variant or cross-over between pemphigus foliaceous and lupus, is more common in dogs than cats (rare) and is usually limited to erosions and crusts of the face and pinnae including the **planum nasale**. Visualization of intact vesicles or bullae is rare. Collies, German shepherds and Shetland sheepdogs are affected more frequently than other breeds.
- *Pemphigus vulgaris* is a rare form of pemphigus involving the formation of suprabasilar clefts that result in vesicles, bullae and erosions which crust when ruptured. **Mucocutaeous junctions, axillae, groin, and nail beds** are favoured sites of lesions.

Laboratory Evaluation
- Skin cytology showing acantholytic cells (pinkish, rounded keratinocytes – foliaceous) and the absence of pathogens, as well as the distinctive location and nature of lesions, will give one a presumptive diagnosis of pemphigus, but confirmation is acquired only by skin biopsy and perhaps immunohistochemistry.

MANAGEMENT

A. **Intravenous fluids** for systemically ill animals.

B. **Specific immunotherapies** (*see Author's Protocol below and Pharmacology*) include **prednisone 2 – 4 mg/kg daily** until lesions resolve, then gradually reducing to the lowest alternate day dose which will control the disease. Other drugs such as **azathioprine 1 mg/kg q24h, cyclosporin 3 mg/kg q24h OR chlorambucil** (*see Author's protocol*) may be used in conjunction with glucocorticoids or as the sole therapy.

C. **Soothing tub soaks** may be beneficial.

D. **Antibiotics, cephalexin 30 mg/kg q12h** (or based on culture and sensitivity) for proven secondary bacterial infections.

E. **Vitamin E at a dose of 400 – 800 IU** daily is used by this author in all cases of immune mediated disease.

F. **Gastric protectants** should be administered with high dose steroids. **Omeprazole approximately 1 mg/kg q12h in dogs (20 mg/dog if >20 kg, 10 mg if dog is >5 kg and <20 kg or 5 mg if <5 mg). Cats: 0.7 mg/kg q24h PO** (*see Pharmacology*).

BULLOUS PEMPHIGOID – DIAGNOSIS

Clinical Signs/Physical Examination
- An autoimmune disease of antibodies directed against the lamina lucida of the basement membrane.
- Primary lesions are vesicles and bullae but these are rarely seen. One generally sees deep erosions which may be covered with dark 'bloody'crusts.
- Mucocutaneous junctions, oral cavity, pinnae, nasale planum and pads are characteristic, but a generalized distribution may be present as well.
- Dogs may be anorexic, depressed and febrile.
- This severe disease may be more difficult to control than other autoimmune skin diseases.

Laboratory Evaluation
- Submit **skin biopsies** as diagnosis is confirmed by dermatohistopathology and immunohistochemistry.

MANAGEMENT

A. Fluid therapy if dehydrated.

B. Immunosuppressive therapy (*see Author's Protocol and Pharmacology below*) **prednisone 2 – 4 mg/kg daily, azathioprine 1 mg/kg q12h (initially), cyclosporin 3 mg/kg q12h OR chlorambucil** should be started immediately upon confirming the diagnosis.

C. If lesions are difficult to control, these drugs may be used in combination.

D. Maintenance therapy after remission, is required for life sentence possibly incomplete here.

SYSTEMIC LUPUS ERYTHEMATOSUS – DIAGNOSIS

Clinical Signs/Physical Examination

- An autoimmune diseases characterized by antibody production against many tissues and formation of circulating immune complexes.
- Animals may be severely ill if anemia, joint disease, renal disease etc. are present.
- Deep erosions caused by disruption of the basement membrane, hydropic degeneration of epidermal basal cells and/or vasculitis, occur in a generalized distribution but mucocutaneous junctions, oral mucosa, pinnae, nasale planum and/or foot pads are always involved.
- Antinuclear antibodies (ANA), rheumatoid factor, Lupus erythematosus (LE) cells may be present and cause signs such as fever, and lameness etc.

Laboratory Evaluation

- **CBC.** Anemia and increased white count may be present.
- **Biochemical profile.** Increased creatinine and urea may be present.
- **Urinalysis.** Proteinuria may be present.
- General symptomatic treatment if systemic signs are present.
- **Skin biopsies** for histopathological and immunohistochemical studies generally provide the diagnosis.
- **ANA titres and LE cell preparations** may be helpful but generally are unreliable diagnostic tests.

MANAGEMENT

A. General immunosuppressive therapy (*see Pemphigus Complex p. 218*).
  1. Prognosis is guarded.

VASCULITIS – DIAGNOSIS

Clinical Signs/Physical Examination

- An immune-mediated reaction resulting in damage to blood vessels.
- Certain breeds may be predisposed e.g., Jack Russell Terriers, German Shepherds and Greyhounds, but may present in any breed.
- May be caused by aberrant antigen/antibody reactions, drugs, toxins, various bacteria, rickettsia, and viruses as well as systemic lupus erythematosus and cold agglutinin disease.
- Areas most affected are those where blood turbulence occurs such as pressure points (all bony prominences), nail beds, pinnae, foot pads, and tail.
- Lesions vary from alopecia with erythema and scale to severe deep ulceration, occasionally extending into the muscle layers.
- Prognosis depends generally on severity of the lesions.

Laboratory Evaluation

- **Skin biopsy** from several lesional sites varying in severity will give the best histopathological results.
- **Skin cytology and hair plucks** help to rule out demodicosis and deep pyoderma although the distribution of lesions will be much more typical of vasculitis i.e., nail beds, pinnae and tail are usually included in the list of affected areas.

A. If systemic signs of dehydration, anemia, anorexia etc. are present then treat accordingly.

B. Upon confirmation of the diagnosis treatments may include immunosuppressive doses (*See Author's Protocol and Pharmacology below*) of **prednisone 2 – 4 mg/kg q24h, dapsone (not cats) 1 mg/kg q8h** until clinical improvement and then smallest controlling dose (bone marrow suppression possible at higher doses) (**NB:** Dapsone, although very effective, is no longer readily available), and **pentoxyfylline 200 – 400 mg per day.**

DRUG AND OTHER AGENT REACTIONS

Clinical Signs/Physical Examination

- A severe and unexpected immune reaction to substances such as drugs, biochemicals (endogenous and/or exogenous) or infectious agents.
- The actual pathological and clinical lesions may vary and bear different names. Such as erythema mulitforme (EM), toxic epidermal necrolysis (TEN) and drug eruption (DE).
- EM is characterized by serpiginous, arciform and "target" or "bullseye" shaped lesions which are sharply demarcated, erythematous and ulcerated. They spread peripherally leaving a central "pallor" and affect mucocutaneous junctions, oral cavity, and haired areas of the body.
- TEN is characterized by sloughing of the epidermis caused by total coagulation necrosis of the epithelial surface. This is very severe and life threatening.
- Other reactions can include anything from ulceration to scaling, erythema and urticaria.
- Mild and non-life threatening forms may resolve spontaneously but could require weeks to months for total resolution.

Laboratory Evaluation

- **Skin biopsy** is usually diagnostic. Epidermis is characterized by necrosis varying from single cell to total.
- Other drug reactions may have various non-specific histopathological reactions and depend on a sharp clinician for the diagnosis.
- **CBC** to assess presence or degree of infection that may be present; and a biochemical profile may be beneficial in assessing the general condition of the patient.

MANAGEMENT

A. Supportive fluid therapy may be necessary in severe cases.

B. Discontinue any offending or suspicious drugs or other agents.

C. In the case of infectious agents select an appropriate antibiotic that is not of the same family as previously used treatments.

> **1.** If signs are severe, immunosuppressive doses of prednisone or prednisolone may be helpful. *See Author's protocol and Pharmacology.*

SUPERFICIAL NECROLYTIC MIGRATORY ERYTHEEMA – DIAGNOSIS
(Hepatocutaeous Syndrome and Superficial Necrolytic Dermatitis)

Clinical Signs/Physical Examination

- An epidermal reaction to pathology of the liver or pancreas resulting in epidermal intra- and intercellular edema causing vesicles or "soggy" demarcated lesions which may ooze serum, and form thin painful crusts. Thick parakeratotic crusts are most visible on footpads and planum nasale.
- Skin lesions often precede overt signs of liver, or less frequently, pancreatic disease by weeks to months.
- This is a life-threatening disease with an extremely poor prognosis unless the pancreatic or hepatic pathology can be corrected.

Laboratory Evaluation

- **Skin biopsy:** is diagnostic with extremely typical lesions ("Red, White and Blue" typify the layers of parakeratosis, epidermal edema and a relatively normal dermis).
- **CBC:** should be performed for completeness and to assess degree of inflammation/ infection.
- **Biochemical profile:** may indicate underlying hepatic disease and/or pancreatic disease. Hyperglycemia may be noted as some dogs may be diabetic or acquire diabetes mellitus (may be due to corticosteroid therapy but may occur without).
- **Abdominal ultrasound and biopsy** as suspicious lesions may offer further information on the nature of the lesion (hepatic or pancreatic).

MANAGEMENT

A. **Palliative therapy.** Topical treatment is the mainstay of therapy; warm water soaks or warm epsom salt or aluminium hydroxide (Burosol) soaks, management of bacterial and fungal infections as well as trials using topical corticosteroids are warranted.

B. **Amino acid therapy** [10% Travasol® (Baxter)] amino acid solution without electrolytes, 20 – 25 mL/kg IV via jugular catheter, can be given over 6 – 8hours and repeated weekly. Improvement should be noted by the fourth week if the patient is going to respond. If a central vein is not accessible, a peripheral vein may be used but the solution must be diluted to a maximum of 3.0% solution and administered over 24 hours (*see Peripheral Parenteral Nutrition p. 511*) to avoid vasculitis and slough. Acidosis is common, therefore acid-base monitoring is necessary. We have added sodium acetate, 2 – 3 mEq/kg to the infusion. Do not add sodium bicarbonate as carbon dioxide is produced (it fizzes!).

C. **Oral supplementation** with egg yolks, zinc (zinc methionine is preferred), vitamin E and essential fatty acids may also be helpful.

D. Rarely, **surgical excision of a pancreatic tumour** provides resolution of dermal lesions. However, generalized hepatic disease is much more prevalent and no cure is possible. Palliation, and pain management are required. Most dogs are euthanized due to progressive skin lesions or liver disease. Some cases have been managed for up to 2 years. (if NOT possible then euthanasia is generally advised as this is a painful condition requiring analgesia until the decision is made).

E. **Analgesics.** Opioids can be used in these patients, **codeine (1 – 2 mg/kg q6–8h) or oxycodone (0.3 + mg/kg q8–12h)** as needed. Nonsteroidal anti-inflammatory analgesics have also been used (**meloxicam 0.1 mg/kg q24h**) in our hospital when concurrent corticosteroids are not administered. The requirement for analgesia (benefit) in these animals outweighs the risk of hepatic dysfunction. Careful patient, and liver and renal parameters require monitoring when NSAIAs are administered.

F. **Prednisone 0.5 mg/kg** has resulted in some improvement in some patients, however, a possible correlation with the development of diabetes mellitus exists. Corticosteroids have been used in a final attempt at management of these cases in our hospital.

EPITHELIOTROPIC LYMPHOMA (Mycosis Fungoides) – DIAGNOSIS

Clinical Signs/Physical Examination

- Epitheliotropic lymphoma is a skin neoplasia with invasion of the dermis and epidermis by neoplastic T-lymphocytes.
- Varying lesions of plaques, nodules, ulcerations and erythema with large white scales have a wide pattern of distribution including muco-cutaneous and oral cavity locations.
- Differential diagnoses include all the other immune mediated diseases (often called a great imitator).
- Most common in middle aged to older dogs and cats.
- The prognosis is grave with most animals being euthanized within weeks of diagnosis unless lesions are minimal and scarce.

Laboratory Evaluation

Skin biopsy is usually diagnostic.

MANAGEMENT

A. Palliative therapy of warm water baths may improve the comfort level in dogs.

B. Most therapies are ineffective although if diagnosed early with only small areas of affected skin, **prednisone, cytotoxic drugs or isotretinoin** may be helpful (*see Author's protocol and Pharmacology below*).

FELINE PARANEOPLASTIC ALOPECIA – DIAGNOSIS

Clinical Signs/Physical Examination

- Rapid onset of symmetrical alopecia with a glossy appearance to the skin.
- Probably the same etiology as Superficial Necrolytic Migratory Erythema in dogs (i.e., pancreatic or hepatic/biliary neoplasia).
- Systemic signs of anorexia, weight loss and lethargy.

Laboratory Evaluation

- **Skin biopsy** is diagnostic with miniaturization of hair follicles being the key finding.
- **CBC** may reflect inflammation/infection and biochemical profile may show increases in ALT, amylase, lipase and, if dehydrated, creatinine and urea.
- **Abdominal ultrasound** may further define hepatic or pancreatic pathology.
- The prognosis is poor unless the neoplasia can be completely surgically excised.

MANAGEMENT

A. Standard supportive therapy is indicated while diagnostic testing is carried out.

FELINE PLASMA CELL PODODERMATITIS – DIAGNOSIS

Clinical Signs/Physical Examination

- Typically ulceration of the foot pads is the only skin lesion although occasionally may also involve the oral mucosa.
- The etiology is unknown although immune mediated mechanisms and perhaps vasculitis (Parker) are suspected.
- Pad lesions generally begin with swelling and a glossy appearance with scale which progresses to ulceration. Ulcers tend to be central rather than peeling from the edges. Eventual resolution leaves pads scarred, flat and hollow.
- The prognosis is variable but treatment is indicated as results may be rewarding.

Laboratory Evaluation

- Cytology of the lesions (fine needle, impressions or tape) may show many plasma cells.
- Biopsy of the lesion is usually diagnostic (be sure to include a portion of intact epithelium).

MANAGEMENT

A. Immunosuppressive doses (*see Author's protocol and Pharmacology below*) of prednisone or prednisolone should be started immediately upon diagnosis.

B. If poorly responsive then begin **aurothioglucose starting at 1 mg/kg IM weekly** and gradually reduce frequency when lesions resolve.

Author's Protocol for Dermatologic Immunosuppressive Therapy

- Begin **prednisone** therapy at a dose of **2 – 3 mg/kg q48h** administered in the morning.
- Give **azathioprine** at a dose of **1 – 2 mg/kg q48h** in the morning of the non-prednisone days.
- Check WBC weekly for several weeks to ensure there is no bone marrow suppression.
- When lesions begin to heal, gradually reduce the dose of prednisone keeping the dose of azathioprine the same.
- After many months of satisfactory control, the dose of azathioprine may gradually be reduced to the minimal controlling dose.
- Dogs with severe pemphigus will likely require both prednisone and azathioprine therapy for life but many cases of discoid lupus have been successfully controlled with twice weekly doses of azathioprine alone.
- These being very rare diseases, one should not hesitate to <u>contact</u> a <u>dermatologic</u> <u>specialist</u> <u>for</u> <u>advice</u> <u>regarding</u> <u>diagnosis</u> <u>and</u> <u>treatment</u>.

PHARMACOLOGY

1) **Azathioprine (Imunran®):** This is an imidazole derivative, cytotoxic drug used in the control of many immune-mediated diseases by modulating cell-mediated immunity and T-lymphocyte-dependent antibody synthesis. Although a dose as high as 2 mg/kg PO q24h can be used in dogs, I generally start much lower, as stated above, and reserve the higher doses for life-threatening situations. The most frequently encountered side effect is bone marrow suppression especially at the higher dose levels. This drug is generally contraindicated in cats. The risk of azathioprine toxicity is increased if administered with allopurinol.

2) **Cyclosporin A (Neoral®):** This is a decapeptide drug derived from a soil fungus and reduces many of the functions of T-lymphocytes. Immunosuppression can be achieved in dogs with doses of 2-5 (start with 3) mg/kg PO q24h and in cats as low as 1 mg/kg PO q24h especially in combination with prednisone. The dose should be reduced over a 4 month period. Toxicity is relatively uncommon in dogs and cats with soft stool being the most commonly reported side effect in cats.

3) **Chlorambucil:** An alkylating agent which is more frequently used in controlling immune-mediated diseases in cats. Doses range from 0.2 mg/kg PO q24h or q48h to 1.4 mg/kg PO q1-4 weeks in both dogs and cats. Myelosuppression is the most frequently encountered side effect.

4) **Pentoxyfylline (Trental®):** This is a methylxanthine derivative which is believed to enhance capillary blood flow by allowing increased flexibility of erythrocytes thus reducing ischemic effects. It has been recommended only for use in dogs and horses. Most frequently reported side effects are inappetance and vomiting.

5) **Aurothioglucose (Solganal®):** This is a water soluble gold salt which has anti-inflammatory and immunomodulating effects that are not well understood. When used in <u>dogs</u>, azathioprine should be discontinued for one month and then aurothioglucose administered at a dose of 1 mg/5kg IM weekly for 10 weeks and then monthly. In <u>cats</u>, give a test dose of 1 mg IM on week 1 and then 2 mg IM on week 2. If no adverse effects are noticed then give 1mg/kg IM per week until clinical remission or for 20 weeks. Then reduce to the minimal controlling dose. Pain at the injection site is a frequent finding and clinicians should be alert for signs of thrombocytopenia.

6) **Omeprazole** is proton pump inhibitor which acts to decrease gastric acid secretion. Omeprazole may be superior to the H2-receptor antagonists in the blockade of acid production and is the therapy of choice at OVC.

SUGGESTED READING

1. Muller and Kirk's Small Animal Dermatology, 6th edition: Scott DW, Miller Wm H Jr. and Griffin CE. WB Saunders Company, Toronto.
2. Small Animal Dermatology: Medleau L and Hnilica KA. WB Saunders Company, Toronto.
3. Small Animal Clinical Pharmacology: Maddison JE, Page SW and Church D. WB Saunders Company, Toronto.
4. Veterinary Drug Handbook: Plumb DC. Iowa State University Press, Ames, Iowa.

NOTES

INTRODUCTION

Animals with severe otitis externa, or associated aural hematoma (*see p. 214*) may present as an emergency due to the high level of discomfort and owner anxiety associated with this problem. In addition, it is not unusual for otitis externa to develop in individuals requiring critical care, especially those that have had bouts of otitis externa previously or may be suffering from sub-clinical disease. Stress may be a significant factor in the development of the condition in the critically ill patient. Ear cytology is a very useful diagnostic aid, however, the results *must* be interpreted in the light of history and clinical findings. The primary aim of therapy should be to reduce inflammation within the ear canal, which, in turn, will help eliminate secondary organism involvement before considering antibiotic therapy.

Complete resolution of an ear problem is very unlikely unless predisposing, primary and perpetuating factors are identified.

- *Predisposing factors* – increase the risk of development of otitis externa, e.g., conformation (congenital stenosis – Shar-Pei; excessive hair – poodles), lifestyle (grooming, swimming, excessive ear care), obstructive lesions (neoplasms, polyps), systemic disease (pyrexia, immune suppression, viruses, debilitation), stress.
- *Primary factors* – incite the condition, e.g., foreign bodies, hypersensitivity disorders (atopy, adverse food reactions, drug reactions), immune-mediated (pemphigus complex), parasites (Otodectes), seborrheic disorders (idiopathic seborrhea), glandular disorders (excessive cerumen/sebum accumulation, sebaceous adenitis).
- *Perpetuating factors* – prevent the resolution of the problem, e.g., organism overgrowth (bacteria, yeast), pathological change (epidermal/glandular hyperplasia, stenosis, calcification, otitis media), over-treatment with topical ear medications.

DIAGNOSIS

The diagnosis of otitis externa and assessment of severity should be based on a thorough history, clinical examination findings, cytology, and if indicated, the results of bacterial culture.

History

- The progression of the case is a crucial part of the clinical assessment. If the condition is pre-existing, ask the client how often the pet bothers the ear (ear rubbing or head shaking, number of times per hour or day). This will provide important information on the severity of the clinical signs. Potential predisposing or primary factors (e.g., ear care, exposure to water, general health, parasites, etc.) should also be explored.

Clinical Signs/Physical Examination

- Don't assume that it is 'just an ear problem'. Perform a full dermatological exam as part of your evaluation.
- Look for evidence of a generalized hypersensitivity disorder affecting the skin. Foot chewing may suggest an underlying environmental hypersensitivity. Food hypersensitivity has been seen in dogs presenting with only otitis externa. Drug reactions and other immune-mediated diseases (pemphigus foliaceus) may present with otitis externa.
- Assess severity of the clinical signs (this may help guide your treatment recommendations). Tilting of the head to the affected side may be noted in acute cases.
- Always examine both ears, even if there is apparently only one ear affected. The apparently normal ear will often tell you more about potential predisposing factors (excessive cerumen accumulation), and primary factors (erythema associated with atopy or food allergy). Include the pinna in the examination.
- A transilluminator can facilitate examination of the majority of the ear canal, especially if the ear canal is very inflamed or the animal is in a lot of discomfort.
- Examine the ear canal for evidence of ulceration, hyperplasia or discharge/debris (describe). Use an otoscope to try and visualize the tympanic membrane. Note whether the tympanic membrane was visualized and if possible, describe its appearance.
- If the patient resents the examination because of severe pain or inflammation, or if significant amounts of discharge prevent examination, institute empirical anti-inflammatory therapy and re-evaluation a few days later (*see MANAGEMENT I General Considerations, below*).

- Ear mites result in intense pruritus around the ears. The ear canals will contain varying amounts of dry brown-red wax mixed with blood, mite exudate and live mites. In classic cases this material may have a coffee ground appearance. The mites are usually visible as tiny white specks with the naked eye. Although the mites live in the ear canals, they may affect other areas of the body, particularly around the head and rump areas in severe cases, especially in cats. Spread to other areas may indicate a degree of immunosuppression and underlying immunosuppressive disorders (i.e., FeLV/FIV) should be investigated in this situation.

Ear Canal Cytology

- Samples should be taken from the vertical canal – horizontal canal junction using a Q-tip, and after heat fixing and staining with Diff-Quik, examined under high power or oil immersion.
- A cytology sample from the inner pinna around the canal orifice with acetate tape may also be useful if secondary Malassezia is suspected.
- Assessment should be made for bacteria, yeast, inflammatory cells and epithelial cells (acanthocytes in pemphigus foliaceus).
- Results must be interpreted in the light of the history, and clinical findings, not by themselves. The number of organisms and/or inflammatory cells should be determined at each visit. Current texts suggest that in dogs, greater than 5 Malassezia and 25 bacteria per x40 field are abnormal, and in cats, greater than 12 yeast and 15 bacteria are abnormal. It is important to remember that increased numbers of organisms may be noted in dogs with any degree of pathologic change associated with a chronic ear problem.
- Increased numbers of bacteria and yeast does not mean that aggressive therapy is indicated. The presence of organisms is not synonymous with infection. If bacteria or yeast are noted within the cerumen or on epithelial cells, and there are no inflammatory cells present, this indicates colonization, not infection. Colonization is common in dogs with any degree of pathologic change within the ear canal.
- If inflammatory cells or large numbers of bacteria are noted on ear canal cytology, consider performing a bacterial culture.
- Cytology should be repeated every two weeks to assess response to therapy.

Bacterial Culture

- Bacterial culture is performed when inflammatory cells or large numbers of bacteria are noted on ear cytology.
- Bacteria cultured may not require specific treatment if the underlying inflammation is controlled. Due to concerns for resistant bacterial ear infections, including those complicated by Pseudomonas, topical and systemic antibiotics must be used appropriately (*see MANAGEMENT*).
- Cytology has been shown to be a far superior method of diagnosing Malassezia than culture.

Imaging

- Radiography, under general anesthesia, may be useful to diagnose middle ear involvement, when the tympanic membrane cannot be observed or there is a doubt as to whether it is intact. However, radiographic findings may fail to diagnose otitis media in ~25% of cases.
- MRI and CT show promise as imaging techniques for the bulla.

MANAGEMENT

I.   General Considerations

A. Treatment should be aggressive enough to avoid the development of chronic pathological changes. It is important not to lose sight of the need to identify predisposing and primary factors.

B. The initial aim of therapy should be to **reduce inflammation** within the ear canal, as this will provide comfort for the patient and may significantly decrease secondary`organism involvement.

C. **Corticosteroids,** topically or systemically, are very beneficial in the treatment of otitis externa and should be first line therapy. Weaning down is possible to an as needed basis. Steroid therapy has been shown to significantly aid in the elimination of resistant *Pseudomonas* strains through changes in the microclimate that no longer favor the growth of the bacteria.

1. **Systemic steroids** at anti-inflammatory doses (**prednisone 1 – 2 mg/kg/day**) should be used to decrease severe inflammation, in acute cases, especially during the early stages of therapy. Rule out any contraindication for this prior to institution.

2. **Topical therapy** using 1% hydrocortisone either combined with an astringent, 2% Burow's solution (aluminum acetate) in propylene glycol or with boric acid may be all that is required for the treatment of mild cases. Systemic antibiotics are not generally helpful in the treatment of otitis externa as they can encourage the overgrowth and colonization by resistant strains of bacteria, in particular *Pseudomonas* spp. Overuse and injudicious use of topical antibiotics may produce the same effect.

II. Otitis Externa Complicated by Bacteria

A. A thorough clinical assessment for underlying etiologies should be performed while instituting a treatment protocol utilizing topical and/or systemic steroids, ear flushing and then, if necessary, topical antibiotics. **Topical antibiotic** therapy may not be required. Assess clinical and cytological response to steroid therapy alone before **determining** if topical antibiotic therapy is required. If the patient is responding favourably, consider instituting an ear flush rather than topical antibiotic therapy. Many apparently resistant bacterial infections will self-cure if inflammation is controlled and they are given time to resolve.

B. **Mild cases** should be initially treated with **1% hydrocortisone with 2% Burow's solution in propylene glycol.** Topical flucinolone (Synotic, Wyeth) is an alternative in more severe cases if oral corticosteroids are to be avoided.

C. **More severe** (acute) cases should receive **oral prednisone** in a gradual reducing regimen starting at 1 – 2 mg/kg/day.

D. **Topical antibiotic** therapy should be considered if topical, systemic corticosteroid therapy and ear flushing does not produce a favourable clinical and cytological response at re-evaluation. Suitable topical antibiotics include:

1. **gentamicin** (Otomax; Schering-Plough, Gentocin Otic; Schering-Plough),
2. **polymixin B** (Surolan; Merial, Cortisporin Otic; Glaxo Wellcome),
3. **ciprofloxacin** (Cipro HC; Alcon), OR
4. **enrofloxacin – silver sulfadiazine** (Baytril-Otic; Bayer).

E. Because of concerns for **development of resistant bacteria,** proprietary products should be used sparingly, observing closely for a lack of response or recurrence/relapse.

F. Flushing debris from the ear canal can be of great benefit, however, flushing should never be attempted in the face of severe inflammation as it may lead to erosion and ulceration of the ear canal.

1. A warm solution of white vinegar in water (1 part of white vinegar to 3 – 5 parts water) makes an excellent general flush, if well tolerated. This solution appears to be safe in the presence of a ruptured tympanum. Vinegar and water flushing is normally carried out every 2 – 3 days during the treatment protocol.
2. Acidifying ear cleaners such as Malacetic from Dermapet may be used in the same way.
3. Flushing the ear canal with the surfactant product, Tris-EDTA, may significantly increase the sensitivity of *Pseudomonas* to topical gentamicin and the other aminoglycosides. The EDTA has a direct effect on the organism by chelating metal ions, destabilizing the cell wall. Tromethamine (Tris) enhances the effect of the EDTA on the organism. The recommended protocol is to flush the canal 15 minutes prior to topical antibiotic use. Tris-EDTA solution is available as TrizEDTA, from Dermapet through Central Sales in North America or can be compounded (6.05 g edetate disodium with 12 g tromethamine (Trizma base) and bring to liter by adding double distilled water. Adjust pH to 8 with hydrochloric acid. Autoclave before use) 100 mL of white vinegar can also be added.

III. Otitis Externa Complicated by Malassezia

A. Although any of the combination products containing an antifungal should be effective, in eliminating Malassezia you should consider carefully whether treatment is needed.

1. Many mild cases will respond to an acidifying ear cleaner and a 1% topical hydrocortisone ear medication as described in IIB above.

2. More severe cases require definitive treatment. Topical 3 in 1 products such as:

    a. Otomax (Schering-Plough; gentamicin, betamethasone, and clotrimazole) or Surolan (Merial; miconazole, polymixin B, prednisolone) should be effective, but their use should be controlled to avoid the development of resistant bacterial strains.

    b. A combination of enilconazole (Imaverol, Merial) in Oticalm ear cleaner (DVM-3M) 1:50 solution appears to be successful in mild cases where inflammation is not an issue.

    c. Ketoconazole 5 mg/kg q12h or 10 mg/kg PO q24h for 2 – 4 weeks appears to work very well in severe infections or where topical therapy has not controlled the problem.

Assessment for underlying etiologies is again very important. Because of concerns regarding liver toxicity, blood work should be performed prior to ketoconazole therapy.

IV. Ear Mites

A. Cats presenting with generalized otodectic mange should be checked for FeLV/FIV status.

B. Traditional treatment relies on the use of a topical miticidal agent. Topical products containing parasiticides, which should be used per the manufacturers recommendations, are:

1. **pyrethrins**
2. **rotenone**
3. **milbemycin** (MilbeMite; Novartis)
4. **thiabendazole** (Tresaderm; Merial)

C. **Gentle ear cleaning** prior to using the drops may be beneficial.

D. Ear products **without parasiticides such as Surolan** (Merial), have also been shown to be effective in eliminating ear-mites. They are believed to be effective by making the environment unsuitable for the mite.

E. **Selamectin** (Revolution; Pfizer) is approved for the treatment of ear mites in cats and dogs with one dose monthly for two doses.

V. Otitis Media/Ruptured Tympanic Membrane

- Cytology and culture/sensitivity from the middle ear is highly recommended.
- Systemic corticosteroids may be of great benefit in decreasing inflammation.
- Systemic antibiotic therapy based on culture/sensitivity and/or systemic fungal therapy is recommended
- Topical therapy should be avoided.
- Flushing the canal and bulla completely with saline under general anesthesia may be beneficial. Flushing the canal with saline or white vinegar in water (1:3) every 2 – 3 days can be used to keep the canal clear of debris.

PHARMACOLOGY

1) **1% hydrocortisone with 2% Burow's solution with propylene glycol** is available from *The Veterinary Pharmacy* in Guelph, ON, Canada (800) 446-8689, (888) 677-0437 (Fax) and *Riverstone Veterinary Pharmacy* (978) 768-0040 in the US. Typical doses are 2-3 drops q12h for small dogs, and 4-6 drops q12h for large dogs. Weaning down to an as needed basis is possible once the problem is under control.

SUGGESTED READING

1. Gotthelf LN: Small Animal Ear Diseases, WB Saunders Co, Philadelphia, 2004.
2. Matousek JL (ed): Vet Clin North America: Small Animal Practice, WB Saunders Co, Philadelphia, 2004.
3. Scott DW, Miller WH, Griffin CE: Muller and Kirk's Small Animal Dermatology, WB Saunders Co, Philadelphia, 2000:1204-1231.

PREPARATION: Using the chart below, find hourly rate in mL of butorphanol at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. Add **mL (10 mg/mL) butorphanol/h to mL fluid/h in burette. A maximum of 6-hour infusion is recommended.** Mix well by inversion. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (i.e., q1h volumes). Butorphanol appears to be compatible with most crystalloid fluids including Plasma-Lyte® A, Plasma-Lyte® 148 and 0.9% NaCl.

INDICATIONS: For managing mild to moderate pain, or sedation (*see Analgesics and Sedatives p. 84*).

CAUTION: *See Analgesics and Sedatives p. 84.*

DOSE: This infusion rate is based on 0.1 – 0.4 mg/kg/h.

COMPATIBILE: Since butorphanol is infused with the maintenance fluids, it is important to know which drugs are compatible. Common compatible drugs include:

| Atropine | Metoclopramide | Propofol (for 1 h only) |

INCOMPATIBLE: These drugs should not be administered in the line while butorphanol is running:

| Midazolam | Pentobarbital |

*Note: Other drugs have not been tested, and therefore should be considered incompatible.

BUTORPHANOL INFUSION IN CRYSTALLOID FLUIDS (original concentration 10 mg/mL)

The volume (mL/h) is the volume of a 10 mg/mL concentration of butorphanol to be added to each hour of IV fluids.

BW kg (lbs)	1 (2.2)	2 (4.4)	3 (6.6)	4 (8.8)	5 (11)
Dose (mg/h)	0.1-0.4	0.2-0.8	0.3-1.2	0.4-1.6	0.5-2.0
Volume (mL/h)	0.01-0.04	0.02-0.08	0.03-0.12	0.04-0.16	0.05-0.20
BW kg (lbs)	6 (13.2)	7 (15.4)	8 (17.6)	9 (19.8)	10 (22)
Dose (mg/h)	0.6-2.4	0.7-2.8	0.8-3.2	0.9-3.6	1.0-4.0
Volume (mL/h)	0.06-0.24	0.07-0.28	0.08-0.32	0.09-0.36	0.10-0.40
BW kg (lbs)	11 (24.2)	12 (26.4)	13 (28.6)	14 (30.8)	15 (33)
Dose (mg/h)	1.1-4.4	1.2-4.8	1.3-5.2	1.4-5.6	1.5-6.0
Volume (mL/h)	0.11-0.44	0.12-0.48	0.13-0.52	0.14-0.56	0.15-0.60
BW kg (lbs)	16 (35.2)	17 (37.4)	18 (39.6)	19 (41.8)	20 (44)
Dose (mg/h)	1.6-6.4	1.7-6.8	1.8-6.8	1.9-7.6	2.0-8.0
Volume (mL/h)	0.16-0.64	0.17-0.68	0.18-0.72	0.19-0.72	0.20-0.80
BW kg (lbs)	21 (46.2)	22 (48.4)	23 (50.6)	24 (52.8)	25 (55)
Dose (mg/h)	2.1-8.4	2.2-8.8	2.3-9.2	2.4-9.6	2.5-9.6
Volume (mL/h)	0.21-0.84	0.22-0.88	0.23-0.92	0.24-0.96	0.25-1.0
BW kg (lbs)	26 (57.2)	27 (59.4)	28 (61.6)	29 (63.8)	30 (66)
Dose (mg/h)	2.6-10.4	2.7-10.8	2.8-11.2	2.9-11.6	3.0-12.0
Volume (mL/h)	0.26-1.0	0.27-1.1	0.28-1.1	0.29-1.2	0.30-1.2
BW kg (lbs)	31 (68.2)	32 (70.4)	33 (72.6)	34 (74.8)	35 (77)
Dose (mg/h)	3.1-12.4	3.2-12.8	3.3-13.2	3.4-13.6	3.5-14.0
Volume (mL/h)	0.31-1.2	0.32-1.3	0.33-1.3	0.34-1.4	0.35-1.4
BW kg (lbs)	36 (79.2)	37 (81.4)	38 (83.6)	39 (85.8)	40 (88)
Dose (mg/h)	3.6-14.4	3.7-14.8	3.8-15.2	3.9-15.6	4.0-16.0
Volume (mL/h)	0.36-1.4	0.37-1.5	0.38-1.5	0.39-1.6	0.40-1.6

BW kg (lbs)	41 (90.2)	42 (92.4)	43 (94.6)	44 (96.8)	45 (99)
Dose (mg/h)	4.1-16.4	4.2-16.8	4.3-17.2	4.4-17.6	4.5-18.0
Volume (mL/h)	0.41-1.6	0.42-1.7	0.43-1.7	0.44-1.8	0.45-1.8
BW kg (lbs)	46 (101.2)	47 (103.4)	48 (105.6)	49 (107.8)	50 (110)
Dose (mg/h)	4.6-18.4	4.7-18.8	4.8-19.2	4.9-19.6	5.0-20.0
Volume (mL/h)	0.46-1.8	0.47-1.9	0.48-1.9	0.49-2.0	0.50-2.0
BW kg (lbs)	51 (112.2)	52 (114.4)	53 (116.6)	54 (118.8)	55 (121)
Dose (mg/h)	5.1-20.4	5.2-20.8	5.3-21.2	5.4-21.6	5.5-22.0
Volume (mL/h)	0.51-2.0	0.52-2.1	0.53-2.1	0.54-2.2	0.55-2.2
BW kg (lbs)	56 (123.2)	57 (125.4)	58 (127.6)	59 (129.8)	60 (132)
Dose (mg/h)	5.6-22.4	5.7-22.8	5.8-23.2	5.9-23.6	6.0-24.0
Volume (mL/h)	0.56-2.2	0.57-2.3	0.58-2.3	0.59-2.4	0.60-2.4
BW kg (lbs)	61 (134.2)	62 (136.4)	63 (138.6)	64 (140.8)	65 (143)
Dose (mg/h)	6.1-24.4	6.2-24.8	6.3-25.2	6.4-25.6	6.5-26.0
Volume (mL/h)	0.61-2.4	0.62-2.5	0.63-2.5	0.64-2.6	0.65-2.6
BW kg (lbs)	66 (145.2)	67 (147.2)	68 (149.6)	69 (151.8)	70 (154)
Dose (mg/h)	6.6-26.4	6.7-26.8	6.8-27.2	6.9-27.6	7.0-28.0
Volume (mL/h)	0.66-2.6	0.67-2.7	0.68-2.7	0.69-2.8	0.70-2.8
BW kg (lbs)	71 (156.2)	72 (158.4)	73 (160.6)	74 (162.8)	75 (165)
Dose (mg/h)	7.1-28.4	7.2-28.8	7.3-29.2	7.4-29.6	7.5-30.0
Volume (mL/h)	0.71-2.8	0.72-2.9	0.73-2.9	0.74-3.0	0.75-3.0
BW kg (lbs)	76 (167.2)	77 (169.4)	78 (171.6)	79 (173.8)	80 (176)
Dose (mg/h)	7.6-30.4	7.7-30.8	7.8-31.2	7.9-31.6	8.0-32.0
Volume (mL/h)	0.76-3.0	0.77-3.1	0.78-3.1	0.79-3.2	0.80-3.2
BW kg (lbs)	81 (178.2)	82 (180.4)	83 (182.6)	84 (184.8)	85 (187)
Dose (mg/h)	8.1-32.4	8.2-32.8	8.3-33.2	8.4-33.6	8.5-34.0
Volume (mL/h)	0.81-3.2	0.82-3.3	0.83-3.3	0.84-3.4	0.85-3.4
BW kg (lbs)	86 (189.2)	87 (191.4)	88 (193.6)	89 (195.8)	90 (198)
Dose (mg/h)	8.6-34.4	8.7-34.8	8.8-35.2	8.9-35.6	9.0-36.0
Volume (mL/h)	0.86-3.4	0.87-3.5	0.88-3.5	0.89-3.6	0.90-3.6

PREPARATION: Add 250 mg dobutamine (20 mL of 12.5 mg/mL) to 500 mL 5% Dextrose in Water (D5W), 0.9% NaCl or 0.45% NaCl for a concentration of 0.5 mg/ml. LRS may also be used, but **not Plasma-Lyte® 148 or Plasma-Lyte® A.** The chart is based on 2 – 10 μg/kg/min. Titrate up or down to effect. Use the solution within 24 hours if not in a dextrose solution. Dextrose containing fluids are recommended to maintain activity of the drug.

INDICATIONS: Has potent inotropic effects (increased cardiac contractility and output). Used in patients with known dilated cardiomyopathy or mitral insufficiency with known poor contractility. Often used concurrently with sodium nitroprusside in patients with life-threatening congestive heart failure. *See Congestive Heart Failure p. 150.*

CAUTION: Do not use for cats with hypertrophic cardiomyopathy. Can be used for cats cautiously if no other vasopressors have worked. *See CongestiveHeart Failure p. 152.*

DOSE: **Dogs:** Start at 5 μg/kg/min and titrate up or down to effect. **Cats (caution):** Start at 1 μg/kg/min to a maximum of 4 μg/kg/min.

BURETTE: **As an alternative** to the above infusion, dobutamine may be added to a burette containing 100 mL of fluids. This may be desirable in the case of a small patient, or for short term use of the solution since *the solution is only stable for 24 hour* when not in D5W. To make a smaller volume of solution, add 50 mg or 4 mL dobutamine to 100 mL of D5W, 0.9% NaCl or 0.45% NaCl to make a 0.5 mg/mL solution. Administer per rates on chart.

COMPATIBILE: Since dobutamine is infused by 'piggy-backing' onto the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Diazepam	Diltiazem	Dopamine
Famotidine	Fentanyl Citrate	Hydromorphone
Insulin (Regular)	Lidocaine	Morphine Sulphate
Norepinephrine	Propofol (for 1 h only)	Ranitidine
Sodium nitroprusside		

INCOMPATIBLE: These drugs should not be administered in the line while dobutamine is running:

Calcium Gluconate	Sodium Bicarbonate	Thiopental
Heparin	Magnesium Sulphate	Furosemide

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

Note: Can add two to four vials (500 mg total) dobutamine to 500 mls 5% D5W, 0.9% NaCl or 0.45% NaCl to create a higher concentration (1 – 2 mg/mL). Rates (mL/h) in chart will need to be halved or quartered depending on concentration or dose required. **CAUTION IS REQUIRED WITH HIGH CONCENTRATIONS, ESPECIALLY IN SMALL PERIPHERAL VESSELS, a central vein is preferred. THIS SHOULD ONLY BE CONSIDERED IN SEVERELY FLUID RESTRICTED SITUATIONS.**

Dobutamine 250 mg in 500 mL 5% Dextrose in Water Infusion/Hour (0.5 mg/ml)
Range: 2 – 10 μg/kg/min

Volume (mL/h) is the volume of the above solution

BW kg (*lbs*)	**1** (*2.2*)	**2** (*4.4*)	**3** (*6.6*)	**4** (*8.8*)	**5** (*11*)
Dose (mg/h)	0.1-0.6	0.2-1.2	0.4-1.8	1.5-2.4	0.6-3.0
Volume (mL/h)	0.2-1.2	0.5-2.4	0.7-3.6	1.0-4.8	1.2-6.0
BW kg (*lbs*)	**6** (*13.2*)	**7** (*15.4*)	**8** (*17.6*)	**9** (*19.8*)	**10** (*22*)
Dose (mg/h)	0.7-3.6	0.8-4.2	1.0-4.8	1.1-5.4	1.2-6.0
Volume (mL/h)	1.4-7.0	1.7-8.5	1.9-9.5	2.2-11	2.4-12

BW kg (lbs) Dose (mg/h) Volume (mL/h)	11 (24.2) 1.3-6.6 3-13	12 (26.4) 1.4-7.2 3-14	13 (28.6) 1.6-7.8 3-15	14 (30.8) 1.7-8.4 3-17	15 (33) 1.8-9.0 4-18
BW kg (lbs) Dose (mg/h) Volume (mL/h)	16 (35.2) 2-9.5 4-19	17 (37.4) 2-10 4-20	18 (39.6) 2-11 4-21	19 (41.8) 2-11.5 5-23	20 (44) 2-12 5-24
BW kg (lbs) Dose (mg /h) Volume (mL/h)	21 (46.2) 3-12.5 5-25	22 (48.4) 3-13 5-26	23 (50.6) 3-14 6-27	24 (52.8) 3-14.5 6-29	25 (55) 3-15 6-30
BW kg (lbs) Dose (mg /h) Volume (mL/h)	26 (57.2) 3-15.5 6-31	27 (59.4) 3-16 6-32	28 (61.6) 3-17 7-33	29 (63.8) 3-17.5 7-35	30 (66) 4-18 7-36
BW kg (lbs) Dose (mg /h) Volume (mL/h)	31 (68.2) 4-18.5 7-37	32 (70.4) 4-19 8-38	33 (72.6) 4-20 8-39	34 (74.8) 4-20.5 8-41	35 (77) 4-21 8-42
BW kg (lbs) Dose (mg /h) Volume (mL/h)	36 (79.2) 4-21.5 9-43	37 (81.4) 4-22 9-44	38 (83.6) 5-23 9-45	39 (85.8) 5-23.5 9-47	40 (88) 5-24 10-48
BW kg (lbs) Dose (mg /h) Volume (mL/h)	41 (90.2) 5-24 10-49	42 (92.4) 5-25 10-50	43 (94.6) 5-26 10-51	44 (96.8) 5-26.5 11-53	45 (99) 5-27 11-54
BW kg (lbs) Dose (mg /h) Volume (mL/h)	46 (101.2) 6-27 11-55	47 (103.4) 6-28 11-56	48 (105.6) 6-29 12-57	49 (107.8) 6-29.5 12-59	50 (110) 6-30 12-60
BW kg (lbs) Dose (mg /h) Volume (mL/h)	51 (112.2) 6-30.5 12-61	52 (114.4) 6-31 12-62	53 (116.6) 6-32 13-63	54 (118.8) 6-34 13-65	55 (121) 7-33 13-66
BW kg (lbs) Dose (mg /h) Volume (mL/h)	56 (123.2) 7-33.5 13-67	57 (125.4) 7-34 14-68	58 (127.6) 7-35 14-69	59 (129.8) 7-35.5 14-71	60 (132) 7-36 14-72
BW kg (lbs) Dose (mg /h) Volume (mL/h)	61 (134.2) 7-36 15-73	62 (136.4) 7-37 16-74	63 (138.6) 8-38 16-76	64 (140.8) 8-38.5 17-77	65 (143) 8-39 17-78
BW kg (lbs) Dose (mg /h) Volume (mL/h)	66 (145.2) 8-39.5 16-79	67 (147) 8-40 16-80	68 (149.6) 8-41 16-81	69 (151.8) 8-41.5 17-83	70 (154) 8-42 17-84
BW kg (lbs) Dose (mg /h) Volume (mL/h)	71 (156.2) 9-42.5 17-85	72 (158.4) 9-43 17-86	73 (160.6) 9-44 18-87	74 (162.8) 9-44.5 18-89	75 (165) 9-45 18-90
BW kg (lbs) Dose (mg /h) Volume (mL/h)	76 (167.2) 9-45.5 18-91	77 (169.4) 9-46 18-92	78 (171.6) 9-47 19-93	79 (173.8) 9-47.5 19-95	80 (176) 10-48 19-96
BW kg (lbs) Dose (mg /h) Volume (mL/h)	81 (178.2) 10-48.5 19-97	82 (180.4) 10-49 20-98	83 (182.6) 10-50 20-99	84 (184.8) 10-50.5 20-101	85 (187) 10-51 20-102
BW kg (lbs) Dose (mg /h) Volume (mL/h)	86 (189.2) 10-51.5 21-103	87 (191.4) 10-52 21-104	88 (193.6) 11-53 21-105	89 (195.8) 11-53.5 21-107	90 (198) 11-54 22-108

PREPARATION: 1 vial (5 mL) of 40 mg/mL into 250 mL of 5% Dextrose in Water (D5W), 0.9% NaCl, or LRS. *Note:* this is double the concentration suggested in the package to decrease the fluid volume delivered to the patient and which is used in the chart below. The recommended concentration on the package is 400 μg/mL (1 5 mL vial/500 mL D5W). Dextrose-containing solution preserves activity of the drug if stored or hung for long periods of time. If placed directly into the burrette, NaCl or LRS is suitable.

INDICATIONS: For criteria for treatment with therapy *see Shock p. 606*, *Sepsis/Septic Shock p. 592* .

CAUTION: Abrubt withdrawal of therapy should be avoided. Risk of extravasation, or high concentration necrosis at insertion site. **Use central line (jugular) or 22 – 20G and 1.88" in length peripheral catheter to minimize this complication. Maintain strict asepsis of catheter site and ensure patency and positioning of catheter on regular basis during therapy. Reduce concentration as soon as possible.** Blood pressure must be continuously monitored during therapy, preferably directly, or reliable indirect at a minimum of q5min to avoid hypertension. Measurement interval can be increased once desired BP is reached, but must still be judiciously evaluated.

COMPATIBILE: Other drugs should not be administered through the dopamine IV set. However, since dopamine will probably be connected to maintenance fluids via a 'piggy-back', it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Diltiazem	Dobutamine	Epinephrine
Famotidine	Fentanyl Citrate	Heparin Sodium
Hydromorphone	Lidocaine	Metronidazole
Morphine Sulfate	Norepinephrine	Ondansetron
Propofol (for 1 h only)	Ranitidine	Sodium Nitroprusside

INCOMPATIBLE: These drugs should not be administered in the line while dopamine is running:

Insulin (regular)

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

DOSE: This infusion rate is based on 5 – 20 μg/kg/min. **The concentration of Dopamine in this solution is 800 μg/mL).** Dopamine infusion should be administered separately from maintenance fluids to allow for adjustment in dosing. Maintenance fluid rate should be calculated with a reduction in volume according to that administered with the Dopamine infusion. More commonly, dopamine solution is titrated to effect within the dosing limits. Halve the lower and higher rates in the chart for 2.5 – 10 μg/kg/min.

DOPAMINE IN D5W, LRS OR 0.9% NaCl, INFUSION/HOUR (800 µg/mL)

Note: The volume (mL/h) give below is the volume of the solution prepared as above.

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	0.3-1	0.6-2	0.9-4	1.2-5	1.5-6
Volume (mL/h)	0.4-2	0.8-3	1.1-5	1.5-6	1.9-8
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (mg/h)	1.8-7	2.1-8	2.4-10	2.7-11	3.0-12
Volume (mL/h)	2.3-9	2.6-11	3.0-12	3.4-14	3.8-15
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (mg/h)	3.3-13	3.6-14	3.9-16	4.2-17	4.5-18
Volume (mL/h)	4.1-17	4.5-18	4.9-20	5.3-21	5.6-23
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (mg/h)	4.8-19	5.1-20	5.4-22	5.7-23	6.0-24
Volume (mL/h)	6.0-24	6.4-26	6.8-27	7.1-29	7.5-30

BW kg (lbs) Dose (mg/h) Volume (mL/h)	21 (46.2) 6.3-25 7.9-32	22 (48.4) 6.6-26 8.3-33	23 (50.6) 6.9-28 8.6-35	24 (52.8) 7.2-29 9.0-36	25 (55) 7.5-30 9.4-38
BW kg (lbs) Dose (mg/h) Volume (mL/h)	26 (57.2) 7.8-31 10-39	27 (59.4) 8.1-32 10-41	28 (61.6) 8.4-34 10-42	29 (63.8) 8.7-35 11 -44	30 (66) 9.0-36 11-45
BW kg (lbs) Dose (mg/h) Volume (mL/h)	31 (68.2) 9.3-37 12 -47	32 (70.4) 9.6-38 12-48	33 (72.6) 10-40 12-50	34 (74.8) 10-41 13-51	35 (77) 10-42 13-53
BW kg (lbs) Dose (mg/h) Volume (mL/h)	36 (79.2) 11-43 13-54	37 (81.4) 11-44 14-56	38 (83.6) 11-46 14-57	39 (85.8) 12-47 15-59	40 (88) 12-48 15-60
BW kg (lbs) Dose (mg/h) Volume (mL/h)	41 (90.2) 12-49 15-62	42 (92.4) 13-50 16-63	43 (94.6) 13-52 16-65	44 (96.8) 13-53 16-66	45 (99) 13-54 17-68
BW kg (lbs) Dose (mg/h) Volume (mL/h)	46 (101.2) 14-55 17-69	47 (103.4) 14-56 17-71	48 (105.6) 14-58 18-72	49 (107.8) 15-59 18-74	50 (110) 15-60 19-75
BW kg (lbs) Dose (mg/h) Volume (mL/h)	51 (112.2) 15-61 19-77	52 (114.4) 16-62 20-78	53 (116.6) 16-64 20-80	54 (118.8) 16-65 20-81	55 (121) 16-66 21-83
BW kg (lbs) Dose (mg/h) Volume (mL/h)	56 (123.2) 17-67 21-84	57 (125.4) 17-68 21-86	58 (127.6) 17-70 22-87	59 (129.8) 18-71 22-89	60 (132) 18-72 23-90
BW kg (lbs) Dose (mg/h) Volume (mL/h)	61 (134.2) 18-73 23-92	62 (136.4) 19-74 23-94	63 (138.6) 19-76 24-95	64 (140.8) 19-77 24-96	65 (143) 19-78 24-98
BW kg (lbs) Dose (mg/h) Volume (mL/h)	66 (145.2) 20-79 25-99	67 (147.2) 20-80 25-101	68 (149.6) 20-82 26-102	69 (151.8) 21-83 26-104	70 (154) 21-84 26-105
BW kg (lbs) Dose (mg/h) Volume (mL/h)	71 (156.2) 21-85 27-107	72 (158.4) 22-86 27-108	73 (160.6) 22-88 27-110	74 (162.8) 22-89 28-111	75 (165) 23-90 28-113
BW kg (lbs) Dose (mg/h) Volume (mL/h)	76 (167.2) 23-91 29-114	77 (169.4) 23-92 29-116	78 (171.6) 23-94 29-117	79 (173.8) 24-95 30-119	80 (176) 24-96 30-120
BW kg (lbs) Dose (mg/h) Volume (mL/h)	81 (178.2) 24-97 30-122	82 (180.4) 25-98 31-123	83 (182.6) 25-100 31-125	84 (184.8) 25-101 32-126	85 (187) 26-102 32-128
BW kg (lbs) Dose (mg/h) Volume (mL/h)	86 (189.2) 26-103 32-129	87 (191.4) 26-104 33-131	88 (193.6) 26-106 33-132	89 (195.8) 27-107 33-134	90 (198) 27-108 34-135

PREPARATION: 4 mL of 1 mg/mL (1:1000) epinephrine in 500 mL 5%Dextrose in Water (D5W), LRS or 0.9% NaCl. The solution is more concentrated than other recommendations so as to deliver less fluid, and is the concentration used in the chart below. If standard concentration is required add 4 mL (1 mg/mL) to 1 Litre. Dextrose solutions are recommended to maintain activity of epinephrine. Solution may become discoloured over time from pink to brownish, this should be discarded.

INDICATIONS: For criteria for treatment with epinephrine *see Shock p. 606, Sepsis/Septic Shock p. 592.*

CAUTION: Abrubt withdrawal of therapy should be avoided. Risk of extravasation, or high concentration necrosis at insertion site. **Use central line (jugular) or 22–20G and 1.88" in length peripheral catheter to minimize this complication. Maintain strict asepsis of catheter site and ensure patency and positioning of catheter on regular basis during therapy. Reduce concentration as soon as possible.**

Blood pressure must be continuously monitored during therapy, preferably directly, or reliable indirect at a minimum of q5min to avoid hypertension. Measurement interval can be increased once desired BP is reached, but must still be judiciously evaluated.

COMPATIBILE: Other drugs should not be administered through the epinephrine IV set. However, since epinephrine will probably be connected to maintenance fluids via a 'piggy-back', it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Dobutamine	Diltiazem	Dopamine
Famotidine	Fentanyl Citrate	Furosemide
Heparin Sodium	Hydromorphone	Midazolam
Morphine Sulfate	Norepinephrine	Propofol (for 1 h only)
Ranitidine		

INCOMPATIBLE: These drugs should not be administered while epinephrine is running:

Ampicillin	Thiopental	Lidocaine
Sodium Bicarbonate		

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

DOSE: This infusion rate is based on $0.1 - 0.5$ $\mu g/kg/min$. **The concentration of Epinephrine in this solution is 8 mg/mL).** Epinephrine infusion should be administered separately from maintenance fluids to allow for adjustment in dosing. Maintenance fluid rate should be calculated with a reduction in volume according to that administered with the Epinephrine infusion. **Should a more concentrated solution be required to reduce fluids administered (this should be considered with higher doses), add 8 mL of 1 mg/mL epinephrine to 500 mL(solution will be 16 mg/mL) and administer at half the infusion rate below.** More commonly, epinephrine solution is titrated to effect within the dosing limits.

EPINEPHRINE IN 5% DEXTROSE OR 0.9% NaCl INFUSION/HOUR (8µg/mL)

Note: The volume (mL/h) is the volume of solution prepared above and rounded to closest whole mL

BW kg (*lbs*)	1 (*2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (µg/h)	6-30	12-60	18-90	24-120	30-150
Volume (mL/h)	1-4	2-8	2-11	3-15	4-19
BW kg (*lbs*)	6 (*13*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (µg/h)	36-180	42-210	48-240	54-270	60-300
Volume (mL/h)	4-22	5-26	6-30	7-34	7-37
BW kg (*lbs*)	11 (*24*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (µg/h)	66-330	72-360	78-390	84-420	90-450
Volume (mL/h)	8-41	9-45	10-49	10-52	11-56
BW kg (*lbs*)	16 (*35*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (µg/h)	96-480	102-510	108-540	114-570	120-600
Volume (mL/h)	12-60	13 -64	13-67	14-71	15-75

BW kg (lbs)	21 (46)	22 (48.4)	23 (50.6)	24 (52.8)	25 (55)
Dose (µg/h)	126-630	132-660	138-690	144-720	150-750
Volume (mL/h)	16-79	16-82	17-86	18-90	19-94
BW kg (lbs)	**26** (57)	**27** (59.4)	**28** (61.6)	**29** (63.8)	**30** (66)
Dose (µg/h)	156-780	162-810	168-840	174-870	180-900
Volume (mL/h)	19-97	20-101	21-105	22-109	22-112
BW kg (lbs)	**31** (68)	**32** (70.4)	**33** (72.6)	**33** (72.6)	**33** (72.6)
Dose (µg/h)	186-930	192-960	198-990	204-1020	210-1050
Volume (mL/h)	23-116	24-120	25-124	25-127	26-131
BW kg (lbs)	**36** (79)	**37** (81.4)	**38** (83.6)	**39** (85.8)	**40** (88)
Dose (µg/h)	216-1080	222-1110	228-1140	234-1170	240-1200
Volume (mL/h)	27-135	28 -139	28-142	29-146	30-150
BW kg (lbs)	**41** (90)	**42** (92.4)	**43** (94.6)	**44** (96.8)	**45** (99)
Dose (µg/h)	246-1230	252-1260	258-1290	264-1320	270-1350
Volume (mL/h)	31-154	31-157	32-161	33-165	34-169
BW kg (lbs)	**46** (101)	**47** (103.4)	**48** (105.6)	**49** (107.8)	**50** (110)
Dose (µg/h)	276-1380	282-1410	288-1440	294-1470	300-1500
Volume (mL/h)	34-172	35-176	36-180	37-184	37-187
BW kg (lbs)	**51** (112)	**52** (114.4)	**53** (116.6)	**54** (118.8)	**55** (121)
Dose (µg/h)	306-1530	312-1560	318-1590	324-1620	330-1650
Volume (mL/h)	38-191	39-195	40-199	40-202	41-206
BW kg (lbs)	**56** (123)	**57** (125.4)	**58** (127.6)	**59** (129.8)	**60** (132)
Dose (µg/h)	336-1680	342-1710	348-1740	354-1770	360-1800
Volume (mL/h)	42-210	43-214	43-217	44-221	45-225
BW kg (lbs)	**61** (134)	**62** (136.4)	**63** (138.6)	**64** (140.8)	**65** (143)
Dose (µg/h)	366-1830	372-1860	378-1890	384-1920	390-1950
Volume (mL/h)	46-229	46-232	47-236	48-240	49-244
BW kg (lbs)	**66** (145)	**67** (147.2)	**68** (149.6)	**69** (151.8)	**70** (154)
Dose (µg/h)	396-1980	402-2010	408-2040	414-2070	420-2100
Volume (mL/h)	50-248	50-251	51-255	52-259	53-263
BW kg (lbs)	**71** (156)	**72** (158.4)	**73** (160.6)	**74** (162.8)	**75** (165)
Dose (µg/h)	426-2130	432-2160	438-2190	444-2220	450-2250
Volume (mL/h)	53-266	54-270	55-274	56-278	56-281
BW kg (lbs)	**76** (167)	**77** (169.4)	**78** (171.6)	**79** (173.8)	**80** (176)
Dose (µg/h)	456-2280	462-2310	468-2340	474-2370	480-2400
Volume (mL/h)	57-285	58-289	59-293	59-296	60-300
BW kg (lbs)	**81** (178)	**82** (180.4)	**83** (182.6)	**84** (184.8)	**85** (187)
Dose (µg/h)	486-2430	492-2460	498-2490	504-2520	510-2550
Volume (mL/h)	61-304	62-308	62-311	63-315	64-319
BW kg (lbs)	**86** (189)	**87** (191.4)	**88** (193.6)	**89** (195.8)	**90** (198)
Dose (µg/h)	516-2580	522-2610	528-2640	534-2670	540-2700
Volume (mL/h)	65-323	65-326	66-330	67-334	68-338

PREPARATION: Using the chart below, find hourly rate in mL of fentanyl at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. **Add mL per hour of fentanyl (50 µg/mL) required to hourly fluid rate in the burette.** Mix well by inversion. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (i.e., q1h volumes). Fentanyl appears to be compatible with most crystalloid fluids including Plasma-Lyte® A, Plasma-Lyte® 148, 0.9% NaCl.

INDICATIONS: For criteria for treatment with fentanyl *see Analgesics and Sedatives p. 83.*

CAUTION: Fentanyl is a potent opioid. Patient must be closely watched for signs of dysphoria or respiratory depression (at higher doses).

DOSE: This infusion rate is based on 3 – 6 µg/kg/h. A bolus of 3 – 5 µg/kg fentanyl is given prior to starting the infusion. **When dealing with extreme pain, fentanyl can be administered to effect, occasionally exceeding 10 µg/kg/h as long as patient is being closely monitored.**

COMPATIBILE: Since fentanyl is infused with the maintenance fluids, it is important to know which drugs will be compatible. More common compatible drugs include:

Atracurium	Heparin	Midazolam
Norepinephrine		

INCOMPATIBLE: These drugs should not be administered in the line while fentanyl is running:

Butorphanol
★Note: Other drugs have not been tested, and therefore should be considered incompatible.

FENTANYL INFUSION IN CRYSTALLOID FLUIDS (original concentration 50 µg/mL)

NOTE: The volume (mL/h) is the volume of full strength fentanyl.
Use this number to determine how much fentanyl to add to hourly fluids.

BW kg (lbs)	1 (2.2)	2 (4.4)	3 (6.6)	4 (8.8)	5 (11)
Dose (µg/h)	3.0-6.0	6.0-12.0	9.0-12.0	12.0-24.0	15.0-30.0
Volume (mL/h)	0.06-0.12	0.12-0.24 0	0.18-0.36	0.24-0.48	0.30-0.60
BW kg (lbs)	6 (13.2)	7 (15.4)	8 (17.6)	9 (19.8)	10 (22)
Dose (µg/h)	18.0-36.0	21.0-42.0	24.0-48.0	27.0-54.0	30.0-60.0
Volume (mL/h)	0.36-0.72	0.42-0.84	48-0.96	0.54-1.08	0.60-1.20
BW kg (lbs)	11 (24.2)	12 (26.4)	13 (28.6)	14 (30.8)	15 (33)
Dose (µg/h)	33.0-66.0	36.0-72.0	39.0-78.0	42.0-84.0	45.0-90.0
Volume (mL/h)	0.66-1.32	0.72-1.44	0.78-1.56	0.84-1.68	0.90-1.80
BW kg (lbs)	16 (35.2)	17 (37.4)	18 (39.6)	19 (41.8)	20 (44)
Dose (µg/h)	48.0-96.0	51.0-102.0	54.0-108.0	57.0-114.0	60.0-120.0
Volume (mL/h)	0.96-1.92	1.0-2.0	1.1-2.2	1.1-2.3	1.2-2.4
BW kg (lbs)	21 (46.2)	22 (48.4)	23 (50.6)	24 (52.8)	25 (55)
Dose (µg/h)	63.0-126.0	66.0-132.0	69.0-138.0	72.0-144.0	75.0-150.0
Volume (mL/h)	1.3-2.5	1.3-2.6	1.4-2.8	1.4-2.9	1.5-3.0
BW kg (lbs)	26 (57.2)	27 (59.4)	28 (61.6)	29 (63.8)	30 (66)
Dose (µg/h)	78.0-156.0	81.0-162.0	84.0-168.0	87.0-174.0	90.0-180.0
Volume (mL/h)	1.6-3.1	1.6-3.2	1.7-3.4	1.7-3.5	1.8-3.6
BW kg (lbs)	31 (68.2)	32 (70.4)	33 (72.6)	34 (74.8)	35 (77)
Dose (µg/h)	93.0-186.0	96.0-192.0	99.0-198.0	102.0-204.0	105.0-210.0
Volume (mL/h)	1.86-3.72	1.92-3.84	1.98-3.96	2.04-4.08	2.10-4.20

BW kg (lbs) Dose (μg/h) Volume (mL/h)	36 (79.2) 108.0-216.0 2.2-4.3	37 (81.4) 111.0-222.0 2.2-4.4	38 (83.6) 114.0-228.0 2.3-4.6	39 (85.8) 117.0-234.0 2.3-4.7	40 (88) 120.0-240.0 2.4-4.8
BW kg (lbs) Dose (μg/h) Volume (mL/h)	41 (90.2) 123.0-246.0 2.5-4.9	42 (92.4) 126.0-252.0 2.5-5.0	43 (94.6) 129.0-258.0 2.6-5.2	44 (96.8) 132.0-264.0 2.6-5.3	45 (99) 135.0-270.0 2.7-5.4
BW kg (lbs) Dose (μg/h) Volume (mL/h)	46 (101.2) 138.0-276.0 2.76-5.52	47 (103.4) 141.0-282.0 2.82-5.64	48 (105.6) 144.0-288.0 2.88-5.76	49 (107.8) 147.0-294.0 2.94-5.88	50 (110) 150.0-300.0 3.00-6.00
BW kg (lbs) Dose (μg/h) Volume (mL/h)	51 (112.2) 153.0-306.0 3.1-6.1	52 (114.4) 156.0-312.0 3.1-6.2	53 (116.6) 159.0-318.0 3.2-6.4	54 (118.8) 162.0-324.0 3.2-6.5	55 (121) 165.0-330.0 3.3-6.6
BW kg (lbs) Dose (μg/h) Volume (mL/h)	56 (123.2) 168.0-336.0 3.4-6.7	57 (125.4) 171.0-342.0 3.4-6.8	58 (127.6) 174.0-348.0 3.5-7.0	59 (129.8) 177.0-354.0 3.5-7.1	60 (132) 180.0-360.0 3.6-7.2
BW kg (lbs) Dose (μg/h) Volume (mL/h)	61 (134.2) 183.0-366.0 3.7-7.3	62 (136.4) 186.0-372.0 3.7-7.4	63 (138.6) 189.0-378.0 3.8-7.6	64 (140.8) 192.0-384.0 3.8-7.7	65 (143) 195.0-390.0 3.9-7.8
BW kg (lbs) Dose (μg/h) Volume (mL/h)	66 (145.2) 198.0-396.0 4.0-7.9	67 (147.2) 201.0-402.0 4.0-8.0	68 (149.6) 204.0-408.0 4.0-8.2	69 (151.8) 207.0-414.0 4.1-8.3	70 (154) 210.0-420.0 4.2-8.4
BW kg (lbs) Dose (μg/h) Volume (mL/h)	71 (156.2) 213.0-426.0 4.3	72 (158.4) 216.0-432.0 4.3	73 (160.6) 219.0-438.0 4.4	74 (162.8) 222.0-444.0 4.4	75 (165) 225.0-450.0 4.5
BW kg (lbs) Dose (μg/h) Volume (mL/h)	76 (167.2) 228.0-456.0 4.6-9.1	77 (169.4) 231.0-462.0 4.6-9.2	78 (171.6) 234.0-468.0 4.7-9.4	79 (173.8) 237.0-474.0 4.7-9.5	80 (176) 240.0-480.0 4.8-9.6
BW kg (lbs) Dose (μg/h) Volume (mL/h)	81 (178.2) 243.0-486.0 4.9-9.7	82 (180.4) 246.0-492.0 4.9-9.8	83 (182.6) 249.0-498.0 5.0-10.0	84 (184.8) 252.0-504.0 5.0-10.1	85 (187) 255.0-510.0 5.1-10.2
BW kg (lbs) Dose (μg/h) Volume (mL/h)	86 (189.2) 258.0-516.0 5.2-10.3	87 (191.4) 261.0-522.0 5.2-10.4	88 (193.6) 264.0-528.0 5.3-10.6	89 (195.8) 267.0-534.0 5.3-10.7	90 (198) 270.0-540.0 5.4-10.8

PREPARATION: Using the chart below, find hourly rate in mL of furosemide at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. **Add mL/h of furosemide (50 mg/mL) required to hourly fluid rate in the burette.** Mix well by inversion. Furosemide has been tested compatible with 5% Dextrose in Water (D5W), 0.9% NaCl and LRS, and appears to be compatible with Plasma-Lyte® A, Plasma-Lyte® 148, but has not been rigorously tested. Fluids used must have a pH >5.5 or furosemide will precipitate.

INDICATIONS: For criteria for treatment with furosemide *see Acute Renal Failure p. 713, Sepsis/Septic Shock p. 592.*

CAUTION: Electrolyte abnormalities and alkalosis may occur with high dosages or continuous infusions.

DOSE: This infusion rate is based on 0.2 – 0.5 mg/kg/h). **The concentration of furosemide is 50 mg/mL.**

COMPATIBILE: Since furosemide is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 4 hours or less include:

Epinephrine	Famotidine	Fentanyl Citrate
Heparin sodium	Hydromorphone	Norepinephrine
Propofol (for 1 h only)	Ranitidine	

INCOMPATIBLE: These drugs should not be administered in the line while furosemide is running:

Diltiazem	Dopamine	Gentamicin
Metoclopramide	Morphine	Ondansetron

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

FUROSEMIDE INFUSION/HOUR (50 mg/mL)
Note: volume mL/h is volume of drug in the above concentration

BW kg (lbs) Dose (mg/h) Volume (mL/h)				
1 (*2.2*) 0.2-1 0.004-0.01	**2** (*4.4*) 0.4-1 0.01-0.02	**3** (*6.6*) 0.6-2 0.01-0.03	**4** (*8.8*) 0.8-2 0.02-0.04	**5** (*11*) 1.0-3 0.02-0.05
6 (*13.2*) 1.2-3 0.02-0.06	**7** (*15.4*) 1.4-4 0.03-0.07	**8** (*17.6*) 1.6-4 0.03-0.08	**9** (*19.8*) 1.8-5 0.04-0.09	**10** (*22*) 2.0-5 0.04-0.10
11 (*24.2*) 2.2-6 0.04-0.11	**12** (*26.4*) 2.4-6 0.05-0.12	**13** (*28.6*) 2.6-7 0.05-0.13	**14** (*30.8*) 2.8-7 0.06-0.14	**15** (*33*) 3.0-8 0.06-0.15
16 (*35.2*) 3.2-8 0.06-0.16	**17** (*37.4*) 3.4-9 0.07-0.17	**18** (*39.6*) 3.6-9 0.07-0.18	**19** (*41.8*) 3.8-10 0.08-0.19	**20** (*44*) 4.0-10 0.08-0.20
21 (*46.2*) 4.2-11 0.08-0.21	**22** (*48.4*) 4.4-11 0.09-0.22	**23** (*50.6*) 4.6-12 0.09-0.23	**24** (*52.8*) 4.8-12 0.10-0.24	**25** (*55*) 5.0-13 0.10-0.25
26 (*57.2*) 5.2-13 0.10-0.26	**27** (*59.4*) 5.4-14 0.11-0.27	**28** (*61.6*) 5.6-14 0.11-0.28	**29** (*63.8*) 5.8-15 0.12-0.29	**30** (*66*) 6.0-15 0.12-0.30
31 (*68.2*) 6.2-16 0.12-0.31	**32** (*70.4*) 6.4-16 0.13-0.32	**33** (*72.6*) 6.6-17 0.13-0.33	**34** (*74.8*) 6.8-17 0.14-0.34	**35** (*77*) 7.0-18 0.14-0.35

BW kg (lbs)	36 (79.2)	37 (81.4)	38 (83.6)	39 (85.8)	40 (88)
Dose (mg/h)	7.2-18	7.4-19	7.6-19	7.8-20	8.0-20
Volume (mL/h)	0.14-0.36	0.15-0.37	0.15-0.38	0.16-0.39	0.16-0.40
BW kg (lbs)	41 (90.2)	42 (92.4)	43 (94.6)	44 (96.8)	45 (99)
Dose (mg/h)	8.2-21	8.4-21	8.6-22	8.8-22	9.0-23
Volume (mL/h)	0.16-0.41	0.17-0.42	0.17-0.43	0.18-0.44	0.18-0.45
BW kg (lbs)	46 (101.2)	47 (103.4)	48 (105.6)	49 (107.8)	50 (110)
Dose (mg/h)	9.2-23	9.4-24	9.6-24	9.8-25	10.0-25
Volume (mL/h)	0.18-0.46	0.19-0.47	0.19-0.48	0.20-0.49	0.20-0.50
BW kg (lbs)	51 (112.2)	52 (114.4)	53 (116.6)	54 (118.8)	55 (121)
Dose (mg/h)	10.2-26	10.4-26	10.6-27	10.8-27	11.0-28
Volume (mL/h)	0.20-0.51	0.21-0.52	0.21-0.53	0.22-0.54	0.22-0.55
BW kg (lbs)	56 (123.2)	57 (125.4)	58 (127.6)	59 (129.8)	60 (132)
Dose (mg/h)	11.2-28	11.4-29	11.6-29	11.8-30	12.0-30
Volume (mL/h)	0.22-0.56	0.23-0.57	0.23-0.58	0.24-0.59	0.24-0.60
BW kg (lbs)	61 (134.2)	62 (136.4)	63 (138.6)	64 (140.8)	65 (143)
Dose (mg/h)	12.2-31	12.4-31	12.6-32	12.8-32	13.0-33
Volume (mL/h)	0.24-0.61	0.25-0.62	0.25-0.63	0.26-0.64	0.26-0.65
BW kg (lbs)	66 (145.2)	67 (147.2)	68 (149.6)	69 (151.8)	70 (154)
Dose (mg/h)	13.2-33	13.4-34	13.6-34	13.8-35	14.0-35
Volume (mL/h)	0.26-0.66	0.27-0.67	0.27-0.68	0.28-0.69	0.28-0.70
BW kg (lbs)	71 (156.2)	72 (158.4)	73 (160.6)	74 (162.8)	75 (165)
Dose (mg/h)	14.2-36	14.4-36	14.6-37	14.8-37	15.0-38
Volume (mL/h)	0.28-0.71	0.29-0.72	0.29-0.73	0.30-0.74	0.30-0.75
BW kg (lbs)	76 (167.2)	77 (169.4)	78 (171.6)	79 (173.8)	80 (176)
Dose (mg/h)	15.2-38	15.4-39	15.6-39	15.8-40	16.0-40
Volume (mL/h)	0.30-0.76	0.31-0.77	0.31-0.78	0.32-0.79	0.32-0.80
BW kg (lbs)	81 (178.2)	82 (180.4)	83 (182.6)	84 (184.8)	85 (187)
Dose (mg/h)	16.2-41	16.4-41	16.6-42	16.8-42	17.0-43
Volume (mL/h)	0.32-0.81	0.33-0.82	0.33-0.83	0.34-0.84	0.34-0.85
BW kg (lbs)	86 (189.2)	87 (191.4)	88 (193.6)	89 (195.8)	90 (198)
Dose (mg/h)	17.2-43	17.4-44	17.6-44	17.8-45	18.0-45
Volume (mL/h)	0.34-0.86	0.35-0.87	0.35-0.88	0.36-0.89	0.36-0.90

PREPARATION: Using the chart below, find hourly rate in mLs of hydromorphone at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. **PLEASE note that we have two charts for two concentrations – 2 mg/mL and 10 mg/mL. Select the chart from the concentrations used in your practice.**

Add mL/h of hydromorphone required to hourly fluid rate in burette. Mix well by inversion. Avoid mixing >6 hours of solution and protect from light. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (i.e., q1h volumes). Another option is to mix a burette that is separate and infuse via injection port into the maintenance fluids. Put the calculated amount of oxymorphone per the chart into 10 mL/h of fluids, then raise or lower the hourly rate depending on the amount of analgesia required. Hydromorphone has been tested compatible with 5% Dextrose in Water (D5W), LRS and 0.9% NaCl and appears to be compatible Plasma-Lyte® A, Plasma-Lyte® 148.

INDICATIONS: For criteria for treatment with hydromorphone *see Analgesics and Sedatives p. 82*.

CAUTION: *See Analgesics and Sedatives p. 82.*

DOSE: This infusion rate is based on 0.01 – 0.03 mg/kg/h. Hydromorphone infusions may be administered with maintenance fluids when practical.

COMPATIBILE: Since hydromorphone is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 4 hours or less include:

Cefoxitin	Ceftazidime	Dopamine
Diltiazem	Dobutamine	Heparin Sodium
Famotidine	Fentanyl Citrate	Morphine Sulfate
Norepinephrine	Metronidazole	Propofol (for 1 h only)
Ranitidine	Ondansetron	
Atropine	Clindamycin	

INCOMPATIBLE: These drugs should not be administered in the line while hydromorphone is running:

Diazepam	Thiopental	Ampicillin Sodium
Cefazolin		

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

HYDROMORPHONE INFUSION IN CRYSTALLOID FLUIDS Original concentration 2 mg/mL
NOTE: The volume (mL/h) is the volume of full strength hydromorphone.
Use this number to determine how much hydromorphone to add to hourly fluids.

HYDROMORPHONE CRI 0.01 – 0.03 mg/kg/h

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	0.01-0.03	0.02-0.06	0.03-0.09	0.04-0.12	0.05-0.15
Volume (mL/h)	0.01-0.02	0.01-0.03	0.02-0.04	0.02-0.06	0.03-0.08
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (mg/h)	0.06-0.18	0.07-0.21	0.08-0.24	0.09-0.27	0.1-0.3
Volume (mL/h)	0.03-0.09	0.03-0.10	0.04-0.12	0.04-0.13	0.05-0.15
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (mg/h)	0.11-0.33	0.12-0.36	0.13-0.39	0.14-0.42	0.15-0.45
Volume (mL/h)	0.05-0.16	0.06-0.18	0.06-0.19	0.07-0.21	0.07-0.22
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (mg/h)	0.16-0.48	0.17-0.51	0.18-0.54	0.19-0.57	0.2-0.6
Volume (mL/h)	0.08-0.24	0.08-0.26	0.09-0.27	0.09-0.29	0.1-0.3

BW kg (lbs)	**21** (46.2)	**22** (48.4)	**23** (50.6)	**24** (52.8)	**25** (55)
Dose (mg/h)	0.21-0.63	0.22-0.66	0.23-0.69	0.24-0.72	0.25-0.75
Volume (mL/h)	0.10-0.32	0.11-0.33	0.11-0.35	0.12-0.36	0.12-0.37
BW kg (lbs)	**26** (57.2)	**27** (59.4)	**28** (61.6)	**29** (63.8)	**30** (66)
Dose (mg/h)	0.26-0.78	0.27-0.81	0.28-0.84	0.29-0.87	0.3-0.9
Volume (mL/h)	0.13-0.39	0.14-0.40	0.14-0.42	0.15-0.44	0.15-0.45
BW kg (lbs)	**31** (68.2)	**32** (70.4)	**33** (72.6)	**34** (74.8)	**35** (77)
Dose (mg/h)	0.31-0.93	0.32-0.96	0.33-0.99	0.34-1.02	0.35-1.05
Volume (mL/h)	0.16-0.47	0.16-0.48	0.17-0.50	0.17-0.51	0.18-0.53
BW kg (lbs)	**36** (79.2)	**37** (81.4)	**38** (83.6)	**39** (85.8)	**40** (88)
Dose (mg/h)	0.36-1.08	0.37-1.11	0.38-1.14	0.39-1.17	0.4-1.2
Volume (mL/h)	0.18-0.54	0.19-0.56	0.19-0.57	0.20-0.59	0.20-0.6
BW kg (lbs)	**41** (90.2)	**42** (92.4)	**43** (94.6)	**44** (96.8)	**45** (99)
Dose (mg/h)	0.41-1.23	0.42-1.26	0.43-1.29	0.44-1.32	0.45-1.35
Volume (mL/h)	0.21-0.62	0.21-0.63	0.22-0.65	0.22-0.66	0.23-0.68
BW kg (lbs)	**46** (101.2)	**47** (103.4)	**48** (105.6)	**49** (107.8)	**50** (110)
Dose (mg/h)	0.46-1.38	0.47-1.41	0.48-1.44	0.49-1.47	0.5-1.5
Volume (mL/h)	0.23-0.69	0.24-0.71	0.24-0.72	0.25-0.74	0.25-0.75
BW kg (lbs)	**51** (112.2)	**52** (114.4)	**53** (116.6)	**54** (118.8)	**55** (121)
Dose (mg/h)	0.51-1.53	0.52-1.53	0.53-1.59	0.54-1.62	0.55-1.65
Volume (mL/h)	0.26-0.77	0.26-0.77	0.27-0.80	0.27-0.81	0.28-0.83
BW kg (lbs)	**56** (123.2)	**57** (125.4)	**58** (127.6)	**59** (129.8)	**60** (132)
Dose (mg/h)	0.56-1.68	0.57-1.71	0.58-1.74	0.59-1.77	0.6-1.8
Volume (mL/h)	0.28-0.84	0.29-0.86	0.29-0.87	0.3-0.89	0.30-0.90
BW kg (lbs)	**61** (134.2)	**62** (136.4)	**63** (138.6)	**64** (140.8)	**65** (143)
Dose (mg/h)	0.61-1.83	0.62-1.86	0.63-1.89	0.64-1.92	0.65-1.95
Volume (mL/h)	0.31-0.92	0.31-0.93	0.32-0.95	0.32-0.96	0.33-0.98
BW kg (lbs)	**66** (145.2)	**67** (147.2)	**68** (149.6)	**69** (151.8)	**70** (154)
Dose (mg/h)	0.66-1.98	0.67-2.01	0.68-2.04	0.69-2.07	0.7-2.1
Volume (mL/h)	0.33-0.99	0.34-1.0	0.34-1.0	0.35-1.0	0.35-1.0
BW kg (lbs)	**71** (156.2)	**72** (158.4)	**73** (160.6)	**74** (162.8)	**75** (165)
Dose (mg/h)	0.71-2.13	0.72-2.16	0.73-2.19	0.74-2.22	0.75-2.25
Volume (mL/h)	0.36-1.1	0.36-1.1	0.37-1.1	0.37-1.1	0.38-1.1
BW kg (lbs)	**76** (167.2)	**77** (169.4)	**78** (171.6)	**79** (173.8)	**80** (176)
Dose (mg/h)	0.76-2.28	0.77-2.31	0.78-2.34	0.79-2.37	0.8-2.4
Volume (mL/h)	0.38-1.1	0.39-1.25	0.39-1.2	0.40-1.2	0.4-1.2
BW kg (lbs)	**81** (178.2)	**82** (180.4)	**83** (182.6)	**84** (184.8)	**85** (187)
Dose (mg/h)	0.81-2.43	0.82-2.46	0.83-2.49	0.84-2.52	0.85-2.55
Volume (mL/h)	0.41-1.2	0.41-1.2	0.42-1.2	0.42-1.3	0.43-1.3
BW kg (lbs)	**86** (189.2)	**87** (191.4)	**88** (193.6)	**89** (195.8)	**90** (198)
Dose (mg/h)	0.86-2.58	0.87-2.61	0.88-2.64	0.89-2.67	0.9-2.7
Volume (mL/h)	0.43-1.3	0.44-1.3	0.44-1.3	0.45-1.3	0.45-1.3

HYDROMORPHONE INFUSION IN CRYSTALLOID FLUIDS Original concentration 10 mg/mL

NOTE: the volume (mL/h) is the volume of full strength hydromorphone.
Use this number to determine how much hydromorphone to add to hourly fluids.

HYDROMORPHONE CRI 0.01 – 0.03 mg/kg/h

BW kg (lbs)	1 (2.2)	2 (4.4)	3 (6.6)	4 (8.8)	5 (11)
Dose (mg/h)	0.01-0.03	0.02-0.06	0.03-0.09	0.04-0.12	0.05-0.15
Volume (mL/h)	0.001-0.003	0.002-0.006	0.003-0.009	0.004-0.01	0.005-0.01
BW kg (lbs)	**6 (13.2)**	**7 (15.4)**	**8 (17.6)**	**9 (19.8)**	**10 (22)**
Dose (mg/h)	0.06-0.18	0.07-0.21	0.08-0.24	0.09-0.27	0.1-0.3
Volume (mL/h)	0.006-0.02	0.007-0.02	0.008-0.02	0.01-0.03	0.01-0.03
BW kg (lbs)	**11 (24.2)**	**12 (26.4)**	**13 (28.6)**	**14 (30.8)**	**15 (33)**
Dose (mg/h)	0.11-0.33	0.12-0.36	0.13-0.39	0.14-0.42	0.15-0.45
Volume (mL/h)	0.01-0.03	0.01-0.04	0.01-0.04	0.01-0.04	0.01-0.04
BW kg (lbs)	**16 (35.2)**	**17 (37.4)**	**18 (39.6)**	**19 (41.8)**	**20 (44)**
Dose (mg/h)	0.16-0.48	0.17-0.51	0.18-0.54	0.19-0.57	0.2-0.6
Volume (mL/h)	0.02-0.05	0.02-0.05	0.02-0.05	0.02-0.06	0.02-0.06
BW kg (lbs)	**21 (46.2)**	**22 (48.4)**	**23 (50.6)**	**24 (52.8)**	**25 (55)**
Dose (mg/h)	0.21-0.63	0.22-0.66	0.23-0.69	0.24-0.72	0.25-0.75
Volume (mL/h)	0.02-0.06	0.02-0.07	0.02-0.07	0.02-0.07	0.02-0.07
BW kg (lbs)	**26 (57.2)**	**27 (59.4)**	**28 (61.6)**	**29 (63.8)**	**30 (66)**
Dose (mg/h)	0.26-0.78	0.27-0.81	0.28-0.84	0.29-0.87	0.3-0.9
Volume (mL/h)	0.03-0.08	0.03-0.08	0.03-0.08	0.03-0.09	0.03-0.09
BW kg (lbs)	**31 (68.2)**	**32 (70.4)**	**33 (72.6)**	**34 (74.8)**	**35 (77)**
Dose (mg/h)	0.31-0.93	0.32-0.96	0.33-0.99	0.34-1.02	0.35-1.05
Volume (mL/h)	0.03-0.09	0.03-0.1	0.03-0.1	0.03-0.1	0.03-0.1
BW kg (lbs)	**36 (79.2)**	**37 (81.4)**	**38 (83.6)**	**39 (85.8)**	**40 (88)**
Dose (mg/h)	0.36-1.08	0.37-1.11	0.38-1.14	0.39-1.17	0.4-1.2
Volume (mL/h)	0.04-0.11	0.04-0.11	0.04-0.11	0.04-0.12	0.04-0.12
BW kg (lbs)	**41 (90.2)**	**42 (92.4)**	**43 (94.6)**	**44 (96.8)**	**45 (99)**
Dose (mg/h)	0.41-1.23	0.42-1.26	0.43-1.29	0.44-1.32	0.45-1.35
Volume (mL/h)	0.04-0.12	0.04-0.13	0.04-0.13	0.04-0.13	0.04-0.13
BW kg (lbs)	**46 (101.2)**	**47 (103.4)**	**48 (105.6)**	**49 (107.8)**	**50 (110)**
Dose (mg/h)	0.46-1.38	0.47-1.41	0.48-1.44	0.49-1.47	0.5-1.5
Volume (mL/h)	0.05-0.14	0.05-0.14	0.05-0.14	0.05-0.15	0.05-0.15
BW kg (lbs)	**51 (112.2)**	**52 (114.4)**	**53 (116.6)**	**54 (118.8)**	**55 (121)**
Dose (mg/h)	0.51-1.53	0.52-1.53	0.53-1.59	0.54-1.62	0.55-1.65
Volume (mL/h)	0.05-0.15	0.05-0.15	0.05-0.16	0.05-0.16	0.05-0.16
BW kg (lbs)	**56 (123.2)**	**57 (125.4)**	**58 (127.6)**	**59 (129.8)**	**60 (132)**
Dose (mg/h)	0.56-1.68	0.57-1.71	0.58-1.74	0.59-1.77	0.6-1.8
Volume (mL/h)	0.06-0.17	0.06-0.17	0.06-0.17	0.06-0.18	0.06-0.18
BW kg (lbs)	**61 (134.2)**	**62 (136.4)**	**63 (138.6)**	**64 (140.8)**	**65 (143)**
Dose (mg/h)	0.61-1.83	0.62-1.86	0.63-1.89	0.64-1.92	0.65-1.95
Volume (mL/h)	0.06-0.18	0.06-0.19	0.06-0.19	0.06-0.19	0.06-0.19
BW kg (lbs)	**66 (145.2)**	**67 (147.2)**	**68 (149.6)**	**69 (151.8)**	**70 (154)**
Dose (mg/h)	0.66-1.98	0.67-2.01	0.68-2.04	0.69-2.07	0.7-2.1
Volume (mL/h)	0.07-0.2	0.07-0.2	0.07-0.2	0.07-0.21	0.07-0.21

BW kg (lbs)	71 (156.2)	72 (158.4)	73 (160.6)	74 (162.8)	75 (165)
Dose (mg/h)	0.71-2.13	0.72-2.16	0.73-2.19	0.74-2.22	0.75-2.25
Volume (mL/h)	0.07-0.21	0.07-0.22	0.07-0.22	0.07-0.22	0.07-0.22
BW kg (lbs)	76 (167.2)	77 (169.4)	78 (171.6)	79 (173.8)	80 (176)
Dose (mg/h)	0.76-2.28	0.77-2.31	0.78-2.34	0.79-2.37	0.8-2.4
Volume (mL/h)	0.08-0.23	0.08-0.23	0.08-0.23	0.08-0.24	0.08-0.24
BW kg (lbs)	81 (178.2)	82 (180.4)	83 (182.6)	84 (184.8)	85 (187)
Dose (mg/h)	0.81-2.43	0.82-2.46	0.83-2.49	0.84-2.52	0.85-2.55
Volume (mL/h)	0.08-0.24	0.08-0.25	0.08-0.25	0.08-0.25	0.08-0.25
BW kg (lbs)	86 (189.2)	87 (191.4)	88 (193.6)	89 (195.8)	90 (198)
Dose (mg/h)	0.86-2.58	0.87-2.61	0.88-2.64	0.89-2.67	0.9-2.7
Volume (mL/h)	0.09-0.26	0.09-0.26	0.09-0.26	0.09-0.27	0.09-0.27

PREPARATION: Using the chart below, find hourly rate in mLs of ketamine at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. **Add mL (100 mg/mL) of ketamine/h to hourly fluid in burette.** Mix well by inversion. Avoid mixing more than 6 hours of solution and protect from light. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (i.e., q1h volumes). Another option is to mix a burette that is separate and 'piggy-backed' onto the maintenance fluids. Put the calculated amount of ketamine per the chart into 10 mL/h of fluids, then raise or lower the hourly rate depending on the amount of analgesia required. Ketamine is stable in D5W and 0.9% NaCl.

INDICATIONS: For criteria for treatment with ketamine *see Anesthesia p. 114 , Analgesics and Sedatives p. 92.*

CAUTION: As ketamine at higher dosages will interfere with blinking, ensure eye ointment is administered q2–4h.

DOSE: This infusion rate is based on **0.2 – 2 mg/kg/h.**

COMPATIBILE: Since ketamine is infused with the maintenance fluids, it is important to know which drugs will be compatible. More common compatible drugs include:

Propofol (for 1 h only)   Meperidine

INCOMPATIBLE: These drugs should not be administered in the line while ketamine is running:

Barbiturates   Diazepam⊕

⊕*Note: Diazepam loses activity when combined with ketamine. Can be used immediately after mixing, but prolonged contact of the two drugs is not recommended.*
*Note: Other drugs have not been tested, and therefore should be considered incompatible.

KETAMINE INFUSION IN CRYSTALLOID FLUIDS (original concentration 100 mg/mL)

NOTE: The volume (mL/h) is the volume of full strength ketamine.
Use this number to determine how much ketamine to add to hourly fluids.

BW kg (lbs)	1 (2.2)	2 (4.4)	3 (6.6)	4 (8.8)	5 (11)
Dose (mg/h)	0.2-2	0.4-4	0.6-6	0.8-8	1.0-10
Volume (mL/h)	0.002-0.02	0.004-0.04	0.006-0.06	0.01-0.08	0.01-0.10
BW kg (lbs)	6 (13.2)	7 (15.4)	8 (17.6)	9 (19.8)	10 (22)
Dose (mg/h)	1.2-12	1.4-14	1.6-16	1.8-18	2.0-20
Volume (mL/h)	0.01-0.12	0.01-0.14	0.02-0.16	0.02-0.18	0.02-0.20
BW kg (lbs)	11 (24.2)	12 (26.4)	13 (28.6)	14 (30.8)	15 (33)
Dose (mg/h)	2.2-22	2.4-24	2.6-26	2.8-28	3.0-30
Volume (mL/h)	0.02-0.22	0.02-0.24	0.03-0.26	0.03-0.28	0.03-0.30
BW kg (lbs)	16 (35.2)	17 (37.4)	18 (39.6)	19 (41.8)	20 (44)
Dose (mg/h)	3.2-32	3.4-34	3.6-36	3.8-38	4.0-40
Volume (mL/h)	0.03-0.32	0.03-0.34	0.04-0.36	0.04-0.38	0.04-0.40
BW kg (lbs)	21 (46.2)	22 (48.4)	23 (50.6)	24 (52.8)	25 (55)
Dose (mg/h)	4.2-42	4.4-44	4.6-46	4.8-48	5.0-50
Volume (mL/h)	0.04-0.42	0.04-0.44	0.05-0.46	0.05-0.48	0.05-0.50
BW kg (lbs)	26 (57.2)	27 (59.4)	28 (61.6)	29 (63.8)	30 (66)
Dose (mg/h)	5.2-52	5.4-54	5.6-56	5.8-58	6.0-60
Volume (mL/h)	0.05-0.52	0.05-0.54	0.06-0.56	0.06-0.58	0.06-0.60

BW kg (*lbs*)	31 (*68.2*)	32 (*70.4*)	33 (*72.6*)	34 (*74.8*)	35 (*77*)
Dose (mg/h)	6.2-62	6.4-64	6.6-66	6.8-68	7.0-70
Volume (mL/h)	0.06-0.62	0.06-0.64	0.07-0.66	0.07-0.68	0.07-0.70
BW kg (*lbs*)	36 (*79.2*)	37 (*81.4*)	38 (*83.6*)	39 (*85.8*)	40 (*88*)
Dose (mg/h)	7.2-72	7.4-74	7.6-76	7.8-78	8.0-80
Volume (mL/h)	0.07-0.72	0.07-0.74	0.08-0.76	0.08-0.78	0.08-0.80
BW kg (*lbs*)	41 (*90.2*)	42 (*92.4*)	43 (*94.6*)	44 (*96.8*)	45 (*99*)
Dose (mg/h)	8.2-82	8.4-84	8.6-86	8.8-88	9.0-90
Volume (mL/h)	0.08-0.82	0.08-0.84	0.09-0.86	0.09-0.88	0.09-0.90
BW kg (*lbs*)	46 (*101.2*)	47 (*103.4*)	48 (*105.6*)	49 (*107.8*)	50 (*110*)
Dose (mg/h)	9.2-92	9.4-94	9.6-96	9.8-98	10.0-100
Volume (mL/h)	0.09-0.92	0.09-0.94	0.10-0.96	0.10-0.98	0.10-1.0
BW kg (*lbs*)	51 (*112.2*)	52 (*114.4*)	53 (*116.6*)	54 (*118.8*)	55 (*121*)
Dose (mg/h)	10.2-102	10.4-104	10.6-106	10.8-108	11.0-110
Volume (mL/h)	0.10-1.0	0.10-1.0	0.11-1.0	0.11-1.1	0.11-1.1
BW kg (*lbs*)	56 (*123.2*)	57 (*125.4*)	58 (*127.6*)	59 (*129.8*)	60 (*132*)
Dose (mg/h)	11.2-112	11.4-114	11.6-116	11.8-118	12.0-120
Volume (mL/h)	0.11-1.1	0.11-1.1	0.12-1.2	0.12-1.2	0.12-1.2
BW kg (*lbs*)	61 (*134.2*)	62 (*136.4*)	63 (*138.6*)	64 (*140.8*)	65 (*143*)
Dose (mg/h)	12.2-122	12.4-124	12.6-126	12.8-128	13.0-130
Volume (mL/h)	0.12-1.2	0.12-1.2	0.13-1.3	0.13-1.3	0.13-1.3
BW kg (*lbs*)	66 (*145.2*)	67 (*147.2*)	68 (*149.6*)	69 (*151.8*)	70 (*154*)
Dose (mg/h)	13.2-132	13.4-134	13.6-136	13.8-138	14.0-140
Volume (mL/h)	0.13-1.3	0.13-1.3	0.14-1.4	0.14-1.4	0.14-1.4
BW kg (*lbs*)	71 (*156.2*)	72 (*158.4*)	73 (*160.6*)	74 (*162.8*)	75 (*165*)
Dose (mg/h)	14.2-142	14.4-144	14.6-146	14.8-148	15.0-150
Volume (mL/h)	0.14-1.4	0.14-1.4	0.15-1.5	0.15-1.5	0.15-1.5
BW kg (*lbs*)	76 (*167.2*)	77 (*169.4*)	78 (*171.6*)	79 (*173.8*)	80 (*176*)
Dose (mg/h)	15.2-152	15.4-154	15.6-156	15.8-158	16.0-160
Volume (mL/h)	0.15-1.5	0.15-1.5	0.16-1.6	0.16-1.6	0.16-1.6
BW kg (*lbs*)	81 (*178.2*)	82 (*180.4*)	83 (*182.6*)	84 (*184.8*)	85 (*187*)
Dose (mg/h)	16.2-162	16.4-164	16.6-166	16.8-168	17.0-170
Volume (mL/h)	0.16-1.6	0.16-1.6	0.17-1.7	0.17-1.7	0.17-1.7
BW kg (*lbs*)	86 (*189.2*)	87 (*191.4*)	88 (*193.6*)	89 (*195.8*)	90 (*198*)
Dose (mg/h)	17.2-172	17.4-174	17.6-176	17.8-178	18.0-180
Volume (mL/h)	0.17-1.7	0.17-1.7	0.18-1.8	0.18-1.8	0.18-1.8

PREPARATION: 1 g Lidocaine without Epinephrine (50 mL 2% Lidocaine) in 500 mL 5% Dextrose in Water (D5W), 0.45% or 0.9% saline, Plasma-Lyte® 148 (not Plasma-Lyteâ A), Normasol® R or Lactated Ringer's solution.

INDICATIONS: For criteria for treatment with lidocaine *see Ventricular Arrhythmias p. 181, Analgesics and Sedatives p. 91, Sepsis/Septic Shock p. 591.*

CAUTION: Not to be used in cats. May precipitate seizures and dysrrhythmia, nausea and vomiting.

DOSE: This infusion rate is based on 30 – 50 μg/kg/min. **The concentration of Lidocaine in this solution is 2 mg/mL, 1/10 of original concentration.** Lidocaine infusion should be administered separately from maintenance fluids to allow for adjustment in dosing. Maintenance fluid rate should be calculated with a reduction in volume according to that administered with the lidocaine infusion. Rarely the infusion can be increased to **60 μg/kg/min (multiply the lower range by 2 on the chart, for dose) or 80 μg/kg/min (add the lower + upper range on the chart, for dose). Should a more concentrated solution be required to reduce fluids administered, add two 50 mL 2% lidocaine to 500 mL and administer at half the infusion rate.**

BURETTE: **As an alternative** to the above infusion, the lidocaine dose per hour can be added to a burette containing the hourly fluid rate. Dose of 'original strength' lidocaine is obtained from chart by taking the weight of the animal, noting the infusion (mL/h) and dividing this by 10. i.e., 10 kg dog requires 9 – 15 mL of infusion, which is 0.9 – 1.5 mL (18 – 30 mg/h) of a 2% lidocaine solution. Solutions with pH >6.5 (i.e., Plasma-Lyte® A pH 7.4) may precipitate or alter kinetics.

COMPATIBILE: Since lidocaine is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Cefazolin sodium	Diltiazem	Dobutamine
Dopamine	Famotidine	Heparin sodium
Morphine	Propofol (1 h only)	Sodium nitroprusside

INCOMPATIBLE: These drugs should not be administered in the line while lidocaine is running:

Thiopental sodium

Note: Other drugs have not been tested, and therefore should be considered incompatible.

LIDOCAINE IN D5W, saline or balanced electrolyte solution INFUSION/HOUR (2 mg/mL)
CRI 30 – 50 μg/kg/min

NOTE: The volume (mL/h) is the volume of fluid with lidocaine made to 500 mL.

If administering **2% lidocaine only** (i.e., not pre-mixed with fluids) in a burette, the volume (mL/h) is 1/10 of that listed on this chart (i.e., 10 kg dog = 0.9 – 1.5 mL/h lidocaine only).

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (μg/h)	1.8 – 3.0	3.6 – 6.0	5.4 – 9.0	7.2 – 12.0	9.0 – 15.0
Volume (mL/h)	1.0 – 1.5	2.0 – 3.0	3.0 – 4.5	4 – 6	5 – 8
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (μg/h)	10.8 – 18.0	12.6 – 21.0	14.4 – 24.0	16.2 – 27.0	18.0 – 30
Volume (mL/h)	5 – 9	6 – 11	7 – 12	8 – 14	9 – 15
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (μg/h)	20-33	22-36	24-39	25-42	27-45
Volume (mL/h)	10-17	11-18	12-20	13-21	14-23
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (μg/h)	29 – 48	30 – 51	32- 54	34 – 57	36 – 60
Volume (mL/h)	14 – 24	15 – 25	16 – 27	17 – 29	18 – 30

BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**21** (*46.2*) 38 – 63 19 – 32	**22** (*48.4*) 40 – 66 20 – 33	**23** (*50.6*) 41 – 69 21 – 35	**24** (*52.8*) 43 – 72 22 – 36	**25** (*55*) 45 – 75 23 – 38
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**26** (*57.2*) 47 – 78 23 – 39	**27** (*59.4*) 49 – 81 25 – 41	**28** (*61.6*) 50 – 84 25 – 42	**29** (*63.8*) 174-870 26 – 44	**30** (*66*) 54 – 90 27 – 45
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**31** (*68.2*) 56 – 93 28 – 47	**32** (*70.4*) 58 – 96 29 – 48	**33** (*72.6*) 59 – 99 30 – 50	**33** (*72.6*) 61 – 102 31 – 51	**33** (*72.6*) 63 – 105 32 – 53
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**36** (*79.2*) 65 – 108 32 – 54	**37** (*81.4*) 67 – 111 33 – 56	**38** (*83.6*) 68 – 114 34 – 57	**39** (*85.8*) 70 – 117 35 – 59	**40** (*88*) 72 – 120 36 – 60
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**41** (*90.2*) 74 – 123 37 – 62	**42** (*92.4*) 76 – 126 38 – 63	**43** (*94.6*) 77 – 129 39 – 65	**44** (*96.8*) 79 – 132 40 – 66	**45** (*99*) 81 – 135 41 – 68
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**46** (*101.2*) 80 – 140 40 – 70	**47** (*103.4*) 85 – 142 42 – 71	**48** (*105.6*) 87 – 144 43 – 72	**49** (*107.8*) 88 – 147 44 –74	**50** (*110*) 90 – 150 40 – 75
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**51** (*112.2*) 92 – 153 46 – 77	**52** (*114.4*) 94 – 156 47 – 78	**53** (*116.6*) 95 – 159 48 – 80	**54** (*118.8*) 97 – 162 49 – 81	**55** (*121*) 99 – 165 50 – 83
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**56** (*123.2*) 101 – 168 50 – 84	**57** (*125.4*) 103 – 171 51 – 86	**58** (*127.6*) 104 – 174 52 – 87	**59** (*129.8*) 106 – 177 53 – 89	**60** (*132*) 108 – 182 54 – 90
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**61** (*134.2*) 110 – 183 55 – 92	**62** (*136.4*) 112 – 186 56 – 93	**63** (*138.6*) 113 – 189 57 – 95	**64** (*140.8*) 115 – 192 58 – 96	**65** (*143*) 117 – 195 59 – 98
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**66** (*145.2*) 119 – 198 59 – 99	**67** (*147.2*) 121 – 201 60 – 101	**68** (*149.6*) 122 – 204 61 – 102	**69** (*151.8*) 124 – 207 62 – 103	**70** (*154*) 126 – 210 63 – 105
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**71** (*156.2*) 128 – 213 64 – 107	**72** (*158.4*) 130 – 216 65 – 108	**73** (*160.6*) 131 – 219 69 – 110	**74** (*162.8*) 133 – 222 67 – 111	**75** (*165*) 135 – 225 68 – 113
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**76** (*167.2*) 137 – 228 68 – 114	**77** (*169.4*) 139 – 231 69 – 116	**78** (*171.6*) 140 – 234 70 – 117	**79** (*173.8*) 142 – 237 71 – 119	**80** (*176*) 144 – 240 72 – 120
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**81** (*178.2*) 146 – 243 73 – 122	**82** (*180.4*) 148 – 246 74 – 123	**83** (*182.6*) 149 – 208 75 – 124	**84** (*184.8*) 151 – 252 76 – 126	**85** (*187*) 153 – 255 77 – 128
BW kg (*lbs*) Dose (µg/h) Volume (mL/h)	**86** (*189.2*) 155 – 258 77 – 129	**87** (*191.4*) 157 – 261 78 – 131	**88** (*193.6*) 158 – 264 79 – 132	**89** (*195.8*) 160 – 267 80 – 134	**90** (*198*) 162 – 270 81 – 135

PREPARATION: Using the chart below, find hourly rate in mL of metoclopramide (5 mg/mL) at the dosing level desired and add to the hourly fluid rate. Tested compatible with 5% dextrose in water (D5W), Total Parenteral Nutrition and 0.9% NaCl. May be added directly to hourly maintenance fluids. Mix well by inversion. For smaller animals, or when fluid rates are being adjusted frequently, the use of a burette may be a more practical solution.

INDICATIONS: For criteria for treatment with metoclopramide *see Vomiting p. 78*.

CAUTION: May cause changes in mentation or behaviour in both dogs and cats. *See Vomiting p. 78*.

DOSE: This infusion rate is based on 1 – 2 mg/kg/day.

COMPATIBILE: Since metoclopramide is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 4 hours or less include:

Butorphanol	Clindamycin	Dexamethasone
Diltiazem	Famotidine	Fentanyl Citrate
Heparin Sodium	Insulin (regular)	Lidocaine
Morphine Sulfate	Ranitidine	

INCOMPATIBLE: These drugs should not be administered while metoclopramide is running:

Ampicillin Sodium	Furosemide	Propofol
Sodium Bicarbonate		

Note: Other drugs have not been tested, and therefore should be considered incompatible.

METOCLOPRAMIDE INFUSION CRYSTALLOID FLUIDS (original concentration 5 mg/mL)

NOTE: The volume (mL/h) is the volume of a 5 mg/mL concentration of metoclopramide.

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	0.042 – 0.084	0.08 – 0.16	0.13 – 0.26	0.17 – 0.34	0.21 – 0.42
Volume (mL/h)	0.008 – 0.016	0.02 – 0.03	0.03 – 0.05	0.03 – 0.07	0.04 – 0.08
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (mg/h)	0.25 – 0.5	0.29 – 0.58	0.33 – 0.67	0.38 – 0.75	0.42 – 0.83
Volume (mL/h)	0.05 – 0.1	0.06 – 0.12	0.07 – 0.13	0.08 – 0.15	0.08 – 0.17
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (mg/h)	0.46 – 0.92	0.50 – 1.00	0.54 – 1.08	0.58 – 1.17	0.63 – 1.25
Volume (mL/h)	0.09 – 0.18	0.10 – 0.20	0.11 – 0.22	0.12 – 0.23	0.13 – 0.25
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (mg/h)	0.67 – 1.33	0.71 – 1.42	0.75 – 1.50	0.79 – 1.58	0.83 – 1.67
Volume (mL/h)	0.13 – 0.27	0.14 – 0.28	0.15 – 0.30	0.16 – 0.32	0.17 – 0.33
BW kg (*lbs*)	21 (*46.2*)	22 (*48.4*)	23 (*50.6*)	24 (*52.8*)	25 (*55*)
Dose (mg/h)	0.88 – 1.75	0.92 – 1.83	0.96 – 1.92	1.00 – 2.00	1.04 – 2.08
Volume (mL/h)	0.18 – 0.35	0.18 – 0.37	0.19 – 0.38	0.20 – 0.40	0.21 – 0.42
BW kg (*lbs*)	26 (*57.2*)	27 (*59.4*)	28 (*61.6*)	29 (*63.8*)	30 (*66*)
Dose (mg/h)	1.08 – 2.17	1.13 – 2.25	1.17 – 2.25	1.21 – 2.42	1.25 – 2.50
Volume (mL/h)	0.22 – 0.43	0.23 – 0.45	0.23 – 0.47	0.24 – 0.48	0.25 – 0.50
BW kg (*lbs*)	31 (*68.2*)	32 (*70.4*)	33 (*72.6*)	34 (*74.8*)	35 (*77*)
Dose (mg/h)	1.29 – 2.58	1.33 – 2.67	1.38 – 2.75	1.42 – 2.83	1.46 – 2.92
Volume (mL/h)	0.26 – 0.52	0.27 – 0.53	0.28 – 0.55	0.28 – 0.57	0.29 – 0.58
BW kg (*lbs*)	36 (*79.2*)	37 (*81.4*)	38 (*83.6*)	39 (*85.8*)	40 (*88*)
Dose (mg/h)	1.50 – 3.00	1.54 – 3.08	1.58 – 3.17	1.63 – 3.25	1.67 – 3.33
Volume (mL/h)	0.30 – 0.60	0.31 – 0.62	0.32 – 0.63	0.33 – 0.65	0.33 – 0.67

BW kg (lbs)	41 (90.2)	42 (92.4)	43 (94.6)	44 (96.8)	45 (99)
Dose (mg/h)	1.71 – 3.42	1.75 – 3.50	1.79 – 3.58	1.83 – 3.67	1.88 – 3.75
Volume (mL/h)	0.34 – 0.68	0.35 – 0.70	0.36 – 0.72	0.37 – 0.73	0.38 – 0.75
BW kg (lbs)	46 (101.2)	47 (103.4)	48 (105.6)	49 (107.8)	50 (110)
Dose (mg/h)	1.92 – 3.83	1.96 – 3.92	2.00 – 4.00	2.04 – 4.08	2.08 – 4.17
Volume (mL/h)	0.38 – 0.77	0.39 – 0.78	0.40 – 0.80	0.41 – 0.82	0.42 – 0.83
BW kg (lbs)	51 (112.2)	52 (114.4)	53 (116.6)	54 (118.8)	55 (121)
Dose (mg/h)	2.13 – 4.25	2.17 – 4.33	2.21 – 4.42	2.25 – 4.50	2.29 – 4.58
Volume (mL/h)	0.43 – 0.85	0.43 – 0.87	0.44 – 0.88	0.45 – 0.90	0.46 – 0.92
BW kg (lbs)	56 (123.2)	57 (125.4)	58 (127.6)	59 (129.8)	60 (132)
Dose (mg/h)	2.33 – 4.67	2.38 – 4.75	2.42 – 4.83	2.46 – 4.92	2.50 – 5.00
Volume (mL/h)	0.47 – 0.93	0.48 – 0.95	0.48 – 0.97	0.49 – 0.98	0.50 – 1.00
BW kg (lbs)	61 (134.2)	62 (136.4)	63 (138.6)	64 (140.8)	65 (143)
Dose (mg/h)	2.5 – 5.1	2.6 – 5.2	2.6 – 5.2	2.7 – 5.3	2.7 – 5.4
Volume (mL/h)	0.51 – 1.0	0.52 – 1.0	0.53 – 1.1	0.53 – 1.1	0.54 – 1.1
BW kg (lbs)	66 (145.2)	67 (147.2)	68 (149.6)	69 (151.8)	70 (154)
Dose (mg/h)	2.7 – 5.5	2.8 – 5.6	2.8 – 5.7	2.9 – 5.8	2.9 – 5.8
Volume (mL/h)	0.55 – 1.1	0.56 – 1.1	0.57 – 1.1	0.58 – 1.2	0.58 – 1.2
BW kg (lbs)	71 (156.2)	72 (158.4)	73 (160.6)	74 (162.8)	75 (165)
Dose (mg/h)	3.0 – 5.9	3.0 – 6.0	3.0 – 6.1	3.1 – 6.2	3.1 – 6.3
Volume (mL/h)	0.59 – 1.2	0.60 – 1.2	0.61 – 1.2	0.62 – 1.2	0.63 – 1.3
BW kg (lbs)	76 (167.2)	77 (169.4)	78 (171.6)	79 (173.8)	80 (176)
Dose (mg/h)	3.2 – 6.3	3.2 – 6.4	3.3 – 6.5	3.3 – 6.6	3.3 – 6.7
Volume (mL/h)	0.6 – 1.3	0.6 – 1.3	0.7 – 1.3	0.7 – 1.3	0.7 – 1.3
BW kg (lbs)	81 (178.2)	82 (180.4)	83 (182.6)	84 (184.8)	85 (187)
Dose (mg/h)	3.4 – 6.8	3.4 – 6.8	3.5 – 6.9	3.5 – 7.0	3.5 – 7.1
Volume (mL/h)	0.7 – 1.4	0.7 – 1.4	0.7 – 1.4	0.7 – 1.4	0.7 – 1.4
BW kg (lbs)	86 (189.2)	87 (191.4)	88 (193.6)	89 (195.8)	90 (198)
Dose (mg/h)	3.6 – 7.2	3.6 – 7.3	3.7 – 7.3	3.7 – 7.4	3.8 – 7.5
Volume (mL/h)	0.7 – 1.4	0.7 – 1.5	0.7 – 1.5	0.7 – 1.5	0.8 – 1.5

PREPARATION: Using the chart below, find hourly rate in mL of morphine sulphate at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. Add **mL of morphine sulphate to be administered/h to a volume of fluid to be administered/h (i.e., 10 mL/h) into a burette.** Mix well by inversion. Avoid mixing >6 hours of solution and protect from light. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (i.e., q1h volumes). Increase or decrease the hourly rate depending on the amount of analgesia required. Morphine sulphate has been tested compatible with 5% Dextrose in Water (D5W), LRS and 0.9% NaCl and appears to be compatible Plasma-Lyte® A, Plasma-Lyte® 148.

INDICATIONS: Pain necessitating repeated administration of analgesics. *See Analgesics and Sedatives p. 82.*

INITIAL LOADING DOSE: 0.3 mg/kg morphine sulphate I.M or VERY slow IV push. **The infusion rate is based on 0.1 mg/kg/h.** Morphine sulphate infusions may be administered with maintenance fluids when practical.

COMMENTS: The above dose is for mild to moderate pain. For severe pain, the loading dose should be increased to 0.5 mg/kg and the infusion increased to 0.2 mg/kg. The infusion dose can be decreased as the pain subsides.

COMPATIBILE: Since morphine sulphate is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Ampicillin Sodium	Cefazolin Sodium	Cefotaxime Sodium
Cefoxitin	Ceftazidime	Clindamycin
Dexamethasone	Diltiazem	Dobutamine
Dopamine	Epinephrine	Famotidine
Fentanyl Citrate	Fluconazole	Gentamicin
Heparin Sodium	Hydromorphone	Insulin (Regular) (1 h only)
Lidocaine	Magnesium Sulphate	Metoclopramide
Metronidazole	Midazolam	Norepinephrine
Ondansetron	Potassium Chloride	Propofol (1 h only)
Ranitidine (1 h only)	Sodium Bicarbonate	Sodium Nitroprusside

INCOMPATIBLE: These drugs should not be administered in the line while morphine sulphate is running:
Furosemide   Thiopental

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

MORPHINE SULPHATE INFUSION IN CRYSTALLOID FLUIDS (Original concentration 15 mg/mL)

NOTE: The volume (mL/h) is the volume of full strength morphine sulphate.
Use this number to determine how much morphine sulphate to add to hourly fluids.

Morphine CRI 0.1 mg/kg/h, 15 mg/mL original concentration

BW kg (lbs)	1 (2.2)	2 (4.4)	3 (6.6)	4 (8.8)	5 (11)
Dose (mg/h)	0.1	0.2	0.3	0.4	0.5
Volume (mL/h)	0.01	0.01	0.02	0.03	0.03
BW kg (lbs)	6 (13.2)	7 (15.4)	8 (17.6)	9 (19.8)	10 (22)
Dose (mg/h)	0.6	0.7	0.8	0.9	1.0
Volume (mL/h)	0.04	0.05	0.05	0.06	0.07
BW kg (lbs)	11 (24.2)	12 (26.4)	13 (28.6)	14 (30.8)	15 (33)
Dose (mg/h)	1.1	1.2	1.3	1.4	1.5
Volume (mL/h)	0.07	0.08	0.09	0.09	0.10
BW kg (lbs)	16 (35.2)	17 (37.4)	18 (39.6)	19 (41.8)	20 (44)
Dose (mg/h)	1.6	1.7	1.8	1.9	2.0
Volume (mL/h)	0.11	0.11	0.12	0.13	0.13

BW kg (lbs) Dose (mg/h) Volume (mL/h)	**21** (*46.2*) 2.1 0.14	**22** (*48.4*) 2.2 0.15	**23** (*50.6*) 2.3 0.15	**24** (*52.8*) 2.4 0.16	**25** (*55*) 2.5 0.17
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**26** (*57.2*) 2.6 0.17	**27** (*59.4*) 2.7 0.18	**28** (*61.6*) 2.8 0.19	**29** (*63.8*) 2.9 0.19	**30** (*66*) 3.0 0.20
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**31** (*68.2*) 3.1 0.21	**32** (*70.4*) 3.2 0.21	**33** (*72.6*) 3.3 0.22	**34** (*74.8*) 3.4 0.23	**35** (*77*) 3.5 0.23
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**36** (*79.2*) 3.6 0.24	**37** (*81.4*) 3.7 0.25	**38** (*83.6*) 3.8 0.25	**39** (*85.8*) 3.9 0.26	**40** (*88*) 4.0 0.27
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**41** (*90.2*) 4.1 0.27	**42** (*92.4*) 4.2 0.28	**43** (*94.6*) 4.3 0.29	**44** (*96.8*) 4.4 0.29	**45** (*99*) 4.5 0.30
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**46** (*101.2*) 4.6 0.31	**47** (*103.4*) 4.7 0.31	**48** (*105.6*) 4.8 0.32	**49** (*107.8*) 4.9 0.33	**50** (*110*) 5.0 0.33
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**51** (*112.2*) 5.1 0.34	**52** (*114.4*) 5.2 0.35	**53** (*116.6*) 5.3 0.35	**54** (*118.8*) 5.4 0.36	**55** (*121*) 5.5 0.37
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**56** (*123.2*) 5.6 0.37	**57** (*125.4*) 5.7 0.38	**58** (*127.6*) 5.8 0.39	**59** (*129.8*) 5.9 0.39	**60** (*132*) 6.0 0.40
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**61** (*134.2*) 6.1 0.41	**62** (*136.4*) 6.2 0.41	**63** (*138.6*) 6.3 0.42	**64** (*140.8*) 6.4 0.43	**65** (*143*) 6.5 0.43
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**66** (*145.2*) 6.6 0.44	**67** (*147.2*) 6.7 0.45	**68** (*149.6*) 6.8 0.45	**69** (*151.8*) 6.9 0.46	**70** (*154*) 7.0 0.47
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**71** (*156.2*) 7.1 0.47	**72** (*158.4*) 7.2 0.48	**73** (*160.6*) 7.3 0.49	**74** (*162.8*) 7.4 0.49	**75** (*165*) 7.5 0.5
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**76** (*167.2*) 7.6 0.51	**77** (*169.4*) 7.7 0.51	**78** (*171.6*) 7.8 0.52	**79** (*173.8*) 7.9 0.53	**80** (*176*) 8.0 0.53
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**81** (*178.2*) 8.1 0.54	**82** (*180.4*) 8.2 0.55	**83** (*182.6*) 8.3 0.55	**84** (*184.8*) 8.4 0.56	**85** (*187*) 8.5 0.57
BW kg (lbs) Dose (mg/h) Volume (mL/h)	**86** (*189.2*) 8.6 0.57	**87** (*191.4*) 8.7 0.58	**88** (*193.6*) 8.8 0.59	**89** (*195.8*) 8.9 0.59	**90** (*198*) 9.0 0.6

PREPARATION: 4 mL of 1 mg/mL norepinephrine in 500 mL in 5% Dextrose in Water (D5W) or Dextrose in NaCl (8 μg/mL). Dextrose solutions are recommended to preserve activity of epinephrine. Note: **this is double the concentration suggested in the package to decrease the fluid volume delivered to the patient.** If lower concentration is preferred add 4 mL of 1 mg/mL to 1 litre (**4 μg/mL**) and double volume administered on the chart.

See **CAUTIONS**. This drug is light sensitive, and extended use should be protected from light (bag only, no need to protect the line).

INDICATIONS: For criteria for treatment with standard norepinephrine therapy see appropriate chapters.

CAUTION: Abrubt withdrawal of therapy should be avoided. Risk of extravasation, or high concentration necrosis at insertion site. **Use central line (jugular) or 22 – 20G and 1.88" in length peripheral catheter to minimize this complication. Maintain strict asepsis of catheter site and ensure patency and positioning of catheter on regular basis during therapy. Reduce concentration as soon as possible.**

Blood pressure must be continuously monitored during therapy, preferably directly, or reliable indirect at a minimum of q 5 minutes to avoid hypertension. Measurement interval can be increased once desired BP is reached, but must still be judiciously evaluated.

COMPATIBILE: Other drugs should not be administered through the norepinephrine IV set. However, since norepinephrine will probably be connected to maintenance fluids through an injection port, it is important to know which drugs will be compatible. Compatible drugs for 4 hours or less include:

Diltiazem	Famotidine	Fentanyl Citrate
Dopamine	Furosemide	Heparin Sodium
Hydromorphone	Midazolam	Morphine Sulfate
Potassium Chloride	Ranitidine	

INCOMPATIBLE: These drugs should not be administered in the line while norepinephrine is running:

Insulin	Pentobarbital	Phenobarbital
Thiopental		

Note: Other drugs have not been tested, and therefore should be considered incompatible.

DOSE: (This infusion rate is based on 0.1 – 0.5 μg/kg/min). **The concentration of norepinephrine in this solution is 8 μg/mL).** Norepinephrine infusion should be administered separately from maintenance fluids to allow for adjustment in dosing. Maintenance fluid rate should be calculated with a reduction in volume according to that administered with the norepinephrine infusion. Rarely the infusion can be increased to **1.0 μg/kg/min (multiply the upper range by 2 on the chart, for dose).** More commonly, norepinephrine solution is titrated to effect within the dosing limits.

BURETTE: Because norepinephrine requires titration to effect, a separate line is always necessary. Since norepinephrine is incompatible with alkalinizing crystalloid solutions, the use of a burette with NaCl + dextrose is recommended.

NOREPINEPHRINE IN D5W, OR DEXTROSE + NaCl, INFUSION/HOUR (8 µg/mL)

NOTE: The volume (mL/h) is the volume to be administered of the 4 mL (1 mg/mL) in 500 mL solution.

BW kg (*lbs*)	**1** (*2.2*)	**2** (*4.4*)	**3** (*6.6*)	**4** (*8.8*)	**5** (*11*)
Dose (μg/h)	6-30	12-60	18-90	24-120	30-150
Volume (mL/h)	1-4	2-8	2-11	3-15	4-19
BW kg (*lbs*)	**6** (*13*)	**7** (*15.4*)	**8** (*17.6*)	**9** (*19.8*)	**10** (*22*)
Dose (μg/h)	36-180	42-210	48-240	54-270	60-300
Volume (mL/h)	4-22	5-26	6-30	7-34	7-37
BW kg (*lbs*)	**11** (*24.2*)	**12** (*26.4*)	**13** (*28.6*)	**14** (*30.8*)	**15** (*33*)
Dose (μg/h)	66-330	72-360	78-390	84-420	90-450
Volume (mL/h)	8-41	9-45	10-49	10-52	11-56

BW kg (lbs) Dose (µg /h) Volume (mL/h)	**16** (*35*) 96-480 12-60	**17** (*37.4*) 102-510 13-64	**18** (*39.6*) 108-540 13-67	**19** (*41.8*) 114-570 14-71	**20** (*44*) 120-600 15-75
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**21** (*46*) 126-630 16-79	**22** (*48.4*) 132-660 16-82	**23** (*50.6*) 138-690 17-86	**24** (*52.8*) 144-720 18-90	**25** (*55*) 150-750 19-94
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**26** (*57*) 156-780 19-97	**27** (*59.4*) 162-810 20-101	**28** (*61.6*) 168-840 21-105	**29** (*63.8*) 174-870 22-109	**30** (*66*) 180-900 22-112
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**31** (*68*) 186-930 23-116	**32** (*70.4*) 192-960 24-120	**33** (*72.6*) 198-990 25-124	**34** (*74.8*) 204-1020 25-127	**35** (*77*) 210-1050 26-131
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**36** (*79*) 216-1080 27-135	**37** (*81.4*) 222-1110 28-139	**38** (*83.6*) 228-1140 28-142	**39** (*85.8*) 234-1170 29-146	**40** (*88*) 240-1200 30-150
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**41** (*90*) 246-1230 31-154	**42** (*92.4*) 252-1260 31-157	**43** (*94.6*) 258-1290 32-161	**44** (*96.8*) 264-1320 33-165	**45** (*99*) 270-1350 34-169
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**46** (*101*) 276-1380 34-172	**47** (*103.4*) 282-1410 35-176	**48** (*105.6*) 288-1440 36-180	**49** (*107.8*) 294-1470 37-184	**50** (*110*) 300-1500 37-187
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**51** (*112*) 306-1530 38-191	**52** (*114.4*) 312-1560 39-195	**53** (*116.6*) 318-1590 40-199	**54** (*118.8*) 324-1620 40-202	**55** (*121*) 330-1650 41-206
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**56** (*123*) 336-1680 42-210	**57** (*125.4*) 342-1710 43-214	**58** (*127.6*) 348-1740 43-217	**59** (*129.8*) 354-1770 44-221	**60** (*132*) 360-1800 45-225
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**61** (*134*) 366-1830 46-229	**62** (*136.4*) 372-1860 46-232	**63** (*138.6*) 378-1890 47-236	**64** (*140.8*) 384-1920 48-240	**65** (*143*) 390-1950 49-244
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**66** (*145*) 396-1980 50-248	**67** (*147*) 402-2010 50-251	**68** (*149.6*) 408-2040 51-255	**69** (*151.8*) 414-2070 52-259	**70** (*154*) 420-2100 53-263
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**71** (*156*) 426-2130 53-266	**72** (*158.4*) 432-2160 54-270	**73** (*160.6*) 438-2190 55-274	**74** (*162.8*) 444-2220 56-278	**75** (*165*) 450-2250 56-281
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**76** (*167*) 456-2280 57-285	**77** (*169.4*) 462-2310 58-289	**78** (*171.6*) 468-2340 59-293	**79** (*173.8*) 474-2370 59-296	**80** (*176*) 480-2400 60-300
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**81** (*178*) 486-2430 61-304	**82** (*180.4*) 492-2460 62-308	**83** (*182.6*) 498-2490 62-311	**84** (*184.8*) 504-2520 63-315	**85** (*187*) 510-2550 64-319
BW kg (lbs) Dose (µg /h) Volume (mL/h)	**86** (*189*) 516-2580 65-323	**87** (*191.4*) 522-2610 65-326	**88** (*193.6*) 528-2640 66-330	**89** (*195.8*) 534-2670 67-334	**90** (*198*) 540-2700 68-338

PREPARATION: Using the chart below, find hourly rate in mL of oxymorphone (10 mg/mL) at the dosing level desired. Administration via syringe pump for ease of titration is ideal, but not always practical. Alternative administration would be via burette. Add the **mL per hour of oxymorphone required to the burette containing a number of mL/hour to be delivered (i.e., 10 mL/h).** Mix well by inversion. Keep in mind while mixing it is often necessary to change the dose given depending on level of pain, therefore it may be prudent to only mix small volumes (ie q1hr volumes). This should be separate from the maintenance fluids and can be 'piggy-backed' onto the maintenance fluid line. The rate of infusion may be increased or dereased

INDICATIONS: For criteria for treatment with standard oxymorphone therapy *see Analgesics and Sedatives p. 81.*

CAUTION: *See Analgesics and Sedatives p 81.*

DOSE: This infusion rate is based on 0.0125 mg/kg/h. This dose may be safely doubled, or more to effect, if the patient's pain is not controlled. Changing to a fentanyl (*p. 83*) infusion may be more cost effective in this circumstance, or in the case of larger patients. Oxymorphone infusions may be administered with maintenance fluids when practical.

COMPATIBILE: Since oxymorphone is infused with the maintenance fluids, it is important to know which drugs will be compatible. More common compatible drugs include:

Acepromazine★   Atropine★   Glycopyrrolate
Ranitidine

★*These drugs have not been tested but appear to be compatible in syringe. Use immediately after mixing.*

INCOMPATIBLE: ★Note: Other drugs have not been tested, and therefore should be considered incompatible.

OXYMORPHONE INFUSION IN CRYSTALLOID FLUIDS (original concentration 10mg/mL)

NOTE: The volume (mL/h) is the volume of full strength oxymorphone.
Use this number to determine how much oxymorphone to add to hourly fluids.

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	0.012	0.025	0.038	0.05	0.06
Volume (mL/h)	0.008	0.017	0.025	0.03	0.04
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (mg/h)	0.075	0.088	0.1	0.11	0.125
Volume (mL/h)	0.05	0.06	0.07	0.08	0.08
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (mg/h)	0.14	0.15	0.16	0.175	0.19
Volume (mL/h)	0.09	0.1	0.11	0.12	0.13
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (mg/h)	0.2	0.2	0.225	0.24	0.25
Volume (mL/h)	0.13	0.14	0.15	0.16	0.17
BW kg (*lbs*)	21 (*46.2*)	22 (*48.4*)	23 (*50.6*)	24 (*52.8*)	25 (*55*)
Dose (mg/h)	0.26	0.28	0.29	0.3	0.31
Volume (mL/h)	0.18	0.18	0.19	0.2	0.21
BW kg (*lbs*)	26 (*57.2*)	27 (*59.4*)	28 (*61.6*)	29 (*63.8*)	30 (*66*)
Dose (mg/h)	0.325	0.34	0.35	0.36	0.38
Volume (mL/h)	0.22	0.23	0.23	0.24	0.25
BW kg (*lbs*)	31 (*68.2*)	32 (*70.4*)	33 (*72.6*)	34 (*74.8*)	35 (*77*)
Dose (mg/h)	0.39	0.4	0.41	0.43	0.44
Volume (mL/h)	0.26	0.27	0.28	0.28	0.29

BW kg (*lbs*)	**36** (*79.2*)	**37** (*81.4*)	**38** (*83.6*)	**39** (*85.8*)	**40** (*88*)
Dose (mg/h)	0.45	0.46	0.48	0.49	0.5
Volume (mL/h)	0.3	0.31	0.32	0.33	0.33
BW kg (*lbs*)	**41** (*90.2*)	**42** (*92.4*)	**43** (*94.6*)	**44** (*96.8*)	**45** (*99*)
Dose (mg/h)	0.51	0.53	0.54	0.55	0.56
Volume (mL/h)	0.34	0.35	0.36	0.37	0.38
BW kg (*lbs*)	**46** (*101.2*)	**47** (*103.4*)	**48** (*105.6*)	**49** (*107.8*)	**50** (*110*)
Dose (mg/h)	0.58	0.59	0.6	0.61	0.63
Volume (mL/h)	0.38	0.39	0.4	0.41	0.42
BW kg (*lbs*)	**51** (*112.2*)	**52** (*114.4*)	**53** (*116.6*)	**54** (*118.8*)	**55** (*121*)
Dose (mg/h)	0.64	0.65	0.66	0.68	0.69
Volume (mL/h)	0.43	0.43	0.44	0.45	0.46
BW kg (*lbs*)	**56** (*123.2*)	**57** (*125.4*)	**58** (*127.6*)	**59** (*129.8*)	**60** (*132*)
Dose (mg/h)	0.7	0.71	0.73	0.74	0.75
Volume (mL/h)	0.47	0.48	0.48	0.49	0.5
BW kg (*lbs*)	**61** (*134.2*)	**62** (*136.4*)	**63** (*138.6*)	**64** (*140.8*)	**65** (*143*)
Dose (mg/h)	0.76	0.78	0.79	0.8	0.81
Volume (mL/h)	0.51	0.52	0.53	0.53	0.54
BW kg (*lbs*)	**66** (*145.2*)	**67** (*147.2*)	**68** (*149.6*)	**69** (*151.8*)	**70** (*154*)
Dose (mg/h)	0.83	0.84	0.85	0.86	0.88
Volume (mL/h)	0.55	0.56	0.57	0.58	0.58
BW kg (*lbs*)	**71** (*156.2*)	**72** (*158.4*)	**73** (*160.6*)	**74** (*162.8*)	**75** (*165*)
Dose (mg/h)	0.89	0.9	0.91	0.93	0.94
Volume (mL/h)	0.59	0.6	0.61	0.62	0.63
BW kg (*lbs*)	**76** (*167.2*)	**77** (*169.4*)	**78** (*171.6*)	**79** (*173.8*)	**80** (*176*)
Dose (mg/h)	0.95	0.96	0.98	0.99	1.0
Volume (mL/h)	0.63	0.64	0.65	0.66	0.67
BW kg (*lbs*)	**81** (*178.2*)	**82** (*180.4*)	**83** (*182.6*)	**84** (*184.8*)	**85** (*187*)
Dose (mg/h)	1.01	1.03	1.04	1.05	1.06
Volume (mL/h)	0.68	0.68	0.69	0.7	0.71
BW kg (*lbs*)	**86** (*189.2*)	**87** (*191.4*)	**88** (*193.6*)	**89** (*195.8*)	**90** (*198*)
Dose (mg/h)	1.08	1.09	1.1	1.1	1.1
Volume (mL/h)	0.72	0.73	0.73	0.74	0.75

PREPARATION: 1 g procainamide (10 mL of 100 mg/mL procainamide) in 500 mL 0.45% or 0.9% NaCl for concentration of 2 mg/mL. **Incompatible with 5% Dextrose in Water (D5W)**, not tested in Plasma-Lyte® 148, Plasma-Lyte® A, Normosol® R or LRS.

INDICATIONS: For criteria for treatment with procainamide *see Supraventricular Tachycardia p. 174, Ventricular Tachycardia p. 182.*

CAUTION: See chapters above.

DOSE: This infusion rate is based on 25 – 50 μg/kg/min. **The concentration of procainamide in this solution is 2 mg/mL.** Procainamide infusion should be administered separately from maintenance fluids to allow for adjustment in dosing. Maintenance fluid rate should be calculated with a reduction in volume according to that administered with the procainamide infusion. **Should a more concentrated solution be required to reduce fluids administered, add two 10 mL of 100 mg/mL vials to 500 mL fluids (4 mg/mL) and administer at half the infusion rate on the chart.**

BURETTE: **As an alternative** to the above infusion, procainamide can be made up in aliquots of 100 mL using the same dilution as above (2 mL of 100 mg/mL procainamide in 100 mL fluids = 2 mg/mL) then administer as per chart. This may be a more reasonable approach for a smaller patient.

COMPATIBILE: Since procainamide is infused with the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 4 hours or less include:

Diltiazem	Dobutamine	Famotidine
Heparin sodium	Ranitidine	

INCOMPATIBLE: *Note: Other drugs have not been tested, and therefore should be considered incompatible.

PROCAINAMIDE IN NaCl INFUSION/HOUR (2 mg/mL)

NOTE: The volume (mL/h) is the volume of fluid with procainamide added (2 mg/mL)
as described above and NOT the volume of original drug, rounded to closest mL.

BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**1** (*2.2*) 1.5-3.0 1-2	**2** (*4.4*) 3.0-6.0 2-3	**3** (*6.6*) 4.5-9.0 2-5	**4** (*8.8*) 6.0-12.0 3-6	**5** (*11*) 7.5-15.0 4-8
BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**6** (*13.2*) 9.0-18.0 5-9	**7** (*15.4*) 10.5-21.0 5-11	**8** (*17.6*) 12.0-24.0 6-12	**9** (*19.8*) 13.5-27.0 7-14	**10** (*22*) 15.0-30.0 8-15
BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**11** (*24.2*) 16.5-33.0 8-17	**12** (*26.4*) 18.0-36.0 9-18	**13** (*28.6*) 19.5-39.0 10-20	**14** (*30.8*) 21.0-42.0 11-21	**15** (*33*) 22.5-45.0 11-23
BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**16** (*35.2*) 24.0-48.0 12-24	**17** (*37.4*) 25.5-51.0 13-26	**18** (*39.6*) 27.0-54.0 14-27	**19** (*41.8*) 28.5-57.0 14-29	**20** (*44*) 30.0-60.0 15-30
BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**21** (*46.2*) 31.5-63.0 16-32	**22** (*48.4*) 33.0-66.0 17-33	**23** (*50.6*) 34.5-69.0 17-35	**24** (*52.8*) 36.0-72.0 18-36	**25** (*55*) 37.5-75.0 19-38
BW kg (*lbs*) Dose (mg/h) Volume (mL/h)	**26** (*57.2*) 39.0-78.0 20-39	**27** (*59.4*) 40.5-81.0 20-41	**28** (*61.6*) 42.0-84.0 21-42	**29** (*63.8*) 43.5-87.0 22-44	**30** (*66*) 45.0-90.0 23-45

BW kg (lbs)	31 (68.2)	32 (70.4)	33 (72.6)	34 (74.8)	35 (77)
Dose (mg/h)	46.5-93.0	48.0-96.0	49.5-99.0	51.0-102.0	52.5-105.0
Volume (mL/h)	23-47	24-48	25-50	26-51	26-53
BW kg (lbs)	36 (79.2)	37 (81.4)	38 (83.6)	39 (85.8)	40 (88)
Dose (mg/h)	54.0-108.0	55.5-111.0	57.0-114.0	58.5-117.0	60.0-120.0
Volume (mL/h)	27-54	28-56	29-57	29-59	30-60
BW kg (lbs)	41 (90.2)	42 (92.4)	43 (94.6)	44 (96.8)	45 (99)
Dose (mg/h)	61.5-123.0	63.0-126.0	64.5-129.0	66.0-132.0	67.5-135.0
Volume (mL/h)	31-62	32-63	32-65	33-66	34-68
BW kg (lbs)	46 (101.2)	47 (103.4)	48 (105.6)	49 (107.8)	50 (110)
Dose (mg/h)	69.0-138.0	70.5-141.0	72.0-144.0	73.5-147.0	75.0-150.0
Volume (mL/h)	35-69	35-71	36-72	37-74	38-75
BW kg (lbs)	51 (112.2)	52 (114.4)	53 (116.6)	54 (118.8)	55 (121)
Dose (mg/h)	76.5-153.0	78.0-156.0	79.5-159.0	81.0-162.0	82.5-165.0
Volume (mL/h)	38-77	39-78	40-80	41-81	41-83
BW kg (lbs)	56 (123.2)	57 (125.4)	58 (127.6)	59 (129.8)	60 (132)
Dose (mg/h)	84.0-168.0	85.5-171.0	87.0-174.0	88.5-177.0	90.0-180.0
Volume (mL/h)	42-84	43-86	44-87	44-89	45-90
BW kg (lbs)	61 (134.2)	62 (136.4)	63 (138.6)	64 (140.8)	65 (143)
Dose (mg/h)	91.5-183.0	93.0-186.0	94.5-189.0	96.0-192.0	97.5-195.0
Volume (mL/h)	46-92	47-93	47-95	48-96	49-98
BW kg (lbs)	66 (145.2)	67 (147.2)	68 (149.6)	69 (151.8)	70 (154)
Dose (mg/h)	99.0-198.0	100.5-201.0	102.0-204.0	103.5-207.0	105.0-210.0
Volume (mL/h)	50-99	50-101	51-102	52-104	53-105
BW kg (lbs)	71 (156.2)	72 (158.4)	73 (160.6)	74 (162.8)	75 (165)
Dose (mg/h)	106.5-213.0	108.0-216.0	109.5-219.0	111.0-222.0	112.5-225.0
Volume (mL/h)	53-107	54-108	55-110	56-111	56-113
BW kg (lbs)	76 (167.2)	77 (169.4)	78 (171.6)	79 (173.8)	80 (176)
Dose (mg/h)	114.0-228.0	115.5-231.0	117.0-234.0	118.5-237.0	120.0-240.0
Volume (mL/h)	57-114	58-116	59-117	59-119	60-120
BW kg (lbs)	81 (178.2)	82 (180.4)	83 (182.6)	84 (184.8)	85 (187)
Dose (mg/h)	121.5-243.0	123.0-246.0	124.5-249.0	126.0-252.0	127.5-255.0
Volume (mL/h)	61-122	62-123	62-125	63-126	64-128
BW kg (lbs)	86 (189.2)	87 (191.4)	88 (193.6)	89 (195.8)	90 (198)
Dose (mg/h)	129.0-258.0	130.5-261.0	132.0-264.0	133.5-267.0	135.0-270.0
Volume (mL/h)	65-129	65-131	66-132	67-134	68-135

PREPARATION: Longer term administration via syringe pump to minimize handling of drug is ideal, but not always practical. A burette and dedicated line and pump would be the alternative, with this 'piggy-backed' into IV fluids. Do not dilute propofol prior to use, put straight into burette and line. Vial should be used within 6 hours of opening. Ideally, burette and lines should be discarded and replaced q6h, or at minimum flushed with saline prior to introducing new propofol. Propofol appears to be compatible with most crystalloid solutions.

INDICATIONS: For criteria for treatment with propofol therapy *see p. 114.*

CAUTION: **Propofol is a lipid based product that can support bacterial growth quite readily. Use strict aseptic technique when handling. Monitor catheter site for phlebitis, monitor patient for sepsis.** The vial should be swabbed with alcohol at the 'break' point and allowed to dry for a moment prior to breaking. This prevents bacteria from entering the solution.

DOSE: This infusion rate is based on 0.1 mg/kg/min but can be titrated to effect depending on the level of sedation required. Anesthesia is often maintained at 0.4 mg/kg/min (4 X dose on chart).

COMPATIBILE: Other drugs should not be administered through the propofol IV set. However, since propofol will probably be connected to maintenance fluids via an injection port, it is important to know which drugs will be compatible. Compatible drugs for 1 hour or less include:

Ampicillin Sodium	Butorphanol	Cefazolin Sodium
Cefotaxime Sodium	Ceftazadime	Clindamycin
Dexamethasone	Dobutamine	Dopamine
Famotidine	Fentanyl Citrate	Furosemide
Glycopyrrolate	Heparin Sodium	Hydromorphone
Insulin	Ketamine	Lidocaine
Meperidine	Midazolam	Morphine
Naloxone	Pentobarbital	Phenobarbital
Ranitidine		

INCOMPATIBLE: These drugs should not be administered in the line while propofol is running:

Diazepam	Gentamicin	Methylprednisolone Sodium Succinate

★Note: Other drugs have not been tested, and therefore should be considered incompatible.

PROPOFOL INFUSION (10 mg/mL)

NOTE: The volume (mL/h) is the volume of 10 mg/mL (full-strength) propofol.

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	6	12	18	24	30
Volume (mL/h)	0.6	1.2	1.8	2.4	3.0
BW kg (*lbs*)	6 (*13.2*)	7 (*15.4*)	8 (*17.6*)	9 (*19.8*)	10 (*22*)
Dose (mg/h)	36	42	48	54	60
Volume (mL/h)	3.6	4.2	4.8	5.4	6.0
BW kg (*lbs*)	11 (*24.2*)	12 (*26.4*)	13 (*28.6*)	14 (*30.8*)	15 (*33*)
Dose (mg/h)	66	72	78	84	90
Volume (mL/h)	6.6	7.2	7.8	8.4	9.0
BW kg (*lbs*)	16 (*35.2*)	17 (*37.4*)	18 (*39.6*)	19 (*41.8*)	20 (*44*)
Dose (mg/h)	96	102	108	114	120
Volume (mL/h)	9.6	10.2	10.8	11.4	12.0
BW kg (*lbs*)	21 (*46.2*)	22 (*48.4*)	23 (*50.6*)	24 (*52.8*)	25 (*55*)
Dose (mg/h)	126	132	138	144	150
Volume (mL/h)	12.6	13.2	13.8	14.4	15.0

BW kg (*lbs*)	**26** (*57.2*)	**27** (*59.4*)	**28** (*61.6*)	**29** (*63.8*)	**30** (*66*)
Dose (mg/h)	156	162	168	174	180
Volume (mL/h)	15.6	16.2	16.8	17.4	18.0
BW kg (*lbs*)	**31** (*68.2*)	**32** (*70.4*)	**33** (*72.6*)	**34** (*74.8*)	**35** (*77*)
Dose (mg/h)	186	192	198	204	210
Volume (mL/h)	18.6	19.2	19.8	20.4	21.0
BW kg (*lbs*)	**36** (*79.2*)	**37** (*81.4*)	**38** (*83.6*)	**39** (*85.8*)	**40** (*88*)
Dose (mg/h)	216	222	228	234	240
Volume (mL/h)	21.6	22.2	22.8	23.4	24.0
BW kg (*lbs*)	**41** (*90.2*)	**42** (*92.4*)	**43** (*94.6*)	**44** (*96.8*)	**45** (*99*)
Dose (mg/h)	246	252	258	264	270
Volume (mL/h)	24.6	25.2	25.8	26.4	27.0
BW kg (*lbs*)	**46** (*101.2*)	**47** (*103.4*)	**48** (*105.6*)	**49** (*107.8*)	**50** (*110*)
Dose (mg/h)	276	282	288	294	300
Volume (mL/h)	27.6	28.2	28.8	29.4	30.0
BW kg (*lbs*)	**51** (*112.2*)	**52** (*114.4*)	**53** (*116.6*)	**54** (*118.8*)	**55** (*121*)
Dose (mg/h)	306	312	318	324	330
Volume (mL/h)	30.6	31.2	31.8	32.4	33.0
BW kg (*lbs*)	**56** (*123.2*)	**57** (*125.4*)	**58** (*127.6*)	**59** (*129.8*)	**60** (*132*)
Dose (mg/h)	336	342	348	354	360
Volume (mL/h)	33.6	34.2	34.8	35.4	36.0
BW kg (*lbs*)	**61** (*134.2*)	**62** (*136.4*)	**63** (*138.6*)	**64** (*140.8*)	**65** (*143*)
Dose (mg/h)	366	372	378	384	390
Volume (mL/h)	36.6	37.2	37.8	38.4	39.0
BW kg (*lbs*)	**66** (*145.2*)	**67** (*147.2*)	**68** (*149.6*)	**69** (*151.8*)	**70** (*154*)
Dose (mg/h)	396	402	408	414	420
Volume (mL/h)	39.6	40.2	40.8	41.4	42.0
BW kg (*lbs*)	**71** (*156.2*)	**72** (*158.4*)	**73** (*160.6*)	**74** (*162.8*)	**75** (*165*)
Dose (mg/h)	426	432	438	444	450
Volume (mL/h)	42.6	43.2	43.8	44.4	45.0
BW kg (*lbs*)	**76** (*167.2*)	**77** (*169.4*)	**78** (*171.6*)	**79** (*173.8*)	**80** (*176*)
Dose (mg/h)	456	462	468	474	480
Volume (mL/h)	45.6	46.2	46.8	47.4	48.0
BW kg (*lbs*)	**81** (*178.2*)	**82** (*180.4*)	**83** (*182.6*)	**84** (*184.8*)	**85** (*187*)
Dose (mg/h)	486	492	498	504	510
Volume (mL/h)	48.6	49.2	49.8	50.4	51.0
BW kg (*lbs*)	**86** (*189.2*)	**87** (*191.4*)	**88** (*193.6*)	**89** (*195.8*)	**90** (*198*)
Dose (mg/h)	516	522	528	534	540
Volume (mL/h)	51.6	52.2	52.8	53.4	54.0

PREPARATION: Dissolve contents of one 50 mg vial with 3 mL 5% Dextrose in Water (D5W). Add 50 mg Nitroprusside to 500 mL D5W = 100 μg/mL (0.1 mg/mL). (Always use 5% Dextrose). Cover fluid bag and lines with aluminum foil to protect from light. Solution may have a brownish or light orange colour. Discard solution if it is blue, green or dark red.

INDICATIONS: Short-term management of severe, acute, life-threatening heart failure or severe systemic hypertension. It is especially useful in canine patients with severe heart failure due to dilated cardiomyopathy. Can be administered with dobutamine. *See Congestive Heart Failure p. 152.*

CAUTION: The most common side effect is hypotension. **Blood pressures must be monitored very closely.** Continuous direct arterial pressure monitoring is preferred. If using an indirect method, blood pressures should be measured at least every 5 – 10 min. **Nitroprusside is metabolized to thiocyanate.** There is a danger of toxicity if nitroprusside is used greater than 2 – 3 days. Cyanide accumulation can result in lactic acidosis, altered behaviour, convulsions, and death.

DOSE: Initial infusion rates in dogs are 1 – 5 μg/kg/min. Titrate to effect by increasing the infusion by 3 – 5 μg/kg/min every 10 minutes. Must be administered accurately through the use of an infusion pump.

BURETTE: For patients not able to withstand the fluid rates in the chart below, nitroprusside can be added to a burette to make a more concentrated solution. Dissolve contents of one 50 mg vial with 3 mL D5W. Add 50 mg nitroprusside to 100 mL of D5W in a burette. This will make a **0.5 mg/mL** solution. Protect from light by wrapping burette and fluid line with aluminum foil. **Calculate fluid rates as 1/5 those in the chart.**

COMPATIBILE: Since nitroprusside is infused by piggybacking onto the maintenance fluids, it is important to know which drugs will be compatible. Compatible drugs for 3 hours or less include:

Diltiazem	Dobutamine	Dopamine
Heparin	Lidocaine (diluted)	Regular insulin

INCOMPATIBLE: Avoid any drugs not listed as compatible, or run sodium nitroprusside through a dedicated IV catheter.

Sodium Nitroprusside in D5W Infusion/Hour (0.1 mg/mL)
Dose Range: 1 – 10 μg/kg/min

NOTE: The volume (mL/h) is the volume to be infused/h based on the 50 mg/500 mL.

BW kg (*lbs*)	1 (*2.2*)	2 (*4.4*)	3 (*6.6*)	4 (*8.8*)	5 (*11*)
Dose (mg/h)	0.1-0.6	0.1-1.2	0.2-1.8	0.2-2.4	0.3-3
Volume (mL/h)	0.6-6.0	1.2-12	2-18	2-24	3-30
BW kg (*lbs*)	**6 (*13.2*)**	**7 (*15.4*)**	**8 (*17.6*)**	**9 (*19.8*)**	**10 (*22*)**
Dose (mg/h)	0.4-1.7	0.4-2.1	0.5-2.4	1.5-2.7	0.6-6.0
Volume (mL/h)	4-18	4-21	5-24	5-27	6-60
BW kg (*lbs*)	**11 (*24.2*)**	**12 (*26.4*)**	**13 (*28.6*)**	**14 (*30.8*)**	**15 (*33*)**
Dose (mg/h)	0.7-6.6	0.7-7.2	0.8-7.8	0.8-8.4	0.9-9
Volume (mL/h)	7-66	7-72	8-78	8-84	9-90
BW kg (*lbs*)	**16 (*35.2*)**	**17 (*37.4*)**	**18 (*39.6*)**	**19 (*41.8*)**	**20 (*44*)**
Dose (mg/h)	1.0-10	1.0-10	1.1-11	1.1-11	1.2-12
Volume (mL/h)	10-96	10-102	11-108	11-114	12-120
BW kg (*lbs*)	**21 (*46.2*)**	**22 (*48.4*)**	**23 (*50.6*)**	**24 (*52.8*)**	**25 (*55*)**
Dose (mg/h)	1.3-13	1.3-13	1.4-14	1.4-14	1.5-15
Volume (mL/h)	13-126	13-132	14-138	14-144	15-150
BW kg (*lbs*)	**26 (*57.2*)**	**27 (*59.4*)**	**28 (*61.6*)**	**29 (*63.8*)**	**30 (*66*)**
Dose (mg/h)	1.6-16	1.6-16	1.7-17	1.7-17	1.8-18
Volume (mL/h)	16-156	16-162	17-168	17-174	18-180

BW kg (*lbs*)	**31** (*68.2*)	**32** (*70.4*)	**33** (*72.6*)	**34** (*74.8*)	**35** (*77*)
Dose (mg/h)	2-19	2-19	2-20	2-20	2-21
Volume (mL/h)	19-186	19-192	20-198	20-204	21-210
BW kg (*lbs*)	**36** (*79.2*)	**37** (*81.4*)	**38** (*83.6*)	**39** (*85.8*)	**40** (*88*)
Dose (mg/h)	2-22	2-22	2-23	2-23	2-24
Volume (mL/h)	22-216	22-222	23-228	23-234	24-240
BW kg (*lbs*)	**41** (*90.2*)	**42** (*92.4*)	**43** (*94.6*)	**44** (*96.8*)	**45** (*99*)
Dose (mg/h)	2-25	3-25	3-26	3-26	3-27
Volume (mL/h)	25-246	25-252	26-258	26-264	27-270
BW kg (*lbs*)	**46** (*101.2*)	**47** (*103.4*)	**48** (*105.6*)	**49** (*107.8*)	**50** (*110*)
Dose (mg/h)	3-28	3-28	3-29	3-29	3-30
Volume (mL/h)	28-276	28-282	29-288	29-294	30-300
BW kg (*lbs*)	**51** (*112.2*)	**52** (*114.4*)	**53** (*116.6*)	**54** (*118.8*)	**55** (*121*)
Dose (mg/h)	3-31	3-31	3-32	3-32	3-33
Volume (mL/h)	31-306	31-312	32-318	32-324	33-330
BW kg (*lbs*)	**56** (*123.2*)	**57** (*125.4*)	**58** (*127.6*)	**59** (*129.8*)	**60** (*132*)
Dose (mg/h)	3-34	3-34	3-35	4-35	4-36
Volume (mL/h)	34-336	34-342	35-348	35-354	36-360
BW kg (*lbs*)	**61** (*134.2*)	**62** (*136.4*)	**63** (*138.6*)	**64** (*140.8*)	**65** (*143*)
Dose (mg/h)	4-37	4-37	4-38	4-38	4-39
Volume (mL/h)	37-366	37-372	38-378	38-384	39-390
BW kg (*lbs*)	**66** (*145.2*)	**67** (*147.2*)	**68** (*149.6*)	**69** (*151.8*)	**70** (*154*)
Dose (mg/h)	4-40	4-40	4-41	4-41	4-42
Volume (mL/h)	70-396	40-400	41-408	41-414	42-420
BW kg (*lbs*)	**71** (*156.2*)	**72** (*158.4*)	**73** (*160.6*)	**74** (*162.8*)	**75** (*165*)
Dose (mg/h)	4-43	4-43	4-44	4-44	5-45
Volume (mL/h)	43-426	43-432	44-438	44-444	45-450
BW kg (*lbs*)	**76** (*167.2*)	**77** (*169.4*)	**78** (*171.6*)	**79** (*173.8*)	**80** (*176*)
Dose (mg/h)	5-46	5-46	5-47	5-47	5-48
Volume (mL/h)	46-456	46-462	47-468	47-474	48-480
BW kg (*lbs*)	**81** (*178.2*)	**82** (*180.4*)	**83** (*182.6*)	**84** (*184.8*)	**85** (*187*)
Dose (mg/h)	5-49	5-49	5-50	5-50	5-51
Volume (mL/h)	49-486	49-492	50-498	50-504	51-510
BW kg (*lbs*)	**86** (*189.2*)	**87** (*191.4*)	**88** (*193.6*)	**89** (*195.8*)	**90** (*198*)
Dose (mg/h)	5-52	5-52	5-53	5-53	5-54
Volume (mL/h)	52-516	52-522	53-528	53-534	54-540

INTRODUCTION

Diabetic ketoacidosis (DKA) results from insulin deficiency, increased levels of the stress hormones epinephrine, cortisol, glucagon, growth hormone, which antagonize insulin, and dehydration. Insulin deficiency and antagonism result in hyperglycemia and lipolysis, releasing fatty acids. These are converted to ketone bodies (β-hydroxybutyrate, acetoacetate, acetone), which cause the ketosis and acidosis of DKA. Stress hormones may be elevated because of concurrent diseases or because of unregulated diabetes. Concurrent diseases include infections (infection has been positively correlated with mean plasma glucose levels and infection promotes release of glucagon, the most ketogenic of the stress hormones), pancreatitis, heart failure, hepatic diseases, renal failure, neoplasia, and specific stress hormone disorders (corticosteroid therapy, endocrine neoplasia, diestrus). Dehydration results from osmotic diuresis and other typical causes (e.g., vomiting); this in turn increases stress hormone levels and exacerbates hyperglycemia.

Dogs or cats with DKA may have been previously diagnosed with diabetes, and now due to some complicating factor develop DKA. They may also present without prior documentation of diabetes. A DKA crisis is diagnosed when the patient is clinically ill, with various degrees of depression, dehydration, inappetence, and vomiting, and there is concurrent acidemia, ketonuria/ketonemia and hyperglycemia. Because acid-base determinations are often not available, the diagnosis of a DKA crisis is frequently made on the basis of a sick diabetic animal demonstrating ketonuria or ketonemia. Alert diabetic animals which are eating, etc., but have a positive ketone reaction on a urine dipstick, are not in a DKA crisis and do not require the intensive management described in this chapter.

Non-diabetic ketosis occurs rarely in dogs and uncommonly in cats. It is characterized by a positive ketone reaction but negative glucose reaction on a urine test strip. Blood glucose levels are normal or low. This may occur in various conditions where there is increased fat metabolism, such as starvation and the later stages of pregnancy. These animals should not be treated with insulin. (*Note:* gestational diabetes and DKA also occur occasionally and must be differentiated from non-diabetic ketosis).

Occasionally cats, and rarely dogs, in a DKA crisis, may not show a positive ketone reaction on a urine test strip. These strips use a nitroprusside reaction to detect acetoacetate, and acetone to a lesser degree, but not β-hydroxybutyrate. The latter may be the predominant ketone and the only one to reach renal threshold (*see Laboratory Evaluation/Diagnostic Imaging below*). Depressed diabetic animals with negative ketonuria on a urine test strip may also have the **hyperglycemic hyperosmolar syndrome (HHS)** (*see p. 279*).

The reported mortality rate of DKA is approximately 25%. Death is due to concurrent disease, DKA and its complications (severe acidosis, hyperosmolality, acute renal failure), complications of therapy (hypokalemia, hypophosphatemia, cerebral edema), euthanasia due to poor response or cost of therapy, and management errors (hyperkalemia, fluid overload). DKA may recur, especially in cats.

DIAGNOSIS

History/Signalment
- Most commonly seen in cats older than 8 years of age and female dogs ~7 – 9 years of age; may occur in any breed.
- Typically the animal has been sick for 1 – 7 days, with depression, inappetence ± reduced drinking, but there may be a history of previous polyuria, polydipsia, polyphagia, and weight loss, due to diabetes.
- There may be a history of a precipitating event: change in insulin treatment, corticosteroid therapy, acute and chronic signs of concurrent diseases.
- Vomiting and diarrhea are common and may be a consequence of DKA or sign of a disorder initiating DKA such as pancreatitis.
- Time of last urination should be noted as acute renal failure can complicate DKA.

Clinical Signs/Physical Examination
- Physical examination findings include weakness, dehydration, signs of diabetes (poor muscle mass and hair coat, hepatomegaly, cataracts in dogs, plantigrade stance in cats), icterus, and signs of concurrent diseases.
- Fever may be present due to infection (e.g., pyelonephritis, pyometra, prostatitis, pneumonia) or non-septic inflammation (e.g., pancreatitis, neoplasia). However, infected DKA animals may not have an appropriate febrile response (normothermic) or may be in shock (hypothermic).
- Abdominal pain ± distension are common and may be a consequence of DKA or due to pancreatitis, other causes of vomiting and diarrhea, aerophagia, and abdominal organ infection.

- The respiratory pattern may be deep and rapid with an acetone odour to the breath. Polypnea/dyspnea may also be due to pain, anemia, fever and concurrent diseases (e.g., pneumonia, heart failure). Pleural effusion may also be identified secondary to heart failure.

Laboratory Evaluation/Diagnostic Imaging

The goals of work-up are to:
- Confirm the diagnosis.
- Identify underlying or complicating diseases, especially infections (e.g., urinary tract infection).
- Identify consequences of DKA (e.g., hypophosphatemia).

Stat
- **PCV** may be increased if dehydrated; normal; or low if hypophosphatemic (usually not until after therapy). The PCV may decrease with fluid therapy thereby unmasking anemia in animals with a normal PCV on presentation.
- **TS** maybe increased if dehydrated, or altered due to a concurrent condition yet to be identified.
- **Blood glucose.** Hyperglycemia is usually >17 mmol/L (300 mg/dl), but may be as low as 11 mmol/L (200 mg/dl). Hyperglycemia >28 mmol/L (500 mg/dl) is indicative of severe dehydration and/or renal insufficiency.
- **Urea and creatinine** are frequently increased.
- **Phosphorus** may be normal but frequently decreases with insulin therapy.
- **Blood gases** (or **total CO$_2$**). To measure the degree of acidosis present (*see Acid-Base Assessment p. 406*).
- **Electrolytes.** Changes may include hyper/hyponatremia, hypo/hyperkalemia. Many cats are hypokalemic. Caution: If hypokalemic, potassium will decrease further with correction of acidosis.
- Calculate effective **serum osmolality (mOsm/kg):**
  - **SI Units: mOsm/kg** = [1.86 X (Na$^+$ + K$^+$)] + glucose + 9, all units in mmol/L; (i.e., calculated serum osmolality minus urea).
  - **Traditional units:** mOsm/kg = [1.86 X (Na$^+$ + K$^+$)(mEq/L)] + [glucose (mg/dL)/18]; (i.e., calculated serum osmolality minus BUN).
  - Consider hyperosmolar if effective serum osmolality >320 mOsm/kg in **dogs** (normal 290 – 310), or >330 mOsm/kg in **cats** (290 – 330).
- **Urine test strip** (obtain urine via cystocentesis if culture required). If the urine test strip is negative for **ketones:**
  - Test heparinized plasma on the urine test strip to detect levels of acetoacetate below renal threshold. A negative test makes ketosis unlikely.
  - Add several drops of hydrogen peroxide to the urine sample in an effort to convert β-hydroxybutyrate to acetoacetate. A negative result does not rule-out ketosis.
  - Test serum on a test strip used to detect β-hydroxybutyrate in bovine milk (Keto-Test, Elanco)(not well-evaluated in dogs and cats).
  - Test blood in a point-of-care instrument used to detect β-hydroxybutyrate in humans (not well-evaluated in dogs and cats).
  - Submit serum to a commercial laboratory that offers a test for β-hydroxybutyrate.

Extended Labotatory Data Base
- A **CBC** usually shows a stress leukogram. Infection or non-septic inflammation (e.g., pancreatitis) should be ruled-out with neutrophil counts >25 – 30 x 10^9/L, a left shift, or toxic changes. Heinz bodies are often seen in cats.
- **Serum chemistry profile,** including magnesium for cats. In addition to hyperglycemia and increased anion gap metabolic acidosis, various alterations in pancreatic, liver and renal parameters may be detected as concurrent conditions that may be contributing factors or consequences of DKA. Consider T4 for cats.
- Consider measuring **serum osmolality** if available (see formula in *Stat* laboratory evaluation above).
- **FeLV** and **FIV** tests for cats.
- Complete **urinalysis** and **urine culture** as urinary tract infections may precipitate DKA in diabetic animals. Urine specific gravity is variable. Because glucose causes an osmotic diuresis and directly affects specific gravity, it cannot be used to assess urine concentrating ability.
- **Blood cultures** if febrile but no obvious cause or localising signs of infection. If there are localising signs of infection, obtain appropriate culture (e.g,. airway wash if signs of pneumonia).
- Obtain other tests as clinically indicated, e.g:
  - Thoracic radiographs if polypnea, dyspnea, or abnormal lung sounds are present.
  - Abdominal radiographs and/or ultrasound examinations if vomiting, abdominal pain or an abdominal mass are present, or if there is laboratory evidence of liver, pancreatic or renal disease.
- **ECG** (establish baseline for monitoring potassium therapy).

MANAGEMENT

DAY 0. *Initial therapy. (Act promptly but correct the metabolic abnormalities slowly over 24 – 48h).*

A. **Monitor** attitude, hydration, temperature, respiration (auscultate), pulse, and urine production (palpation of bladder, urination) q2–6h. Urine ketones and glucose should be measured whenever the animal urinates (q2–4h if catheterized). (Alternatively plasma ketones may be measured when blood glucose samples are obtained).

B. **Venous access.** A jugular catheter is usually recommended to facilitate frequent blood sampling and fluid therapy, especially in small dogs and cats. Use strict aseptic technique whenever handling the catheter. If a through-the-needle catheter is used, handle it gently to prevent cracking at the needle hub. If renal or heart failure are present, attach a central venous pressure (CVP) manometer or other recording device (*see p. 371*).

C. **Fluids.** Place a burette in the IV line as frequent fluid adjustments are necessary. **Caution:** Lowering osmolality too rapidly with over-aggressive fluid therapy will cause cerebral edema, due to the presence of organic osmolytes (idiogenic osmoles) formed in the brain in response to serum hyperosmolality.

    1. If in **shock** (*p. 606*), or acute oliguric renal failure (*p. 709*), administer fluids ONLY TO establish normal intravascular volume, to reverse clinical signs of shock, and to establish urine flow (0.5 – 1 mL/kg/h); administer fluids over 1 hour to establish this then reduce. The authors' fluid preference is 3(a) below. Rates from 50 – 90 mL/kg/h in the dog or 20 – 60 mL/kg/h in the cat may be needed initially. If shock is not resolving, consider 2.5 mL/kg boluses of synthetic colloid in addition to crystalloids, to prevent rapid reduction in osmolality. The fluid rate should then be reduced and the patient re-assessed with regard to hydration status and serum glucose levels, which will be reduced by fluid therapy. At this stage, the estimated deficit volume should be administered as described in 2 and 3 below, in addition to maintenance fluids and fluids to replace ongoing losses (i.e., vomiting, urine in excess of 2 mL/kg/h).

    2. Replace estimated deficits over 24 – 48h. Monitoring electrolytes in 4 hours to ensure that a change in sodium of greater than 0.5 mEq/L does not occur (*see p. 381*).

    3. Normal (0.9%) saline, lactated Ringer's solution, Plasma-Lyte® 148 or A, or Normasol® have been used and each has advantages and disadvantages.

        a. **Plasma-Lyte® 148 and A and Normasol®** are alkalinizing solutions and have a higher sodium content [140 mmol/L Na^+] than lactated Ringer's solution. For these reasons these solutions are preferred by the authors. The theoretical concern for the acetate component to promote ketogenesis is not a clinical concern when treating the ketonemia. Ketones are bicarbonate precursors that will ultimately increase pH. If hyponatremia (Na^+ <130 mEq/L) is present, the slower correction of serum Na^+ is also preferred to that which occurs when 0.9% saline is used.

        b. **Normal saline** has been advocated as the best choice for volume expansion, maintaining serum osmolality while serum glucose is reduced, and correcting the inevitable sodium deficit [saline contains 154 mmol/L Na^+]. However, this may promote dilutional acidosis, in addition to the existing acidosis and therefore, may increase the requirement for bicarbonate therapy initially.

        c. **Lactated Ringer's** solution is an alkalinizing solution, but is lower in sodium [130 mmol/L Na^+] and may more rapidly reduce plasma osmolality. Depending on the response of the fluids above, LRS may be indicated in certain serum sodium derangements (*p. 381*).

        d. Intravascular volume and hydration status must be assessed and the volume of fluid required to correct the deficit calculated (*p. 349*). As this calculation includes several physical findings a more accurate assessment will be made after consulting *Fluid Therapy (p. 347)*. Begin fluids at 4 mL/kg/h (~ twice maintenance) pending more accurate calculations.

        e. If hyper/hyponatremic, initiate (a) above and refer to *Hyper/Hyponatremia p. 381* for ongoing fluid guidelines.

D. **Electrolytes.** Measure venous blood gases and electrolytes q2h for the first 6h, then q4 – 6h. The frequent blood sampling can cause anemia in cats and small dogs – collect the minimum blood volumes required for sampling.

    1. **Potassium – supplement with KCl.** Do not give if suspect renal failure (oliguria), serum K^+ >5.5 mmol/L, or evidence of hyperkalemia on ECG. *See Table 1 and 2.*

TABLE 1. Potassium Supplementation for FIRST 6 – 12 hours of Treatment of DKA.

Serum K+ (mmol/L)*	K+ supplement (mEq) per volume of fluids**			
	125 mL***	250 mL	500 mL	1 L
> 5.5++++	2.5	5.0	10	20
4.0 – 5.5	5.0	10	20	40
< 4.0	7.5	15	30	60

*   If serum K+ not known then supplement at 40 mEq/L administered at maintenance rate. Monitor ECG if K+ cannot be monitored or if arrhythmia detected.

**   This table assumes a MAINTENANCE fluid rate. Adjust KCl supplementation according to fluid rate to not exceed delivery of >0.5 mEq/kg/h unless animal is closely monitored and a higher delivery rate (up to 1 mEq/kg/h) is necessary due to low serum K+. Check the K+ already present in your selected fluid.

*** Most burettes hold 150 mL fluids.

**** Wait 2 – 4h of fluid therapy and re-check K+ prior to this K+ supplement.

TABLE 2. Potassium Supplementation AFTER first 6 – 12 hours of Treatment of DKA.

Serum K+ (mmol/L)*	K+ supplement (mEq) per volume of fluids**			
	125 mL***	250 mL	500 mL	1 L
>3.5	2.5	5.0	10	20
3.1 – 3.5	3.7	7.5	15	30
2.6 – 3.0	5.0	10	20	40
2.1 – 2.5	7.5	15	30	60
<2.0	10	20	40	80

*   If serum K+ not known then supplement at 20 mEq/L. Monitor ECG if K+ cannot be monitored or if arrhythmia detected.

**   This table assumes a MAINTENANCE fluid rate. Adjust KCl supplementation according to fluid rate to not exceed delivery of >0.5 mEq/kg/h unless animal is closely monitored and a higher delivery rate (up to 1 mEq/kg/h) is necessary due to low serum K+. Check the K+ already present in your selected fluid.

*** Most burettes hold 150 mL fluids.

2. **Magnesium – supplement with MgSO$_4$.** (*see Hypo/Hypermagnesemia p. 403*). If hypokalemia is present requiring high dose supplementation (>0.5 mEq/kg/h), or magnesium levels <0.7 mmol/L, treat with magnesium. Administer 30 mg/kg over 4 h. Repeat twice more in a 24 period if necessary. Alternatively, deliver 60 – 125 mg/kg/24h (0.6 – 1 mEq/kg/day) by constant rate infusion. Use the lower dose if renal insufficiency is present. Repeat serum K+ in 2 hours and reduce the potassium supplementation based on rate of improvement. Magnesium supplementation is also recommended if hypophosphatemia is present. Frequent (q4–6h) measurements of potassium and phosphorous levels, and daily magnesium levels are necessary while supplementing with these electrolytes (*see chapters on individual electrolytes*).

3. **Bicarbonate – supplement with NaHCO$_3$** In general, bicarbonate therapy should not be administered. Ketones are bicarbonate precursors and bicarbonate therapy may result in alkalosis once ketoacidosis is resolved. Human studies have shown no proven benefit, and bicarbonate therapy is not routinely used at OVC, especially in cats. Only consider treatment if HCO$_3^-$ or total CO$_2$ remains <10 mmol/L, pH <7.1, after re-hydration and animal is normovolemic, and the patient's overall condition is not improving. (Note: Total CO$_2$ levels may be low if tubes are transported or allowed to sit open prior to testing). As the authors rarely administer NaHCO$_3$ to patients with DKA, and as there are various formulas suggested to derive a dose of NaHCO$_3$, the authors are reluctant to advise specific therapy. Based on published formulas a suggested compromise is: **Dose HCO$_3^-$ (mmol/L) = BW (kg) x (12 – patient HCO$_3^-$) x 0.2, given over 1 – 2 hours.** A previously published empirical dose is NaHCO$_3$ = 0.5 – 1.0 mEq/kg, given over 2 hours. If HCO$_3^-$ or total CO$_2$ level is not known, do not give bicarbonate therapy unless animal is markedly depressed or is not responding to fluid and insulin therapy (*see below*). If hyponatremia is a concern NaHCO$_3$ therapy may be indicated (*see Hyper/Hyponatremia p. 388*).

4. **Phosphate – supplement with KPO₄.** Hypophosphatemia (*p. 390*) may cause weakness, neurologic signs, and hemolysis. Treat if measure or anticipate phosphorus <0.35 mmol/L (most likely to occur after insulin therapy, on day 2). Dose = 0.01 – 0.03 mmol/kg/h for 6 hours and then re-measure serum phosphate level. Reduce KCl dose by amount of K^+ being given with KPO4 supplementation. (*See sections on potassium and magnesium above p. 403 and Hypophosphatemia p. 390*). Occasionally higher doses of phosphate are required (up to 0.12 mmol/kg/h) using sodium phosphate ($NaPO_4$). Serum calcium, phosphorus and sodium levels must be monitored with high dose phosphate supplementation to avoid hypocalcemia, hyperphosphatemia, soft tissue calcification and hypernatremia.

If serum phosphorus level is not known, add 20 mmol KPO₄/L (reduce KCl supplementation by 20 mEq/L for a total initial K^+ supplementation of 40 mEq/L). A practical initial approach is to add 20 mmol/L KPO₄ and 20 mEq/L KCL to fluids delivered at **maintenance rate.**

E. **Insulin.** Use Regular (Toronto) insulin (human).
Three efficacious protocols have been described, based on IV, IM, and SC administration. The dose of insulin required to prevent ketogenesis is less than the dose required to prevent hyperglycemia. Rapid control of blood glucose (BG) is not important and hypoglycemia and rapid decline in osmolality are **potentially devastating,** therefore it is best to err on the low end of the insulin dose. Ideally BG should drop by 3 – 5.5 mmol/L/h (50 – 100 mg/dL/h) to 11 – 14 mmol/L (200 – 250 mg/dl) during initial insulin therapy.

a. **Continuous IV infusion** for sick, dehydrated patients.
1. Give an IV bolus of 0.1U/kg. Prepare the infusion to begin 1 hour later.
2. Set up a separate IV bag of saline with a burette, dedicated to giving insulin. (The patient's fluid therapy should be delivered from a separate bag).
3. Fill the burette with 100 mL saline and add a calculated amount of insulin for a rate of 0.1 U/kg/h based on a fluid rate that delivers a small volume relative to the patient's fluid needs, e.g., 5 – 10 mL/h.
4. Run this solution through the line, and then let it sit in the line and burette, ideally for 1 hour, as insulin binds to the plastic. Discard this solution, and make up a fresh solution before starting the infusion. Begin the infusion 1 hour after giving the initial IV bolus of insulin.
5. Measure BG hourly.
6. Once BG drops to 14 mmol/L (250 mg/dl), reduce the insulin infusion rate by half (i.e., to 0.05 U/kg/h), and add 50% dextrose to the IV fluids **to make a 5% solution (10 mL/100 mL IV fluids)** (*see D below*).
7. Continue initially to measure BG hourly. Adjust insulin infusion rate to maintain BG between 9.0 – 12.0 mmol/L (160 – 220 mg/dl). Once a stable insulin rate has been determined, less frequent BG testing is needed (q2–4h).
8. When the patient is well hydrated, insulin therapy should be continued via the subcutaneous route q6–8h (*see c below*).

b. **Hourly IM injection.**
1. Give 0.2 U/kg IM (quadriceps), then 0.1 U/kg IM hourly until blood BG <17 mmol/L (300 mg/dl).
2. Measure BG prior to each insulin dose. If BG is dropping at too fast a rate, reduce insulin dose to 25 – 75% of previous dose.
3. Once BG drops to 14 mmol/L (250 mg/dl), give 0.1 – 0.4 U/kg IM q4–6h **if dehydrated,** OR 0.1 – 0.5 U/kg SC q6–8h **if well hydrated,** and add 50% dextrose to the IV fluids to make a 5% solution (10 mLs/100 mL IV fluids, *see Day 1 D*). Monitor BG q2–4h. Adjust insulin dose based on BG level and response to previous doses. The dose of insulin should be titrated to maintain BG between 9.0 – 12.0 mmol/L (160 – 220 mg/dl). Once the animal's response to insulin is understood, a chart can be prepared to guide the veterinarians and technicians in giving subsequent insulin doses based upon BG level.

c. **Intermittent SC injection.**
1. Insulin is given SC q4–6h. The initial dose is 0.25 U/kg (give IM if moderate to severe dehydration is present). This is **a test dose** and further insulin doses are adjusted based upon response.
2. Measure BG in 4 – 6 hours.
a. If hyperglycemia (>22 – 28 mmol/L [400 – 500 mg/dl]) is still present and BG has been dropping at desired rate, repeat the initial dose.

    b. If hyperglycemia (>28 mmol/L [500 mg/dl]) has not responded to insulin appropriately, then increase the insulin dose by 50 – 100% the initial dose.

    c. If the BG is <22 mmol/L (400 mg/dl), reduce insulin dose to 50% of initial dose.

    d. If the BG is <14 mmol/L (250 mg/dl), reduce insulin dose to 25% of initial dose and add 5 – 10mL 50% dextrose to 100 mL IV fluids to make a 2.5 – 5.0 % dextrose solution. The dose of insulin should be titrated to maintain BG between 9.0 – 12.0 mmol/L (160 – 220 mg/dl). Once the animal's response to insulin is understood, a chart can be prepared to guide the veterinarians and technicians in giving subsequent insulin doses based upon BG level. (In this protocol BG is only measured prior to each insulin dose, which reduces the number of BG measurements. This reduces cost and is advantageous in reducing the number of venipunctures if jugular catheter placement is not feasible. However, if the response to insulin is not clear or if hypoglycemia is suspected, additional BG measurements are required).

F. **Antibiotics.** Give after urine (± other) culture(s) have been obtained. Use ampicillin 20 mg/kg IV q6–8h unless other choice indicated by clinical findings.

G. **Acute Renal Failure.** *See p. 709.* **Do not use** mannitol or glucose to help promote urine formation. Urinary catheterization should be avoided if possible, especially in females, because of patient susceptibility to urinary tract infection. If oliguria is suspected (<0.3 mL/kg/h), assess by palpating the bladder or imaging with ultrasound, or if urine output must be more accurately monitored, ASEPTICALLY catheterize bladder and attach a closed collection system for the shortest time possible.

DAY 1. *"The Next Day"*

A. **Monitor** vital signs q4–8h and other parameters (e.g., ECG) as indicated.

B. **Fluids.** Continue rehydration/maintenance fluids. Continue to monitor urine production by free catch each time walked, or palpate bladder if necessary q4–8h, weight, hydration and respiration (auscultate).

Continue to balance "ins" and "outs": adjust fluids and electrolyte supplementation as indicated.

TABLE 3. Fluid Therapy in Resolving DKA crisis.

Serum Na$^+$ (mmol/L)	Fluid
<140	Normal saline
140–155	Plasma-Lyte® 148 or A, lactated Ringer's
>155	0.45% saline, 0.3% saline/3.3% dextrose,★
	Plasma-Lyte® 56,★ or Normasol M★ OR
	1:1of 5% dextrose:Plasma-Lyte® 148 OR
	:Plasma-Lyte® A OR
	:Normasol R® OR
	:lactated Ringer's

★Assuming BG being controlled – *see Glucose below.*

C. **Electrolytes.** Monitor acid-base/electrolytes q4 – 8h.

    1. **Potassium.** Adjust according to measured values. If normal urine output, the minimum supplementation to maintain normokalemia is 20 mEq/L, but up to 40 mEq/L fluids may be required (check K$^+$ already present in fluid). If hypokalemia is persisting, add 40 – 60 mEq KCl/L fluids. These doses assume MAINTENANCE fluid rate. Adjust KCl supplementation according to fluid rate to not exceed delivery of >0.5 mEq/kg/h unless animal is closely monitored and a higher delivery rate (up to 1 mEq/kg/h) is necessary due to low serum K$^+$.

    2. **Bicarbonate.** See above DAY 0 (D3); usually not necessary.

    3. **Phosphate.** See above DAY 0 (D4). This is when hypophosphatemia is most likely to occur.

D. Glucose. When BG <14 mmol/L (250 mg/dl), aseptically add glucose to fluids to make a 2.5 % or 5% solution in the bag depending on fluid rate (e.g., a 2.5% glucose solution given at twice maintenance rate = 5% solution given at maintenance).

    1. For an approximately 2.5% solution, add 50 mL 50% dextrose TO a 1L bag. For sterility purposes, fluid is not withdrawn from the bag. (In burette mix 95 mL fluids and 5 mL 50% dextrose).

    2. For an approximately 5% solution add 100 mL 50% dextrose TO a 1L bag. (In burette mix 90 mL fluids and 10 mL 50% dextrose).

    3. NOTE: When adding substances to a bag potentially requiring more than one aspiration from bulk container (i.e., using 60 mL syringe for 100 mL aspiration), NEVER touch the body of the plunger of the syringe with your hands, grasp only the distal portion. Hands contaminate the plunger that is then pushed inside the barrel.

    4. Pre-mixed solutions containing dextrose include 0.3% saline/3.3% dextrose, and Plasma-Lyte® 56 and Normasol M®, which contains 5% dextrose.

E. Insulin. Continue **Regular (Toronto) insulin** infusion/injection until ketoacidosis resolves and the patient is eating and drinking. Measure blood glucose q2–4h. Measure urine ketones and glucose whenever urine is available. (Alternatively plasma ketones may be measured when blood glucose samples are obtained). Note that blood ketone levels will not fall as rapidly as blood glucose values, and ketonuria may persist for 48 – 96 hours. Indeed, urine and plasma ketones may paradoxically rise when ketoacidosis improves, especially in cats, from conversion of β-hydroxybutyrate to acetoacetate. Judge whether increasing ketonuria/ketonemia means worsening or improving ketoacidosis on the basis of clinical signs and BG control (and, if necessary, on β-hydroxybutyrate measurements).

F. Antibiotics. Continue until infection ruled-out. Switch to oral route if animal is eating.

G. Nutrition. Offer low fat food and water as soon as patient is brighter and not vomiting.

DAYS 2 – 4. *The Next Few Days.*

A. Gradually reduce intensity of monitoring.

B. Wean off fluid therapy when patient is eating and drinking normally. Leave jugular catheter in place for BG and electrolyte monitoring.

C. Begin intermediate/long-acting insulin as soon as patient is clinically stable, maintaining hydration without fluid support, eating well, and electrolyte abnormalities have resolved. Do **not** attempt to re-regulate animal for several days to a week following resolution of DKA crisis.

SUGGESTED READING

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INTRODUCTION

Hyperadrenocorticism (HAC) is diagnosed when there is an excess of steroid hormone within the body. The excess may be due to a functional adrenal tumor (AT), occurrence 15 – 20%, or may be pituitary dependent (PDH), occurrence 80%. Any breed can develop HAC but small terriers, poodles, dachshunds, Bull and Staffordshire Terriers appear to be at greater risk for PDH. Iatrogenic HAC may occur whilst receiving exogenous corticosteroids. Dogs with naturally occurring HAC tend to be middle-aged to older and typically do not present with acute, emergent disease. However, several conditions that may be associated with HAC in the dog may cause severe, acute illness. Hypertension is recognized in greater than 50% of dogs that are tested, and can cause acute collapse, weakness, blindness (rare), or exacerbate left ventricular hypertrophy, heart failure and glomerulopathies. Steroid hormone excess can reduce the ability of neutrophils and macrophages to function, predisposing the animal to infection. Urinary tract infections causing pyelonephritis and even sepsis can cause severe disease in dogs with HAC. Dogs with HAC may present with acute respiratory distress due to pulmonary thromboembolism (PTE). PTE is rare, but has been associated with HAC in dogs. Predisposing factors for PTE include a hypercoagulable state, obesity, hypertension, increased hematocrit, prolonged recumbency and sepsis. Dogs that are medically managed for HAC using o,p'-DDD may develop iatrogenic hypoadrenocorticism and can present acutely ill. Finally, dogs that have chronic HAC may develop a secondary condition such as pancreatitis or diabetes mellitus/diabetic ketoacidosis and may present with a severe metabolic crisis (dehydrated, hypernatremic, acidemic). Pituitary or adrenal tumor hemorrhage may result in acute collapse.

DIAGNOSIS

History/Signalment

- A thorough history should verify the chronicity of the signs. Typical physical findings of HAC coupled with a long history of polyuria and polydipsia, polyphagia and weight gain, preceding a peracute onset of illness should prompt the clinician to look for underlying disease (pancreatitis, diabetic ketoacidosis, sepsis, heart failure, hypertension).
- The history will also identify those HAC dogs that may have iatrogenic hypoadrenocorticism.
- Suspicion of HAC is dependent upon a thorough history and physical examination. A definitive diagnosis can be difficult to make in some cases due to concurrent diseases such as diabetes mellitus. Sepsis and a focus of infection may be difficult to identify due to the relative lack of an inflammatory response, caused by severe glucocorticoid excess. Concurrent diseases will be diagnosed with a thorough physical examination and work-up. This protocol is designed to treat the patient that you suspect has HAC, and presented as acutely ill.

Clinical Signs/Physical Examination

- Clinical signs of uncomplicated HAC are usually chronic in nature and include polyuria and polydipsia, panting, polyphagia, cutaneous abnormalities, weight gain, weakness and lethargy.
- Physical findings may include obesity, a pendulous/enlarged abdomen, hepatomegaly, an enlarged urinary bladder, bilaterally symmetrical alopecia, weakness and muscle wasting.
- Clinical signs of **hypertension** may include acute collapse, intermittent or persistent weakness, acute blindness (with HAC rarely see detached retina or retinal hemorrhage with ophthalmological examination), epistaxis, polyuria and polydipsia, or signs of heart failure (dyspnea and coughing due to pulmonary edema, decreased breath sounds on thoracic auscultation due to pleural effusion, poor capillary refill time, cool extremities and weakness).
- **Neurological signs**, slowly progressive, associated with an expanding pituitary lesion may be evident, but are often not recognized by the owner or veterinarian. Acute collapse alone may occur with hemorrhage of an adrenal tumour or associated with neurological deficits and stupor/coma with hemorrhage of a pituitary tumor. Extensor rigidity associated with myotonia may be present.
- Clinical signs associated with **iatrogenic** hypoadrenocorticism include lethargy, anorexia, ataxia, vomiting and/or diarrhea.
- Clinical signs associated with **secondary diseases** such as sepsis, pancreatitis, diabetic ketoacidosis, hypokalemia and hypernatremia are nonspecific and are described elsewhere in this text.

- Clinical signs associated with **PTE/HAC** in some cases include a severe, acute onset of respiratory distress and orthopnea. Physical examination may reveal cyanosis and jugular pulses; a split second heart sound, during thoracic auscultation.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV** may be increased due to HAC or if dehydrated.
- **Total solids** may be increased in dehydration and if lipemia is present (common).
- **Stick BUN, urea, creatinine** may all be increased in dehydration; however, creatinine, urea and stick BUN may be normal to decreased.
- **ACT** may be <70 seconds if hypercoagulable or increased if septic.
- **Blood glucose** may be increased (common).
- **Blood gases** (arterial if dyspneic). If suspect PTE the Pa 0_2 is <80 mm/Hg and $PaCO_2$ is normal to decreased. Otherwise obtain a venous sample to assess acid-base status.
- **Electrolytes** may reveal hypernatremia (*see Hypernatremia p. 381*) and hypokalemia (*see Hypokalemia p. 394*).
- **Urinalysis** (aseptically collected) including glucose/ketones, specific gravity and culture. Urine specific gravity is typically <1.015 with HAC and can be <1.008. Infection is often present and undetected in dilute urine, culture is always recommended.
- **Blood pressure** to assess for hypertension (*see Hypertension p. 205*).
- **ECG** to assess heart rate, rhythm and chamber size.

Extended Laboratory Data Base

- Relevant tests, based on physical exam and emergency data base, to definitively diagnose underlying or associated disease.
- **Complete blood count.** Changes typical of HAC include the following: a stress leukogram (neutrophilia, lymphopenia, eosinopenia), increased hematocrit/platelets. However, these may be altered with associated illness.
- **Serum biochemical profile.** Increased ALP, lipase/amylase (to assess for pancreatitis). Increased ALT, cholesterol and blood glucose (rarely due to diabetes) may be noted.
- **ACTH stimulation test** and **dexamethasone suppression** tests are required for a definitive diagnosis of HAC. However, in critical illness responses may be altered. It is advised to treat the patient and allow a return to relative normal health prior to performing the following tests, <u>because false positive results are commonly seen.</u>

ACTH Stimulation Test

Obtain 0.5 mL plasma or serum for baseline cortisol.
For confirmation of adrenal function either of the following tests can be utilized:

1a. Synthetic ACTH (Cortrosyn®) 0.25 mg (1 ampule) IV (dogs >5 kg) or 0.125 mg IV (dogs <5 kg). Obtain 1.0 mL blood (0.5 mL serum) at 30 – 60 min. Place in serum tube.

1b. A low-dose ACTH stimulation test has been described (5 µg/kg) and is equal to the high dose protocol (250 µg/dog [0.25 mg]). In addition, reconstituted cosyntropin can be frozen and stored in plastic syringes at -20°C for up to 6 months with no adverse effects.

2. ACTH gel (Cortigel-40®) 2.2 mg/kg IM. Obtain 1.0 mL blood (require at least 0.5 mL serum) at 0 and 120 minutes. Place in a serum tube. Test should be delayed until adequate perfusion of muscle is obtained.

Either test has to be performed prior to, or at least 48 hours after, administration of prednisone, prednisolone sodium succinate or methylprednisolone sodium succinate. There is no cross-reactivity with dexamethasone however, cortisol will be suppressed in patients with an intact hypothalamic-pituitary-adrenal axis.

Normal resting cortisol is 32 – 300 nmol/L (normal published values in United States of America, non-SI Units 2 – 5 µg/dl which is considerably lower than normal values at the Ontario Veterinary College, and those published for humans. Conversion factor 27.59 from mg/dl to nmol/L). An appropriate natural stress response or a post-ACTH stimulation response would result in 400 – 600 nmol/L (7.2 – 16.3 µg/dl) or greater. An exaggerated response post-ACTH, confirming HAC, should be >600 nmol/L (>21.7 µg/dl). However, we have seen baselines much greater than normal with stimulation to >1,200 nmol/L in dogs dying of peracute, severe, septic pneumonia without evidence of HAC. Caution is required in interpretation as baseline values within normal range, and reduced response to stimulation, may be present if iatrogenic HAC (due to adrenocortical suppression).

Low-dose dexamethasone screening test (LDDST)

Collect baseline sample. Administer 0.01 mg/kg **dexamethasone sodium-phosphate** IV. Collect blood for cortisol levels 4 and 8 hours later. Cortisol values >40 nmol/L (1.5 μg/dL) at 8 hours is diagnostic for dogs with adrenal-dependent HAC (ADH) and ~ 90% of pituitary-dependent HAC (PDH). Animals with AT do not significantly suppress at 4 hours. However, associated stress may 'break' the immunosuppressive effect of dexamethasone. Suppression of cortisol to <30 nmol/L (<1.1 μg/dL) at 4 hours with a rebound escape of suppression at 8 hours, would be suggestive of PDH.

- **Chest radiographs** if dyspneic, to assess lungs and heart size. Radiographic findings of PTE may be normal; OR abnormal with: hyperlucent lung fields, alveolar infiltrates, blunting of pulmonary vasculature. (*see Pulmonary Hypertension p. 191*). Systemic hypertension (*see Systemic Hypertension p. 207*) may cause overcirculation of vasculature and pleural effusion. May see an alveolar lung pattern with pulmonary edema secondary to heart failure (*see Congestive Heart Failure p. 150*).
- **Abdominal radiographs** to assess liver size (usually enlarged with HAC), the urinary bladder and the presence of an adrenal mass (may be calcified). Dystrophic calcification may be seen in the skin, airways and great vessels.
- **Abdominal ultrasound** to further assess adrenal size, liver and the pancreas (if indicated).
- **Echocardiography** (if indicated) to further assess for chamber enlargement, pulmonary hypertension (*see Pulmonary Hypertension p. 191*) and fractional shortening.
- **Ophthalmological examination** if hypertension is suspected or blindness is present.

MANAGEMENT

Treatment is based upon the emergent disease process.
If pancreatitis (*see p. 47*), heart failure (*see p. 150*), sepsis (*see p. 588/591*), diabetic ketoacidosis (*see p. 265*), hypernatremia (*see p. 384*), or hypertension (*see p. 208*). If iatrogenic hypoadrenocorticisim is suspected, o,p'-DDD therapy should be discontinued and emergent therapy commenced (*see Hypoadrenocorticism p. 276*).

A. If dyspneic, **oxygen** supplementation should be provided, initially using flow-by, and later by nasal cannulation.

B. Place a large bore **IV catheter.**

C. **Fluids.** Administer a balanced electrolyte solution (Plasma-Lyte® 148, Normasol®R, Lactated Ringer's) at a rate based upon perfusion and hydration status (*see Fluid Therapy p. 351*). Caution is required if any respiratory or cardiovascular compromise exists.

D. **Electrolytes.** Potassium should be supplemented based upon serum potassium measurement [3.6 – 5.5 mEq/L] (*see Hypo/Hyperkalemia p. 394*). Sodium and chloride should be maintained within the normal range [Na⁺ 142 – 152 mEq/L] (*see Hypo/Hypernatremia p. 381*).

E. **Anticoagulant therapy** should be administered if **PTE** is suspected (*see Thromboembolic Disease in Dogs p. 201*).
  1. **Heparin 100 U/kg IV initially, followed by 100 U/kg/h constant rate infusion.** Measure ACT or PT/PTT within 4 hours to ensure patient is not over-heparinized, then daily. Subcutaneous administration of 250 U/kg SC q8h may be used if a CRI cannot be monitored. Therapy should be adjusted to maintain the PTT (or ACT) at 1.5 – 2 times control values or 150 – 200 seconds (ACT). The **prophylactic dose of heparin** used is half of the above therapeutic dose. After 1 – 3 days of therapy, the dog should be slowly weaned off the heparin (over 48 – 72 h) and warfarin (0.1 mg/kg PO q24h) therapy should be initiated concurrently.
  2. Low molecular weight heparin (LMWH) may have a more predictable anticoagulant effect as it only inhibits factor Xa. LMWH has not been well studied in veterinary patients, but a dosage of **dalteparin at 100 units/kg q12h** did not produce any bleeding complications in one dog study.

F. **Analgesics** (opioids: morphine 0.1 mg/kg, oxymorphone 0.02 mg/kg or methadone 0.01 mg/kg, or more, to effect).

G. **Nutritional support** (*see Nutritional Support p. 499*).

H. **Antibiotic** therapy is recommended if infection is suspected (i.e., pyelonephritis) with broad spectrum, bacteriocidal activity. This should be initiated after a urine culture has been obtained. **Cefoxitin 20 mg/kg IV q6h OR a combination of ampicillin 20 mg/kg IV q6h and enrofloxacin 5 mg/kg slowly IV q12h** are good choices. **Fluid therapy should be adjusted to correct for dehydration and provide diuresis of at least two times maintenance.** Long-term (6 – 8 wk) oral antibiotics should be initiated after the patient is eating and not vomiting.

I. Specific therapy for HAC should be considered after the acute illness has resolved and a definitive diagnosis established. *See Suggested Reading for therapy.*

PHARMACOLOGY

1) **Heparin sodium** is used as an anticoagulant for the treatment of thromboembolic disease. Bleeding and thrombocytopenia are the most severe adverse effects of the drug. The PTT/ACT should be monitored regularly (4 hours post-injection) and maintained at 1.5 – 2 times normal. The dose of heparin should be weaned gradually to prevent a rebound effect. If bleeding occurs, protamine (1 mg protamine/1 mg heparin slowly IV as 1% solution) can be used as an antidote.

2) **Warfarin sodium** is an anticoagulant that interferes with the action of vitamin K1 and prevents synthesis of the coagulation factors II, VII, IX, X. It is used for the treatment/prevention of thromboembolic disease. The primary adverse effect is hemorrhage, which is <u>not predictable</u> based upon dosage. The drug is highly protein bound and has multiple drug interactions. Warfarin therapy <u>requires extremely</u> close veterinary monitoring and owner compliance. The PT, PTT or PIVKA protein levels can be used for monitoring. Warfarin therapy should be initiated as heparin dosage is decreased to prevent a rebound coagulation effect (proteins C and S anticoagulants may be decreased).

SUGGESTED READING

1. Canine and Feline Endocrinology and Reproduction, 3rd edition, Feldman and Nelson (eds), St. Louis, MO. Saunders. 2003:358-393.
2. Clinical Medicine of the Dog & Cat, Schaer M (ed). London, Manson Publishing. 2003:388-399.
3. Veterinary Internal Medicine, 5th edition, Ettinger and Feldman (eds), Philadelphia, PA. WB Saunders. 2000:1460-1487.

NOTES

INTRODUCTION

Hypoadrenocorticism (Addison's Disease) results in reduced production of glucocorticoids and/or mineralocorticoids by the adrenal glands. Primary hypoadrenocorticism is the most common type and results from atrophy of the adrenal glands secondary to immune-mediated disease, hemorrhage, fungal, viral or bacterial disease, neoplasia, o-p-DDD toxicity, exogenous glucocorticoid administration or idiopathic causes. Secondary hypoadrenocorticism results from a pathologic condition of the anterior pituitary and reduced, or lack of, production of ACTH. With decreased ACTH production, atrophy of the adrenal glands occur. Secondary hypoadrenocorticism can be caused by the same mechanisms as primary hypoadrenocorticism. Glucocorticoid deficiency exists with both primary and secondary hypoadrenocorticism, whereas mineralocorticoid production and function may be normal with secondary hypoadrenocorticism but abnormal with primary hypoadrenocorticism. The disease is uncommon in dogs and extremely rare in cats. Although it is an uncommon disease, it is one that every veterinarian will be presented with and possibly may have difficulty diagnosing. Cortisol resistance or low cortisol levels associated with decreased adrenal response to critical illness may be a consequence of severe illness. Due to the diverse functions of glucocorticoids, clinical signs, biochemical and hematological findings can mimic several other diseases, hence hypoadrenocorticism is often referred to as the 'great pretender'.

DIAGNOSIS

History/Signalment

- A careful history should be obtained with regards to duration of illness.
- Precipitating events such as stressful situations.
- Response to any therapy that was given in the past.
- Frequency of occurrences.
- Recent history of corticosteroid withdrawal or o-p-DDD therapy.

Clinical Signs/Physical Examination

- Clinical signs vary with the severity of adrenal atrophy or dysfunction and associated lack of glucocorticoid and mineralocorticoid production.
- A chronic history of minor infections (otitis externa, pyoderma etc.), intermittent vomiting and diarrhea, anorexia, weight loss, polyuria/polydipsia, lethargy and weakness.
- Neurological signs such as shivering or seizures and coma (secondary to hypoglycemia) may be present or associated with an enlarging pituitary tumour (blindness, walking aimlessly, circling, ataxia etc.).
- Animals can present depressed and in shock, with weak pulses, frequently red mucous membranes and fast capillary refill time(CRT), as though septic, or may have a slow CRT with paler mucous membranes; **the heart rate may be normal or low which is atypical for the physical findings of shock (this is a key finding with hypoadrenocorticism)**. Hypovolemic shock, enterotoxemia and disseminated intravascular coagulation may be present in these cases.
- Bowel loops may be distended with absent gut sounds. Hemorrhagic gastroenteritis or gastric ulceration and hemorrhage can be severe in rare cases. Megaesophagus may also be present resulting in aspiration pneumonia.
- Assess hydration status (*see Fluid Therapy p. 349*).
- Although hypoadrenocorticism can present in any size and breed of dog (or cat) of any age, Standard Poodles, Great Danes, Labrador retrievers, Rottweilers, Portugese waterdogs, Nova Scotia Duck tolling retrievers, Wheaton and West Highland White terriers, and females, tend to be over represented.
- A stressed animal, such as those with severe illness as in sepsis or other debilitating, prolonged illness; mineralocorticoid function is normal in these cases.

  Because of the variable clinical signs and physical findings, the list of differential diagnoses includes:
  a) renal insufficiency/failure,
  b) hemorrhagic gastroenteritis, parvo-viral enteritis, gastrointestinal foreign body
  c) pancreatitis
  d) ethylene glycol and other toxic substance ingestion
  e) sepsis of unknown cause
  f) insulinoma
  g) primary chronic otitis externa, pyoderma and several others.
  h) intestinal parasitism (trichuriasis, salmonellosis and ancylostomiasis), fecal examination should be conducted

ACTH Stimulation Test

For confirmation of adrenal function either of the following tests can be utilized:

1) **Synthetic ACTH (Cortrosyn®) 0.25 mg (1 ampule) IV (dog) or 0.125 mg IV (cat).** Obtain 1.0 mL blood (0.5 mL serum) at 0 and 60 min (dog) and 0, 30, and 60 min (cat). Place in serum tube.

2) **ACTH gel (Cortigel-40®) 2.2 mg/kg IM.** Obtain 1.0 mL blood (require at least 0.5 mL serum) at 0 and 120 minutes (dogs), and 0, 60 and 90 minutes (cats). Place in a serum tube. Test should be delayed until adequate perfusion of muscle is obtained.

Either test has to be performed prior to, or at least 48 hours after, administration of prednisone, prednisolone sodium succinate or methylprednisolone sodium succinate. The test can be performed however, if dexamethasone sodium phosphate is administered.

Normal resting cortisol in Dogs: 32 – 300 nmol/L and **Cats:** 30 – 390 nmol/L (normal published values in United States of America, non-SI Units 2 – 5 μg/dL which is considerably lower than normal values at the Ontario Veterinary College and those published for humans Conversion factor 27.59 from μg/dL to nmol/L). Hypoadrenocortism is confirmed by baseline cortisol values commonly less than, or low, normal and post-ACTH stimulation cortisol levels frequently below or at, the baseline cortisol level. These results are obtained with both primary and secondary hypoadrenocorticism. Caution is required in interpretation as baseline values within normal range may still be abnormal for a stressed, ill patient or in the early stages of the disease. An appropriate natural stress response or a post-ACTH stimulation response would result in 400 – **600** nmol/L or greater.

Plasma Endogenous ACTH

Blood for this test must be collected before any glucocorticoids, including dexamethasone, have been administered. Collect 1.0 mL blood, place in EDTA tube and spin immediately. Place plasma in a PLASTIC TUBE NOT GLASS, and freeze immediately. ACTH levels above normal range indicates primary hypoadrenocorticism, whereas levels below normal, indicate secondary (or pituitary) hypoadrenocorticism. Normal values are 7 – 40 pg/L (less than this indicates secondary hypoadrenocorticism, greater, primary hypoadrenocorticism).

Blood aldosterone

There is no clear demarcation in blood aldosterone concentrations between dogs with primary or secondary adrenal atrophy; 146 – 519 pg/mL was reported in normal dogs.

If hypoadrenocorticism is suspected due to illness, surgery or trauma, perform resting TSH and T4 as these may also be low if the hypothalmic-pituitary axis is a probable cause of the problem.

- **CBC.** Eosinophilia and lymphocytosis may or may not be present (both may be within normal limits which is inappropriately high for a stressed animal), neutrophil count may be low, normal or above normal. Hypoadrenocorticism should be suspected when normal or elevated lymphocyte counts are present in an ill dog. Anemia may be present due to gastrointestinal blood loss or reduced red cell production, OR hemoconcentration may be present due to urinary water loss.
- **Total solids** may be increased or decreased if associated with urinary or GI blood loss, respectively.
- **Serum Electrolytes** may be normal in the early stage of disease or if secondary hypoadrenocorticism. Potassium may be high normal and sodium low normal, chloride also may be normal or increased; sodium/potassium may be <27. Due to aldosterone deficiency potassium may be extremely high (>8 mEq/L) and sodium may be very low. ADH secretion and water retention will contribute to sodium dilution in hypovolemic states.
- **Venous Blood Gases.** Acidemia is usually present due to poor perfusion or retention of hydrogen ion.
- **BUN, Urea and Creatinine** may be mildly to moderately increased due to volume contraction, reduced renal perfusion and glomerular filtration rate. This is pre-renal azotemia; there is no primary renal pathology. Serum urea and BUN may be extremely high and does not correlate with serum creatinine measurements.
- **Blood Glucose.** Hypoglycemia may be present due to reduced gluconeogenesis and glycogenesis.
- **Serum Calcium.** Hypercalcemia may be present due to dehydration or decreased affect of corticosteroid mediated calcium metabolism.
- **Urinalysis.** Isosthenuria or hyposthenuria is usually present due to sodium diuresis and reduced medullary concentration gradient. Renal casts or tubular epithelial cells may be present due to acute ischemic necrosis. There is no primary renal pathology, this is due to pre-renal causes.
- **ECG.** Bradycardia, peaked T-wave, heart block, atrial standstill, widened QRS complex, reduced R wave.

- **Abdominal Radiographs.** Dilated loops of bowel due to ileus or enteritis. Glucocorticoids influence gastric and intestinal motility through their inhibitory action on CRH production. Increased CRH inhibits release of motilin a hormone responsible for the initiation of the migrating contractions.
- **Chest Radiographs.** If taken may show microcardia, narrow vena cava and dark lung fields (reduced vascular pattern) due to hypovolemia. Dilated esophagus may be evident (aperistaltic esophageal dilation) a possible mechanism may be similar to ileus described above.
- **Fecal analysis.** The presence of trichuriasis, salmonellosis and ancylostomiasis is likely the cause of the presenting signs.
- **Systemic blood pressure & ECG. Hypotension and/or bradycardia** potentially due to lack of glucocorticoid effects on blood pressure modulation and cardiac adrenergic receptor function.

MANAGEMENT

Management will depend on the clinical findings. Only treatment for Addisonian crisis will be outlined.

A. MOST IMPORTANT, fluid resuscitation is aimed at restoring intravascular volume, increasing renal perfusion and lowering serum potassium.

For smaller animals place a burette in line to avoid fluid overdose. Commence fluid therapy, Plasma-Lyte®-148, Normasol® at 20 – 90+ mL/kg/h is the author's preference. Initially, the lower rate should be considered for extremely dehydrated, bradycardic animals, especially those with underlying cardiac disease, to ascertain their tolerance of high fluid rate. Tachypnea, worsening of bradycardia or tachycardia, pulmonary crackles, general decline or rapid increase in CVP, indicates too rapid infusion. If tolerated after 10 minutes, the fluid rate may be increased until the CVP has increased >4 cm H_2O above baseline with a slow decline, or up to 90 mL/kg/h (higher if needed). A reduction in fluid rate will depend on response to the higher rate; intolerance or improvement. In almost all instances, rapid fluid administration results in marked improvement of clinical signs, reduction in serum potassium and resolution of cardiac arrhythmias.

B. If shock due to acute gastric or duodenal hemorrhage:

1. **Whole blood transfusion is necessary.** While crystalloids are administered, commence blood transfusion. Calculate volume required to raise PCV to ~ 30% (*see Transfusion of Blood Products p. 667*). Synthetic hemoglobin products may be used as an alternative to blood (*see Hemorrhage p. 625*). **Do not raise mean arterial pressure above 70 mmHg or systolic pressure above 90 – 100 mmHg until hemorrhage has stopped.**

2. **1 – 2 g sucralfate** (1 or 2 tablets pulverized with water or 5 – 10 mL suspension – preferred)/**small to large dog and 0.5 g per cat PO as soon as possible. Repeat at half the dose q1h for 3 treatments,** tapering off to q4h then q8h for 7 days. There are **NO** concerns for overdose.

3. **Famotidine 0.5 mg/kg IV (dogs), SC (cats) q12h, or pantoprazole 1 mg/kg IV, maximum of 30 mg, q24h.** Require new vial each time as only stable for 6 hours.

C. After establishment of fluid therapy, assess **cardiac arrhythmias**, usually bradycardia or ventricular tachycardia associated with hyperkalemia.

1. **Life-threatening bradycardia,** escape beats only (rate < 40/min) which is usually associated with potassium > 8 mEq/L. To protect the myocardium against the deleterious effects of hyperkalemia, administer, **with continuous ECG monitoring, calcium gluconate 0.5 – 1.0 mL/kg of 10% over 2 – 5 min.** The infusion should be stopped if the heart rate decreases further or if a new arrhythmia is encountered. Do not use if hypercalcemic. This therapy is rarely required and will not lower potassium but will buy a ~ 20 minutes until a reduction in serum potassium can be achieved by performing (i or ii below) or (D) below. <u>NOTE</u>: **Early stages of hyperkalemia result in tachycardia.**

2. **If serum potassium > 8 mEq/L, with clinical signs,** reduce by administration of
   i. **50% dextrose 1.0 – 2.0 mL/kg, dilute with 0.9% sodium chloride, IV slow bolus, OR**
   ii. **2 g dextrose (4 mL of 50% dextrose) per Unit Regular insulin (0.25 – 0.5 U/kg) IV followed by 2.5% dextrose (50 mL of 50% dextrose/L fluids) CRI.**

D. If moderate to severely **acidemia** (venous pH <7.2 or base deficit > -12), if HCO_3^- or total CO_2 <12 mmol/L (**Note**: total CO_2 may be low if tubes are transported or allowed to sit open prior to test) and hyperkalemic with cardiac arrhythmias, **HCO_3^- therapy** may be an alternative treatment to dextrose for intracellular translocation of potassium. Administer IV **$NaHCO_3$ 0.5 – 1.0 mEq/kg, half over 5 minutes, reassess, continue with the remainder over 30 – 60 min, OR calculate dose, $NaHCO_3$ = [BW (kg) x base deficit] x 0.2 OR, = [BW (kg) x (12- patient's HCO_3^-)] x 0.3 and administer as above**. This will raise the HCO_3^- to -12 (base deficit of 12). Alkalinizing solutions and rapid volume resuscitation usually correct the acidemia.

E. If **hypoglycemic** administer up to **1 mL/kg 50% dextrose** diluted with **1 – 2 mL/kg 0.9%** sodium chloride or administer as a slow push, high in the IV line to dilute it, then add **50 mL of 50% dextrose** to each litre of fluids (2.5% solution). Measure q8–12h initially to avoid hyperglycemia.

F. Place a urinary catheter, measure urine volume, specific gravity and examine sediment.

G. Assess response to therapy by q5min examination of pulse pressure and rate, blood pressure, capillary refill time, mentation, urine output. As these parameters normalize (MAP > 70 mmHg, systolic pressure > 100 mm Hg, CRT <2 sec, improved mentation, urine production >1.0 mL/kg/h) reduce fluid rate to 20 – 30 mL/kg/h. Continue to monitor, improvement may be temporary and an increase in fluid rate may be required. The high fluid rate may be necessary for longer than one hour due to vasodilation and dehydration.

H. **Glucocorticoid** therapy should be administered after aggressive fluid resuscitation. If the ACTH test is planned **dexamethasone sodium phosphate 0.1 – 2.0 mg/kg IV** should be administered then **0.05 – 0.1 mg/kg q12h**. Alternatively **prednisolone sodium succinate at 2 – 5 mg/kg IV**, (preferred for its glucocorticoid and mineralocorticoid effects) over 20 minutes OR **methylprednisolone 2 – 5 mg/kg IV (if mineralocorticoid therapy is not required**) administered over 20 minutes. Depending on severity, lower dosages with repeat to effect is recommended. Repeat at half the initial dose in 6 hours, or sooner, if necessary. After stabilization decrease to 1 mg/kg q12h for 48 hours and reduce to 0.25 mg/kg daily. **Hydrocortisone sodium succinate 1.25 mg/kg IV, then 0.5 – 1.0 mg/kg IV q8h**, to be administered over 20 minutes, is recommended for critical illness associated hypoadrenocorticism in human patients which may also be beneficial in dogs and cats. Alternatively **prednisolone sodium succinate 0.5 – 1.0 mg/kg IV, then 0.25 mg/kg q12–24h until recovered**, with a reducing dose over 2 weeks.

I. **Mineralocorticoid** supplementation (primary Addisonion only), both **immediate and long term therapy, with desoxycorticosterone pivalate (DOCP) 2.2 mg/kg by IM injection every 25 – 30 days is an alternative to fludrocortisone acetate 0.01–0.02 mg/kg PO, divided q12h** administration when vomiting ceases. Serum electrolytes should be measured every 12 – 25 days after each of the first two or three DOCP injections. The next dose should be increased by 10% should the patient still be hyponatremic or hypokalemic. Reduction is also required should the electrolytes be increased. The treatment dosing and dosing interval has to be titrated to the patient's needs, therefore, monitoring is essential for both DOCP and fludrocortisone acetate, where the dose can be very variable and higher than the initial recommendation.

J. **Once the patient is stabilized**, reassess hydration. The remainder of the deficit (or corrected deficit), in addition to normal maintenance volume and increased urinary losses (at least 3 – 5 mL/kg/h), should be delivered over 24 – 48 hours. Urine output should gradually increase over this period of time to at least 1 – 2 mL/kg/h.

K. If urine output is not established after aggressive , and more than adequate, fluid resuscitation, administer **furosemide 2 mg/kg**. This is rarely required. Furosemide should result in diuresis within 30 minutes and will also lower serum potassium (*see Acute Renal Failure p. 713*).

L. Prognosis is good to excellent with **chronic fludrocortisone therapy 0.01 – 0.02 mg/kg divided q12h,** or DOCP (I. above) and physiological doses (0.25 mg/kg) of glucocorticoid (prednisone) daily or on alternate days. Increase glucocorticoid therapy by 2 – 10 times the maintenance physiological dose during times of stress. Re-check visits at 2 weeks then 1 – 3 months. Fludrocortisone has glucocorticoid activity therefore additional glucocorticoid may not be required.

PHARMACOLOGY

1) **Fludrocortisone acetate (Florinef®Acetate, SquibbMark)** is a potent corticosteroid with both glucocorticoid and significant mineralocorticoid activity. It is approximately 10 – 15 times as potent a glucocorticoid agent as hydrocortisone but 125 more potent as a mineralocorticoid.

2) **Hydrocortisone sodium succinate** also known as cortisol, is secreted by the adrenal gland and has both glucocorticoid and mineralocorticoid activity. It has a relative anti-inflammatory potency of 1. Duration of action <12h.

3) **Prednisolone sodium succinate (Solu-delta-cortef®, Upjohn)** is a synthetic glucocorticoid with some mineralocorticoid activity. It has a relative anti-inflammatory potency of 4. Duration of action 12 – 36h.

4) **Methylprednisolone sodium phosphate (Solu-medrol®, Upjohn)** is a synthetic glucocorticoid with no mineralocorticoid activity. It has a relative anti-inflammatory potency of 5. Duration of action 12 – 36h.

5) **Dexamethasone sodium phosphate** is a synthetic glucocorticoid with no mineralocorticoid activity. It has a relative anti-inflammatory potency of 30 with a duration of action >48h.

SUGGESTED READING

1. Bollaert PE et al. Reversal of late septic shock with supraphysiologic doses of hydrocortisone. Crit Care Med 1998; 26(4):645-650.
2. Briegel et al. Low-dose hydrocortisone infusion attenuates the systemic inflammatory response syndrome. The Clinical Investigator. 1994; 72:782-787.
3. Endocrine disorders: In small animal Internal Medicine, Nelson & Couto (eds) St. Louis, Mosby, 2003:804-809.
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   *In a select population of human patients, glucocorticoid deficiency may be associated with acute illness such as post-surgery, trauma or sepsis.
5. Meduri U. Steroid therapy in sepsis: Septic shock – new understanding in the relationship between exaggerated host defense response and endogenous glucocorticoid function. 27th Society Critical care Medicine Educational and Science Symposium Proceedings, San Antonio Texas. 1998:152.
6. Merry WH et al. Postoperative acute adrenal failure caused by transient corticotropin deficiency. Surgery. 1994; 116:1095-1100.

NOTES

INTRODUCTION

The hyperglycemic hyperosmolar syndrome (HHS) is a differential diagnosis for DKA in a sick diabetic animal. It is characterized by marked dehydration (potentially associated with hypovolemic shock), absence of ketoacidosis based on urine test strip measurement, blood glucose >33 mmol/L (600 mg/dl), and serum osmolality > 350 mOsm/kg, or effective serum osmolality >330 mOsm/kg in cats, and slightly less than this in dogs (*see DKA p. 263*). (Effective serum osmolality in humans is >320 mOsm/L. Dogs may fall between cats and humans). The HHS is less common than DKA. The pathogenesis of HHS is similar to DKA, but it appears that there is sufficient insulin to block lipolysis but insufficient to control hyperglycemia. The most common concurrent disease, which likely contributes to development of HHS, is chronic renal failure; other common concurrent diseases are infection, heart failure, neoplasia, and gastrointestinal tract disorders. These disorders are more common in HHS than DKA. Pancreatitis and liver diseases, however, appear to be less common in HHS than DKA in cats.

The prognosis for HHS is worse than for DKA. In one case series of cats, 35% survived hospitalization and long-term survival was 12%. Prognostic factors are not known.

DIAGNOSIS

History/Signalment

- More common in cats than in dogs.
- Compared to DKA:
    - Animals tend to be **older** and to have a **history of treated diabetes.**
    - There is a longer pre-critical course with insidious signs, but a **shorter course** of critical illness.
    - There is a history of **chronic renal failure** in over half the cases.

Clinical Signs/Physical Examination

- Physical examination findings are similar to DKA, except that icterus is uncommon, there is no acetone odour, and **neurologic signs are more common** (because of cerebral dehydration). Neurologic signs include stupor, coma, seizures, and cranial nerve deficits.

Laboratory Evaluation/Diagnostic Imaging

- The work-up for HHS is similar to DKA. In contrast to DKA:
    - By definition **urine ketones on a urine test strip are negative.** Serum ketones have not been well-evaluated in HHS in animals.
    - Serum **urea and creatinine** levels are more elevated. This is frequently due to renal failure. Dehydration is also a contributing factor.
    - **Hyperphosphatemia** is commonly present in cats, whereas most animals with DKA have normal or low serum phosphate values.
    - Cats tend to have **normal K⁺.**
    - **Lactate** levels tend to be higher in HHS contributing to acidosis, whereas the ketones in DKA contribute to acidosis. Acidosis in HHS may also be due to respiratory acidosis and uremia.

MANAGEMENT

A. The treatment regimen for HHS is similar to that of DKA except that the insulin requirements are usually less as animals with HHS are more sensitive to exogenous insulin therapy.
   1. Animals are at a greater risk for cerebral edema resulting from too rapid a lowering of serum osmolality. Calculate fluid deficit and correct dehydration over 24 – 48 hours; however shock must be corrected rapidly but with careful monitoring (*see DKA p. 265*).
   2. Reassess mentation, electrolytes and blood glucose after 2 hours. Reduce fluid rate if patient is brighter and urinary bladder is filling; reassess these parameters again at 4 hours.
   3. Initiate insulin at this time (i.e., at 4 hours) (*follow instructions as for DKA p. 267*) except halve the dose.

SUGGESTED READING
1. Koenig A, Drobatz KJ, Beale AB, King LG. Hyperglycemic, hyperosmolar syndrome in feline diabetes: 17 cases (1995-2001). J Vet Emerg Crit Care 2004;14:30-41.

INTRODUCTION

Hypoglycemia is defined as a blood glucose less than 3.5 mmol/L (65 mg/dL). Insulin is responsible for glucose uptake and utilization while inhibiting gluconeogenesis and glycogenolysis. Hypoglycemia normally inhibits insulin secretion and is a potent stimulus for the release of epinephrine, cortisol, glucagon and growth hormone, which antagonize insulin. In addition, these hormones act together to raise blood glucose levels. Some of the clinical manifestations of hypoglycemia are related to the actions of these hormones (see clinical signs below). Overall, glucose homeostasis is dependent on multiple factors making it important to recognize that hypoglycemia is indicative of an underlying disease process (*see algorithm*). Hypoglycemia may be detected incidentally while investigating other illnesses or as a primary presentation for signs associated with hypoglycemia. Clinical signs are dependent on the rate of decline of serum glucose concentration, and are most commonly related to the nervous system. These signs may be precipitated by an incident requiring an increase in glucose requirements (exercise, or excitement), or during fasting (i.e., an excess of insulin is administered to a diabetic, or in a patient with an insulinoma). The brain is an obligate consumer of glucose. Other cells in the body prefer to use glucose, but unlike the brain they can use ketone bodies or fatty acids in hypoglycemic states. The most sensitive area of the nervous system is the cerebral cortex and cerebellum resulting in the clinical signs described below. The least sensitive area of the nervous system is the peripheral nerves but note that prolonged hypoglycemia can lead to peripheral nerve demyelination and axonal degeneration and subsequent clinical signs consistent with a polyneuropathy. The most severe consequences of hypoglycemia relate to potential irreversible brain injury or DIC related to seizure-induced hyperthermia.

Fasting/Malnutrition in the normal ADULT dog or cat RARELY if ever causes hypoglycemia, therefore an underlying cause must be identified (*see algorithm*). Malabsorptive conditions alone do not result in sufficient nutrient loss to cause hypoglycemia.

Severe hypoglycemia, collapse, and seizures can occur after consuming a large quantity of sugar-free gum sweetened with the sugar-alcohol xylitol. In humans, xylitol has little to no effect on plasma insulin or glucose levels, but in dogs xylitol is a strong promoter of insulin release and can cause severe hypoglycemia with ataxia, collapse and seizures. With the increased appearance of xylitol-sweetened products in the US, xylitol toxicosis in dogs may become more common.

DIAGNOSIS

History/Signalment

- A thorough history is essential due to the long list of differentials (*see algorithm*).
- Question the owner regarding insulin administration. Insulin overdose is based on coincidental historical information regarding clinical signs and insulin injection, recent insulin dose change, insulin bottle almost empty (i.e., insulin potentially concentrated if poor mixing techniques occurred).
- Consider history of declining insulin needs in a cat (possible transient diabetes).
- Inquire about a change in concurrent steroid therapy, or concurrently treating for hyperadrenocorticism.
- Insulin given despite poor appetite or anorexia due to concurrent illness can cause hypoglycemia.
- Neonates have immature regulatory mechanisms and are at risk for hypoglycemia.

Clinical Signs/Physical Examination

- A rapid fall in blood glucose concentration leads to adrenergic manifestations of hypoglycemia .
  - **Dilated pupils, tachycardia, tremors, nervousness, vocalization and intense hunger.**
- With a slower onset of hypoglycemia the patient presents with neuroglucopenic signs.
  - **Hypothermia, visual impairment, weakness, ataxia, mental dullness or depression, bizarre behaviour, seizures and bradycardia.** If not treated, these signs will progress to
- Life threatening signs:
  - **Decerebrate rigidity, miotic pupils, loss of spinal reflexes and coma.**
- Overall the most common presenting clinical signs in an animal with hypoglycemia are behavioural changes, seizures and coma.

Physical Examination

See algorithm for details based on history and signalment.

Laboratory Evaluation/Diagnostic Imaging

- **Blood or serum glucose <3.5** mmol/L (65 mg/dL).
- Confirm that hypoglycemia is not a laboratory error. The most common causes for laboratory error are:
    - Allowing the blood sample to sit for a prolonged period of time before separating the serum as blood cells consume glucose.
    - A profound leukocytosis or polycythemia, inappropriate handling will increase this possibility.
    - Correct handling/processing of the blood sample should result in an accurate blood glucose determination. If laboratory error is a possibility, collect blood in a Sodium Fluoride (gray-top) tube.
    - If normal on glucometer but low on laboratory analysis, consider discordant test results due to
        - ◆ potential technical problems (equipment, supplies, sampling time)
        - ◆ polycythemia or severe leukocytosis.
- If glucose is not as low as expected based on history (i.e., seizures), consider:
    - increase in glucose secondary to hypoglycemia-induced epinephrine surge.
    - intermittent episodes of hypoglycemia and glucose is not low at this time; consider a period of supervised fasting to document hypoglycemia in this case.
- Recent seizure activity in small breed dogs may result in hypoglycemia rather than seizures being a consequence of hypoglycemia. The difference must be identified.
- See algorithm for specific laboratory tests based on history and physical findings.
- A complete hematologic and biochemial evaluation should be performed in comatose, severely mentally altered or depressed animals. See algorithm for interpretation of lab results together with history and physical examination.

Extended Laboratory Data Base/Diagnostic Imaging

- Additional diagnostic testing will depend on the index of suspicion for the cause of hypoglycemia. Please refer to other chapters for definitive diagnosis and treatment.
- Collect serum insulin levels (serum – red top tube) while the patient is hypoglycemic to diagnose insulinoma. During a hypoglycemic crisis the insulin level should be extremely low; therefore, demonstration of a normal or increased insulin level in a hypoglycemic patient is consistent with a diagnosis of insulinoma.
- Abdominal ultrasound can be used to look for masses within the pancreas and potential metastasis. Both limbs of the pancreas should be evaluated and a standing abdominal ultrasound may be necessary to accomplish this (personal communication Dr. Nykamp). Consider surgical exploration for mass removal if index of suspicion is high.

MANAGEMENT

A. **50% Karo/Corn syrup** on the gums if no IV access available (neonate 0.25 – 0.625 mL/62 g or ounce body weight.) or if owner calls from home. Do not advise an owner to administer oral dextrose solutions to seizuring animals.

B. Obtain IV (peripheral or central), or intraosseous access (neonate/pediatric). NOTE: Never administer dextrose subcutaneously as this will likely cause cellulitis and sloughing of the skin.

C. **Dextrose bolus.** 50% dextrose (50 g/100 mL) administer 0.5 g/kg (0.5 mL of 50%/kg) ALWAYS diluted 1:4 with normal saline.

   1. Bolus is given during a seizure only until the seizure stops (*see Seizures Cat p. 456, Dog p. 460*).
   2. Patients with an insulinoma, do not induce hyperglycemia as this can lead to refractory hypoglycemia secondary to further insulin release (***see E below if known insulinoma***).

D. **Establish a CRI of 2.5 – 5.0% dextrose** (50 – 100 mL/L of 50% dextrose), or 7.5 – 10% (150 – 200 mL/L) if needed through a central line if available as this is very hyperosmolar.

   1. Dextrose CRI's should be given to maintain a blood glucose level so that clinical signs of hypoglycemia are not apparent.
   2. Maintain blood/serum glucose levels within normal range.

HYPOGLYCEMIA –
BLOOD GLUCOSE (BG) <3.5 mmol/L

NEONATE *
History of stressful precipitating event such as, hypothermia, hypoxia, diarrhea, dehydration, ineffective nursing, premature or low birth weight, septicemia, viremia, parasite burden etc., can cause hypoglycemia

PE: Neuroglycopenic signs since there is not an epinephrine surge leading to adrenergic signs i.e., weakness, ataxia, paresis, seizures, depression to moribund

BG <1.8 mmolL in newborn
BG <2.5 mmol/L 14d → 6 mo

See Chapter 83/109

*Consider Toy Breed Hypoglycemia or Glycogen Storage Disease (GSD) if sick neonate or juvenile patient

GSD Breeds
Cats :
Norwegian Forest cat
Persian

Dogs:
English Springer Spaniel
German Shepherd
Lapland Terrier
Maltese Terrier

HISTORY OF DIABETES MELLITUS OR
History of owner with Diabetes and oral hypoglycemic medications in the house – consider sulfonylurea induced hypoglycemia if any chance of pill consumption
Toxin Effect*

PE: Weakness, ataxia, moderate to severe depression, seizures

Consider **INSULIN OVERDOSE** or Transient Diabetes in Cats (Non-Insulin Dependent Diabetes)

See Management

CONSIDERATIONS
- Do not administer insulin until animal has been tapered off the dextrose CRI and is persistently hyperglycemic
- Re-institute Insulin at 50% of the original dose at least

*TOXIN
- Note excessive consumption of xylitol in dogs can cause life threatening hypoglycemia
- Xylitol is commonly found in chewing gum

History of previous chemotherapy, severe vomiting, diarrhea, abdominal pain, cough, difficulty breathing, depression, lethargy, inappetence or any other systemic signs

PE: Fever, injected mucus membranes and sclera, hypotension and tachycardia, tachypnea. Evidence of underlying infection (i.e., pyometra, pancreatitis, pneumonia, prostatitis, peritonitis)

Lab: Neutrophilia +/- left shift, neutropenia, toxic neutrophils, non-regenerative anemia

Consider **SEPSIS**
See Chapter 86

History includes **hunting dog** breed, lean & high strung
History of exercise

PE: Weakness, trembling, ataxia, collapse

Consider **Hunting Dog Syndrome** – Minimal Information on pathophysiology

CONSIDERATIONS
- Client Education is Key – cautious exercise and carry Karo/Corn Syrup on long walks
- Watch for early signs such as confusion and weakness
- Consider hypoadrenocorticism as a primary ruleout

History of poor growth, poor doer, PUPD, vomiting, diarrhea, pica. Clinical signs of hypoglycemia noted in between meals and/or association of neurological signs after a meal

PE: Variable concurrent neurological signs: Star gazing, head pressing, circling, drooling (especially cats). Thin, abnormal growth.

Lab: CBC: Microcytic anemia +/- thrombocytosis
Chemistry: Low urea, low albumin, low cholesterol, increased liver enzymes
U/A: ammonium biurate crystals low USG

CONGENITAL/ACQUIRED PSS
End Stage Liver disease/Acute severe hepatic necrosis
(**see Hepatic Failure** p. 37)

See General Therapy Guidelines
• Feed small frequent meals as long as not showing signs of HepaticEncephalopathy p. 38

Consider **ENCEPHALOPATHY**

1. Pre and Post Bile Acids
2. Resting/Fasting Ammonia level elevation
3. Radiographs: microhepatica, and/or renomegaly, ascites (rare with congenital PSS)
4. Abdominal Ultrasound looking for microhepatica, an anomalous vessel/s, renomegaly, urate stones/crystals in the bladder or evidence of severe liver architecture abnormalities associated with end stage liver disease

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History: exercise intolerance, weakness, bizarre behaviour including personality change i.e., aggression, muscle tremors, seizures, polyphagia or weight gain. Clinical signs of hypoglycemia noted during exercise, excitement or after a meal
Middle age to older dog/cat

PE: generalized weakness, may see mild conscious proprioceptive deficits +/- facial nerve paralysis, +/- peripheral polyneuropathy (rare)

Consider **INSULINOMA**

See Management
BE AWARE OF INDUCING REFRACTORY HYPOGLYCEMIA WITH DEXTROSE THERAPY
Note: many of these dogs have adjusted to a blood glucose level or 20 – 30 mg/dl (1.0 – 2.0 mmol/L with few to no clinical signs

CONSIDERATIONS
1. Obtain a Red Top Tube for a Serum Insulin Level when hypoglycemia is documented
2. Consider abdominal Ultrasound to look for a mass in the pancreas +/- abdominal exploratory if index of suspicion is high (ideal therapy is surgical removal/debulking of tumor
3. Note hyperglycemia and potentially DKA can develop post surgery
4. Additional medical management includes prednisone, diazoxide and /or somatostatin
5. Chemotherpeutic options include streptomomycin (toxic)

History of: waxing and waning illness especially during times of stress
• Chronic intermittent diarrhea and vomiting including hemorrhagic gastroenteritis like episodes
• PUPD, weight loss,
• Great Dane, Black Female Std Poodle, Soft Coated Wheaton

PE: Shocky/severe hypotension with bradycardia,
Weakness, muscle tremors, severe hemorrhagic diarrhea, thin, vague abdominal pain

Lab: CBC – mild anemia, lack of stress leukogram +/- lymphocytosis and/or eosinophilia
Chemistry – increased potassium, low sodium +/- hypercalcemia,+/- low albumin

Consider **HYPOADRENOCORTICISM**

• Note electrolytes can be normal in pure glucocorticoid deficiency
• Treat with Dexamethasone and not Prednisone if ACTH stimulation has not been performed yet
See Chapter 43

1. Note other tumors can cause hypoglycemia due to the production of insulin like growth factors
2. Numerous tumors have been reported to cause a **PARANEOPLASTIC** hypoglycemia for e.g.,
• Hepatoma, Fibrosarcoma
• Leiomyoma – older dog with a microcytic anemia and melena +/- palpable abdominal mass

E. Glucagon may be required for refractory hypoglycemia seen with insulinomas. A glucagon continuous rate infusion may also be considered in a patient with insulinoma that presents with severe neurologic signs where it is imperative not to risk a possible rebound hypoglycemia and additional seizure activity, or when neurologic signs do not improve despite euglycemia after dextrose administration.

1. The 1 mg glucagon vial is reconstituted as directed by the manufacturer with diluent provided. A bolus of 50 ng/kg prior to infusion is recommended by some.
2. Glucagon infusion is prepared by adding reconstituted glucagon to 1 L of 0.9% NaCl (a final concentration of solution is 1000 ng/mL) and administered as a CRI of 5 – 15 ng/kg/min but may need to increase up to 40 ng/kg/min.

F. If glucagon is not available then concentrations of dextrose higher than 10% can be given through a central line.

G. Blood glucose should be measured repeatedly initially to ensure euglycemia is established.

1. Patients with (or suspect) an insulinoma can maintain low normal or slightly lower blood glucose levels as significant clinical improvement is usually present at these levels which prevent an insulin surge and subsequent worsening of clinical signs.
2. Once an acceptable blood glucose level is established then glucose should be measured every 2 – 6 hours depending on the clinical situation.

H. Small but frequent meals are recommended to maintain euglycemia prior to weaning off dextrose infusion.

1. For patients with an **insulinoma,** or other insulin-like peptide secreting tumor, small frequent meals rich in protein and complex carbohydrates should be offered to avoid sudden spikes in blood glucose from simple sugars.
2. **Additional treatment** may involve prednisone, surgery or diazoxide or chemotherapeutic agents.
3. **Neonates, toy breeds or liver disorders** also require small frequent meals however protein content should be moderate to low so as to not stimulate a hepatic encephalopathic crisis in liver failure/PSS patients.

I. Always treat the underlying cause if identified (*see appropriate chapters*).

1. **Hypoadrenocorticism,** or Lysodren overdose. Prednisone administration will be required (*see p. 277*).
2. **Hunting Dog Syndrome** – avoid strenuous exercise, carry corn syrup if going on long walks and monitor dog closely during exercise.
3. **Diabetic – Insulin Overdose.** It may take up to THREE days for hyperglycemia to redevelop. Insulin dose should be dropped by 50% or more once hyperglycemia recurs.
4. Glycogen storage disease – Based on Breed and Age. No specific treatment for underlying disease. Testing available at PennGenn: www.vet.upenn.edu/penngen.
   a. Owner's may need to monitor urine glucose on glucose strips at home frequently if insulin requirements are changing, especially in the cat. **Purina® Glucotest™ brand Feline Urinary Glucose Detection System** may be a helpful tool for estimating overall glucosuria trends.

PHARMACOLOGY

1) **Glucagon** is an unbranched chain of 29 amino acids. Glucagon functions to directly oppose insulin, increases glycogenolysis and gluconeogenesis.
2) **Glucose** should be stored in the fridge and the date the bottle is opened should be noted. Wipe the injection port with alcohol prior to use. Do not re-insert needle if it has contacted a patient directly.

SUGGESTED READING

1. Fisher JR, Smith SA, Harkin KR, Glucagon Constant Rate Infusion: A Novel Strategy for the Management of Hyperinsulinemic-Hypoglycemic Crisis in the Dog. J Am Anim Hosp Assoc 2000;(1); 36:27-32.
2. Howerton TL and Shell LG: Neurologic Manifestation of Altered Serum Glucose. Progress in Veterinary Neurology 1992; Vol 3 (2):57-64.
3. Walters PC and Drobatz KJ: Hypoglycemia. Compend Contin Educ Prac Vet. 1992;14 (9):1150-1158.

INTRODUCTION

Hypothyroidism is primarily a dog's disease and will rarely present as an emergency situation. Thyroid hormone can be thought of as a fuel that supplies each cell in the body, and a lack of this hormone causes an overall decrease in metabolism. Hypothyroidism is most often a primary disease caused by an immune-mediated destruction of the gland or caused by idiopathic atrophy of the gland. Other causes of hypothyroidism are rare, but may include neoplastic destruction of the gland or secondary disease due to a lack of thyroid stimulating hormone (TSH). Primary hypothyroidism is most commonly seen in the middle-aged to older dog, and is often recognized in Labrador and Golden retrievers, Cocker Spaniels, and Doberman Pinschers. Clinical signs are slow to develop and are typically not emergent. Several conditions that may present as emergencies include neuromuscular problems (ataxia, weakness, circling, vestibular signs, seizures), cardiovascular problems (bradycardia, arrhythmias), and myxedema coma. Myxedema develops when there is an accumulation of mucopolysaccharides and hyaluronic acid in the dermis, and may be seen in cases of severe hypothyroidism. A cause and effect relationship between laryngeal paralysis and megaesophagus has not been documented. This chapter is directed towards treating the dog with severe signs of hypothyroidism.

DIAGNOSIS

History/Signalment

- Since most dogs are mid-age when they develop hypothyroidism, and signs are slow to develop, many owners attribute changes seen with hypothyroidism to aging.
- History will likely include depression, dullness, lethargy and exercise intolerance. Owners may have noticed changes in the hair coat including alopecia, thinning of the hair, dullness of the hair coat and dryness of the skin.
- Most hypothyroid dogs will maintain a good appetite and will have gained weight.
- Difficulty reported during defecation may be due to constipation.
- Anestrus may be recognized in the intact female.
- Vomiting/diarrhea and polyuria and polydipsia are not typical of a hypothyroid dog, but may be seen with concurrent diseases.

Clinical Signs/Physical Examination

- The typical hypothyroid dog will be overweight, lethargic and have a poor hair coat.
- With more advanced disease, clinical signs include severe mental dullness, depression, weakness, hypothermia, hypoventilation and bradycardia.
- With severe disease the following may be present:
    - hypothermia
    - bradycardia (or other arrhythmias)
    - weak apex beat
    - stupor and even coma may be present
- Alopecia may be bilaterally symmetrical or diffuse, or may only involve the tail ("rat tail"). There may be a secondary pyoderma, but typically, the dog is not pruritic. With myxedema the skin will be thickened, especially over the face and forehead, causing the eyelids to droop ("tragic expression"). A non-pitting edema will be appreciated.
- The most common neuromuscular sign is weakness. Other signs may include facial nerve paralysis, vestibular disease, ataxia, knuckling or circling. Seizures and coma are rare.
- Signs such as hyperemia and chemosis of the conjunctiva, and blepharospasm and/or ocular discharge should alert the clinician to ocular lesions. Occular manifestations of severe hypothyroidism may be emergent and can include uveitis (± glaucoma), or corneal ulceration secondary to corneal lipid accumulation.
- Rectal examination and abdominal palpation may reveal large amounts of feces within the colon, due to constipation.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, TS, stick BUN** to obtain a baseline and assess hydration status.
- **Electrolytes, body weight and blood glucose**, as baseline prior to treatment/fluid therapy. Some dogs with myxedema coma may have hyponatremia and hypoglycemia.
- **Arterial blood gas**, if myxedema coma, may have hypoxemia and hypercarbia due to hypoventilation. Venous blood gases are also appropriate for carbon dioxide measurements.
- **Neurological examination** to localize abnormalities and baseline for trending purposes.
- **Ophthalmological examination** to identify corneal ulceration, uveitis or glaucoma that may occur with hypothyroidism.
- **ECG** may document arrhythmias, first or second degree heart block, decreased amplitude of the P and R waves, bradycardia or chamber enlargement.

Extended Laboratory/Imaging Database

- **CBC** may show a mild normocytic, normochromic non-regenerative anemia. Target cells may also be present due to hypercholesterolemia. White blood cell count and platelet count are usually normal.
- **Biochemical profile** commonly reveals a fasting hypercholesterolemia and hyperlipidemia. Mildly increased liver enzymes due to hepatic lipid accumulation may be present. Creatine kinase may be elevated.
- **Urinalysis** to assess renal function, as most hypothyroid dogs are older.
- **Chest radiographs** to assess heart size, or pulmonary metastasis if neoplasia is the cause of thyroid gland pathology.
- Serum for **thyroid hormone** assessment. Serum is relatively stable. However, if storage is required, recommendations are to freeze and store in plastic. **Thyroxine level (TT4)** will be decreased in hypothyroid, if euthyroid sick syndrome, or with the use of some medications (glucocorticoids, phenobarbitol, sulfonamides or non-steroidal anti-inflammatory analgesics). Free **T4 (fT4)** measurement by equilibrium dialysis is highly recommended to confirm diagnosis. The normal range for both tests is dependent upon the reference range established by the laboratory. Accuracy of point-of-care tests (ELISA) for TT4 should be confirmed at a commercial laboratory. **Endogenous canine TSH level** may be increased, or may be normal with primary thyroid disease. This test should never be used alone to make a diagnosis of hypothyroidism. Secondary hypothyroidism may or may not cause a decrease in TSH. The normal reference range for TT4 and fT4 is lower for sight hounds.
- **Fasting triglyceride levels** are frequently elevated.
- **Cardiac ultrasound** to document chamber enlargement and contractility. Changes similar to those seen with dilated cardiomyopathy may be present with chronic bradycardia. Heart failure due to hypothyroidism has not been recognized; however, certain breeds (i.e. Doberman) may have concurrent hypothyroidism and dilated cardiomyopathy.
- Dogs that are ill for any reason may have a decreased TT4 and fT4 (euthyroid sick syndrome); therefore, the diagnosis of hypothyroidism is confirmed only when thyroid hormone levels are low (TT4 and free T4) **and** typical clinical findings are present.

MANAGEMENT

Acute

Acute management of hypothyroidism is only indicated if myxedema coma is present, as mortality is high with this condition.

A. Hypothermia must be managed as soon as possible (*see Accidental Hypothermia p. 293*).

B. Hypovolemia may be present requiring fluid therapy. Cautious administration of fluids is necessary where contractility is poor. CVP measurement may be helpful in guiding fluid therapy (*see Fluid Therapy p. 349*).

C. Electrolyte abnormalities may be present and should be corrected (see appropriate chapters).

D. Supplemental oxygen may improve hypoxemia slightly, however, assisted ventilation (*see Respiratory Emergencies p. 564*) will be required if the dog is comatose with decreased ventilation.

E. Intravenous thyroid supplementation (levothyroxine sodium, 5 mg/kg every 12 hours IV) is recommended because oral medications will likely not be absorbed. This dose should be lowered (50 – 75%) if decreased contractility or heart failure is present. Oral therapy should be instituted simultaneously. Improvement should be seen within 24 hours, and intravenous thyroid supplementation can be discontinued.

F. Oral supplementation should be initiated using a name brand product, known to be effective in dogs. The starting dose is 0.02 mg/kg orally every 12 hours. This dose should be decreased by (50–75%) in dogs that have decreased cardiac contractility.

G. Treatment of ocular disease (ulceration, uveitis, glaucoma) is described in *Ophthalmological Emergencies p. 520*.

Chronic

A. Supplementation should be continued for at least 6 – 8 weeks before the effectiveness of therapy is evaluated. Improvement in attitude should be appreciated within the first week of therapy. Other signs may resolve over the next few months including changes in the hair coat (hair loss may occur before improvement is noticed), obesity, cardiac changes and muscular weakness. Improvement in neurological signs is not predictable.

B. TT4 or free T4 by equilibrium dialysis are used for monitoring purposes, and should be within the normal range 4 – 6 hours after administration of the oral medication. Therapeutic monitoring is described elsewhere (*see suggested reading below*).

PHARMACOLOGY

1) **Injectable levothyroxine sodium** is commercially available and may be acquired at a hospital.

2) **Oral thyroid hormone replacement** is poorly absorbed from the gastrointestinal tract in dogs. Because of this, only name brand products that have been tested in dogs are recommended for initial therapy. Thyroid hormone supplementation increases metabolism and oxygen consumption by cells. A sudden increase in oxygen and energy demand may cause stress on the heart, therefore, if heart disease is present, a decreased dose is recommended for initial therapy.

SUGGESTED READING

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2. Small Animal Internal Medicine 3rd edition, Nelson and Couto (eds). Mosby, Inc, St. Louis, MO; 2003:691-709.

NOTES

INTRODUCTION

Hyperthyroidism is a disease that is most often recognized cats. It is a rare condition in dogs, usually caused by a functional thyroid tumor (most often carcinoma). Most of the clinical features of canine hyperthyroidism are the same as those observed in the feline. However, a hyperthyroid dog will likely have an obvious mass in the neck/thyroid area. Feline hyperthyroidism is a primary disease of the thyroid gland, and is usually caused by a benign adenomatous change in one, or both, lobes. The etiology of this condition is unknown. Malignant thyroid tumors causing hyperthyroidism in cats are uncommon. Thyroid hormone acts on most cells of the body to increase energy expenditure. Most cats with hyperthyroidism are older (average age is 13 years). Initially, these cats seem active and healthy to the owner, and clinical signs are usually slow to progress. Because hyperthyroid cats tend to be older, many also have concurrent diseases, such as renal or liver disease, or diabetes mellitus. Excessive thyroid hormone can also cause hypertrophy of the cardiac muscle. Thus, some cats may present emergent with congestive heart failure (*see Congestive Heart Failure p. 149*). Older cats with hyperthyroidism may also present with hypertension (*see Hypertension p. 205*). Acute manifestations of hypertension may include: blindness due to retinal hemorrhage, edema or detachment, and/or ataxia; vestibular disease; and seizures or paraparesis due to a cerebrovascular accident. Finally, ventroflexion of the neck (also due to hypokalemia) may be seen. This chapter focuses on cats presenting acutely ill due to hyperthyroidism, and possible concurrent diseases.

DIAGNOSIS

History

- Owners may perceive that their cat was healthy and became acutely ill.
- History may include increased appetite, weight loss, increased drinking and urination.
- Most owners notice that their cat seems very active and even restless. Some cats will be aggressive.
- Vomiting, diarrhea and increased frequency of defecation are often noticed.
- Poor hair coat, with matted hair and seborrheic skin, and a lack of grooming is also frequently noticed. Some cats will groom excessively and exhibit patchy alopecia.
- Uncommon signs include decreased appetite, lethargy, increased respiratory rate, weakness or seizures, and hyperthermia of the ear tips (due to hypertension). These signs may be due to severe hyperthyroidism or concurrent disease.

Clinical Signs/Physical Examination

- The typical hyperthyroid cat has a palpable thyroid nodule (may be bilateral), is in poor body condition/cachexic, and seems very active or restless.
- Thoracic auscultation will often reveal tachycardia, and may also reveal a heart murmur or arrhythmia. If the cat presents in heart failure, an increased respiratory rate/dyspnea will be observed with either increased (pulmonary edema) or decreased (pleural effusion) lung sounds.
- Rectal temperature may be increased.
- Dehydration is common, especially with concurrent diseases.
- Hair coat is generally poor and unkempt in appearance.
- Kidneys may palpate small and irregular if concurrent renal disease/failure.
- Dependent on concurrent diseases, the cat may be weak, depressed, or exhibit ventroflexion (rare) of the neck.
- Neurological signs and/or blindness may be present if the cat is hypertensive.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV, TS, stick BUN** to obtain baseline and assess hydration, renal status.
- **Urine** for specific gravity (to assess concentrating ability), and dipstick to assess for glucose and ketones. Thyroid hormone can have a diuretic action and cause increased medullary blood flow. Thus, cats with hyperthyroidism and normal renal function may have an inappropriate urine specific gravity.
- **Electrolytes, body weight and blood glucose to** assess for hypokalemia and other abnormalities associated with dehydration and diabetes mellitus. Note: many hyperthyroid cats exhibit stress-induced hyperglycemia.
- **Venous blood gases** to assess for metabolic acidosis, especially if concurrent disease (renal failure, diabetes).
- **ECG** may document arrhythmias or chamber enlargement.
- **Neurological** examination to localize abnormalities and baseline for trending purposes.
- **Ophthalmological** examination to identify retinal abnormalities if cat presents blind or is hypertensive.

Extended Laboratory Data Base

- **Biochemical profile** commonly reveals mild to moderately elevated liver enzymes with hyperthyroidism. Concurrent liver disease (cholangiohepatitis, neoplasia, etc.) may also be present in the older cat. If dehydration or concurrent renal disease exists, urea/creatinine may be elevated.
- **Complete blood count** will usually reveal a stress leukogram. If concurrent diseases exist, a mild anemia, or other changes, may also be seen.
- **Urinalysis** to assess for proteinuria (may be seen with concurrent renal disease or hypertension).
- **Blood pressure** assessment using Doppler (*see Hypertension p. 205*).
- **Chest radiographs** to assess heart size and presence of pulmonary changes (edema or metastatic disease if carcinoma), and pleural fluid.
- **Abdominal radiographs** to further assess renal and liver size.
- **Echocardiography** to assess for cardiomyopathy or changes due to hyperthyroidism/hypertension. Highly recommended if heart murmur, arrhythmia, or cardiomegally are documented.
- **Serum** for thyroid hormone assessment. Serum is relatively stable. However, if storage is required, the recommendation is to freeze and store in plastic. Thyroxine level (TT4) will be increased in the majority (>90%) of hyperthyroid cats. Accuracy of point-of-care tests should be confirmed at a commercial laboratory. If TT4 is normal, and hyperthyroidism is suspected based upon clinical signs and the presence of a thyroid nodule, the test should be repeated after non-thyroidal illness is treated/ruled-out. If still not elevated, a free T4 by equilibrium dialysis can be performed to confirm hyperthyroidism.

MANAGEMENT

Acute

A. Dependent upon **concurrent diseases.**

    1. If renal failure *see p. 721.*
    2. If diabetes/DKA *see p. 265.*
    3. If congestive heart failure *see p. 150.*
    4. If hypertensive *see p. 209.*

B. **If dehydrated, begin fluid therapy.** Place a large bore intravenous catheter. Administer balanced electrolyte solution fluids (i.e., Plasma-Lyte® 148, Normosol® R, Lactated Ringers) after calculating fluid volume replacement, based upon hydration status and ongoing losses (*see chapter Fluid Therapy p. 349*). Replace deficit over 8–24h, depending on the clinical condition of the patient. Metabolic acidosis will likely be corrected with fluid therapy.

C. **Electrolyte abnormalities** may be present and should be corrected.

    Potassium supplementation 20 – 40 mEq/L may be indicated depending upon the serum potassium (*see Hypo/hyperkalemia p. 394*). Potassium should be closely monitored (especially dehydrated cats). Sodium and chloride should be maintained within normal range.

D. **Methimazole (2.5 mg PO q12h)** is recommended if abnormalities are due to severe hyperthyroidism, and no other underlying diseases need to be addressed. If underlying renal disease is suspected, begin therapy once daily only and monitor renal values (recheck in one week).

E. **Propranolol 2.5 mg PO q12h or atenolol 6.25 mg/cat/day** should be administered in an acute crisis where tachycardia, or supraventricular tachyarrhythmias are present. Heart rate and rhythm require consant monitoring.

Chronic

A. If underlying renal disease is unmasked, methimazole therapy must be tailored in order to balance hyperthyroidism and decreased renal blood flow. More permanent therapeutic options (Iodine[131] or surgery) are **not** recommended in these cases.

B. Methimazole dosage should be gradually increased by 2.5 mg (every two weeks) if the cat remains hyperthyroid at the two-week recheck. Once the T4 is normal, the dosage should be maintained and T4 rechecked every 3 – 6 months.

C. If more permanent therapeutic options are to be pursued, the cat must have concurrent diseases managed, and be euthyroid prior to surgery/Iodine[131].

PHARMACOLOGY

1) **Methimazole** can be administered in an oral or topical form. The topical form may take longer to have an effect, but by four weeks no difference is noted. Adverse effects are common and usually occur within the first three months. Common adverse reactions include vomiting, anorexia, depression, eosinophilia, lymphocytosis and leukopenia. Less common reactions include facial pruritis/excoriation, agranulocytosis, thrombocytopenia, hepatopathy and immune-mediated hemolytic anemia. Recheck CBC and profile should be performed monthly until 3-4 months. The cat should be rechecked every 3-6 months thereafter.

2) **Propranolol** is a nonspecific beta antagonist used to treat tachyarrythmias and can mask some signs of thyrotoxicosis. Contraindications include heart failure, allergic airway disease, or severe renal or hepatic insufficiency.

3) **Atenolol** is a more specific (ß 2) blocker and can be used to treat tachyarrythmias and hypertension. It is safer to use in cats with allergic airway disease. Also contraindicated in cats with heart failure, renal or liver failure. Not recommended for acute therapy prior to surgery because dosage usually requires gradual titration.

SUGGESTED READING

1. Canine and Feline Endocrinology and Reproduction, 3rd edition. Feldman and Nelson (eds). Saunders, St. Louis, MO. 2004:152-218.
2. Small Animal Internal Medicine, 3rd edition. Nelson and Couto (eds). Mosby, St. Louis, MO. 2003:712-724.

NOTES

INTRODUCTION

Hypothermia is classified as primary or secondary. Primary hypothermia develops as a result of exposure to low environmental temperatures. Principle factors causing accidental hypothermia are cold exposure, immersion in water, trauma and exhaustion. Underlying conditions (secondary hypothermia) such as hypothyroidism, age (very young or very old), cardiac disease or malnutrition may predispose animals to accidental hypothermia. The possibility of human-administered abuse with recreational drugs or alcohol, ethylene glycol and phenothiazines should also be considered, as these can disrupt normal heat production and conservation by impairing perception of changes in ambient temperature, depressing mental status, and inhibiting the shivering response. In addition to the hypothermia-induced abnormalities, clinical signs may correlate with the hypothermia precipitating event (i.e., trauma, hypothyroidism). Anesthesia and surgery frequently reduce the body temperature to low levels, resulting in inability to metabolize administered drugs, which in turn prolongs the hypothermic event. As the body temperature decreases, multiorgan dysfunction occurs which ultimately results in multiorgan failure if left untreated. Hypotension and potentially fatal dysrhythmias can result. Treatment of hypothermia requires extreme care and attention to detail. Effects of re-warming can result in secondary problems, such as afterdrop. Afterdrop denotes a drop in the core temperature as a result of sudden peripheral re-warming and vasodilation where the cold acidemic blood is returned to the core. The pathophysiologic events that occur due to hypothermia and its treatment have major systemic effects.

Low environmental temperatures predispose animals to frost bite of distal limbs, tail and ears or other parts of the body (i.e., tongue, penis, ventral abdomen) in contact with ice or frozen metal. Vasoconstriction due to hypothermia diverts oxygen and nutrients away from the periphery predisposing these tissues to cell death. In addition, intracellular and extracellular ice may form causing cell lysis. Vasculitis and hyperviscosity of the blood may precipitate thrombosis.

DIAGNOSIS

History/Signalment

Frequently, hypothermic patients are lost or abandoned and a thorough history is not available as to the precipitating event, duration of hypothermia or medical history. Where owners are present obtain this information. Where water immersion is the cause, aspiration pneumonia or near-drowning must be considered (*see Near-drowning p. 570*) in addition to the other potential problems discussed. Problems such as injuries associated with trauma, possible abusive elicit drug or alcohol administration or medical problems predisposing to exposure should be identified, and need to be included in the laboratory work-up.

Clinical Signs/Physical Examination

Always handle severely hypothermic animals carefully as ventricular fibrillation can be precipitated very easily.

- Where **moderate to severe hypothermia** is suspected, esophageal or rectal temperatures can be measured using electronic probes which are approximately 8Fr or 10Fr and 1 meter long (Sonatemp 400 – 700 Thermometer, Sheridan, Argyle, NY) that can be placed intra-nasally into the esophagus or into the colon per rectum. Infrared otic thermometers have inherent inconsistencies and are not recommended. The digital thermometers only register to 34°C or 32°C (93° F – 90°F) making an accurate determination of degree of hypothermia difficult.
- Patients may appear 'dead' if the temperature is <28°C (83°F), however, resuscitation should be attempted as occasional success has been recorded in individuals with temperatures <18°C (<6°F). The saying 'you're not dead until you're warm and dead' should be remembered. However, if the patient is not breathing, has a 'flat ECG, is stiff and the blood is clotted, then it is dead.
- Depending on the **degree of hypothermia** the animal may present with:
    - **mild hypothermia 34° – 37°C (93° – 98.7°F),** alert and shivering with pale mucous membranes, tachycardia, tachypnea, increased blood pressure
    - **moderate hypothermia 30° – 34°C (86° – 93°F),** depressed to stuporous, oliguric, dehydrated, bradycardic and bradypneic, hypotensive with acrocyanosis
    - **severe hypothermia 28° – 30°C (83° – 86°F),** worsening brainstem and cardiac function leading to coma and cardiac dysrhythmias, muscular rigidity
    - **temperatures <28°C (83°F) (extremely severe),** cardiopulmonary arrest

- Due to **severe vasoconstriction,** it is often difficult to feel a pulse and weak myocardial contractions are barely, if at all, audible.
- **Complications** of hypothermia are related to hypoxemia, metabolic acidosis, poor splanchnic perfusion, reduced cardiac output, reduced renal perfusion, cold induced coagulopathy, electrolyte disturbances, leukopenia, thrombocytopenia, hemoconcentration, microvascular disruption, disseminated intravascular coagulation and multiorgan failure.
- **Pain** is a consistent finding and can be severe upon resuscitation. The limbs, tail and ears can be excruciatingly painful so handle with care.
- **Hypotension** occurs secondary to hypothermia and cortisol deficiency. Catecholamine receptor dysfunction occurs in these circumstances. Re-warming should correct low blood pressure if hypovolemia or hypoadrenocorticism (primary or secondary) are not features.
- If **trauma** is a precipitating factor, significant blood loss associated with soft tissue and orthopedic injuries may be present.
    - Underlying precipitating events as mentioned above, should be kept in mind.
- **Frostbite** is difficult to assess as to its degree on initial presentation; all exposed areas should be assessed as resuscitation continues.
    - First degree frostbite manifests as erythema after warming.
    - Second degree leads to blistering.
    - Third degree results in skin necrosis, tissue loss and is susceptible to infection.
    - Fourth degree results in devitalization of the whole part (gangrene) and is susceptible to infection.
    - The severity of injury cannot be assessed for several days. In superficial frostbite the skin is white, without blanching or evidence of capillary filling after mild pressure and feels somewhat soft or rubbery to palpation. Deep frostbite, which involves all tissues including bone, produces a hard or wooden-like extremity.

Laboratory Evaluation/Diagnostic Imaging

Stat

In moderately to severe hypothermic animals, it may be difficult to obtain blood samples. Slow gentle handling is mandatory, especially with invasive procedures such as intravenous catheter placement and blood collection to avoid precipitating fatal arrhythmias.

- **PCV and TS** may be increased due to cold diuresis causing isotonic dehydration; or reduced if associated with trauma and hemorrhage.
- **Stick BUN, urea or creatinine** may be increased due to pre-renal azotemia and fluid loses.
- **Glucose** may be increased initially due to stress, catecholamines, cortisol release and peripheral insulin resistance, but may be quite low as time progresses.
- **ACT** is variable depending on severity and duration. Will be increased in DIC.
- **Urine specific gravity** is variable depending on severity and duration of hypothermia.
- **Venous blood gases** progress to significant acidemia.
- **Lactate** may be increased above normal (2.5 mmol/L dog) (1.5 mmol/L cat) and progress as hypothermia worsens.
- **Electrolytes** may be altered due to dehydration, urinary losses of **potassium** initially but may increase as temperature decreases (>10 mmol/L K^+ is considered as an index of irreversibility), or rhabdomyolysis.
- **ECG** (*see B below*).

Extended Laboratory Data Base

Obtain as soon as possible after re-warming.

- **CBC** may have increased red blood cells due to hemoconcentration, white blood cells and platelets may be low due to sequestration within the spleen and perivascular tissue and DIC.
- **Serum biochemical profile, urinalysis** to evaluate systemic illness that may have been pre-existing or as a result of hypothermia and resuscitation (*Pancreatitis p. 45, Acute Renal Failure p. 709, Toxicities p. 638*).
- **Radiographs** (i.e., thorax, abdomen, limbs where indicated) especially where trauma, aspiration or drowning is suspected or respiratory compromise is present.
- **Serum osmolality**, measure and calculate (*suspect Ethylene Glycol Intoxication p. 655, DKA p. 263, Acute Renal Failure p. 709*).
- **Thyroid panel** after recovery, and where hypothyroidism is suspected (*see Hypothyroidism p. 285*). If measured early in the recovery stage, T4 could be increased due to 'euthyroid sick syndrome.' However if myxedema (*see Hypothyroidism p. 285*) is evident, severe hypothyroidism is present.
- **Serum cortisol** if hypoadrenocorticism is suspected either as a cause, or an effect, and poorly responsive (*see Hypoadrenocorticism p. 274*).

MANAGEMENT

A. Oxygen. May reduce the risk of ventricular fibrillation during resuscitation. Initially, establish the A-B-Cs of resuscitation. You must be sure that the patient has arrested prior to commencing cardiopulmonary resuscitation as chest compression frequently causes ventricular fibrillation (VF).

B. ECG monitoring may be difficult due to shivering (may look like VF). A 'flat ECG' may be due to asystole or just bad electrical conductance through cold skin or problems of adhesion of ECG electrodes. Sterile hypodermic needles should be placed through the gel portion of the electrodes, which will improve adhesion and conduction; or place sterile wire through the skin and place the alligator clip to the wire. Asystolic arrest usually occurs with severe hypothermia. The cold myocardium is relatively insensitive to DC shock defibrillation however, administer three shocks immediately and if no response, administer a further three after the patient has been re-warmed to 28 – 30°C (83° – 86°F). The hypothermic heart is unresponsive to pacing and cardioactive drugs. **Medication to treat arrhythmias should not be given until body temperature is 30°C – 32°C (86° – 90.3°F) as drugs are ineffective at temperatures below this.** Atropine is ineffective for bradyarrhythmias at low temperatures. Re-warming alone usually will correct this rhythm. Also, the heart generally cannot sustain rhythmic electrical function until this temperature is reached. Basic cardiopulmonary resuscitation (*see CPR p. 133*) should be performed, if necessary, until the temperature is >32° (90.3°F) when advanced cardiac life support (*the use of medication – see CPR p. 135*) can be added if required. Administration of normal doses, and repeat doses of any medication at temperatuire <30° – 32°C, will lead to accumulation and be toxic to the patient when re-warmed.

C. Associated problems such as injuries due to trauma (*see Triage p. 6*), possible abusive elicit drug or alcohol administration (*see Toxicities p. 630*), drowning (*see Near Drowning p. 570*) or medical problems (*see Hypothyroid p. 285, Hypoadrenocorticism p. 274, Hypoglycemia p. 280, Neonates & Pediatrics p. 542*) predisposing to exposure hypothermia should be identified. Following this, restoration of normothermia is the main objective in managing the hypothermic patient. Re-warming techniques depend on the degree of hypothermia, duration and predisposing events.

D. Intravenous fluids. As even mild hypothermia causes a cold diuresis, all hypothermic animals should receive warmed intravascular fluid support. The volume and rate are assessed based on history (i.e., trauma with blood loss, short term hypothermia with variable degree of dehydration) and physical examination (*see Fluid Therapy p. 348*). Hydration status should be assessed and fluid requirements calculated. While completing the physical examination, it is advisable to administer fluids cautiously (~2 – 10 mL/kg/h) due to:

   1. Possible **depressed cardiac function and intense peripheral vasoconstriction** (*see Fluid Therapy p. 347*). **Central venous pressure (CVP)** is advised during fluid administration where depressed cardiac function is suspected (*see Monitoring p. 354*). In addition, blood pressure measurements should be attempted but may be difficult to obtain until re-warming occurs.
   2. A **jugular vein** may be easier to catheterize than a peripheral vein in severely hypothermic patients. Be gentle and ensure the catheter does not enter the right atrium.
   3. **Hypotension secondary to hypothermia** is common and aggressive fluid administration, if significant loss has not occurred, may predispose to pulmonary edema during and after re-warming, especially in cats. Unless obvious blood loss is noted, a judicious approach to fluid administration is advised initially.
   4. **Plasma-Lyte® 148 or A, or Normasol®R** is recommended as acidosis frequently occurs. Lactated Ringer's should be **avoided in severe hypothermia** as the liver may not be able to metabolize the lactate. Various other solutions such as 0.9%, 0.45% sodium chloride or one-third dextrose with 2/3 saline may be appropriate depending on serum electrolytes, acid-base status and blood glucose. The intravenous fluids should be **warmed to 50°C (120°F) when hung (not delivered directly at this temperature)** with a standard intravenous delivery set or **to 42°C (108°F) when using 60 mL syringes,** short tubing and a syringe pump. The temperature of the fluid drops dramatically due to ambient room temperature even when warmed. Placing the intravenous delivery line between hot water bottles or 'oat/bean/ or rice bags warmed to **42°C (108°F)** will maintain warm fluid temperature. The temperature can be measured by placing a digital thermometer between the 'oat bags' or hot water bottles. **Fluid temperature entering the patient should not exceed 42°C (108°F).**

E. A **urinary catheter** should be placed where necessary, prior to or after re-warming in an aseptic manner to measure urine output (and to facilitate re-warming via lavage *see I below*). Constant assessment is required as the core

temperature increases; fluid therapy can be altered based on blood pressure, central venous pressure, urine production, PCV, TS, mentation and tolerance of fluids delivered (*see Acute Renal Failure p. 709, Fluid Therapy p. 353, Monitoring p. 16*).

F. **External re-warming** is usually adequate for **temperatures >32°C (90.3°F)**. This can be in an active or passive form. If the patient is wet, dry them gently with a towel to remove as much water as possible. **Passive re-warming** is usually adequate for the mildly hypothermic animal ≥34°C (93.5°F), and consists of placing them in a warm room wrapped in a blanket with the addition of other insulating material where the animal can re-warm themselves via shivering and heat conservation. The head should also be covered. With this method the temperature can increase by 0.4 – 2°C/h (0.75 – 4°F/h). Peripheral vasoconstriction is maintained which minimizes the risk of both hypotension and the temperature afterdrop.

G. **Active re-warming** is required for patients with **moderate to severe hypothermia, core temperatures below 34°C (93.5°F). This may be preferable also in patients with a temperature >34°C that are hypoglycemic, hypothyroid, adrenal insufficient or have other disorders that limit endogenous thermogenesis. Patients with diabetic ketoacidosis or have an unstable cardiovascular system may also benefit from rapid normalization of core body temperature. Active re-warming must be performed in any patient, whatever the degree of hypothermia, if initial passive re-warming methods fail to elevate body temperature.** Active external re-warming can be accomplished by hot water bottles, heated blankets, or warmed incubators for small animals. Also, holding a small patient close to your body then covering with a blanket, is an efficient means of re-warming. **Warming the ambient air and cage with hot water bottles will reduce heat loss.** Fans should not be used, as stationary air is less conducive to heat losses by radiation. However, **forced air enclosed around the patient**, has proved effective in core re-warming in humans. Temperatures of 28.8 ± 2.5°C (86°F) increased by 2.4 ± 1.0°C/h (36.3 ± ~2 – 4°F/h) using the forced air system (Bair Hugger, Model 500; Augustine Medical Incorporated, Minn.). This is our preferred method of re-warming. The capacity of even forced air to increase core temperature may be restricted by afterdrop or thermoregulatory vasoconstriction which decreases transfer of applied heat from peripheral to central tissues. **Caution** is required with active re-warming any animal. Cutaneous burns may occur due to inability to move and initial vasoconstriction in these patients blocks dissipation of heat from surface tissues. The temperature of external heat sources therefore, should not exceed 45°C (113°F). A barrier (towel, fleece, blanket) should be placed between the animal and the heat source.

H. **Blood pressure must be monitored and a fluid bolus administered should hypotension occur.** Caution must be used with fluid administration (*see D above*). Afterdrop may develop with external heat sources, which may predispose to, or exacerbate cardiac arrhythmias. Also, vasodilation associated with warming of the limbs may precipitate further hypotension. It has been recommended that limiting the application of external heat to the trunk can minimize the after-drop effect. Further hemodynamic instability may occur if the hypothermic heart is unable to respond adequately to the rising metabolic requirements of the re-warmed exterior tissue shell. The risk of circulatory collapse is determined primarily by the patient's degree of tolerance of intravenous fluids, the extent of hypothermia and intensity of re-warming. If **intolerance to fluids or colloids** (*see signs in Fluid Therapy p.354*) is demonstrated and ventricular function is impaired, **slowly titrate dobutamine starting at 1 μg/kg/min slowly increasing to effect and a maximum of 5 μg/kg/min until re-warmed then a further increase may be instituted.**

I. **Invasive internal re-warming is recommended for animals that have hypothermia-induced cardiac arrest, core temperatures <30°C (86°F) or higher if cardiovascular function is unstable and where other forms of re-warming are unsuccessful (if the Bair Hugger, or other similar device, is available this is preferred to invasive measures).** Core re-warming minimizes afterdrop and potential deterioration as well as hastens normalization of body temperature. In addition to using warm intravenous fluids, lavage of the urinary bladder with 42°C (107.5°F) sterile saline via an indwelling urinary catheter is recommended. Allow the fluid to flow into the bladder by gravity and flow out as the bladder fills. If a Foley catheter is used, deflate the balloon when the bladder increases in size. Allow a 10 – 15 minute dwell time. Similarly, **peritoneal dialysis or warm lavage of the pleural space with 10 mL/kg of 42°C (107.5°F) 0.9% saline or 1.5% dextrose dialysis fluid** has been suggested to be effective. Administer fluid with caution so as not to jeopardize ventilation. Do not use Plasma-Lyte® or Normasol® as these appear to be painful when placed into the abdomen. An exchange every 30 minutes is recommended. The dialysate must be kept at ~42°C (108°F) or core re-warming may not occur and, in fact, a temperature drop may be encountered. Peritoneal or pleural dialysis should not be performed in patients with suspected trauma within these cavities, or where surgery was recently performed. Gastric or colonic lavage with 42°C, 0.9% saline or tap water has also been suggested, but should only be used as a last resort due to potential for regurgitation/aspiration, alterations in electrolytes and inability to obtain accurate rectal or esophageal temperature. Heating inspiratory oxygen may assist in warming the patient but is not very effective. This may be

accomplished by applying a heat and moisture exchange between the oxygen tubing and the endotracheal tube or face mask. Placing a hot water bottle (42° – 46°C, 108° – 114.8°F) on the tubing, OR warming the humidifier on the ventilator, may warm the inspired air.

NOTE: There is no definitive recommendation on the rate of re-warming other than a more rapid technique may be desirable to facilitate treatment of associated medical problems that appear to play a major role in hypothermia-associated mortality. Quickly increasing the temperature to 30°C (86°F) may reduce the risk of ventricular fibrillation and cardiovascular collapse and improve myocardial performance. Rapid re-warming may also minimize acidosis and hypoxia associated with slower methods. **Do not correct the acidosis** until after fluid administration as acidosis causes a shift of the oxyhemoglobin dissociation curve to the right, which will counter the shift to the left produced by hypothermia. If pH remains <7.1 judicious correction is advised. In sub-acute hypothermia (definition not given but likely longer than 12 hours where organic osmolytes have formed in the brain in concert with dehydration), the rate of re-warming should not exceed 0.5°C/h to avoid development of pulmonary/cerebral edema.

J. **Pain always occurs and can be severe in these patients.** Once temperature has reached 37°C (98.5°F), analgesics are recommended for those patients whose temperature was <34°C (93°F) as pain is reported in humans following the extensive shivering that occurs during development and recovery from hypothermia. This has also been noted in animals (Mathews unpublished observations). If a fentanyl patch is placed, morphine 0.2 – 0.5 mg/kg IM, SC or as a CRI oxymorphone or hydromorphone at 0.02 – 0.1 mg/kg IV, IM, SC or as a CRI, should be given until adequate fentanyl blood levels are reached (6 – 12 hours in the cat and 12 – 36 hours in the dog), and used in addition to the fentanyl patch if required. A fentanyl (4 – 6+ μg/kg/h) CRI alone is easy to implement and adjust as needed for neurological assessment if this is required (*see Analgesia p. 83*). When perfusion is established and gastrointestinal and renal abnormalities are ruled out, a non-steroidal anti-inflammatory analgesic can be administered (*see NSAIAs p. 85*).

K. **Continuous monitoring is essential** as the re-warmed patient is at risk for developing multiple complications. **Pancreatitis** occurs in 50% of humans with moderate to severe hypothermia and also occurs in animals (Mathews unpublished observations). Amylase and lipase should be monitored as pancreatitis may occur prior to or after eating. If the patient is dehydrated and azotemic, these enzymes may be increased due to renal failure. Offer only frequent, small amounts of low fat food initially. As **acute tubular necrosis** may occur, urine production should be carefully monitored and treatment for oliguria should be instituted if urine output is inadequate after temperature, fluid and pressure resuscitation (*see Acute Renal Failure p. 712*). **Pneumonia and other infections** are common sequelae due to severe hypothermia therefore appropriate preventive measures should always be considered and instituted (e.g., aseptic technique, airway protection). **Other complications, such as pulmonary edema, rhabdomyolysis, electrolyte disturbances, gastric hemorrhage, pancreatic necrosis, intravascular thromboses, DIC and frostbite of peripheral tissues (ears, tail and distal limbs – *see M below*) may also occur.**

L. **Laboratory evaluation** PCV, TS, activated clotting time, serum electrolytes, stick BUN and glucose in addition to a complete physical examination and measurement of vital signs, should be performed at least once daily to monitor for potential problems (*see K above*). Biochemical profile, complete blood count and urinalysis (monitor for casts), are recommended once body temperature has normalized to assess underlying predisposing medical problems or problems associated with the hypothermic event. Endocrine evaluation including full thyroid panel, resting and stimulated cortisol levels should be performed if indicated. Electrolytes, especially potassium must be monitored. Caution with K^+ supplementation as overdose may occur as temperature stabilizes.

While the above are guidelines, not all hypothermic animals will present as described nor will they necessarily require the re-warming technique described. However, initial presentation and trending will dictate the appropriate therapeutic modality to pursue.

M. **Frostbitten tissues should be rapidly warmed. Immerse the affected part in water of 40 – 42°C (104 – 108°F) for at least 20 minutes or until thawing is complete.** Dry heat should not be used. **Never rub or massage the tissues.** Application of soft, dry bandages to the injured part is required to protect the area from self-inflicted, or other, trauma. Cage rest is required to reduce injury. **Analgesics must be given as this injury is extremely painful** (*see J above*), Topical antiseptics may help prevent infection of necrotic tissue or ruptured blisters. Large blisters may be aspirated aseptically. Prophylactic antibiotics are not recommended. Culture of an infected wound and antibiogramme should be performed to select the appropriate antibiotic. Should the wound on a distal limb

become superficially infected, topical administration of sugar or honey with daily rinsing and bandaging until cleared (usually 3 days), works very well. Surgical management should be delayed until spontaneous amputation of necrotic tissue has occurred and is complete. Definitive surgical management is based on the individual injury. Heparin or low-molecular weight dextrans have not proven beneficial in preventing ischemic necrosis.

PHARMACOLOGY

1) **Bair Hugger, Model 500.** Augustine Medical Incorporated, Minn. is a forced air system comprised of disposable plastic, paper covers, and a heat source that directs warm air across the skin. This system simultaneously provides convective heat transfer and shielding against radiant heat loss. Studies indicate that forced air transfers far more heat than other external methods, and was also more effective than peritoneal dialysis in one study. However, the capacity of even forced air to increase core temperature may be restricted by afterdrop or thermoregulatory vasoconstriction that decreases transfer of applied heat from peripheral to central tissues. This forced air system is used in our institution for re-warming post-operative hypothermia and has proved to be very effective in severe accidental hypothermic animals.

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NOTES

INTRODUCTION

Hyperthermia is defined as as a body temperature above the range of normal (~39.5°C [102.5°F]). The temperature of the body is maintained within a normal diurnal range (~38.2 – 39.5°C [101.5 – 102.5°F]) called the set-point. Hyperthermia may be due to an exogenous (infectious) or endogenous (inflammatory e.g., pancreatitis) pyrogenic (fever), or non-pyrogenic etiology. Despite their physiologic differences, hyperthermia and fever cannot be differentiated clinically on the basis of the height of the temperature or its pattern.

Pyrogenic (infectious and inflammatory) disorders alter the hypothalamic thermoregulatory set-point via cytokines and prostaglandins. During pyrogenesis the body responds to the new set-point through 'generating heat' via shivering, peripheral vasoconstriction and increased metabolism. This is a physiologic response and the temperature should not be reduced unless critical (~≥41.5°C [106°F], or lower if rising rapidly) because this will result in increasing overall energy expenditure or 'work' attempting to maintain the temperature at the new set-point. Treating the underlying cause of infection or inflammation is necessary. **Non-pyrogenic** hyperthermia is an increase in body temperature above the normal set-point. Hyperthermia in this setting is a result of a heat load exceeding the animal's ability to dissipate it. Causes include, increased activity, hot environmental conditions, **medical conditions** (*see History and Physical Examination below*), and impaired heat dissipating mechanisms (i.e., neuroleptic drugs, inability to pant). A rise in temperature signals the thermoregulatory center, which in turn stimulates panting and increased perfusion to the tongue; dissipation of heat occurs via the countercurrent mechanism of the sublingual vessels and airways of dogs and cats. Increased cardiac output and vasodilation facilitates heat loss through the skin via radiation and convection. Minimal heat dissipation, via sweating, also occurs via the footpads and other non-haired regions of the body. The animal also exhibits behavioural patterns such as seeking out shade, cold floors, and assumes a frog-leg position. Hyperthermia, associated with hot environmental situations (worsened by increasing humidity) may be exhibited as **heat stress** (thirst, discomfort associated with physical activity, fluid and electrolyte disorders), progressing to **heat exhaustion** (intense thirst, weakness, discomfort, anxiety, syncope, associated with physical activity), or **heatstroke** (**classical** – severe illness associated with central nervous system abnormalities and multi-organ involvement not associated with exercise; **exertional heatstroke** – similar clinical presentation but associated with physical activity). While heatstroke initially is due to a non-pyrogenic mechanism, the subsequent multi-organ involvement results in the systemic inflammatory response syndrome (SIRS). Progression to multi-organ dysfunction syndrome (MODS) is secondary to the acute physiological alterations occurring (e.g., circulatory failure, hypoxia, increased metabolic demand, inflammatory response of the host, initiation of the coagulation cascade and direct cytotoxicity of heat). While hyperthermia may have been present initially, the temperature may drop due to shock or cooling prior to presentation; therefore, the actual temperature experienced by the animal may not be known. Temperatures ≥ 43°C (109°F) result in enzyme dysfunction and denaturation of proteins resulting in significant injury. At extreme body temperatures 49°C – 50°C (120°F) all cellular structures are destroyed and cellular necrosis occurs in less than 5 minutes.

Malignant hyperthermia (MH) is a life-threatening myopathy involving excessive release of calcium from the sarcoplasmic reticulum in response to anesthetic agents and some neuroleptic drugs. This occurs rarely in dogs anesthetized with halothane (most potent trigger) or isoflurane. Onset of hyperthermia is rapid with an increased oxygen requirement by striated muscle. Muscle contraction, sympathetic activation and increased muscle cellular permeability occurs. Rapid identification and treatment is necessary to prevent death.

Miscellaneous causes of hyperthermia include dehydration/hypoperfusion alone, heavy body bandages, and poor air circulation. In animals that must exert themselves excessively to breathe (i.e., neuropathic disorders, upper airway pathology), temperatures may reach 43°C (109°F).

DIAGNOSIS

History/Signalment

It will be necessary to commence management (*below p. 300*) while taking a history and performing the physical examination.

> **Heat associated illness** can affect any animal.
> - A thorough history regarding the predisposing cause for heat-associated illness is necessary as this will assist the veterinarian in assessing the potential severity of the situation, especially if the owner has attempted cooling, or the animal is in shock and the temperature may be declining. Question the owner as to their attempts at cooling the animal.

- Those more prone to classic heatstroke are brachycephalic breeds, animals with upper airway pathology, geriatric, obese and pregnant animals.
- Dogs tethered without shade are at high risk.
- Increased activity such as exertional hyperthermia, or the more advanced exertional heatstroke tends to be seen in younger, active, larger breed dogs, especially with thick haircoats. Some English Springer Spaniels and Labrador Retrievers may be predisposed. Working dogs or those exercising with owners will frequently run until they stagger and 'drop'. Seasonal changes from cool to warm weather may predispose exercising dogs to heat-related illness as a period of acclimatization to the hotter weather has not occurred.
- Exercise can be hazardous to people in high humidity, and during heatwaves (3 consecutive days of >32.2°C [90°F]), so assume these conditions will affect animals also.
- A common cause is an animal confined in a closed vehicle during warm weather, where there is direct sunlight. Even in cooler outdoor temperatures, the temperature inside the car may exceed 48°C (120°F) in 20 minutes, or when car heaters are left running for prolonged periods of time.
- A previous episode of heatstroke may predispose the animal to subsequent episodes due to permanent injury to the thermoregulatory centre.
- Consider toxin exposure (e.g., metaldehyde, macadamia nuts, *see Toxicological Emergencies p. 630*).
- Other **medical problems** may be the cause of hyperthermia (*hyperthyroidism p. 288, hypocalcemia p. 377, eclampsia p. 753, tetany p. 486, seizures in dogs p. 460 , or cats p. 456, infection p. 588, pheochromocytoma p. 206*). Ask appropriate questions for the disorder.
- Where heat-asssociated illness is ruled out based on history, rule out sepsis and the refer to *Fever of Unknown Origin p. 422* for potential etiologies.
- **Miscellaneous causes.** In addition to medical problems above, consider ingestion of neuroleptic drugs, (including phenothiazines), amphetamines, diuretics, or beta-blockers. Basically any drug or situation that reduces peripheral perfusion (or increases vasoconstriction) may reduce heat dissipation. If a medium to large dog, in your clinic, recent hyperthermia may be associated with a confined area and poor circulation. Consider a neuropathy and increased work of breathing (respiratory failure). Thyrotoxicosis following thyroid tumour removal.
- **Malignant hyperthermia (MH)** must be identified quickly as it is rapid in onset with high mortality. Heavily muscled dogs (e.g., Rottweiller, greyhounds) are predisposed. MH frequently occurs during inhalant anesthesia but is also associated with neuroleptic drugs in humans. The author has observed an MH-like syndrome in 2 dogs with polyradiculoneuritis and rapid-onset paralysis requiring mechanical ventilation. This was not associated with 'work of breathing' as this occurred during ventilation.

Clinical Signs/Physical Examination

I.   If an owner calls for **advice** and hyperthermia is highly likely, go to Management below *p. .*

II. The severity of **heat-induced** illness is dependent upon the circumstances and duration of **heat exposure.** Consider **sepsis** when the history is not consistent with associated illness. Septic animals do not pant or seek cool areas. Refer to *Fever of Unknown Origin p. 422* if septic focus not identified. Once heatstroke is identified:

- Place the animal directly on a cool surface (steel examination table).
- If moribund with weak to absent pulses start treatment immediately (*below p. 300*) while taking rectal temperature. Do not apply cooling measures if temperature at or below 39.5°C (102.5°F).
- Rectal temperature may be low in advanced shock, or if cooling has been performed by the owner. A thermometer measuring up to 45°C (113°F) is required to establish the actual degree of hyperthermia.
- Peripheral pulses may be bounding initially due to a hyperdynamic state; more commonly pulses are weak due to dehydration and poor cardiac output.
- Heart rate may be increased (normal response to hyperthermia), normal (mild hyperthermia or declining due to condition or cooling) or low (shock or cooling).
- Mucous membranes are hyperemic initially with a CRT <1 second with prolongation associated with cardiovascular collapse.
- Respiratory rate may be increased, panting, normal, or decreased if in shock. Stridor may be evident with upper airway obstruction (brachycephalic syndrome, laryngeal paralysis, mass, collapsing trachea). Lung sounds may be quiet with panting, loud with respiratory effort, crackles may be present if aspiration of vomitus occurred during a seizure or as a result of heat induced vomiting, or hemorrhage secondary to DIC *p. 417*.
- Mentation will vary. Alert and anxious in the early stages; more commonly, depressed. In advanced stages cerebral edema or hypoglycemia may result in coma. Liver injury may result in hepatic encephalopathy. Intra-parenchymal hemorrhage of the brain due to hyperthermia may cause seizures, therefore, seizures may be a result of, rather than a cause of, hyperthermia. Cortical blindness, depression, stupor or coma may be present.

- Ataxia may be due to weakness. Cerebellar dysfunction can occur, and may be permanent.
- Assess hydration status. Dehydration and hypovolemia can be severe due to evaporative and gastrointestinal losses.
- Vomiting and diarrhea, with or without blood, are noted in moderate to severe situations.
- Petechiae and ecchymoses may be present secondary to DIC.
- The urinary bladder may be very small due to oliguria or anuria.

III. Malignant hyperthermia is associated with drug or inhalant anesthesia administration and exclusion of other central and systemic causes of hyperthermia. Go **immediately to Management** below *p. 300*.
Clinical signs include:
- Tachycardia and tachypnea
- Rapidly rising end-tidal CO_2, $PvCO_2$ and $PaCO_2$
- Muscle rigidity
- Folowing extubation patients are dyspneic and may eventually become apneic

Laboratory/Imaging Evaluation

Stat
- **Obtain rectal temperature immediately.**
- **PCV and TS** increased due to dehydration or within normal limits in early stages. If hemorrhage present PCV is decreased. If septic or SIRS, TS may be decreased due to loss through vascular permeability. Note hemoglobinemia or myoglobinemia.
- **Stick BUN, urea or creatinine** may be increased due to pre-renal azotemia and fluid losses.
- **Glucose** may be increased initially due to stress, catecholamines, cortisol release and peripheral insulin resistance, but may be quite low as time progresses and if septic.
- **ACT** variable depending on severity and duration of hyperthermia. Increased (>120 seconds dogs, 90 seconds cats) in DIC.
- **Urine,** specific gravity variable depending on severity and duration of hyperthermia; increased initially due to dehydration and potentially low if renal tubular injury occurs. Hemoglobin or myoglobin may be present with rhabdomyolysis. Inappropriate glucosuria and casts are associated with renal tubular injury. May be anuric due to MODS.
- **Venous blood gases** initially show a respiratory alkalosis with progression to significant acidemia as perfusion and cardiac output decrease. Respiratory alkalosis may co-exist with non-respiratory acidosis due to increased lactate. $PvCO_2$ (and $PaCO_2$) rises rapidly with MH.
- **Lactate** is frequently increased above normal (2.5 mmol/L), especially with exertional hyperthermia and increases rapidly as hyperthermia worsens.
- **Electrolytes** may be altered due to dehydration (serum sodium increased), urinary and gastrointestinal losses. Potassium may be low or slightly increased initially, but increased with renal compromise or rhabdomyolysis. Calcium and phosphorous may be increased or decreased, which contributes to patient deterioration.
- **ECG** exhibits sinus tachycardia in early stages followed by ventricular arrhymias in the late stage.
- **Systemic blood pressure (SBP)** as the patient may be in shock (SBP ≤90, MAP ≤60 mmHg).

Extended Laboratory/Imaging Data Base
- Obtain as soon as possible.
- **CBC** may have increased red blood cell count due to hemoconcentration or decreased due to hemorrhage; nucleated red blood cells and schistocytes may be observed; leukocytosis or leukopenia, and thrombocytopenia due to endothelial injury and DIC.
- **Serum biochemical profile, urinalysis** to evaluate systemic illness (MODS) that may be a result of hyperthermia (*Pancreatitis p. 46, Acute Renal Failure p. 711, Hepatic Encephalopathy p. 40, Hypophosphatemia p. 390, Hypocalcemia p. 377*). Serum calcium may be normal but respiratory alkalosis reduces ionized calcium which may induce tetany. Creatinine kinase will be increased proportional to degree of injury and peaks at ~ 48 hours.
- **Thoracic radiographs,** when patient is stable, where respiratory compromise is present i.e., potential aspiration pneumonia, hemorrhage.
- **Further testing** is based on history, clinical and physical findings (differential diagnoses for cause of, rather than effect of, hyperthermia i.e., seizures may be a primary or secondary cause of hyperthermia).

If the owner calls for advice, telephone instructions should include taking the rectal temperature if possible, while cooling the animal by gentle hosing with cool water, placing the animal into a cool bath, pool, lake or ocean. Avoid putting the head near the water surface as aspiration may occur due to anxiety and tachypnea. Water immersion should be for a short period of time (15 minutes) before the temperature should be retaken. Depending on the condition (i.e., otherwise stable) continue to cool; if not stable (i.e., in shock) transport to the clinic with ice packs (i.e., include frozen food packs if needed), do not dry the animal, travel with car windows open and air conditioner on. While cooling the animal is important, reducing the temperature to lower than high normal range (39.5°C [102.5°F]) worsens outcome. As the thermoregulatory centre may be temporarily dysfunctional, thermoregulation may be impaired and hypothermia will not trigger endogenous heat production, therefore, continual monitoring of rectal temperature is essential. It is advised that all animals come to the clinic. If temperature has been reduced to the hypothermic range *see Accidental Hypothermia p. 291* for re-warming.

I.   **Malignant Hyperthermia.** Treatment must begin immediately as the temperature rises very rapidly and is difficult to control.

   1. **Discontinue inhalant** or other suspicious agent immediately. Remove anesthetic machine and use other source of oxygen and ventilation
   2. **Begin cooling as in D1 a–e below** while accessing.
   3. **Dantrolene 2 – 5 mg/kg IV.**
   4. **Propofol 0.1 – 0.2 mg/kg/min CRI (to effect) with top up 0.5 – 1.0 mg/kg** can be used in combination with dantrolene to continue anesthsia. Caution with hypotension.
   5. **Continue treatment below.**

II. **GENERAL MANAGEMENT**

A.   **Oxygen.** Initially, establish the Airway-Breathing (*Respiratory Emergencies p. 564*) where needed.

B.   **Butorphanol 0.2 mg/kg and dexamethasone 0.25 mg/kg** for animals with upper airway pathology.

C.   **IV catheter and IV fluids, while performing D below.** Plasma-Lyte® 148 or A, Normasol• R, or Lactated Ringer's. If serum **sodium > 160 mmol/L** 0.45% sodium chloride and 2.5% dextrose. As hypernatremia is acute, there is no concern for rapid reduction. As even mild hyperthermia causes fluid loss, all animals should receive IV fluids. The volume and rate is assessed based on history (i.e., blood loss, degree of dehydration), body temperature and physical examination (*see Fluid Therapy p. 347*). If the patient is septic *see Sepsis/Septic Shock p. 591* for fluid therapy. Avoid fluid overload (*see Monitoring during Fluid Therapy p. 358*).

   1. Animals **obviously in shock (Heatstroke)** SBP ≤90 mmHg, MAP ≤60 mmHg should receive:
      a. **Crystalloids at 1.5 – 5.0 mL/kg/min** initially with response to therapy monitored q5min to an approximate volume of 60 mL/kg (cats) – 90 mL/kg (dogs) with reduction if colloids are co-administered. As capillary leak and pulmonary edema may be a complication, vigilance is required. The rate should be increased or decreased based on response. **ADD**
      b. **Whole blood** if PCV <25%.
      c. **Synthetic colloid (dextran 70, 6% Hetastarch, 6% Pentastarch** – all acidifying solutions) in aliquots of **5 – 10 mL/kg (dog) or 2 – 5 mL/kg (cat)** to a maximum of 20 mL/kg (dog), 10 mL/kg (cat), over >15 minutes if hypotension persists.
      d. **If not hypernatremic,** and hypotension persists consider **hypertonic saline 5% (6 – 10 mL/kg max), OR 7.5% (4 – 8 mL/kg max) at 1 mL/kg/min** for dogs, **quarter of this for cats,** [with rapid administration respiratory arrest and/or vagoreflex bradycardia may occur, treat with 0.02 mg/kg atropine].
      e. **Fresh frozen plasma** 10 mL/kg CRI over 2 hours initially. If ACT prolonged, administer second infusion over 4 hours.
   2. Animals sufering from heat stress (**not in shock**), administer fluids cautiously (~2 – 10 mL/kg/h) until full extent of losses are known.

D.   **Cooling techniques**

   1. **Non-pyrogenic (Heat-induced illness).**
      Cooling must begin if temperature **>39.5°C (102.5°F). Continuous monitoring** is required.
      a. **39.5°C (102.5°F) <41.0°C (105°F)** wet with cool water, fan, room temperature fluids.

      b. **41.0°C (105°F) >42.0°C (107.5°F)** as b. above, run fluid line through bowl with ice in water (~4°C). As temperature drops, remove ice water.

      c. **≥42.0°C (107.5°F)** as **b.** above. Pack ice around the patient and close to, but not compressing, jugular veins, and head. Place urinary catheter and instill room temperature saline until bladder distended; allow dwell time of 5 mins, repeat. Offer ice cubes or crushed ice to lick if patient is alert. As temperature drops, follow steps **b. then a.** above. RARELY, room temperature (not ice cold or cold as splanchnic vasoconstriction occurs) enemas may be required if temperature not dropping. Prior to this compare the axillary temperature with the rectal temperature for continuous monitoring as the rectal route will not reflect true body temperature when enemas are used.

      d. The rate of cooling depends on the temperature. Lower as quickly as possible to **42.0°C (107.5°F)** followed by a slower rate beyond this to avoid hypothermia (~30 – 60 mins in total).

      e. Stop cooling measures at **39.5°C (102.5°F)**. Continuously measure temperature.

      f. **Non-steroidal anti-inflammatory drugs (NSAIDs)** should not be administered as the thermoregulatory set-point is not changed.

2. **Pyrogenic (fever).** Temperatures ≥41.5°C (106°F), or if 41.0°C (105°F) and rapidly rising (documented within a ≤10 min. period).

      a. Temperature must be lowered actively until it starts to drop, or stabilizes at ~**41.0°C (105°F)**. Use procedures in **1a–c above** while continually monitoring temperature and administering an **NSAID (b. below)**. Shivering must be avoided.

      b. **NSAIDs** must be administered in this setting to lower the set-point otherwise the shivering and increased metabolism will be induced to maintain the set-point. The following can be used in both cats and dogs, usually once. **Dipyrone** is preferred as there are no renal or gastrointestinal adverse effects. Re-dosing may be required if no effect in 45 – 60 min. The following are lower than analgesic dosages.

          i. Dipyrone 10 mg/kg IV   OR

          ii. Meloxicam 0.05 – 0.1 mg/kg IV   OR

          iii. Carprofen 2 mg/kg IV (do not repeat in cats)   OR

          iv. Ketoprofen 0.5 mg/kg IV   OR

          v. Tolfenamic Acid 1 mg/kg IV   OR

          vi. Acetaminophen drops (dogs only) 10 mg/kg if can take oral meds

      c. *See Sepsis/Septic Shock p. 588* **for further treatment.**

E. Neurologic deficits. If the patient is euvolemic, systolic blood pressure is ≥120 mmHg,

1. Neurological signs are severe or are deteriorating and increased intracranial pressure (*see Head Trauma – Neurological Assessment p. 465*) is suspected, and the patient is **NOT** overhydrated, oliguric (*p. 709*) or anuric (*p. 709*), and pulmonary edema or congestive heart failure (*p. 149*) **have been ruled out,** consider the following:

      a. **If not hypernatremic,** administer **hypertonic saline 5% (6 – 10 mL max), OR 7.5% (4 – 8 mL/kg max) at 1 mL/kg/min** for dogs, **quarter of this for cats** [rapid administration may result in respiratory arrest and/or vagoreflex bradycardia may occur, treat with 0.02 mg/kg atropine]. **OR**

      b. **Mannitol 0.1 – 0.25 g/kg (100 – 250 mg/kg)** over 5 minutes. **Do not use** with capillary leak.

      c. **Repeat mannitol q4–6h** for two more treatments if required. Higher doses of mannitol are not recommended.

      d. **If overhydrated +/- pulmonary edema** treat with **2 mg/kg furosemide IV**. As soon as possible after edema has resolved, give hypertonic saline, as above providing the patient is normotensive and signs are not improved.

2. **Vocalization, dimentia, extreme restlessness (rule out pain, hypoxia etc.), 'discombobulation',** administer **gabapentin 5 – 25 mg/kg PO q8–12h.** Start at 10 mg/kg. Very effective. Reduce dose in renal failure (eliminated by kidneys), wean off slowly over days. Adjust dosage according to level of sedation.

F. Vasopressors or an inotrope may be indicated in refractory hypotension (*see p. 606*).

      a. Dopamine 2 – 10 mg/kg/min   OR

      b. Dobutamine 2 – 10 mg/kg/min   OR

      c. Norepinephrine 0.1 – 0.5 µg/kg/min if not responsive to a or b above.

G. Prednisolone sodium succinate or methylprednisolone 0.5 mg/kg IV may be considered for refractory hypotension.

H. **Hypoglycemia,** glucose <3.5 mmol/L (65 mg/dL).

  1. **Dextrose 50% 0.25 – 0.5 mL/kg bolus** initially.
  2. Based on severity, establish a **CRI of 2.5 – 5.0% dextrose** (50 – 100 mL/L of 50% dextrose), or 7.5 – 10% (150 – 200 mL/L of 50% dextrose) if needed and for short duration, (a central line is required in small animals as this is very hyperosmolar *see Hypoglycemia p. 280*).
  3. Measure blood glucose frequently to **avoid hyperglycemia** which may worsen neurological outcome.

I. **Venous blood gases and lactate.** Should be monitored frequently until stable. **Acidosis** is frequently corrected by restoration of perfusion with alkalinizing crystalloid solutions in D above.

J. **Electrolytes,** should be frequently assessed until normalized. See specific chapters for therapy.

K. **Cardiac arrhythmias,** especially ventricular (*p. 179*) may require therapy. See specific chapters for therapy.

L. **Antibiotics** should be administered when vomiting and diarrhea are present as heat or ischemic injury to the gastrointestinal mucosa may facilitate translocation of enteric bacteria.

  1. **Cefoxitin 20 mg/kg IV q6h (dogs), q8h (cats) OR**
  2. **Ampicillin 20 mg/kgIV q6h (dogs), q8h (cats)**
  3. **Enrofloxacin 5 mg/kg IV (dogs) SC (cats) 1-hour infusion q24h** where mucosal slough noted **in combination with ampicillin OR**
  4. **Imipenem 5 mg/kg IV 30-min infusion q8h** as a single agent **OR**
  5. **Meropenem 20 mg/kg IV q12h, 8 mg/kg SC q12h (cats and dogs)**

M. **Gastrointestinal protectants** where gastrointestinal involvement is noted

  1. **Famotidine 0.5 mg/kg IV (dogs), SC (cats) q12h.**

N. A **urinary catheter** should be placed where necessary, prior to or after cooling, in an aseptic manner, to measure urine output. Constant assessment is required. Fluid therapy can be altered based on blood pressure, central venous pressure, urine production, PCV, TS, mentation and tolerance of fluids delivered (*see Acute Renal Failure p. 709, Fluid Therapy p. 353, Monitoring p. 16*).

O. Systemic blood pressure must be monitored and a fluid or colloid bolus administered should hypotension occur.

P. **Analgesics. Pain** is always a concern; analgesics should be administered where there is muscle or gastrointestinal involvement. For cats and dogs:

  1. **Morphine 0.2 – 0.5 mg/kg IM, SC or as a CRI** (*p. 251*)   **OR**
  2. **Oxymorphone 0.02 – 0.2 mg/kg IV, IM, SC or as a CRI** (*p. 255*)   **OR**
  3. **Hydromorphone 0.02 – 0.2 mg/kg IM, SC**   **OR**
  4. **Fentanyl 4 – 6 + μg/kg/h**
     When perfusion is established and gastrointestinal and renal abnormalities are ruled out, a NSAIA (*see Non-steroidal anti-inflammatory analgesics p. 85*) may be administered.

Q. **Laboratory evaluation** PCV, TS, activated clotting time, serum electrolytes, stick BUN and glucose in addition to weighing the animal, should be performed at least once daily to monitor for potential problems. A complete physical examination and measurement of vital signs should be performed several times daily until stable. Repeat biochemical profile, complete blood count and urinalysis (monitor for casts), are recommended in 24 hours to assess problems associated with the hyperthermic event, and potential predisposing medical conditions. Further testing may be required.

While the above are guidelines, not all hyperthermic animals will present as described nor will they necessarily require the cooling technique described. However, initial presentation and trending will dictate the appropriate therapeutic modality to pursue.

PHARMACOLOGY

1) **Dantrolene** is a muscle relaxant and antipyretic. It suppresses calcium ion release but does not inhibit uptake of calcium in muscle cells.

2) **Vasopressors and inotropes.** *See Cardiopulmonary Resuscitation p. 141.*

3) **Antibiotics.** *See Sepsis p. 593/597.*

4) **Analgesics.** *See analgesics p. 81.*

SUGGESTED READINGS

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NOTES

INTRODUCTION

There are approximately 2,500 species of snakes found on all continents except Antarctica. Snakes can be found in all habitats: plains, forests, jungles, savannahs, deserts, swamps, water and land. There are five groups of venomous snakes: Colubridae (rigid rear-fanged snakes, i.e., boomslang), Elapidae (rigid front-fanged snakes, i.e., cobras, mambas, coral snakes), Viperidae (true vipers, hinged, front-fanged, i.e., adders, vipers), Crotalidae (pit vipers, i.e., rattlesnakes, copperheads, cotton-mouths), and Hydrophiidae (rigid front-fanged sea snakes). In North America, there are two subfamilies of venomous snakes: Crotalidae, the pit vipers (i.e., rattlesnakes, cottonmouth or water moccasins, copperheads) and Elapidae (coral snakes). The crotalids (rattlesnakes) strike and release their prey, and search for the dying animal after it has ceased moving; therefore, their venom is primarily hemotoxic and proteolytic, functioning to immobilize the target and predigest the prey's body tissues. In contrast, the elapids (coral snakes) hold their prey after striking and use its neurotoxic venom to immobilize its prey. Hence venom can be considered functionally as an immobilizing agent with a plethora of predigestive enzymes. Among snake species, there are variable amounts of enzymatic and nonenzymatic proteins in the venom which give various physiologic effects characteristic of a particular snake species.

DIAGNOSIS

History/Signalment

- Severity of snakebite primarily dependent on quantity and toxicity of venom injected by snake.
- Amount and composition of venom is dependent on species of snake, time of year, regenerated volume since last bite, age of the snake, aggressiveness and motivation of the snake.
- Factors affecting the victim are size of the victim (ratio of venom to body weight), site of the snakebite, time elapsed since the bite, and the amount of physical activity after the bite occurred which affects the uptake of venom.
- It is important to identify the particular species of snake to determine that the pet has actually been envenomated. Clients that witness snakebites may claim the snake was venomous merely because it was a snake! If the snake's head is examined appropriate precautions must be taken because venom can be reflexively released several hours after a snake dies.
- Tendency to occur in young mature dogs.

Clinical Signs/Physical Examination

Local Signs
- Acute pain at the bite site.
- Acute erythema and edema at the bite site.
- Puncture wounds. Fang marks may be present as one or more well defined punctures, as a series of small lacerations or scratches, or there may not be any noticeable or obvious markings where the bite occurred. The absence of fang marks does not preclude the possibility of a bite (especially if a juvenile snake is involved). Most often bite on head, front limbs, or hind limbs.
- Local tissue necrosis and slough.

Systemic Signs
- Petechial and ecchymotic hemorrhages on mucous membranes and in tissues.
- Shock, severe hypotension, tachycardia, and shallow respiration.
- Systemic signs can include depression, lethargy, vomiting, diarrhea, arrhythmia, fever.
- Convulsions, bulbar paralysis manifest as cranial nerve deficits (i.e., ptosis, dysphagia, dysphonia).

Patient Evaluation

- Clip fur in the region of the bite while searching for wounds. Local edema may obscure puncture wounds.
- Careful monitoring is important because an apparently mild case of envenomization may rapidly progress to a moderate or severe case over a few hours.
- Each case of snake bite with envenomization is unique; therefore, treatment is directed towards clinical signs present.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, total solids (TS).** Hemoconcentration due to dehydration, shifts of fluids to inflamed areas from circulation, or catecholamine–induced splenic contraction; or decreased PCV due to hypovolemia from shock or anemia from bleeding.
- **Stick BUN** may be elevated with dehydration (elevated urine specific gravity) or multi-organ failure (elevated creatinine).
- **ALT** may be elevated with liver damage.
- **Activated clotting time (ACT)** may be elevated with DIC.
- **Coagulogram [PTT, PT, FDP]** may be elevated with DIC.
- **Creatine kinase** may be elevated due to rhabdomyolysis or muscle damage at snake bite site.
- Measure the circumference of the affected body part above, below and at the bite site to monitor for edema.
- **ECG.** Arrhythmias may be due to cardiotoxin or myocarditis.

Extended Laboratory Data Base

If not already obtained.

- **CBC.** Acute inflammatory reaction characterized by leukocytosis consisting of neutrophilia with or without a left shift, or a stress response of leukocytosis with neutrophilia; thrombocytopenia may occur due to vasculitis, utilization in inflamed tissues, development of DIC.
- **Biochemical profile** including electrolytes, BUN, creatinine, creatine kinase, glucose. BUN and creatinine may be elevated with dehydration or multi-organ failure; ALT, SAP, and GGT may be elevated with liver damage; elevated CK with or without hyperkalemia, hypercalcemia, and hyperphosphatemia due to muscle damage at snake bite site; plasma may be hemolysed or hyperbilirubinemia from hemolysis (venom hemolysin); hyperglobulinemia may be due to increased levels of acute phase proteins.
- **Urinalysis** may have hematuria, hemoglobinuria, or myoglobinuria.
- **Coagulogram [PTT, PT, FDP]** may be prolonged if DIC present.
- Serial measurements of laboratory parameters are necessary to assess changes in the systemic response to envenomation.
- Bacterial culture of wound (aerobic and anaerobic).

MANAGEMENT

Acute

A. If necessary, make sure that responsible snake or snakes have been appropriately and safely contained and are not in danger of inflicting any additional bites.

B. **Subdue and immobilize** the patient as much as possible to slow the uptake of venom. For mild to moderate restraint **butorphanol 0.1 – 0.2 mg/kg IV, IM,** for more profound effect **oxymorphone or hydromorphone 0.05 mg/kg IV or IM (rapid)** or **morphine 0.1 – 0.2 mg/kg IV (slowly), IM** or **methadone 0.1 – 0.2 mg/kg IV, IM.** If inadequate (*see Chemical Restraint p. 97*).

C. **Fluid therapy.** A balanced, isotonic, alkalinizing, crystalloid solution (BES) is preferred (Plasma-Lyte® 148, Plasma-Lyte® A, Lactated Ringers). In hypovolemic shock, rapid, large volume (**1.5 – 2 mL/kg/min BES** or **synthetic colloids 5 – 10 mL/kg titrated to effect**) fluid therapy may be required. (*See Fluid Therapy p. 358 or Shock p. 606*). **Transfusion.** In the presence of coagulopathies, platelet-rich plasma, fresh or fresh-frozen plasma may be needed (*see Transfusion p. 667*).

D. **Antihistamines.** Diphenhydramine 2 mg/kg IM dogs and cats given before antivenin administration (added benefit of sedation).

E. **Antivenin.** The appropriate dose to neutralize signs is determined by *in vivo* titration while monitoring the physical signs and laboratory parameters of the patient. Rarely contraindicated except for patients with a history of anaphylaxis to antivenin. In most cases, if signs of envenomization are evident, antivenin should be given as soon as possible. Treatment delays are more hazardous in smaller animals due to lack of venomdilution.

F. **Epinephrine.** Be prepared to use in cases of anaphylaxis with administration of antivenin (*see Anaphylaxis p. 615*).

G. **Antibiotics.** Based on culture and sensitivity of the wound and ability of the antibiotic to reach appropriate tissue level concentrations. Empiric intravenous first (**cefazolin 20 mg/kg IV q6h, cephalexin 20 mg/kg PO q8h**) or second (**cefoxitin or cefotetan 20 mg/kg IV** to include anaerobic coverage) generation cephalosporins may be used pending culture results.

H. Corticosteroids do not alter the course of envenomation and may contribute to sepsis.

I. Patient should be monitored for at least 24 hours as clinical signs of envenomation may take hours to appear. Don't leave unattended in the clinic, home monitoring is better than none.

J. **Rattlesnake vaccine** (*Crotalus atrox* toxoid). A prophylaxis for healthy dogs who are in rattlesnake habitat. Vaccinates produce antibodies against *Crotalus atrox* (Western diamondback rattlesnake) venom which cross-protects against many U.S.A. rattlesnake venoms. Vaccinates typically experience a moderated course of venom toxicity depending on titer and degree of envenomation; therefore, vaccinates require less therapeutic intervention than unvaccinated dog.

PHARMACOLOGY

1) **Antivenin** acts by neutralizing the venoms in patients via passive immunization of globulins obtained from horses immunized with venom. Cost may limit its use. The most significant adverse effect is anaphylaxis secondary to the equine source of the product. Antivenin (*Crotalidae*) Polyvalent Equine Origin (Fort Dodge or Wyeth). Antivenin (*Micrurus fulvius*) Coral Snake (Wyeth) but not effective for Sonoran or Arizona Coral Snake. To locate nearest Antivenom Resource call Wyeth (610) 688-4400.

2) **Cephalexin, cefazolin** cover gram positive and gram-negative organisms, whereas **cefoxitin and cefotetan** have additional anaerobic coverage.

3) **Rattlesnake vaccine** (*Crotalus atrox* toxoid). Initial vaccination of 2 doses one month (3 – 6 weeks) apart followed by an annual booster one month prior to potential exposure. Dogs at particular risk (e.g., small dog) or in area with extended season of rattlesnake activity may be boostered at 4 – 6 month intervals. Antivenin is not contraindicated in vaccinated dogs and should be used where appropriate. Manufactured by Red Rock Biologics (866) 897-7625 (www.redrockbiologics.com).

SUGGESTED READING

1. http://www.venomdoc.com.
2. Hudelson S, Hudelson P. Pathophysiology of snake envenomization and evaluation of treatments – Part III, Compendium on Continuing Education for the Practicing Veterinarian, 1995; 17:1385-1396.

NOTES

INTRODUCTION

Ticks are one of the most important groups of arthropods affecting pets. They can have deleterious effects directly by injecting saliva or obtaining blood and indirectly by transmitting a variety of disease agents. The epidemiology of tick-borne diseases continues to change as society continues to evolve creating more opportunities for tick-animal contact. As a result, a number of tick-transmitted diseases have begun to emerge in the temperate zones such as Lyme borreliosis and Rocky Mountain spotted fever. Ticks are obligate blood feeders with all active stage (larvae, nymphs, and adults) requiring blood as a source of nutrition and, in the case of adults, for reproduction. Tick salivary secretions play a major role in animal disease because of the transmission of pathogenic organisms. *Dermacentor andersoni*, the Rocky Mountain wood tick, and *Dermacentor variabilis*, the American dog tick, are the principal vectors of *Rickettsia rickettsii* the causative agent of Rocky Mountain spotted fever. The genus *Rhipicephalus sanguineus*, the brown dog tick, is the vector for *Ehrlichia* and *Babesia canis*. The genus Ixodes such as *Ixodes dammini* are major vectors for the spirochete *Borrelia burgdorferi* the causative agent of Lyme borreliosis. *Amblyomma maculatum*, the Gulf Coast tick, is the vector for *Hepatozoon americanum* the causative agent for canine Hepatozoonosis. *Dermacentor variabilis* is the principal vector for transmission of *Cytauxzoon felis* to cats in south-central U.S.A.

DIAGNOSIS

History

- Dogs and cats that roam in wooded areas, fields, may become tick infested; therefore, periodic examinations should be made to remove attached and engorged ticks.
- Care must be taken to remove all of the tick, to not crush the tick and contaminate the bite wound, and to not infect the owner.

Clinical Signs/Physical Examination

- Fever
- Anorexia
- Lymphadenopathy
- Lameness, myalagia, joint pain
- Petechiae and ecchymoses on mucous membranes or skin (e.g., hematuria, epistaxis)
- Cachexia, weight loss
- Anterior uveitis, retinal hemorrhage
- Ataxia, paraparesis, conscious proprioceptive deficits
- Head tilt, nystagmus, seizures

Laboratory Evaluation

Stat
- **PCV.** Mild to marked anemia (usually nonregenerative) depending on blood loss or chronic bone marrow suppression (pancytopenia).
- **TS** may be decreased due to blood loss or hypoalbuminemia from proteinuria.
- **Stick BUN** may be elevated (if renal disease from glomerulonephritis or interstitial nephritis).
- **Glucose** may be mildly increased, or may be artifactually lowered by consumption by markedly elevated neutrophils (Hepatozoon).
- **ACT** may be prolonged.
- **Urine specific gravity** may be within normal limits if no renal involvement or glomeruli affected but may be isosthenuric should interstitial disease compromise tubular function.
- **CSF** may have pleocytosis with elevated protein, may see morulae in leukocytes.

Routine Minimum Data Base

If not already obtained,
- **CBC.** Mild to marked anemia depending on blood loss or chronic bone marrow suppression (pancytopenia) or regenerative anemia (+/- autoagglutination) with immune-mediated hemolytic anemia IMHA (Babesia); leukocytosis (marked neutrophilia [20 – 200 x 10'/L] with Hepatozoon) to leukopenia with chronic bone marrow suppression; thrombocytopenia due to vasculitis, platelet consumption, and decreased platelet half-life from splenic sequestration.
- **Biochemical profile** (including electrolytes, BUN, creatinine, creatine kinase, glucose). Mild to marked elevations in BUN and creatinine (if renal disease from glomerulonephritis or interstitial nephritis); hyperproteinemia with hyperglobulinemia (usually polyclonal but monoclonal can occur); hypoalbuminemia (if proteinuria); nonspecific mild increases in ALT, SAP, and bilirubin; hypercholesterolemia.
- **Urinalysis** may have proteinuria, hematuria.
- **Coagulogram** [PTT, PT, FDP] may be prolonged.
- **Arthrocentesis** with cytological examination +/- bacterial culture. Inflammatory changes with predominately neutrophilic effusion.
- **Bone marrow biopsy** in chronic Ehrlichia may have pancytopenia, granulocytic hyperplasia with erythroid hypoplasia with Hepatozoon.
- **Direct anti-RBC antiglobulin (Coombs') test** for IMHA due to *Babesia*.
- **Blood smear:** occasionally organisms identified in cells on thin blood smears.
- **Serological titers** for *Rickettsia rickettsii, Ehrlichia, Borrelia burgdorferi, Babesia.*
- **Polymerase Chain Reaction (PCR):** available in commercial or research labs (used in conjunction with serology or to monitor therapy).
- **Muscle biopsy** for *Hepatozoon americanum.*

MANAGEMENT

A. Antibiotics.
1. Rickettsia (*Rickettsia rickettsii, Ehrlichia*) and spirochete (*Borrelia burgdorferi*): doxycycline 5 mg/kg PO q12–24h, tetracycline 22 mg/kg PO q8h or chloramphenicol(15 – 20 mg/kg PO q8h.
2. Resistant *Ehrlichia*: imidocarb dipropionate 5 mg/kg IM once every 2 – 3 weeks.
3. *Hepatozoon americanum*: combination of trimethoprim sulfa 15 mg/kg PO q24h, pyrimethamine 0.25 mg/kg PO q24h, and clindamycin 10 mg/kg PO q8h for 2 weeks followed by decoquinate 10 – 20 mg/kg PO q12h.
4. *Babesia*: imidocarb dipropionate 5 – 7.5 mg/kg once every 2 – 3 weeks IM or SC; atovaquone 13.3 mg/kg PO q12h and azithromycin 10 mg/kg PO q24h.

B. Transfusion. In the presence of coagulopathies, platelet-rich plasma, fresh or fresh-frozen plasma may be needed (*see Transfusion, p. 667* and *Thrombocytopenia, p. 451*).

C. Fluid therapy. A balanced, isotonic, alkalinizing, crystalloid solution is preferred (Plasmalyte). In severe cases of hypovolemic shock colloids may be required (*see Fluid Therapy, p. 358 or Shock p. 606*).

D. Prednisone. In presence of immune-mediated hemolytic anemia (*see IMHA, p. 411*).

PHARMACOLOGY

1) **Doxycycline** long-acting, lipid soluble, second generation tetracycline antibiotic especially effective against rickettsia and spirochetes. Readily diffuses into the eye, brain, CSF and prostate. Can be given once daily and absorption is not hindered in the presence of food. The increased cost over tetracycline is cost effective when considering the potential for poor compliance of tetracycline (*see below*).

2) **Tetracycline** is a broad spectrum antibiotic, however dosing is required q8h and must be given in the absence of food within the gastrointestinal tract. Based on this, owner compliance is usually poor and it is almost impossible to have an empty gastrointestinal tract with this dosing schedule. It is therefore suggested that treatment may be more effective with doxycycline.

3) **Imidocarb dipropionate** is an antiprotozoal agent; it is painful upon injection and may cause hypersalivation, lacrimation, diarrhea, dyspnea and depression. Atropine may be used to treat cholinergic signs. Do not use in patients exposed to cholinesterase-inhibiting drugs, pesticides, or chemicals.

4) **Trimethoprim sulfa** broad spectrum antibiotic which has efficacy against protozoa when used in combination with other antimicrobials. Several adverse reactions may occur and these should be noted.

5) **Pyrimethamine** inhibits folic acid metabolism in the parasite and increases the activity of the sulfonamides against *Hepatozoon americanum*. Depression, anorexia, vomiting and reversible bone marrow suppression may occur within 4-6 days with the combination. Cats are especially sensitive. Bone marrow suppression may be mitigated with 50 mg/day folic acid, 100 mg/kg/day Bakers' yeast or 1 mg/kg/day folinic acid, added to the diet.

6) **Chloramphenicol** is a broad spectrum antibiotic. The owners should be cautioned as to the human potential for bone marrow suppression when handling this medication. Gloves and immediate hand washing is advised.

7) **Atovaquone** is an antiprotozoal agent; used in combination with other drugs because in vitro testing found increased resistance.

8) **Azithromycin** is a relatively broad spectrum antibiotic, **which has efficacy against protozoa when used in combination with other antimicrobials.** Contraindicated in animals hypersensitive to macrolides and use with caution in animals with hepatic disease.

SUGGESTED READING

1. Greene CE. Infectious Diseases of the Dog and Cat, 3rd edition, Toronto: WB Saunders; 2006.
2. Macintire DK. Emerging and Re-emerging Infectious Diseases, Vet Clin North Am. Small Anim Pract, Toronto: WB Saunders; 2003.

TABLE 1. Antiparasitics for Tick Control in Dogs (D) and Cats (C)

Drug	Ticks			
	Dermacentor variabilis (American dog tick)	*Rhipicephalus sanguineus* (brown dog tick)	*Ixodes scapularis* (blacklegged tick, deer tick)	*Amblyomma maculatum* (Gulf Coast tick)
Amitraz (Preventic™ collar)	D	D		
Carbaryl (Zodiac™ powder)	C/D	C/D		
Fipronil (Frontline™)	C/D	C/D	C/D	C/D
Fipronil/methoprene (Frontline Plus™)	C/D	C/D	C/D	C/D
Imidacloprid/Permethrin (K9 Advantix™)	D	D	D	D
Permethrin (Defend Exspot™, Proticall™, Active-3™)	D	D	D	
Propoxur (Zodiac™ collar)	C/D	C/D		
Pyrethrins	C/D	C/D		
Selamectin (Revolution™)	D			

Adapted from Allen DG, Handbook of Veterinary Drugs, 3rd edition, Philadelphia: Blackwell Publishing (Lippincott Williams & Wilkins), 2005.

NOTES

INTRODUCTION

Birds have developed effective techniques to mask debility as a survival mechanism in the wild. Many avian "emergencies" reflect decompensation of chronic disease processes. The patient may have been ill far longer than realized by the client but is now presented exhibiting detectable clinical signs that are perceived as acute in onset. The clinician is strongly encouraged to take a detailed history and observe the patient, from a distance if possible, before approaching the cage and restraining the bird.

HISTORY TAKING

- A thorough history is extremely important.
- Nuances of mentation, behaviour and respiratory rate are best appreciated from a distance.
- Is the patient alert?
- Does the bird perch and ambulate normally?
- Does the bird exhibit dyspnea (increased respiratory noises, increased abdominal effort and tail bobbing)?
- A decision regarding the ability of the patient to withstand physical restraint and examination must be made and discussed with the owner at this point.

RESTRAINT AND HANDLING

- Most techniques of clinical investigation require a properly restrained patient.
- Safe, effective means of restraint are essential and are based upon meeting and controlling the defensive and offensive abilities of the particular species you will be handling.
- Parrots, for example, have beak, head and neck adaptations that enable them to generate powerful crushing forces for food prehension and processing. When threatened they will defend themselves by biting.
- Capture and restraint of members of the parrot family therefore focuses upon immobilizing the head and neck region first before controlling the rest of the body.
- An appropriately sized towel, held in the dominant hand of the operator, is used to approach and quickly grasp the parrot's head and neck from behind as the bird turns to flee.
- The wings and body are surrounded by and supported using the remaining towel to achieve control.
- With raptorial birds (falcons, hawks, owls) the focus centers on the quick, strong, feet with their sharp talons. A towel is used to cover the bird from above while even, downward pressure is applied over each flank to force the bird onto its hocks. The operator can then move his or her hands quickly over and around the sides to grasp the feet. It is essential to immobilize both feet simultaneously!
- During the period of restraint the clinician should continually assess how the patient is responding by observing respiratory excursions and effort as well as mentation. If the bird exhibits open mouth breathing or other signs of respiratory distress, restraint should be terminated immediately.
- The patient should be given supplemental oxygen by mask or cage if respiration does not return to normal within one to two minutes.

PHYSICAL EXAMINATION

- An assistant will usually be required to hold the bird while the veterinarian performs the physical examination.
- Begin at the head and examine the eyes, nares and beak.
- A speculum or tape loops will be required to safely hold the beak open in the unanesthetized bird to allow examination of the oral cavity.
- The pectoral limbs should be palpated thoroughly for swelling and/or fractures. Begin at the shoulder and progress down the humerus to the elbow.
- Inspect the forearm, carpus and modified hand paying careful attention to the primary and secondary flight feathers.
- The large pectoral muscle mass of the bird is an excellent indicator of general body condition. This muscle mass should be symmetrical and rise to meet the keel of the sternum on the ventral midline. Atrophy is reflected by an increased concavity of the pectoral muscles and can be graded (Fig. 1).

- Only the most caudal portion of the coelomic cavity is palpable caudal to the large plate-like sternum. The ventriculus may be palpable as a firm mass in the left cranial quadrant of the abdomen. In female birds ready to lay an egg, the egg will be palpable in the left caudal abdomen. Distension of the coelomic cavity with fluid or other firm masses is not normal. The healthy liver does not extend beyond the sternal border in most pet birds.
- The vent lips should be clean and closed due to normal muscle tone. Adherent urates, feces or blood are abnormal findings.

ANESTHESIA

May be required as restraint for further examination, sample collection and diagnostic imaging.
- *Isoflurane* is the anesthetic agent of choice in pet birds. Premedicants are seldom used.
- The bird's crop (located at the thoracic inlet) should be palpated to ensure that it is empty before proceeding in order to prevent regurgitation and aspiration.
- A facemask is placed over the head of the restrained bird and an initial concentration of 5% is administered to achieve rapid induction.
- For procedures longer than 15 minutes or in high-risk patients an uncuffed endotracheal tube is placed into the glottis and the bird maintained with a Bain (or other low resistance, non-rebreathing) circuit
- The inhalent is given to effect, typical maintenance concentrations vary between 1.5 – 3.0 % isoflurane.
- The oxygen flow rate should be not less than 300 mL/min and will typically be between 0.8 L/min and 1.5 L/min. The depth and rate of sternal movements are an excellent indicator of anesthetic plane.

DIAGNOSTIC SAMPLE COLLECTION

Blood Collection & Hematologic Assessment

- Good quality blood samples are important to the definitive diagnosis of avian disease.
- The **right jugular** vein is the largest and most accessible vein for sample collection. The patient is held by an assistant placing the left hand on the mandible and using the right hand to grasp the feet and the tip of the right wing. (Fig. 2a, b) The bird is stretched into left lateral recumbency so that moistening the lateral cervical feathers can expose a featherless area overlying the right jugular vein (Fig. 2c). The highly mobile vein is stabilized with the thumb of the non-dominant hand (Fig. 2d). After collection of a sample equivalent in millilitres to *less than* one percent of an accurately determined body weight in grams (Table 1) the patient is placed back into its cage. Application of pressure to the jugular venipucture site is not recommended as it tends to *increase* hematoma formation. Release the bird and allow the patient to resume a standing position.
- The **basilic vein** is a second choice for collection. This vessel runs the length of the humerus. Its ulnar branch is the most frequently cannulated portion. Unlike the jugular vein, pressure over this site, preferably in advance of removal of the needle, is absolutely necessary to reduce hematoma formation.
- The **medial metatarsal vein** is a useful sample site in selected species such as pigeons, ducks, geese and swans. The vein is covered for part of its length by reptilian-like scales.
- The clipping of toenails is a painful technique that frequently yields blood samples of inadequate volume and quality. We do not recommend this approach for clinical samples.

TABLE 1. Estimating Safe Avian Blood Sample Size

SPECIES	BODY WEIGHT	MAXIMUM SAMPLE
Canary	20 g	0.2 mL
Budgerigar	35 g	0.35 mL
Cockatiel	90 g	0.9 mL
Quaker Parakeet	122 g	1.22 mL
Amazon Parrot	425 g	4.25 mL

Diagnostic Imaging

- Anesthesia is generally required to achieve appropriate positioning while reducing patient stress.
- The patient must be stable.
- Two properly positioned, standard, whole body views (a ventrodorsal and a left to right lateral) should be exposed on high detail cassettes.
- The ventrodorsal survey view is achieved by placing the anesthetized patient in dorsal recumbency with the wings extended symmetrically to each side and the legs extended caudally (Fig. 3a). If properly positioned the V/D view places the keel at a ninety-degree angle to the film *directly* superimposed over the vertebral column and the femurs are parallel.
- For the lateral view the patient is placed in right lateral recumbency with the wings extended over the back and taped to the plate with a lightly adhesive tape (e.g., Transpore, 3M Corporation, Minneapolis, MN) (Fig. 3b). Achieve true lateral positioning by avoiding over rotation of the body. Check the tension applied to the wings before taping in place. The legs are pulled caudally and taped with a similar tape. By convention the dependant (right) limbs are placed slightly cranial to the left limbs. A correctly positioned lateral radiograph is judged by superimposition of the acetabulae and ribs.

EUTHANASIA

- Birds should be euthanized with an intravenous injection of a suitable agent such as pentobarbital.
- General anesthesia (e.g., isoflurane administered by mask) facilitates intravenous administration while preventing movement or vocalization.
- Intrahepatic or intracardiac injections are appropriate in anesthetized birds if peripheral veins cannot be used but are more difficult to perform than in mammals due to the presence of the large, shield-like sternum.
- Some euthanasia products may be rapidly absorbed after injection into the pectoral muscles of small birds (e.g., less than 50 g).
- Intra-coelomic injections are *not appropriate* in birds as accidental injection into an air sac may not provide adequate absorption of the euthanasia solution.

GENERAL SUPPORTIVE CARE for Specific Syndromes below

A. Environmental Support

1. Many pet bird species are originally native to peri-equatorial regions and benefit from thermal support when ill.
2. Supplemental humidity may also be required. Knowing the normal biology of the species being treated is important.
3. Thermal support and variable relative humidity are best provided using an incubator with adjustable controls. Suggested starting point is 30°C (88°F) with humidity of 60%.

B. Fluid Therapy

1. **IV catheters** are challenging to maintain except in anesthetised or moribund birds. The thin overlying dermis and fragility of avian veins make placement and anchoring difficult. The most commonly used sites are the jugular vein and the basilic vein in awake birds.
2. An **intraosseous catheter** may be placed into marrow containing bones such as the ulna or tibia. Catheters in these locations are more stable and difficult for the patient to remove. The ulna is the IO site of choice in most species because the cannula can be taped into the distal ulna in a comfortable yet secure position. A spinal needle of appropriate diameter is recommended (usually 22 g, 1.5 inch for 250 – 900 g birds). The needle is inserted into the distal ulna, on the lateral aspect, at a point just medial to the dorsal ulnar condyle (Fig. 4).
3. **Balanced electrolyte solutions** may be given subcutaneously, intravenously or intraosseously.
4. **Subcutaneous fluids** (do not use acetated solutions as they sting) may be administered in the inguinal region, over the pectoral muscles and/or in the interscapular area. The dorsal cervical region should be avoided as subcutaneous air sacs occur in this location.

C. Respiratory Support

1. Birds have a unique respiratory system based upon flow through, non-expansile lungs and large air sacs.
2. The air sacs provide tidal volume by expanding or contracting in relationship to the bellows like movement of the sternum.
3. Increased environmental oxygen can be supplied using an incubator, face mask or modified cage front.
4. Severely dyspneic birds may be assisted by using alternate methods of ventilation not possible with mammalian lungs.
5. In the case of upper respiratory or tracheal obstruction, cannulation of the caudal thoracic air sac is the safest access point in most species for alternate ventilation.
6. A sterile, uncuffed endotracheal tube (e.g., 3.0 – 4.0 mm, uncuffed) is inserted behind the last rib through a blunt puncture in the body wall. The site is located by noting where the flexor cruris muscle crosses the last rib (Fig. 5a). A skin incision over this point allows the ventral border of the flexor cruris to be located. The ventral edge is bluntly reflected and the body wall is punctured, allowing insertion of a sterile ET tube in a cranial direction (Fig. 5b). Reduction in respiratory effort should be immediate and air flow should be evident through the lumen of the tube. If available, a 2.7 mm endoscope can be inserted through the lumen of the tube to ensure its positioning in the air sac.
7. The ET tube can be secured using a tape butterfly placed around the tube at the body wall and sutured to muscle or the last rib. The tube must be assessed regularly to ensure patency, and should be left in place for the minimum time required.

D. Nutritional Support

1. In pet seed eating birds, gavage feeding with a balanced formula designed for juvenile parrots is an excellent method of meeting the nutritional needs of the debilitated patient. The dry powder is added to a suitable amount of warm water (37.0 – 39.0°C) to make a suspension of approximately cake batter consistency.
2. Carnivorous raptors may be gavage fed using pureed feline recovery diets.
3. Rigid, curved, stainless steel feeding tubes are available in several sizes and are the easiest to manipulate and place in parrots. Rubber and vinyl feeding tubes are flexible and better employed in species without a crushing or cutting bill. They are especially useful in birds with long necks.
4. It is essential to ensure that the tube is in the esophagus before commencing gavage feeding as intratracheal infusion will almost certainly kill the patient.

E. Medical Therapy

1. **Antibiotics:** Broad-spectrum antibiotics are recommended in debilitated birds. Gram negative pathogens predominate but collection of appropriate pretreatment samples for diagnostic evaluation allows the most precise selection of effective therapy. Useful emergency choices are:
   a. **Enrofloxacin 10 – 15 mg/kg IM or PO q12h.**
   b. **Trimethoprim-sulfonamide** combinations **30 – 60 mg/kg SC or PO q12h.**
2. **Analgesia**
   a. Opioids most commonly used for avian analgesia.
      1. **Butorphanol 1 – 3 mg/kg IM q6–8h**
      2. **Meperidine 3 – 5 mg/kg IM q4–6h**
   b. NSAIDS
      1. **Meloxicam 0.3 – 0.5 mg/kg IM, PO q24h** is an excellent non-steroidal anti-inflammatory agent in birds.

SPECIFIC SYNDROMES

"SICK BIRD SYNDROME"

History/Clinical Signs/Physical Examination

- Inappetence, depression, lethargy, fluffed body feathers.
- No evidence of trauma, regurgitation, ataxia or respiratory distress.
- Owner may perceive these as acute signs but a thorough history may suggest longer course.
- Consider systemic bacterial, viral or fungal infection. Guarded prognosis.

Laboratory Evaluation

- CBC for evidence of anemia or leukocytosis suggestive of infection. Biochemical profile particularly for hepatic and renal function.
- Radiographs of appropriate areas.
- Fecal cytology and culture.
- *Chlamydophila psittaci* ELISA and/or PCR.

MANAGEMENT

Prior to treatment collect samples and place in incubator.

A. Begin broad-spectrum antibiotic therapy.

B. Correct and maintain hydration.

C. Gavage feed.

BLEEDING

History/Clinical Signs

- Blood is observed on the cage bottom, perches or walls.
- Blood may be seen on the bird's feathers or beak.

Physical Examination/Laboratory Evaluation

- Is the blood associated with the urofeces? If yes, check the bird's vent for trauma, papillomas or inflammation. Anaesthesia and cloacoscopy may be required to perform a thorough examination. This type of bleeding is more likely to be intermittent.
- If no, examine the patient's feathers carefully, especially those on the wings and tail for a damaged growing feather (a "blood quill"). Anesthesia may be required.
- Check CBC (especially the hematocrit) and blood calcium levels.

MANAGEMENT

A. Damaged blood quills are removed from the feather follicle by grasping them at the base and pulling firmly out *in the direction of feather growth*. Hemostats or needle nosed pliers may be required in larger patients. Apply local pressure to the follicle after removal to completely stop bleeding.

B. Delayed blood clotting may represent a coagulation disorder. The avian blood clotting system is weighted more heavily to the extrinsic pathway. Tissue thromboplastin released during trauma is usually effective in stimulating clotting. **Vitamin K$_1$ (0.5 – 2.5 mg/kg IM) and/or calcium gluconate (50 – 200 mg/kg SC or IM) may be administered.**

C. Transfusions are rarely required but should be considered when the hematocrit drops below 10 – 12.

D. Fluid therapy as needed.

TRAUMA

History/Clinical Signs/Physical Examination

- Clinical Signs: Abnormal wing position, not using leg, ataxia, lacerations
- Thorough examination and palpation under isoflurane anaesthesia
- Evaluate wounds keeping in mind that feathers tend to obscure skin trauma.
- Bruised areas in birds turn green within 3 – 4 days as hemoglobin is converted to biliverdin. This should not be confused with gangrenous tissue, which will be black, cold, and either dried or edematous.

Laboratory Evaluation

- Radiographs.
- CBC. Biochemical profile.

MANAGEMENT

A. Cleanse and dress wounds using standard techniques.

B. Skeletal fractures in birds are often open as birds have very thin skin with minimal soft tissue coverage over bones, and fractures frequently have sharp bone fragments.

C. Stabilize fractures using bandaging and coaptation. For fractures distal to the humerus, a figure 8 bandage incorporating the humerus and distal wing is appropriate (Fig. 6). For injuries to the humerus or pectoral girdle, a body wrap is required in addition to the figure 8 wrap (Fig. 7).

D. Birds are highly sensitive to the immunosuppressive effects of corticosteroids, and their use is discouraged in most situations. Corticosteroid use could be considered for patients with acute head trauma (<24 hours) as a single low dose of dexamethasone at 0.1 – 0.25 mg/kg SC, IM.

E. Broad-spectrum antibiotic.

REGURGITATION AND VOMITING

History/Clinical Signs/Physical Examination

- Head and neck "pumping", expulsion of food material and/or mucus from the oral cavity.
- Variable lethargy and depression.
- True vomit will usually have gastric or duodenal content present (e.g., green colouring due to bile stained ingesta) and will have an acidic pH.
- Differential Diagnoses: Proventricular Dilation Disease (PDD). Acute lead or zinc toxicity. Bacterial ingluvitis. Megabacteriosis (Avian Gastric Yeast). Foreign body ingestion. Renal failure.

Laboratory Evaluation

- CBC. Biochemical profile (especially uric acid to assess renal function).
- Radiographs, barium contrast may also be indicated.
- Zinc determination (plasma, centrifuged and separated immediately, placed in plastic tube or royal blue vacutainer for shipment to laboratory).
- Lead determination (heparinized whole blood).
- Crop cytology and/or crop culture.
- Fecal cytology and/or culture.

MANAGEMENT

A. Collect pre-treatment samples.

B. Begin broad-spectrum antibiotic therapy.

C. Begin chelation therapy (**Calcium EDTA 30 mg/kg BID IM**). It is essential to begin chelation therapy before heavy metal results are back as many pet birds will become *rapidly* toxic due to the amount ingested.

DIARRHEA

History/Clinical Signs/Physical Examination

- True diarrhea is less common than polyuria in pet birds. By definition, with true diarrhea the fecal component of the urofeces will lack the typical, tubular form created by passage through the rectum.
- Variable lethargy and dehydration.
- Feces may have foul odour.
- Differential Diagnoses: Gram negative bacteria (e.g., *Salmonella* sp., *Yersinia* sp., *E. coli*), anaerobic bacteria (e.g., *Clostridium perfringens*), Giardia, Cochlosoma, Coronavirus, Rotavirus.

Laboratory Evaluation

- CBC, particularly for leukocytosis suggestive of enteritis. Biochemical profile, particularly uric acid levels if moderate to severe dehydration is present.
- Fresh fecal wet mount, cytology, Gram stain.
- Fecal culture.
- Viral culture and/or electron microscopy.

A. Environmental support (temperature and/or humidity).

B. Fluid therapy.

C. Antibiotic therapy based upon fecal cytology (while awaiting cultures).

D. Anaerobic bacterial infections are under appreciated due to difficulty in culture. Check Gram stain for large Gram positive rods, especially with spores. If infection with anaerobes is suspected treat with **metronidazole 30 – 50 mg/kg PO q12h.**

ACUTE RESPIRATORY DISTRESS

History/Clinical Signs/Physical Examination

- Inspiratory or expiratory dyspnea.
- Open mouth breathing.
- Abnormal respiratory sounds (wheezing, coughing).
- Altered vocalizations, change in voice.
- Differential Diagnosis: syringeal, pulmonary, or air sac aspergillosis. Tracheal/syringeal obstruction due to aspiration of a seed. Aspiration pneumonia (especially in hand-fed juvenile birds). Inhalation of toxic agents including polytetrafluoroethylene (PTFE) (e.g., non-stick) coatings, aerosolized lipids, carpet shampoos and deodorizers, other volatile sprays.

Laboratory Evaluation

- Assess patient stability, *proceed with caution!*
- Radiographs for increased radio-density in the pulmonary fields (enhanced parabronchial pattern), focal or diffuse densities in the air sacs, visible (thickened) air sac membranes.
- CBC, particularly for leukocytosis as evidence of infection. Biochemical profile.
- Endoscopy to examine trachea to the level of the syrinx, also caudal thoracic air sac approaches to assess the lung and air sacs.

MANAGEMENT

A. Oxygen cage, deliver 100% O_2 and observe for improvement in dyspnea.

B. Stress free environment.

C. Broad-spectrum antibiotics.

D. If no improvement in dyspnea an air sac breathing tube (3.0 – 4.0 mm; placed in the caudal thoracic air sac) may be required. Use survey radiographs to guide side for placement (right or left). If dyspnea does not improve after placement then severe pulmonary pathology is likely present.

E. Endoscopic examination of the lung with the potential for guided biopsy is indicated. This can be performed through the lumen of the air sac tube.

NEUROLOGICAL SIGNS

History/Clinical Signs/Physical Examination

- Ataxia, seizures, head tilt, paresis.
- Differential Diagnoses: Chronic lead toxicity, Proventricular Dilation Disease (PDD), other viral encephalitides, bacterial meningoencephalitis (e.g., *Salmonella* sp., *Chlamydophila psittaci*), trauma, hypocalcemia (more common in some parrots e.g., African species), neural larval migrans (*Baylisascaris procyonis*), hypoglycemia, thiamine deficiency (more common in some species e.g., falcons, fish eating birds fed frozen diet).

Laboratory Evaluation

- CBC, particularly for leukocytosis as evidence of infection. Biochemical profile, particularly glucose and calcium levels.
- Radiographs.
- Lead determination (heparinized whole blood).

MANAGEMENT

A. Collect pre-treatment samples.

B. Begin broad-spectrum antibiotic to cover opportunistic bacterial infections.

C. Chelation therapy (**Calcium EDTA 30 mg/kg BID IM**) to cover for toxicity.

D. **Calcium gluconate (100 – 300 mg/kg, SC)** diluted to less than 5% solution with normal saline if hypocalcemia suspected.

E. Consider **Vitamin B Complex 3 mg/kg, IM** injection calculated by thiamine content.

F. General supportive care to prevent further trauma due to neurological signs.

"EGG BINDING" IN FEMALE BIRDS

History/Clinical Signs/Physical Examination

- During egg laying the left ovary releases large ova that travel to the distal oviduct where the calcified shell is deposited. The time from ovulation to oviposition and laying of the egg is a short period (generally 24 – 48 hours). If calcium is insufficient for shell production the bird may enter a hypocalcemic state. Clinical evidence for hypocalcemia includes depression and lethargy, muscle weakness evidenced by drooped wings, abdominal distension, and straining.
- Gentle palpation, secussion. If the egg is in oviposition (distal oviduct) it will likely be palpable in the caudal coelomic cavity.
- Differential Diagnosis: Neoplasia, hepatomegaly due to chronic infection or neoplasia, fluid accumulation (ascites or abdominal effusion), obesity, herniation or generalized weakness of the abdominal wall.

Laboratory Evaluation

- CBC. Biochemical profile. Note calcium and cholesterol levels especially. Elevated blood cholesterol levels can be indicative of egg production.
- Radiographs. Birds preparing to lay eggs should have evidence of increased medullary bone. This special, loose matrix osteoid should be homogenously deposited in marrow containing bones such as the ulna, tibiotarsus and coracoid. Birds with inadequate reserves will develop hypocalemia when attempting to mobilize calcium for shell deposition.
- Abdominocentesis if fluid wave detected. If egg related peritonitis is present cytology may reveal macrophages with phagocytosed lipid and cholesterol levels in the effusion will be 2 – 5 times higher than the plasma cholesterol levels.

MANAGEMENT

A. Temperature and humidity support (30 – 34°C, 60 – 80% humidity).

B. **Calcium gluconate (100 – 300 mg/kg)** diluted to less than 5% solution with normal saline, subcutaneously or partially IM if more rapid uptake desired.

C. If an egg is not laid within 24 hours of calcium and supportive care, consider hormonal therapy. **PGE_2 (dinoprostone) 1 mL/kg intracloacally** applied to the left lateral wall of the urodeum to stimulate vaginal sphincter relaxation.

D. **Oxytocin (5 IU/kg, IM)** to promote oviductal smooth muscle contractions. Wait at least 30 minutes after the application of PGE_2 to administer. May be repeated again in 2 – 4 hours.

E. Surgical removal of the egg may be necessary in the small proportion of egg bound birds where abnormal eggs or uterine pathology prevent normal laying.

SICK, UNWEANED BIRD

History/Clinical Signs/Physical Examination

- The chicks of altricial birds, such as parrots, are cared for by the parents for relatively long periods of time until they are self-feeding. This may vary from 6 – 14 weeks, depending upon the species.
- It is common for many aviculturalists to rear young parrots for at least a portion of this time.
- Ill chicks may demonstrate a poor feeding response or continue to beg for food (with specific food solicitation vocalization) even after feeding. Crop emptying may be delayed or there may be changes in the appearance of their urofeces.
- The first six to eight weeks after hatch are normally a period of rapid growth. Decrease or levelling off in body weight gain will be noticeable if daily, morning (pre-feeding) body weights are being recorded on a growth chart. Assess general development for poor muscle development, dehydration and/or stunting
- The first six to ten months represent the time of bursal and thymic (B and T cell) lymphocyte maturation and development. Chronic stress (e.g., malnutrition, improper management) can interfere with normal bursal development and may lead to immunodeficiency.

Laboratory Evaluation

- CBC, particularly anemia, leukocytosis as evidence of infection, lymphopenia as evidence of chronic stress and immunosuppression.
- Biochemical profile, particularly for hypoalbuminemia as evidence of inadequate caloric intake, and renal compromise associated with reduced fluid intake from lack of feeding.
- Radiographs –check bone development especially.
- Culture of nasal discharge or abnormal feces.

MANAGEMENT

A. Appropriate temperature and humidity for the age and species of chick (typically 27 – 32°C and 65 – 75% humidity for tropical species. This is best delivered using an incubator.

B. Fluid therapy by SC or IO if *per os* delivery by feeding formula is not adequate.

C. Assessment of dietary program for the chick: nutritional content, amount and timing of feedings and temperature of food are important considerations.

D. Broad spectrum antibiotic therapy may aid chronically stressed chicks. Choice of antibiotic is best guided by culture otherwise begin with a trimethoprim/sulfonamide product.

SUGGESTED READINGS

1. Analgesics/anesthetics for birds. Smith DA, Mathews KA. In: PAIN How to Understand, Recognize, Treat and Stop, CD-ROM. Jonkar Veterinary Systems Ltd., Guelph, Ontario, Canada, 2003.
2. Exotic Animal Formulary, 2nd edition: Carpenter JW, Mashima TY, Rupiper DJ. WB Saunders Co., Philadelphia, 2001.
3. Handbook of Veterinary Drugs, 3rd edition: Allen DG, Dowling T, Pasloske K, Smith DA. Lippincott Williams and Wilkins, Philadelphia, 2004.
4. Manual of Avian Medicine. Olsen GH, Orosz SE. Mosby Inc, St.Louis, 2000.

NOTES

FIGURE 1. Grading scheme for pectoral musculature

cross section
through chest

muscle

keel

chest
cavity

1 emaciated

2 lean

3 ideal

4 plump

5 obese
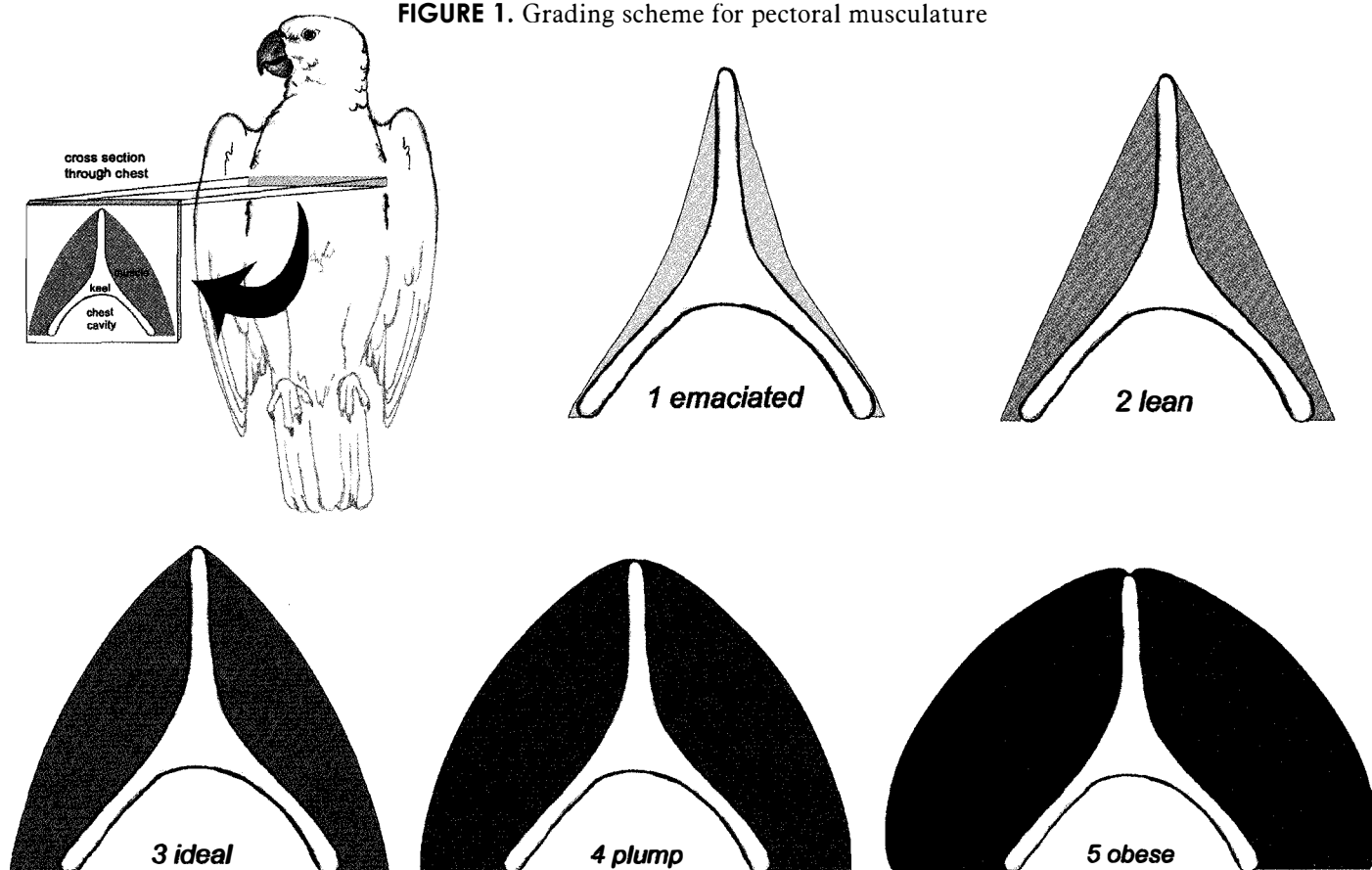
FIGURE 2. Positioning for jugular venipuncture

A

B

C

D
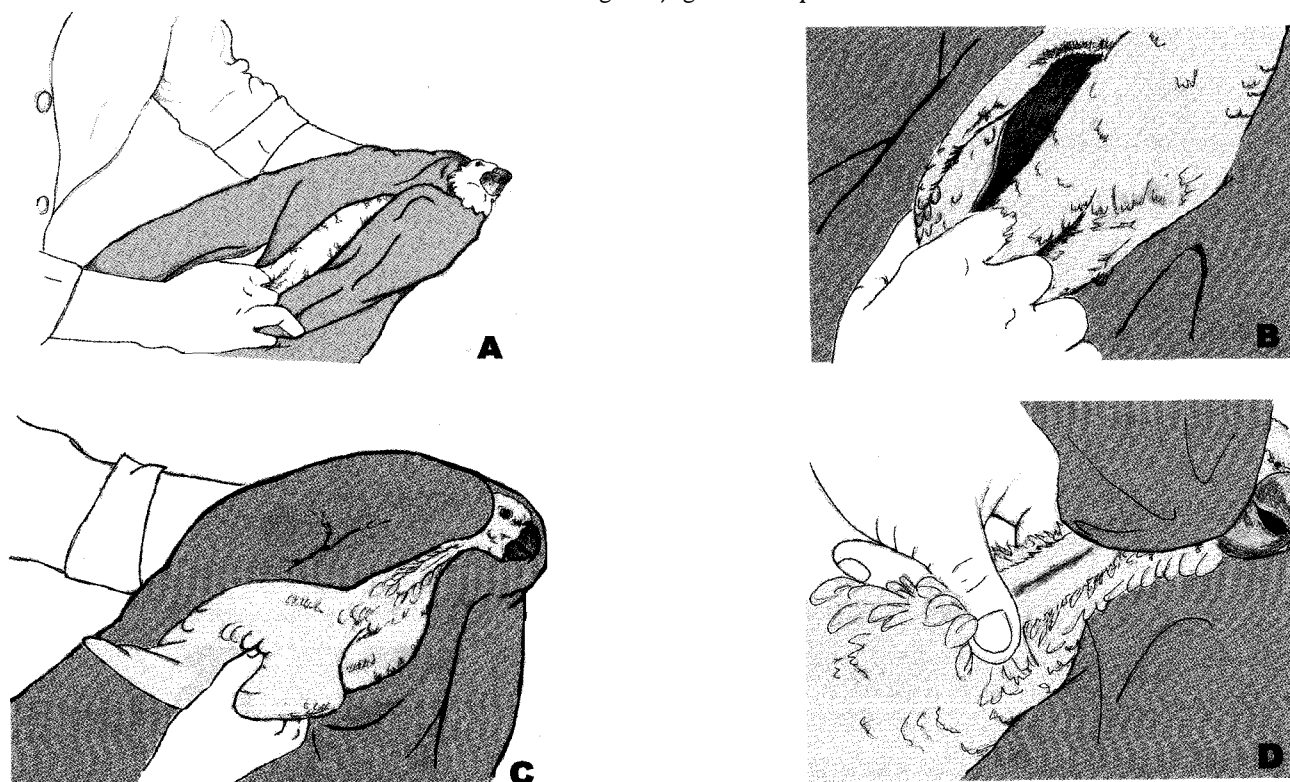
FIGURE 3. Positioning for dorso-ventral and lateral radiographs
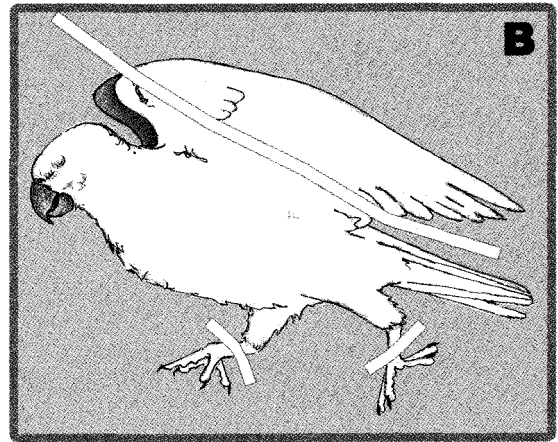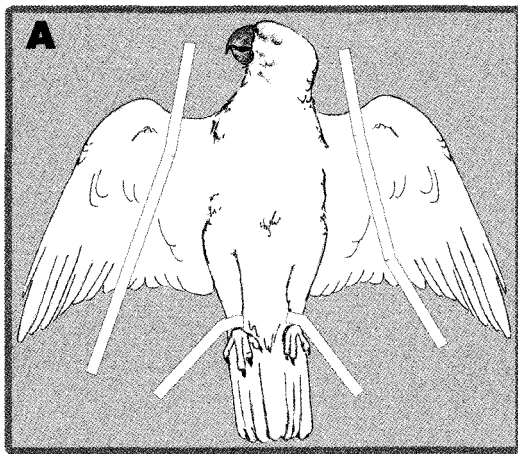
FIGURE 4. Placement of an intraoseous catheter into the ulna
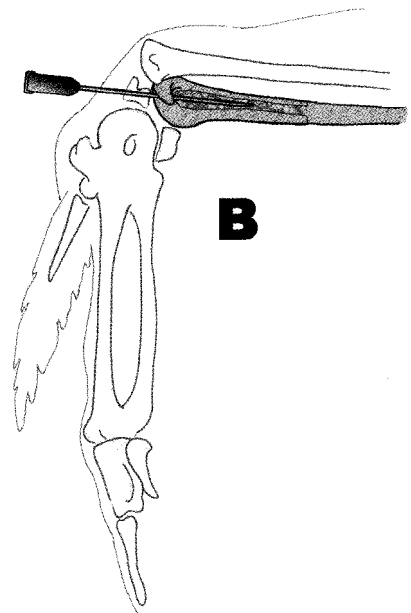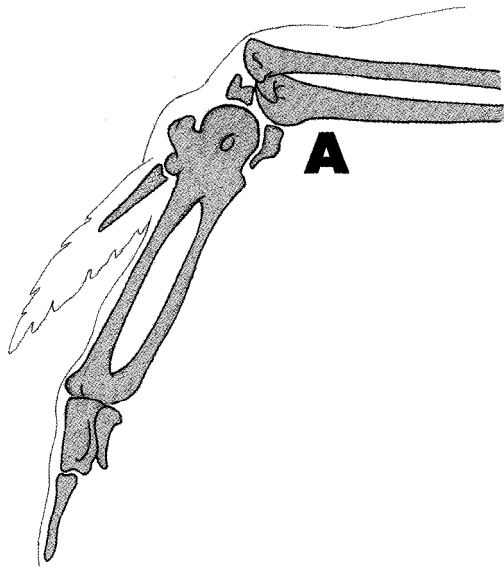
FIGURE 5. Placement of an air sac tube to assist ventilation
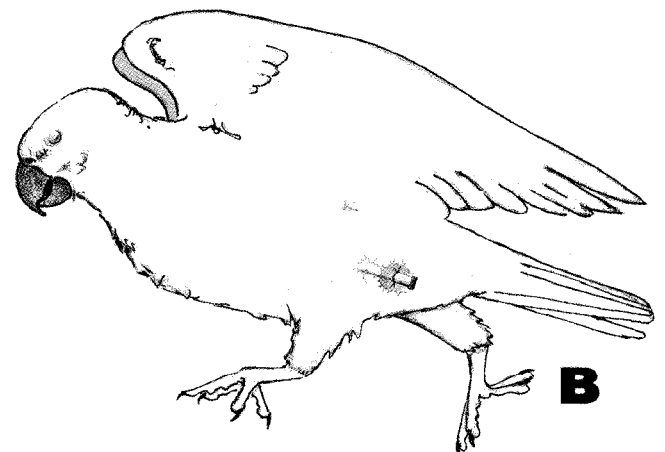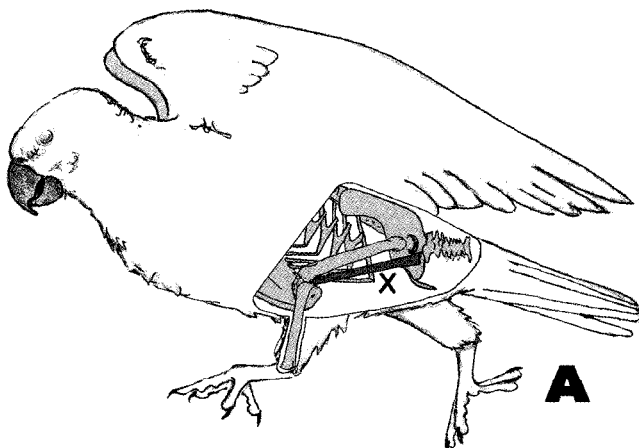
FIGURE 6. Application of a figure-8 wing bandage
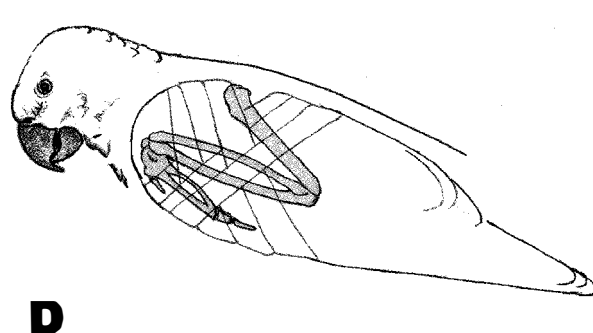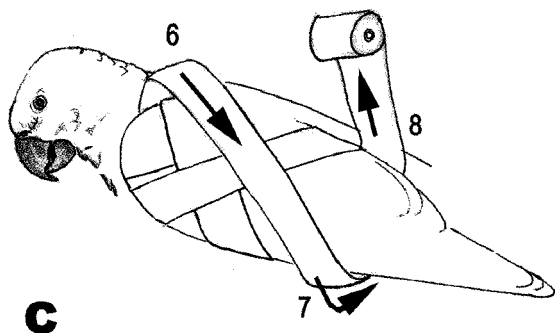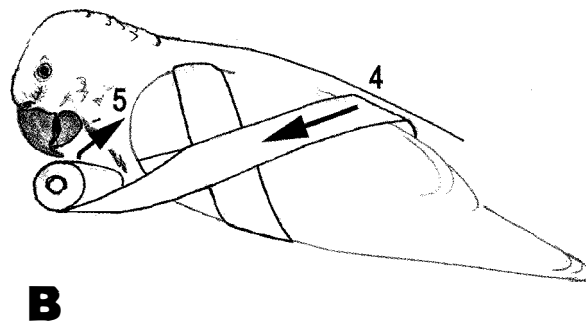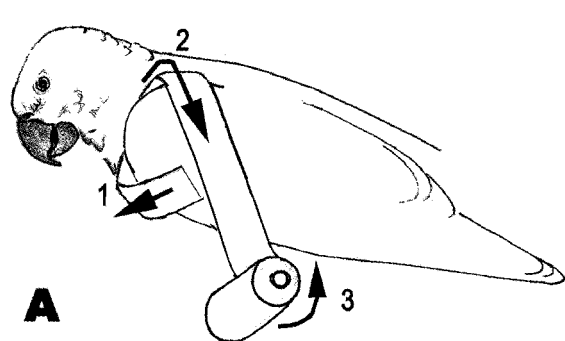
FIGURE 7. Application of a body wrap over a figure-8 wing bandage
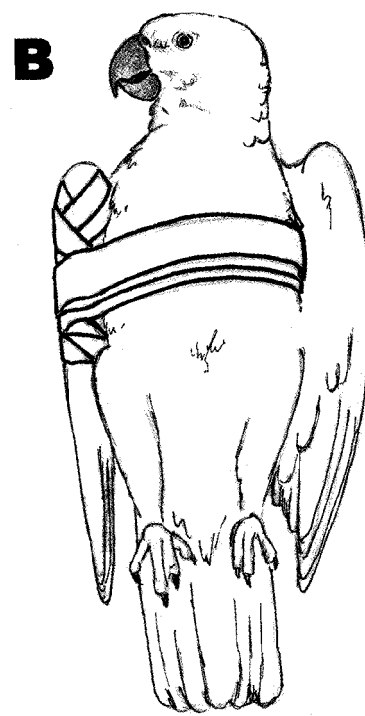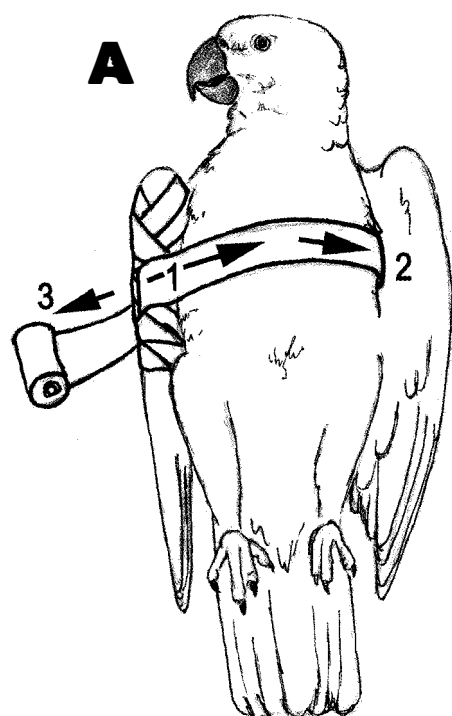
INTRODUCTION

The veterinary care of pet ferrets is very similar to that provided for dogs and cats, and the diagnostic and therapeutic protocols used for these animals are highly appropriate. Supportive care, including pain management, is equally important. The veterinarian should be aware of the small number of disease conditions that are somewhat ferret-specific or are particularly common in ferrets.

HISTORY TAKING

- Most ferrets are neutered and descented as young animals; ensure that this is so as unspayed females are susceptible to pancytopenia and other complications of persistent estrus. Ferrets are induced ovulators.
- A ration specifically formulated for ferrets, or a high quality kitten food should be provided. Water should be supplied ad-lib, preferably through a water bottle to prevent fouling.
- Litter boxes for urination and defecation should be available.
- Ferrets are short lived (6 – 8 years) and may be considered "aged" after approximately 5 years.
- Older ferrets commonly have several concurrent disease processes.
- Ferrets are normally vaccinated for canine distemper and rabies using vaccines licensed for use in this species (currently Fervac-D®, PureVax Ferret®, Imrab-3®).

RESTRAINT AND HANDLING

- Most ferrets are good-natured, well socialized, and used to handling. They will bite if annoyed and may be too active to sit still for detailed examination.
- For minor procedures or injections, ferrets can be distracted with strong tasting products such as Ferrettone® or Nutrical® or other treats.
- Ferrets can be restrained by a firm grip on the scruff of the neck (they will likely open their mouth wide during scruffing) or by a hand cupped over the neck and holding under the jaw.
- Ferrets are very inquisitive and should never be unsupervised as they will enter small holes or crevices. They should be securely housed as they can escape through relatively small openings.
- Ferrets like to burrow and sleep under blankets or other cloth items in their cage.
- Ferrets can be aggressive hunters and must be kept away from other small patients.

PHYSICAL EXAMINATION

- There are no particular cautions or specific concerns when performing a physical examination. Ferrets may struggle when a rectal thermometer is inserted.
- Normal temperature is 37.8 – 39.5°C (rectal), heart rate is 180 – 240 bpm, and respiratory rate is 30 – 40 breaths per minute.
- Abdominal contents can be easily palpated due to the ferret's elongate shape and thin body wall.
- Splenomegaly is common and may not be relevant to the animal's presentation for emergency assessment. Extramedullary hematopoesis and lymphoma are the two major differentials for splenomegaly.
- Multiple enlarged peripheral lymph nodes are suggestive of lymphoma.

ANESTHESIA

- General anesthesia may be required for sample collection and diagnostic imaging.
- General protocols and techniques for the anesthesia of small animal pets are appropriate for ferrets.
- Common premedications include **glycopyrrolate 0.01 – 0.02 mg/kg SC, IM, IV and butorphanol 0.05 – 0.5 mg/kg SC, IM, IV.** For painful procedures, additional analgesia with opiates and/or NSAIDS is frequently required.
- **Isoflurane** is the anesthetic of choice. Ferrets can be mask induced and then intubated. Average cuff sizes (outside diameter) are 2.5 – 3 mm for females and 3 – 3.5 mm for males. Uncuffed Magill or Murphy tubes are recommended. Ferrets maintain jaw tone until a deep plane of anesthesia. Endotracheal tubes should be tied in using tape or gauze straps that cross over the animal's shoulders and run behind the front legs.
- An indwelling catheter can be placed in the cephalic or saphenous vein once the animal is anesthetized.
- Body temperature must be monitored closely and thermal support (e.g., convective air warmer or warmed oat bags) is required for procedures longer than 15 – 30 minutes.

DIAGNOSTIC SAMPLE COLLECTION

Blood Collection

- Venous blood samples can be collected from the cephalic and saphenous veins, from the anterior vena cava/jugular vein, and from the ventral tail artery. All vessels except the anterior vena cava are very small. Anesthesia will likely be required unless the veterinarian is experienced at bleeding ferrets.
- Routine CBC and biochemical profiles can be carried out on ferret blood as they would be for dogs and cats. General concepts of interpretation are as for dogs and cats, but the laboratory should provide reference ranges specific to ferrets.

Diagnostic Imaging

- Although ferrets can be manually restrained for radiographs, anesthesia allows better positioning and stretching.
- Standard lateral and ventro-dorsal views should be taken.
- Ultrasonic imaging is also used extensively for the evaluation of cardiac function and adrenal size, and to identify the presence of gastrointestinal foreign bodies or intra-abdominal or thoracic masses.

EUTHANASIA

- Ferrets should be euthanized with an intravenous injection of a euthanasia agent such as pentobarbital.
- The animal should initially be anesthetized for both humane and practical reasons.
- Intracardiac injection is also appropriate in anesthetized animals.

GENERAL SUPPORTIVE CARE

Heat

- Sick ferrets are prone to hypothermia due to their small size and high metabolic rate.
- Hospitalized ferrets should be kept in warm rooms or in heated incubators (22 – 28°C). Additional heat can be provided with warmed oat bags.
- As body temperature can return rapidly to normal, care must be taken not to overheat the animal. Remove warming devices at 1°C below normal body temperature and recheck in 30 minutes.

Fluid Therapy

- General principles of fluid therapy apply to ferrets (*see Fluid Therapy p. 347*).
- Intravenous catheters can be placed in the cephalic or saphenous veins. In relatively active animals, which may chew an intravenous line, repeated IV bolus dosing can also be used.
- Subcutaneous fluid can be administered over the shoulders, dorsal neck, and upper back.
- An intraosseous catheter (20 or 22 g, 1.5 inch spinal needle) can be placed in the proximal femur if necessary.
- Ferret to ferret blood transfusions can be administered using protocols developed for other small animal species. (*see Tranfusion Therapy p. 667*).Cross-matching is not considered necessary as ferrets do not appear to have different blood groups. Blood replacement products (e.g., Oxyglobin®) have also been used successfully.

Respiratory Support

- Severely dyspneic or moribund ferrets can be provided with oxygen either through a facemask, or within a chamber.

Nutritional Support

- Sick ferrets can be very fussy eaters.
- Anorectic ferrets may be encouraged to eat with strong smelling cat foods, or by drizzling Ferretone®, etc., over their food.
- Ferrets can be syringe fed with diluted ferret or cat food, or liquid critical care products.

Medical Therapy

- Although there are no medications licensed for ferrets, the administration of drugs licensed for use in small animals, at dosages appropriate for cats, is widespread and generally well tolerated.
- Ferrets are difficult to pill, but may take liquid medications well, either in food or directly *per os*.
- IM injections should be given into the larger muscle masses of the hind and forelimbs.
- Antibiotics commonly administered to ferrets include:

a. Enrofloxacin 5 – 15 mg/kg PO, SC, IM.
　　　b. Trimethoprim-sulfonamide combinations 15 – 30 mg/kg PO, SC q12h.
　　　c. Metronidazole 10 – 20 mg/kg PO q12h.
　　　d. Amoxicillin + clavulanic acid (Clavamox®), 10 – 20 mg/kg PO q8–12h.
　　　e. Cephalexin 15 – 30 mg/kg PO q8–12h.

Analgesia

- Opioid analgesics used in ferrets include
  　　a. Butorphanol 0.05 – 0.5 mg/kg SC, IM, IV q2–12h as needed.
  　　b. Buprenorphine 0.01 – 0.05 mg/kg SC, IM, IV q6–12h as needed.
  　　c. Ferrets may become very lethargic when treated with opioids.
- The most frequently recommended non-steroidal anti-inflammatory drug is **meloxicam 0.2 mg/kg initial dose, then 0.1 mg/kg q24h for 2 – 3 days. Reduce to 0.025 mg/kg PO, SC, IM, IV q24–48h for long-term use; where not contraindicated** (*see Analgesics p. 85*).

ACUTE COLLAPSE

History/Clinical Signs/Physical Examination

- Animals may be extremely weak and even appear to have primary neurologic signs.
- Major differential diagnoses: hypoglycemic episode due to pancreatic insulinoma, congestive heart failure and pulmonary edema, severe anemia due to adrenal disease or persistent estrus/hyperestrogenism, anaphylactic/allergic response to a vaccine or other injectable medication.
- Ferrets with insulinomas may have repeated, transient, episodes of weakness and collapse and often improve immediately if given a high energy substance such as corn syrup orally, unlike patients with cardiac disease.
- Female ferrets in persistent estrus will have a swollen vulva.
- Infectious pneumonia is rare in the ferret.

Laboratory Evaluation

- Whole body radiographs or ultrasonographic examination, particularly to evaluate cardiac size, shape (the normal ferret heart is rounded and large), contractility, the presence of pulmonary edema, and the presence of internal masses.
- ECG to evaluate cardiac rate, rhythm and waveform.
- Ferrets are susceptible to heartworm disease.
- Complete blood cell count, with a particular interest in ruling out severe anemia.
- Serum biochemistry to rule out hypoglycemia (may only be present during an episode of clinical hypoglycemia) and to assess hepatic, renal and other organ dysfunction.

MANAGEMENT

A. Insulinoma. Immediately administer orally a high calorie oral supplement, such as glucose or corn syrup, for a hypoglycemic episode. The return to normal activity is generally rapid and a hallmark of uncomplicated insulinomas (*see Hypoglycemia p. 281*). If the animal does not respond inject 50% (**0.5 mL/kg** [dilute 1:4 with saline]) **dextrose IV slowly to effect.** Long term management could include:

　1. Exploratory laparotomy and removal of the neoplasm or
　2. Medical therapy with
　　a. **Prednisone 0.5 – 2.5 mg/kg, PO q12h.** Start with low dose and adjust to effect.
　　b. If prednisone alone is not effective add **diazoxide 5 mg/kg PO daily dose initially, divided q8–12h as necessary, increasing up to 60 mg/kg daily total dose** as needed. Medical therapy may not be as effective as surgical removal.
　3. Instruct owners to feed small meals frequently.

B. Ferrets with congestive heart failure or other cardiac disease can be treated using the same basic principles and drug combinations as used for cats. Careful monitoring for drug effect and adverse reactions is necessary. Cardiac ultrasound is essential for accurate diagnosis. The following suggested starting dosages should be adjusted as appropriate. *See also Life-threatening Congestive Heart Failure p. 149.*

1. Atenolol 3.13 – 6.25 mg/kg PO q24h.
2. Digoxin elixir 0.005 – 0.01 mg/kg PO q12–24h.
3. Diltiazem 1.5 – 7.5 mg/kg PO q6–24h.
4. Enalapril 0.5 mg/kg PO q48h initially, increase dose or decrease frequency as clinically appropriate.
5. Furosemide 1 – 4 mg/kg PO, SC, IM, IV q8–12h and reduce dosage for maintenance.
6. Nitroglycerine ointment 1/8-in. length of 2% ointment applied topically; q12–24h.

C. Ferrets showing **vaccination reactions or anaphylaxis** should be treated with:

1. **mild** reaction, an antihistamine (i.e., **diphenhydramine at 0.5 – 2 mg/kg PO q8–12h; q12h IM**).
2. **moderate** reaction, add a corticosteroid (**dexamethasone sodium phosphate at 0.2 – 1 mg/kg IM, IV**).
3. **Severe** reaction, add **epinephrine 20 μg/kg SC, IM, IV or intratracheally** as appropriate (*see Anaphylaxis p. 617*).

D. The persistent estrus induced by **hyperestrogenism** can be treated with **GnRH 20 μg/ferret SC, IM or HCG 100 IU/ferret IM.** The animal should be spayed as soon as its condition is stable.

"SICK", WEAK, EMACIATED

History/Clinical Signs/Physical Examination

- Major differential diagnoses for more acute conditions: canine distemper virus infection (rare, but ferrets are extremely susceptible), human influenza virus infection (anthroponotic), and acute renal failure.
- Major differential diagnoses for chronic conditions: neoplasia (especially lymphoma, adrenal neoplasia), chronic renal failure, chronic gastrointestinal disease (*see Vomiting p. 74, Diarrhea p. 32*), and persistent estrus/hyperestrogenism.
- The apparent hind end weakness sometimes seen in very sick or emaciated ferrets can be confused with true neurologic ataxia.
- Anorexia may be the primary clinical sign in ferrets with gastric foreign bodies.
- Unspayed females in persistent estrus and animals with chronic adrenal cortical disease can become severely anemic or pancytopenic.
- Ferrets with influenza infection may show lethargy, fever, conjunctivitis, and predominantly upper respiratory signs.
- Careful abdominal palpation may reveal thickened bowel walls (inflammatory bowel disease, intestinal lymphoma) or internal masses.

Laboratory Evaluation

- Complete blood cell count and biochemical profile.
- Full body radiographs or ultrasound.

MANAGEMENT

A. General supportive care.

B. Medical therapy as appropriate to the specific clinical condition(s) diagnosed or suspected.

C. Persistent estrus/hyperestrogenism can be treated with **GnRH 20 μg/ferret SC, IM or HCG 100 IU/ferret IM.** The animal should be spayed when its condition is stable.

D. A variety of chemotherapeutic protocols have been used with varying success to treat lymphoma in ferrets and are detailed in a number of reference sources [1, 2, 4]. Treatment with **prednisone 1 – 2.2 mg/kg PO q24h** is generally effective as a palliative measure.

VOMITING/REGURGITATION

History/Clinical Signs/Physical Examination

- Major differential diagnoses: gastrointestinal foreign bodies, megaesophagus, gastritis and gastric ulceration caused by *Helicobacter mustelae* infection, azotemia, gastric or intestinal obstruction due to neoplasia.
- Affected animals are likely anorexic and may show evidence of nausea or pain.
- Dehydration may be moderate to severe; ferrets dehydrate rapidly with vomiting or diarrhea.
- Foreign bodies or internal masses may be palpable on physical examination.

Laboratory Evaluation

- Radiographs or ultrasonographic examination may be useful to identify internal soft tissue masses or GI foreign bodies. NOTE: ferrets most often ingest rubber or foam materials, which are not radio-opaque.
- Barium contrast radiographs can be used to diagnose megaesophagus or gastrointestinal blockage (*see Acute Abdomen p. 21*).
- Routine CBC and biochemical profile with particular emphasis on acid-base and electrolyte status and renal function.
- Exploratory laparotomy may be necessary to determine the cause of the animal's vomiting (including the identification and removal of foreign objects), and to take appropriate biopsy samples.

MANAGEMENT

A. Provide fluid therapy as appropriate to manage dehydration and acid-base and electrolyte abnormalities (*see Fluid Therapy p. 347*).

B. Use small frequent feedings for animals whose vomiting is not severe.

C. Use an appropriate drug combination to treat infection by *Helicobacter mustelae*. Three examples of treatment regimens are:

1. Amoxicillin 30 mg/kg PO q12h + metronidazole 20 mg/kg PO q12h + bismuth subsalicylate 17.5 mg/kg or 1 mL/kg PO q12h for 14 days minimum OR
2. Clarithromycin 12.5 mg/kg PO q8h + ranitidine bismuth citrate 24 mg/kg, PO q8h for 14 days OR
3. Clarithromycin 50 mg/kg, PO q24h for 14 days + omeprazole 4 mg/kg PO q24h for 28 days;

D. Famotidine 0.25 – 0.5 mg/kg PO, IV q24h or omeprazole 1 – 4 mg/kg PO q24h and/or sucralfate 100 mg/kg PO q6h may also be helpful adjunct therapies in the treatment of gastritis.

DIARRHEA

History/Clinical Signs/Physical Examination

- Major differential diagnoses: rotavirus or coccidiosis in young ferrets, epizootic catarrhal enteritis (putatively a coronavirus) in older ferrets, proliferative bowel disease (*Lawsonia intracellularis*), inflammatory bowel disease, gram-negative bacteria such as *Salmonella* spp., dietary upset.
- Ferrets have a very short GI transit time of 2 – 3 hours.
- Recent exposure to other ferrets may have provided exposure to novel infectious agents.
- Determine whether a correct and adequate diet is being fed, and whether there have been any changes in diet or management.
- Thickened bowel loops may be palpable with proliferative bowel disease.
- Affected animals may be dehydrated.

Laboratory Evaluation

- Complete blood cell count and biochemical profile to assess hematologic, biochemical and electrolyte abnormalities.
- Fecal analysis for the presence of parasites (especially for coccidia) and microbial culture and sensitivity may provide a definitive diagnosis.

MANAGEMENT

A. General supportive care with an emphasis on fluid (p. 347), acid-base (p. 406), and electrolyte management as appropriate.

B. Institute medical therapy treatment as appropriate.
1. **Chloramphenicol 50 mg/kg PO, SC, IM q12h** has been the drug of choice to treat proliferative bowel disease.
2. Sulfonamides such as **sulfadimethoxine 50 mg/kg PO once, then 25 mg/kg daily for 9 days,** or a **trimethoprim-sulfonamide combination 30 mg/kg PO q24h for 14 days** can be used to treat coccidiosis.
3. **Kaolin-pectin products 1 – 2 mL/kg PO q2–6h as needed** can be used as GI protectants.

C. Use bland diets fed in small quantities.

URINARY OBSTRUCTION

History/Clinical Signs/Physical Examination

- In a male ferret, clinical signs suggestive of urethral obstruction in any other species.
- Distension of the bladder or dribbling of urine might be noted.
- Major differential diagnoses: prostatic hyperplasia and urethral compression secondary to chronic adrenal cortical disease, urinary calculi, cystitis.

Laboratory Evaluation

- Radiographs or ultrasonic examination particularly to assess the urinary system, the presence of calculi, the prostate, and the presence of internal masses that might reflect adrenal hyperplasia or neoplasia.
- Urinalysis and urine culture to rule out infection or neoplasia.
- Plasma or serum biochemistry to assess renal function and electrolytes.

MANAGEMENT

A. Parenteral fluids and correct acid base and electrolyte disturbances.

B. Cathetization, cystocentesis, or pre-pubic percutaneous placement of a catheter into the bladder with definitive management of obstruction (see *Urethral Obstruction p. 745*) as performed in other small animals. Catheter passage may be difficult in male ferrets due to the small size of the urethra and the presence of a curved penis.

C. Long term, correction of diet if appropriate.

D. If **prostatic hyperplasia** due to adrenal disease is suspected, commence medical treatment with **leuprolide acetate Lupron®, 100 – 500 μg/ferret; IM once a month,** or consider exploratory laparotomy and adrenal removal once the animal is stable. Response to leuprolide is often rapid, without worsening of clinical signs. The dosage and frequency of administration must be adjusted as appropriate for long term therapy.

ADRENAL CORTICAL HYPERPLASIA AND NEOPLASIA

History/Clinical Signs/Physical Examination

- Although adrenal disease as such is not an emergency condition, the consequences of chronic adrenal disease, including cachexia, urinary obstruction in male ferrets due to prostatic hyperplasia, and anemia or pancytopenia, may result in the presentation of a ferret in critical condition.
- Hyperadrenocorticism refers to a spectrum of hyperplastic to neoplastic proliferation of the adrenal cortex and results in the production of increased levels of steroid hormones including estrogen, progestins, and androgens. This is **NOT a gluco- or mineralo-corticoid based disease.**
- This condition is extremely common in adult and aged ferrets, the left adrenal is affected more frequently but both glands can be involved.
- Alopecia is the most common clinical sign noted in the early stages of the condition. It often starts on the tail and can progress to involve most of the body.
- An extremely enlarged neoplastic adrenal gland can occasionally be palpated.

Laboratory Evaluation

- Radiographs or ultrasonographic examination are used to note the size and shape of the adrenal glands, and identify any additional lesions that could reflect metastasis (which is uncommon).
- CBC to identify the presence of non-regenerative anemia or, less commonly, pancytopenia.
- Serum estradiol, 17-hydroxyprogesterone, and androstenedione can be measured (Ferret Adrenal Panel, University of Tennessee College of Veterinary Medicine).

MANAGEMENT

A. Medical therapy consists of monthly injections of the GnRH-agonist **leuprolide acetate (Lupron®) 100 – 500 μg/ferret IM** to reduce steroid production by the adrenal glands through a negative feedback mechanism.

B. Surgical therapy consists of removal of the affected adrenal gland and thorough examination of the remaining gland. Leuprolide therapy is still likely to be necessary to prevent hyperplasia in the remaining gland.

SUGGESTED READING

1. Handbook of Veterinary Drugs, 3rd edition: Allen DG, Dowling T, Pasloske K, Smith DA. Lippincott Williams and Wilkins, 2004.
2. Exotic Animal Formulary, 2nd edition: Carpenter JW, Mashima TY, Rupiper DJ. WB Saunders Co., Philadelphia, 2001.
3. Analgesics/anesthetics for ferrets. Smith DA, Mathews KA. In: PAIN How to Understand, Recognize, Treat and Stop, CD. Jonkar Veterinary Systems Ltd., Guelph, ON, 2003.
4. Ferrets, Rabbits and Rodents Clinical Medicine and Surgery. 2nd edition: Quesenberry KE, Carpenter JW. WB Saunders, Philadelphia, 2004.

NOTES

INTRODUCTION

The domestic pet rabbits seen in veterinary practice all originate from the European wild rabbit, *Oryctolagus cuniculus*. The rabbit, a prey species, tolerates stressful situations poorly. Careful handling and supportive care, including pain management, are very important.

HISTORY TAKING

- Dwarf rabbits are more prone to the development of malocclusion and of neurologic disease associated with *Encephalitozoon cuniculi* infection.
- Many rabbits are not neutered. It is important to ascertain whether females have been spayed, as they are subject to a variety of diseases of the reproductive tract.
- Rabbits should be fed a high fibre good quality diet. Fibre is essential in stimulating normal gastrointestinal motility.
- Feces described as being small in size and scant in volume often indicate reduced appetite and or GI motility. Rabbits pass firm fibrous pellets during the day and pass softer cecal pellets at night. These cecotrophs are normally re-ingested as they pass from the anus.
- Water should be provided ad-lib, either through a water bottle to prevent fouling or in a water bowl.
- Many rabbits will use a litter box for urination and defecation.
- Rabbits have a life span of approximately 6 – 12 years.
- There are no routinely recommended vaccines for rabbits in North America.
- Tooth grinding can indicate pain.

RESTRAINT AND HANDLING

- It is essential to house rabbits in a quiet area and handle them in a careful manner to prevent stress and ensuing catecholamine release.
- The skeletal system of the rabbit is relatively fragile. Animals that struggle unduly, jump from a table, or fall can fracture a lumbar vertebra. A non-slip surface is important in the cage or on the examination table.
- Rabbits can be restrained by a firm grip on the scruff of the neck and a supporting hand under the rump. They should be held and supported with the animal's head nestled in the crook of the holder's arm, or wrapped up and supported in a towel or cat bag. It is essential that the animal be prevented from kicking backwards and injuring its spine.
- Although most rabbits are docile, they can give the handler deep scratches with the sharp claws on their strong hind legs.
- Both male and female rabbits can be territorial and aggressive, and may thump their hind feet, growl, or bite.

PHYSICAL EXAMINATION

- Normal temperature is 38.5 – 40.0°C (rectal), heart rate is 140 – 260 bpm, and respiratory rate is 30 – 60 breaths per minute.
- The nostrils and conjunctiva should be examined carefully for purulent discharge, and the chest auscultated for evidence of upper or lower respiratory disease.
- Dental disease is common in rabbits, and is an important cause of inappetence. Incisor and molar teeth are open-rooted and grow continuously. The rabbit oral cavity is long and narrow, and the mouth does not open widely, making detailed dental examination difficult without sedation or anesthesia and some type of illuminated otoscope or endoscope. Palpate the head carefully as osteomyelitis and abscesses are common sequelae. Drooling, or a wet chin, can also indicate dental problems.
- Lenticular opacity may reflect aging or infection with the microsporidan parasite *Encephalitozoon cuniculi*. Rabbits do not have a reliable menace response.
- Ear mites (*Psoroptes cuniculi*) can cause crusting and scaling within the external ear canal.
- Abdominal palpation may not be rewarding in an awake animal, as many rabbits will tense their abdomen. In a relaxed animal the cecum, fecal pellets, and the kidneys and bladder may be palpable. The main fat storage depots in rabbits are the abdominal fat pads, which become large in overweight animals.

- Rabbits in good body condition should have strong rounded epaxial musculature. Muscle wasting (palpable over the back and hips), can occur in emaciation or protein-losing diseases while abdominal fat deposits are maintained.
- In unspayed females, the reproductive tract should be assessed for masses or thickening. Mammary hyperplasia or secretions are also suggestive of ovarian or uterine disease.
- The perineal area should be clean and free of feces or discharge. There are two thin-walled inguinal scent pouches that produce a sebaceous secretion.
- In male rabbits, the inguinal rings remain open throughout life, and the testicles, which are located cranial to the penis, can retract back into the abdominal cavity.
- Normal rabbit urine can be red or brown in colour, a result of excretion of dietary pigments, and often contains large quantities of calcium that leave a white granular precipitate when the liquid evaporates.
- Rabbit skin is more delicate than that of the dog or cat and can be torn easily by electric clippers.

ANESTHESIA

- Sedation or general anesthesia may be required to reduce stress for detailed examination, and for sample collection or diagnostic imaging.
- Rabbits are obligate nose breathers; upper respiratory disease increases the risk associated with anesthesia.
- Rabbits are generally mask-induced with either **isoflurane** or **sevoflurane.** In fractious or nervous animals premedication with **midazolam 0.5 – 2 mg/kg IM, acepromazine 0.5 – 1 mg/kg IM,** or **butorphanol 0.1 – 0.5 mg/kg SC, IM** may ease induction. Mask induction of highly stressed rabbits may result in massive catecholamine release and cardiac arrest.
- **Glycopyrrolate 0.01 – 0.2 mg/kg SC, IM** is preferred over atropine as an anticholinergic, as many rabbits produce endogenous atropinase.
- Endotracheal intubation is recommended for long or difficult procedures; however, the long narrow oral cavity, delicate oral and laryngeal mucosa, and the anatomical relationship of the epiglottis to the soft palate combine to make intubation difficult, particularly in small patients. A face mask can be used to maintain anesthesia for most procedures.
- Injectable combinations including **ketamine 15 – 50 mg/kg IM** and a benzodiazepine, an opioid, or acepromazine are described for sedation or short periods of anesthesia.
- An indwelling catheter can be placed in the cephalic or saphenous vein once the animal is anesthetized.
- Body temperature must be monitored closely and thermal support (e.g., convective air warmer or warmed oat bags) is required for procedures longer than 15 –30 minutes.

DIAGNOSTIC SAMPLE COLLECTION

Blood Collection

- Venous blood samples can be collected from the cephalic and saphenous veins, the marginal ear vein, and the central ear artery. Warming the ear improves blood collection.
- Sedation or anesthesia may be required to obtain blood from the anterior vena cava/jugular vein.
- Routine CBC and biochemical profiles can be carried out on rabbit blood as they would be for dogs and cats. General concepts of interpretation apply, but the laboratory should provide reference ranges specific to rabbits.

Diagnostic Imaging

- Although rabbits can be manually restrained for radiographs or ultrasound examination, anesthesia reduces stress and allows better positioning and stretching.
- Standard lateral and ventro-dorsal radiographic views should be taken.
- Large amounts of calcium in the urine may cause the bladder to appear radio-opaque.

Urinalysis

- Urine can be collected from the litter pan, by bladder compression, or by cystocentesis.

EUTHANASIA

- Rabbits should be euthanized with an intravenous injection of a euthanasia agent such as pentobarbital.
- The animal should initially be anesthetized for both humane and practical reasons.
- Intracardiac injection is also appropriate in anesthetized animals.

GENERAL SUPPORTIVE CARE

Heat

- Sick rabbits are prone to hypothermia due to their small size and high surface area:weight ratio.
- Hypothermic rabbits, or animals recovering from anesthesia, should be kept in a warm environment (20 – 25°C) or placed on warmed oat bags.
- Rabbits show heat stress at ambient temperatures approaching 28°C, especially if the relative humidity is high.

Fluid therapy

- General principles of fluid therapy apply to rabbits.
- Subcutaneous fluid can be administered over the shoulders, dorsal neck, and cranial to the thighs.
- Intravenous catheters can be placed in the cephalic or saphenous veins, but sedation or anesthesia may be required. Catheters can also be placed in the ear vein, but subsequent sloughing is more likely at this location. Repeated IV bolus dosing can be used in animals that chew at or are distressed by an IV line.
- An intraosseous catheter (20 or 22 g, 1.5 inch spinal needle) can be placed in the proximal femur or tibia if necessary.

Respiratory Support

- Severely dyspneic or moribund rabbits can be provided with oxygen either via a face mask or within a chamber.

Nutritional Support

- Sick or anorexic rabbits often have GI stasis that further exacerbates inappetance.
- High quality alfalfa hay is highly palatable to most rabbits.
- Rabbits can be syringe fed with a slurry of ground, moistened rabbit pellets, or a commercial rabbit supplement (e.g., Oxbow Pet Products Critical Care for Herbivores®).
- Passing a stomach or nasogastric tube is difficult in an awake rabbit and may result in complications, even in anesthetized animals. Rabbits cannot vomit to relieve an over-distended stomach.
- Indigestible fibre is essential for normal motility of both the stomach and intestinal tract.

Medical Therapy

- Rabbits will rarely take pills, but can be given oral liquid medications syringed into the diastema (the space between the incisor and premolar teeth).
- IM injections should be given into the large epaxial muscles or the quadriceps muscles cranial to the femur.
- Rabbits have a predominantly gram positive anaerobic intestinal flora. Disruption of this flora can lead to dysbiosis (the proliferation of gram negative and clostridial organisms) and fatal enterotoxemia. Orally administered narrow spectrum antibiotics, such as the penicillins and cephalosporins, are most commonly implicated in iatrogenic enterotoxemia.
    1. **Antibiotics** generally safe for administration to rabbits include:
        a. enrofloxacin 5 – 10 mg/kg PO, SC, IM q12h
        b. trimethoprim-sulfonamide combinations 15 – 30 mg/kg PO, SC, IM q12h
        c. metronidazole 20 – 60 mg/kg PO, IV q12h
        d. <u>injectable</u> penicillin products can be used to treat rabbits with abscesses and pasteurellosis; however, treatment must be stopped if there is any evidence of gastrointestinal upset. **Penicillin G (procaine) 40,000 – 60,000 U/kg SC, IM q24h for 2 weeks, then q48h for an additional 2 weeks or longer, or penicillin G (benzathine + procaine) 75,000 U/rabbit weighing <2.5 kg or 150,000 U/rabbit weighing >2.5 kg q72h for 4 weeks**

2. **Metoclopramide 0.5 mg/kg PO, SC q8–12h** is used to stimulate GI motility.

3. **Antiparasitic** drugs include:
   a. ivermectin 200 μg/kg PO, SC
   b. fenbendazole 10 – 20 mg/kg PO q24h for 30 days to treat infection by *E. cuniculi*
   c. albendazole 10 – 30 mg/kg PO q24h for 30 – 90 days to treat infection by *E. cuniculi*
   d. oxibendazole 30 mg/kg PO q24h for 7 – 14 days followed by 15 mg/kg q24h for 30 – 60 days, or indefinitely to treat infection by *E. cuniculi*
   e. trimethoprim + a sulfonamide 30 mg/kg PO q12h for 10 – 14 days
   f. sulfadimethoxine 15 – 30 mg/kg PO q12h for 10 – 14 days
   g. amprolium 0.5 mL of 9.6% in 500 mL drinking water for 10 – 14 days
   h. sulfaquinoxaline 0.25 – 1 mg/mL of drinking water for 10 – 14 days
   i. metronidazole 25 – 50 mg/kg PO q12h for 5 – 10 days

4. **Corticosteroids** should be used sparingly in rabbits due to their immunosuppressive effects.

5. **Analgesia**
   a. **opioid** analgesics used in rabbits include:
      i. butorphanol 0.1 – 0.5 mg/kg SC, IM, IV q2–4h as needed
      ii. buprenorphine 0.01 – 0.05 mg/kg SC, IM, IV q6–12h as needed

6. **Non-steroidal anti-inflammatory drugs** include:
   a. meloxicam 0.3 mg/kg PO, SC, IM q24h
   b. carprofen 1 – 2.2 mg/kg PO q12–24h

ANOREXIA, EMACIATION, GIT STASIS

History/Clinical Signs/Physical Examination

- Owners may not notice reduced appetite if large amounts of pellets and hay are always available.
- Anorexic rabbits often also become dehydrated.
- Diets low in indigestible fibre may result in GI hypomotility. Diets composed of coarse or poor quality roughage may be unpalatable.
- An accumulation of hair in the stomach ("gastric hair ball") is probably a result of poor gastric function and gastric stasis, rather than a cause. An enlarged, doughy stomach may be palpable.
- Rabbits will, on occasion, ingest foreign material such as carpet fibres and can become acutely obstructed.
- Reduction in fecal pellet size and number indicates anorexia and or reduced GI motility.
- Wet fur or dermatitis under the chin can occur with malocclusion.
- A detailed dental evaluation, usually under sedation or anesthesia and employing a speculum, otoscope, or ideally an endoscope, is necessary to assess the teeth and gingiva. Overgrowth of incisors or molars can lead to gingival injury and anorexia. Cellulitis and abscesses are common sequellae.
- Chronic renal disease and GI, or systemic, neoplasia are additional causes of anorexia and emaciation.

Laboratory Evaluation

- CBC is evaluated as for cats and dogs.
- Biochemical profile, particularly to assess renal function.
- Full body radiographs or ultrasonographic examination. Large mats of hair and fibre are sometimes identified in the stomachs of rabbits with hypomotility.
- Urinalysis to assess renal function (e.g., proteinuria) and rule out infection.

MANAGEMENT

A. General supportive care. Correct dehydration, rehydrate gastric contents by syringe feeding with a very liquid oral nutritional supplement, and provide high fibre nutritional support. Anorexic rabbits can develop fatty liver syndrome and ketosis.

B. Perform corrective dentistry and tooth trimming as required

C. Use antibiotics, with broad spectrum aerobic and anaerobic coverage

D. Employ metoclopramide to promote GI motility.

E. Provide other specific medical treatments as indicated.

DIARRHEA, ENTERITIS

History/Clinical Signs/Physical Examination

- Enteritis, in some cases leading to enterotoxemia, is an important clinical problem in pet rabbits.
- Clinical signs include diarrhea, staining of the perineum with feces, dehydration, and toxemia.
- Collect a detailed history, because stress, including environmental or dietary change, is an important predisposing factor in the disruption of the rabbit's normal intestinal flora (dysbiosis).
- Major differential diagnoses: simple dysbiosis caused by environmental and dietary changes (e.g., fibre deficiency, and/or carbohydrate excess), iatrogenic antibiotic induced dysbiosis, mucoid enteritis (young rabbits), coliform enteritis (neonatal and post-weaning), enteric coccidiosis (young rabbits), cryptosporidiosis (young rabbits), rotavirus and coronavirus.
- Enterotoxemia is a severe form of cecal dysbiosis in which *Clostridium spiroforme* proliferate and produce an iota toxin.
- Orally administered antibiotics including penicillins, especially ampicillin, amoxicillin, and clavamox; the cephalosporins; lincomycin and clindamycin; and erythromycin can induce enterotoxemia and are contraindicated.

Laboratory Evaluation

- Complete blood cell count and biochemical profile to assess hematologic, biochemical and electrolyte abnormalities.
- Fecal analysis for the presence of parasites (esp. for coccidia), microbial culture and sensitivity, and clostridial toxin identification by ELISA may provide a definitive diagnosis.

MANAGEMENT

A. Aggressive supportive care with an emphasis on fluid, acid-base, and electrolyte management.

B. Institute medical therapy as appropriate:

    1. Antibiotic therapy to reduce proliferation of pathogenic bacteria, including clostridia, using **metronidazole** with or without a broad spectrum antibiotic such as a **trimethoprim-sulfonamide combination.**

    2. **Sulfonamides** (e.g., **sulfadimethoxine**), a **trimethoprim-sulfonamide combination**, or **amprolium** can be used to treat coccidiosis.

C. Change the environment to remove or reduce identifiable stressors.

D. Provide a diet high in indigestible fibre (e.g., good quality, palatable alfalfa hay) to stimulate normal GI motility. Syringe feed with products described above until appetite returns.

RESPIRATORY DISTRESS

History/Clinical Signs/Physical Examination

- Inquire as to previous episodes of respiratory disease, the health of other rabbits the patient has contact with, whether heat stroke is a possibility, and the air quality in the animal's environment.
- Subclinical infections by *Pasteurella multocida* and *Bordetella bronchiseptica* are common, but both organisms can cause upper (snuffles) and lower respiratory disease, especially in stressed or immunocompromised animals. Respiratory disease can also result from infection by a variety of other bacterial agents, as well as non-infectious causes.
- Classic signs of upper respiratory infection include noisy breathing, sneezing, and a nasal discharge. Rabbits with nasal discharge often have matted fur on their forefeet. Rabbits are obligate nose-breathers.
- Conjunctivitis, lacrimal duct blockage, otitis, bacteremia, and abscesses are frequently seen with infection by *P. multocida*.
- Careful auscultation is needed to differentiate upper from lower respiratory involvement.
- Rectal temperatures above 40.2°C may indicate heat stroke. Animals may show acute respiratory distress or simply collapse.

Laboratory Evaluation

- CBC and biochemical profile to assess general health. Infection is not always reflected by a neutrophilia (heterophilia).
- Radiographic examination, particularly to assess the lungs and thorax, the tympanic bullae, and the sinuses.
- Deep nasal swab for microbial culture and sensitivity.

MANAGEMENT

A. Broad spectrum antibiotic therapy, to be adjusted according to the results of culture and sensitivity.

B. Respiratory support including oxygen therapy and a bronchodilator (i.e., **aminophylline 5 mg/kg PO, IM q8–12h**)

C. Topical antibiotic therapy for conjunctivitis.

D. For heat stroke, reduce the patient's body temperature slowly and provide aggressive fluid therapy and respiratory support as necessary.

E. General supportive care as necessary.

TRAUMA

History/Clinical Signs/Physical Examination

- Rough handling, being dropped or stepped on, or having struggled is often in the history. Spinal injury, including lumbosacral vertebral fracture, may result.
- Limb fractures are most often a result of the animal being stepped on or shut in a door.
- Predatory attacks by dogs, and occasionally cats or ferrets, occur.
- The clinical signs of skeletal, soft tissue, and neurologic damage are similar to those in other species.
- Rabbits do not tolerate pain or severe stress well and may go into shock.

Laboratory Evaluation

- Radiographic evaluation for the presence of fractures.
- CBC or hematocrit to assess blood loss (internal or external).

MANAGEMENT

A. Immediate hemostasis, rehydration, and wound management.

B. Broad spectrum antibiotic coverage for open injuries and bite wounds.

C. Analgesia using opioid and or non-steroidal anti-inflammatory agents.

D. Provision of a quiet, non-stressful environment and supportive care as necessary.

E. Fracture repair as appropriate once the patient is stable.

NEUROLOGIC DISEASE

History/Clinical Signs/Physical Examination

- Clinical signs include sudden onset, or progressive development, of central or peripheral neurologic signs, particularly ataxia, torticollis, nystagmus and seizures, and paresis or paralysis.
- Major differential diagnoses include non-suppurative encephalitis caused by the protozoon parasite *Encephalitozoon cuniculi* (central or peripheral nervous signs, more frequent in dwarf rabbits); meningitis, encephalitis, or otitis interna caused by *Pasteurella multocida* or other bacteria; head or spinal trauma; cerebral larval migrans by the raccoon roundworm *Baylisascaris procyonis*. Lead poisoning is an unusual cause of neurologic signs in rabbits.
- Enquire as to a history of exposure to the outdoors, trauma, and contact with other rabbits that might be shedding infectious agents.
- Perform a neurologic examination to differentiate weakness from true neurologic dysfunction and to localize the lesions. Rabbits do not show a reliable menace response.
- Evaluate the eyes, looking particularly for cataracts and uveitis (seen with *E. cuniculi*), and the ears for evidence of otitis.
- Assess the respiratory system and check for ocular or nasal discharge as evidence of infection with *P. multocida*.

Laboratory Evaluation

- CBC and biochemical profile for general health evaluation.
- Assess renal function as indirect evidence for infection by *E. cuniculi*
- Radiographic examination of the head to evaluate the otic bullae and the whole animal, particularly for evidence of trauma and renal or respiratory disease.
- Serology for *Encephalitozoon cuniculi* is available through Charles River Laboratories, Wilmington, Massachusetts, USA. Clinically normal animals can be seropositive. A rising or high titre is necessary to implicate *E. cuniculi as* the cause of neurologic disease in a given patient.

MANAGEMENT

A. **Broad spectrum antibiotics,** particularly **enrofloxacin** or a **trimethoprim-sulphonamide combination**, if there is a suspicion that bacterial otitis, meningitis, or encephalitis is responsible for the clinical signs.

B. There is currently no effective treatment for *E. cuniculi* encephalitis. Treatment with **fenbendazole, oxibendazole,** or **albendazole** may delay the progression of, or more rarely reduce the severity of, clinical signs.

C. **Diazepam 1 – 5 mg/kg IM, IV** or **midazolam 0.5 – 2 mg/kg IM** can be used in seizuring animals as necessary.

D. Provide supportive care as necessary to deal with nutrition, hydration, and to prevent perineal scalding in incontinent animals.

BLOOD IN URINE or AROUND PERINEUM

History/Clinical Signs/Physical Examination

- Note the gender of the animal and determine whether females have been spayed. Uterine disease is common in mature un-spayed female rabbits.
- Blood in the urine or blood staining of the perineum can reflect renal or uterine disease, such as neoplasia and endometrial venous aneurysms.
- Abnormalities of the reproductive tract or cystic calculi may be palpable.
- Normal rabbit urine can have a deep red or brown colour due to excretion of dietary porphyrin pigments.

Laboratory Evaluation

- Urinalysis and urine culture on urine obtained by cystocentesis to differentiate uterine from urinary disease, and characterize urinary abnormalities.
- Radiographic or ultrasonic examination to identify abdominal abnormalities including renal or cystic calculi and ovarian or uterine masses. Rabbit urine can have very high levels of calcium, and hence appear radio-opaque in normal animals.
- CBC and serum biochemistry, particularly to assess the presence of infection and renal function.

MANAGEMENT

A. **Broad spectrum antibiotic** therapy as indicated for cystitis.

B. Surgical removal of cystic calculi if indicated.

C. Ovariohysterectomy for uterine disease, providing the patient is stable.

D. Supportive care as needed.

LUMPS AND BUMPS

History/Clinical Signs/Physical Examination

- Common locations for abscesses include the face and limbs. Facial abscesses are most frequently odontogenic.
- Left untreated, abscesses can eventually result in severe emaciation and dehydration, particularly if they involve the teeth or oral cavity. Subcutaneous abscesses may also reflect the presence of multiple internal abscesses resulting from bacteremia (e.g., *P. multocida*).
- A complete physical examination and diagnostic work-up should be carried out in severely ill animals to identify additional internal problems.

Laboratory Evaluation

- CBC and biochemical profile to assess general health.
- Radiographic examination, particularly to assess bony involvement and disease of other organs, especially the lung.
- Culture and sensitivity (aerobic and anaerobic) of the lesion. A better sample can be obtained by surgically opening the lesions, as the very thick pus in rabbit abscesses is difficult to draw through a needle. Anaerobic bacteria are the most common isolates from odontogenic abscesses.

MANAGEMENT

A. Antibiotic therapy based on culture and sensitivity results. **Metronidazole** is often used, in combination with other antibiotics, for its activity against anaerobes.

B. Abscesses will require surgical cleaning and debriding at frequent intervals. It is rarely possible to remove the abscess *in toto*. Weekly packing of the abscess cavity with a sterile gauze soaked in an appropriate antibiotic aids in resolution of the lesions (*see reference 6*).

C. Supportive and other medical care should be provided as appropriate to the patient's needs.

SUGGESTED READING

1. Analgesics/anesthetics for rabbits. Smith DA, Mathews KA. *In:* PAIN How to Understand, Recognize, Treat and Stop, CD. Jonkar Veterinary Systems Ltd. Guelph, ON, 2003.
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NOTES

INTRODUCTION

Most reptiles presented to veterinary clinics as emergency patients are in fact suffering from chronic, usually husbandry-related, problems. The owner may have just noticed the abnormality, or the disease may have progressed to the point that the animal is in a state of collapse. Debilitated reptiles are very susceptible to local and systemic bacterial infections. The animal may require a prolonged period of medical care, and the prognosis may be guarded if the disease condition is advanced. Unfortunately, many owners of reptile pets are unable or unwilling to financially support a long or expensive therapeutic plan.

Due to the unfamiliarity of most practicing veterinarians with the handling and management of reptiles, this chapter discusses all the practical aspects separately, and continues into potential presenting problems.

HISTORY TAKING

- As well as basic signalment, collect detailed information on management, and on the development and clinical signs related to the reason for presentation.
- Husbandry: size and type of caging; type of substrate used; environmental temperature in animal's cage or enclosure, methods of provision of supplementary heat, proximity to and possibility of contact with heat source (i.e., thermal burns); lighting regime including full spectrum UV light exposure, distance from animal to UV bulb (should be within 12 – 18 inches), frequency with which UV light source is changed (should be each 6 months), any exposure to outdoor light and sunshine (non-carnivorous reptiles require dietary Vitamin D3 or exposure to broad spectrum UV lighting or sunlight to prevent metabolic bone disease).
- Feeding and nutrition: diet fed, frequency of feeding. For carnivorous species: is prey fed dead or alive (live prey can injure the animal being fed)? Are any calcium or vitamin D supplements used (necessary for insectivores and carnivores if whole prey is not fed)?

RESTRAINT AND HANDLING

- Confirm the identity of the species presented to ensure that it is not venomous, and find out whether the animal is comfortable being handled.
- Reptiles often carry and shed *Salmonella* spp. Handlers should wash their hands after working with reptiles and wear protective examination gloves when possible.
- Inexperienced personnel should not handle venomous snakes or lizards, and should reflect before dealing with very large or potentially dangerous reptiles (e.g., large pythons or monitor lizards, alligators).

Snakes

- Remember that all snakes have sharp teeth and can bite.
- First grip the snake over the back of the cervical area just caudal to the head ensuring that the animal cannot turn and bite.
- Support the remainder of the body of the snake. This may require additional persons, depending on the snake's size.
- Most snakes will try to coil around something, generally the handler's arm, in order to support themselves and feel more secure. Larger snakes can grip quite tightly, and may need to be "peeled off" by a second party.
- Snakes should never be allowed to wrap around a person's body or neck.
- During handling, snakes frequently pass feces, urates, and the contents of their scent glands from the cloaca, which opens ventrally at the base of the tail. These excretions can be extremely malodorous.

Lizards

- Lizards have small pointed teeth and can bite, and will scratch with both fore and hind toenails.
- Larger lizards, such as iguanas, can swing their tails like a whip and scratch the handler with the tail's rough surface.
- Place one hand over the dorsal cervical area behind the mandibles to stabilize the head, and a second hand dorsally over the pelvis to control the hind limbs and base of the tail.
- Fractious lizards can be partially wrapped in a towel.
- NEVER hold a lizard by the tail as the tail may break off as a mechanism to escape from a predator.

Chelonians (turtles and tortoises)

- Chelonians have bony plates covering their upper and lower jaws and may bite. These animals can also scratch with the toenails on their fore and hind legs.
- Most turtles and tortoises withdraw their head and legs as far as possible into the shell, and are very difficult to examine.
- Hold the animal across the middle of their upper shell (carapace).
- If an animal has its head out of the shell, the head may be grasped from the dorsal aspect, just behind the skull, and held. It is almost impossible to extract the head from the shell of a strong animal.
- A limb can be extended in most animals by continuous steady traction on the foot.

PHYSICAL EXAMINATION

- Visually examine and palpate (as is possible) all parts of the animal in a routine manner, starting at the head and moving caudally.
- In snakes and lizards the mouth can be opened by carefully inserting a non-abrasive mouth gag (e.g., a tongue depressor, two strips of adhesive tape, a plastic spatula). Be careful not to injure the delicate oral mucosa or break any teeth.
- Visually assess respiratory rate and pattern at rest by watching movements of the chest.
- Reptiles are difficult to auscultate as the stethoscope head does not seal well against their rigid and irregular skin. A thin towel or wet gauze placed on the stethoscope head may help.
- Heart rate can be auscultated over the cardiac region or, in snakes and lizards, directly palpated over the heart. Peripheral pulses are not readily palpated.
- Reptiles are ectothermic, thus their body temperature directly reflects environmental temperature. Body temperature can be taken via the cloaca, but many clinical thermometers do not measure low temperatures. Rectal temperature is only useful to assess whether the environmental heat sources are sufficient to raise an animal's temperature to the desired level. As reptiles do not control their own body temperature, they cannot produce a fever and do not become hyperthermic or hypothermic when ill.

ANESTHESIA

- **Isoflurane is the anesthetic of choice** for reptiles, particularly for painful or prolonged procedures.
- Long periods of breath holding (i.e., tens of minutes) can make mask or chamber induction impractical. If an animal does not become anesthetized within 5 – 10 minutes of anesthetic exposure an alternate induction technique should be considered.
- Larger snakes and some lizards can be endotracheally intubated under manual restraint and then ventilated with isoflurane until the desired plane of anesthesia is reached.
- Induction using an injectable agent is commonly practiced. Ketamine is the most commonly used agent. Sedation and immobilization occur within 10 – 30 minutes following injection. **Ketamine 20 – 40 mg/kg IM** often provides adequate restraint for simple procedures. The dosage of ketamine necessary for surgical anesthesia is extremely high and may result in mortality or prolonged (several days) recovery.
- Other drugs used alone or in combination with low doses of ketamine for anesthetic induction or sedation include **midazolam 2 mg/kg IM or medetomidine 100 – 200 μg/kg IM or IV. Propofol 5 – 15 mg/kg IV** can be used for induction or for very short periods of anesthesia.
- It is generally recommended that IM injections should be given into the muscles of the forelegs of lizards and turtles, and the cranial half of the body of snakes, to prevent nephrotoxicity or premature elimination of drugs whose pharmacokinetics might be affected by the renal portal system (flow of blood from the hind legs through the kidney before entering the main circulation). Further research is needed on this subject.
- Most reptiles breathe poorly when anesthetized, and manual ventilation (IPPV) is necessary when using isoflurane.
- Monitoring during anesthesia can be difficult, as spontaneous ventilation is rare or irregular, and peripheral pulses are unlikely to be palpable.
- An esophageal stethoscope or Doppler flow monitor placed over the heart, at the thoracic inlet, or on the ventral aspect of the tail allow cardiac monitoring.
- Depth of anesthesia is judged by patient responsiveness and movement.
- Induction and recovery times are strongly affected by body temperature. Supplemental heat is necessary before, during, and after an anesthetic procedure to maintain an animal's temperature as close to the **preferred optimal temperature range** (POTR) as possible (*see General Supportive Care – Heat p. 340*).

DIAGNOSTIC SAMPLE COLLECTION

Blood Collection & Hematologic Assessment

- Blood collection from reptiles is difficult for inexperienced clinicians.
- For snakes and lizards, an appropriately sized needle (e.g., 22 g 1") butterfly catheter can be inserted into the ventral tail vein (on the ventral midline approximately 1/3 of the way down the tail, to the depth of the vertebrae) and light suction applied as the needle is gently withdrawn and repositioned until blood flows through the tubing.
- For chelonians, blood can often be collected from a venous sinus on the dorsum of the tail, just behind the shell. In some species blood may also be obtained from the ventral tail vein or the jugular vein or leg veins, which can sometimes be visualized or palpated.
- Contamination and dilution of blood samples with lymphatic fluid is common.
- These sites can also sometimes be used for a single intravenous injection; catheter placement is generally impractical.
- **No more than 1% of body weight should be collected (i.e., 1 mL/100 g).**
- Assessment of the CBC follows general principles. The heterophil is the equivalent of mammalian neutrophil. Some reptilian species have a type of monocyte referred to as the azurophil.
- Assessment of the biochemical profile follows general principles with the exception that **uric acid**, rather than BUN or creatinine, is used to assess renal function. Hyperphosphatemia and hypocalcemia can be seen with nutritional and metabolic bone disease and renal failure.
- Ideally, reference ranges should be obtained from the laboratory that processes the sample and should be for the species under consideration. This is rarely the case and large generalizations and assumptions are often made from one reptilian species to another.

Diagnostic Imaging

- Radiographs are taken using manual restraint or with the patient confined in a plastic or cardboard container.
- Many lizards will remain still for a brief period after light pressure is applied over the eyeballs (vagal reflex).
- Dorso-ventral and lateral views (repositioning the radiograph machine rather than the patient) are taken using fine detail or extremity cassettes.

EUTHANASIA

- The most practical method to euthanize a reptile is to initially anesthetize the animal, using an inhalant or injectable agent (e.g., high doses of **ketamine: 80 – 100 mg/kg**), and then inject a euthanasia agent directly into the heart if access to a peripheral vein cannot be obtained.
- In snakes, the heart is located at approximately the junction between the proximal and middle third of the animal, and can be palpated through the ventral body wall.
- In lizards, the heart is located quite cranially in the coelomic cavity, between the forelegs.
- The heart in turtles and tortoises is extremely difficult to access, as it is protected by the ventral shell (the plastron). A needle can be inserted between the shell plates on the ventral midline approximately 1/3 of the distance from the front to back of the shell. It may be necessary to pre-drill a hole with a larger bore needle first.
- Intravenous access is difficult or impossible in most seriously ill reptiles (*see blood collection above*). As an alternative, barbiturates (diluted 1:5 to minimize local pain and necrosis) can be given intracoelomically.
- It may be difficult to ascertain when the animal is actually dead, as cardiac electrical activity may continue for some time. This is especially important if the animal is being taken home for burial.
- Freezing and decapitation are not considered professional or humane methods of euthanizing reptiles.

GENERAL SUPPORTIVE CARE

Optimize Environment: Temperature and Humidity

- Sick reptiles should be held at the upper end of their **preferred optimum temperature range** (POTR) to optimize metabolism, appetite, digestion, white blood cell function, and immunity.
- The POTR for most species commonly kept as pets is between 22 and 28° C.
- Thermal support can be provided with a warm environment (e.g., a warm room or incubator) or heat source for basking.

- Basking sources (e.g., heat light, heating pad) should be used with caution, as reptiles seeking heat may place their body directly against the heat source and create thermal burns. Commercial "heat-rocks" are not reliable and may result in burns.
- The body temperature of reptiles held in heated chambers may not increase as anticipated, because the animals generally lie against the cool floor of the chamber. In these circumstances measuring cloacal temperature can help determine the effectiveness of supplementary heat.
- Provide environmental humidity appropriate to the species of patient to help maintain and even improve hydration.
- Water placed in an incubator or warmed environment can also help maintain increased ambient humidity.

Fluid Therapy

- Rehydrate according to general veterinary principles using balanced electrolyte solutions (with up to 1/3 volume of 5% dextrose) or 0.9 % saline. Fluids should be warmed to a temperature appropriate to the species under treatment.
- Alert animals can be rehydrated orally with balanced electrolyte or oral rehydration fluids using a rubber or metal oro-gastric feeding tube (*see Nutritional Support below*).
- Depressed or severely debilitated animals should receive parenteral fluids.
- Fluids can be administered subcutaneously in multiple locations according to the degree of dehydration and the "stretchability" of the skin at the sites of injection.
- Subcutaneous injection of hyper- or hypotonic fluids, fluids containing dextrose or K^+, or large amounts of fluids at one site, may result in skin necrosis and sloughing.
- Fluids can also be administered intracoleomically (right lower quadrant – lizards; right or left caudal quadrant – snakes and turtles).
- Large volumes of fluid (i.e., > 2–3% BW) in the coelomic cavity may result in pulmonary compression (reptiles have no diaphragm).
- The proximal femur or tibia can be used for intraosseous administration using an appropriate sized spinal or hypodermic needle.

Nutritional Support

- Chronically ill reptiles are often emaciated and require urgent nutritional support.
- Short periods of fasting will not harm animals in good body condition. Lizards and turtles might be fed daily or every several days; some snakes can go months without eating. The assessment of true "anorexia" must take into account the owner's descriptions of normal feeding patterns for the species and individual.
- Reptiles can be stomach-tubed using metal or red rubber feeding tubes appropriate to the animal's size. The tube should be inserted to the level of the distal esophagus or stomach.
- Care must be taken not to injure the oral mucosa, particularly in snakes, when opening the mouth. A rubber spatula works well for this purpose.
- A maximum volume of 25 mL/kg BW is appropriate for the green iguana.
- An easily digestible nutritional supplement (e.g., Ensure®, Clinicare®, AD®) can be used initially.
- For longer term feeding the diet should be appropriate for the animal's natural history (i.e. carnivore, insectivore, or herbivore).
- For herbivorous reptiles such as green iguanas, appropriate options for tube feeding include a slurry of pulverized and soaked rabbit pellets or a commercial rabbit supplement (e.g., Oxbow Pet Products Critical Care for Herbivores®).
- Vitamin A deficiency is very common in young red-eared slider turtles that are often kept as pets. They can be supplemented with **Vitamin A 1,000 to 2,000 IU/kg IM or SC** (once).

Antibiotics

- Treat all debilitated and sick reptiles with a parenteral antibiotic, as sepsis is common.
- Suggested antibiotics include: **amikacin 2.5 – 5 mg/kg, IM q72h, enrofloxacin 5 – 10 mg/kg, IM q24h or q48h, trimethoprim-sulfonamide 15 – 30 mg/kg, IM, SC q12–24h, and ceftazidime 20 mg/kg, IM q72h.**
- Injections should be given into the muscles of the forelegs of lizards and turtles and the cranial half of the body of snakes due to concerns regarding the potential for nephrotoxicity or premature elimination of the drug.
- An appropriate formulary should be consulted to determine a regimen for prolonged antibiotic therapy. Dosage and safety of various therapeutic compounds can vary widely among different types of reptiles and with environmental temperature.

Analgesics

- Little research has been carried out on the effectiveness or correct dosing of analgesics in reptiles. It is expected that opioids and non-steroidal anti-inflammatory agents should be effective.
- Suggested analgesics include: **meloxicam 0.1 – 0.2 mg/kg PO q24h** starting dose. Reduce to minimum effective dose after 2 – 3 days; **butorphanol 0.04 – 2 mg/kg IM** as needed; **buprenorphine 0.01 – 0.1 mg/kg IM** as needed.

PRESENTING PROBLEMS

"JUST SICK"

History/Clinical Signs/Physical Examination

- Non-specific clinical signs include inactivity, unresponsiveness, and anorexia. Animals are often emaciated and dehydrated. Lizards such as the green iguana may have an abnormal brown or yellow colour.
- There may be no specific abnormalities on physical examination.
- Precise history taking is essential as inappropriate diet and husbandry requirements are often predisposing or causative factors.
- Owners are often unaware of the proper care of their reptile pet.
- Anorexia normally occurs in female animals late in egg production, and in snakes preparing to shed (undergo ecdysis). Owners may not be aware of this.

Laboratory Evaluation

- Complete blood cell count and biochemical profile if possible.
- Whole body radiographs, particularly to assess bone density (presence of metabolic bone disease), reproductive activity in females, and the presence of ingested foreign objects.
- Reptiles with metabolic bone disease have poorly mineralized cortices and pathological fractures, and may have greatly thickened thighs due to fibrous osteodystrophy.
- If physical examination suggests a focus of infection (e.g., abscessation, ulceration, dermatitis, stomatitis) samples should be collected for microbial culture and sensitivity. Gram negative organisms (e.g., *Pseudomonas* spp., *Aeromonas* spp.) are the most common causes of sepsis.

MANAGEMENT

A. Provide general supportive care.

B. Treat according to the results of the diagnostic testing.

TRAUMA

History/Clinical Signs/Physical Examination

- Gross trauma, including limb or spinal fractures, usually result from an animal falling when roaming freely about the house, being dropped, or being stepped on. Metabolic bone disease (nutritional) is a common predisposing factor. Wild reptiles are frequently run over by motor vehicles.
- Most reptiles with fractures remain bright and active but will not have proper function of the injured limb. Animals with spinal fracture may show paresis or paralysis. Most fractures are closed, but on physical examination crepitus and abnormal mobility can be elicited.
- Snakes can be severely traumatized by live prey (i.e., rats) placed in their cage without supervision.
- Snakes held under improper management conditions may abrade the mucosa of the oral cavity and develop secondary bacterial infection.
- Reptiles, particularly snakes, can develop severe cutaneous burns from close contact with external heat sources.

Laboratory Evaluation

- Complete blood cell count and biochemical profile.
- Whole body radiographs, particularly to assess bone density (presence of metabolic bone disease), and fractures. Reptiles with metabolic bone disease have poorly mineralized cortices and pathological fractures, and may have greatly thickened thighs due to fibrous osteodystrophy.
- If physical examination suggests a focus of infection (e.g., abscessation, ulceration, dermatitis, stomatitis) samples should be collected for bacterial culture and sensitivity.

MANAGEMENT

A. Fractured limbs can be splinted using whatever soft bandaging materials are on hand. Orthopedic repair is generally unnecessary.

B. Animals with spinal fractures should be kept confined to reduce movement. Depending on the degree of spinal injury, they may or may not have bowel and bladder control (in chelonians and lizard species that have bladders).

C. General supportive care including antibiotic therapy as warranted.

D. Dietary correction and oral calcium supplementation must be implemented (e.g., **calcium borogluconate, 50 – 300 mg/kg PO, daily**) for animals with metabolic bone disease.

LUMPS AND BUMPS

History/Clinical Signs/Physical Examination

- Subcutaneous abscesses and granulomas are common in reptiles and, although not emergency conditions, may be associated with systemic illness due to sepsis or disseminated lesions.
- Gram negative organisms and mycobacteria are the most common organisms responsible.
- Also check for fungi and parasites, especially in wild caught species.

Laboratory Evaluation

- Complete blood cell count and biochemical profile to assess systemic involvement.
- Needle aspiration or biopsy can be used for culture and sensitivity, cytology, or histopathologic diagnosis.

MANAGEMENT

A. General supportive care is required, including antibiotic therapy based on culture and sensitivity, where possible, or broad spectrum with good coverage of gram negative organisms.

B. Reptiles do not form liquid pus and therefore lesions do not drain. Excision or debridement is generally necessary.

TREMORS & SEIZURES

History/Clinical Signs/Physical Examination

- Clinical hypocalcemia secondary to chronic dietary deficiency or imbalance, or chronic renal disease, are common causes of this clinical presentation in herbivorous and insectivorous reptiles.
- Females that are reproductively active and are shelling eggs may be more susceptible. Owners are frequently unaware of the reproductive status of their pet reptile.
- Mildly affected animals show minor muscle fasciculation, either continuously or after stimulation.
- More severely affected animals may be unable to rise or move about, and when stimulated may go into tetanic spasms with the forelimbs held tightly against the body and the hind limbs extending caudally. Some animals may show actual convulsions.
- Tongue prolapse can be seen in chameleons.
- Although clinical signs are generally diagnostic, a detailed history is necessary to determine the diet and access to sunlight or artificial UV light.
- In snakes, neurologic signs can be caused by several viral infections for which there is no effective therapy.

Laboratory Evaluation

- Plasma calcium and phosphorus levels reflect the degree of metabolic upset. Calcium: phosphorus ratios and levels in normal animals are similar to those in other species (e.g., 1.5 – 2.5:1). Hypocalcemia and hyperphosphatemia can be seen.
- Mature animals with renal secondary hyperparathyroidism will have elevated uric acid levels.
- Radiographs allow assessment of the degree of skeletal demineralization. Young growing animals are more prone to metabolic bone disease. Mature animals with renal secondary hyperparathyroidism may not show poor bone density.

MANAGEMENT

A. Supplement calcium by subcutaneous or intracoelomic injection of an **injectable calcium product 50 – 300 mg/kg, diluted to a concentration of 5% or less** as needed (*see Hypocalcemia p. 379*).

B. Oral supplementation can be initiated in animals that are still eating and are only mildly affected (e.g., **calcium borogluconate, 25 – 250 mg/kg PO, daily**).

C. Aggressive fluid therapy should be administered to animals with elevated uric acid levels.

D. Provide general supportive care.

E. Long term therapy includes provision of a correct diet and exposure to broad spectrum UV light or direct sunlight.

RESPIRATORY DISTRESS

History/Clinical Signs/Physical Examination

- Respiratory distress most commonly found in snakes and tortoises.
- Clinical signs include dyspnea, bubbling at the nose and open mouth breathing.
- Turtles with pneumonia may "tilt" when floating or swimming in water.
- Bacterial causes are most common but viral, fungal, and parasitic pneumonias can occur.
- Deficiencies in husbandry are important predisposing factors.

Laboratory Evaluation

- Complete blood cell count and biochemical profile to assess systemic complications.
- Lateral and cranio-caudal (in turtles and tortoises) radiographs may show radiodense areas in the lung and asymmetry
- Tracheal or glottal swabs can be used for culture and sensitivity to determine appropriate antibiotic therapy.

MANAGEMENT

A. General supportive care with appropriate antibiotic therapy.

B. Prognosis is poor in severe cases.

STRAINING/DYSTOCIA/EGG BINDING

History/Clinical Signs/Physical Examination

- The majority of reptilian species kept in captivity lay eggs; boid snakes have live births
- The veterinarian must distinguish between an animal that is simply full of eggs, and one that is having difficulty passing eggs. Many reptiles will not start to lay their clutch unless specific environmental conditions are met. The treatment of these animals is not an emergency situation.
- Anorexia is common and not abnormal in reptiles late in the egg production process.
- Lizards with many eggs will have grossly enlarged coeloms and may show dyspnea.
- Egg masses may be visible or palpable in gravid snakes.
- General debility, hypocalcemia, malformed eggs, and uterine infections are the most common causes of dystocia. Depression, unresponsiveness, straining, and cloacal prolapse are signs that an animal is attempting to pass eggs. The owner may relate that some eggs have already been passed.

Laboratory Evaluation

- Radiography is the most effective way of determining the number, position, and shape of the eggs in the oviduct. It may be possible to differentiate between animals with pre-ovulatory stasis (many large ova still on the ovary) and post-ovulatory stasis or dystocia (eggs within the oviduct).
- Monitoring blood calcium levels may help determine the cause of egg stasis and help evaluate the response to treatment.

MANAGEMENT

A. Environmental management: initially correct ambient temperature, hydration, and calcium status (*see Management of Tremors and Seizures p. 343,* and *General Supportive Care p. 340*).

B. Oxytocin is highly effective in promoting egg laying in chelonians, less effective in lizards, and poorly effective in snakes. Oviductal contractions should occur within 30 – 60 minutes. Oxytocin does not relax the utero-vaginal sphincter and can result in deaths in animals with true dystocia.

C. Dosages of **oxytocin: chelonians (turtles and tortoises) : 1 – 10 IU/kg IM; repeat in 2 – 4 h as necessary; lizards and snakes: 10 – 30 IU/kg IM; repeat in 2 – 4 h as necessary.**

D. Caesarian section or ovariohysterectomy is required if environmental management and medical therapy are unsuccessful. Usually several days of supportive therapy are provided before surgical options are considered. Caesarian sections are not performed as emergency surgeries in reptile patients. Consult a reptilian medicine text for details on surgical procedure as this varies significantly among different types of reptiles.

GASTROINTESTINAL DISORDERS

Clinical Signs/Physical Examination

- Anorexia, weight loss, and reduced fecal passage are common, non-specific clinical signs and may simply reflect inadequate diet and husbandry.
- True gastrointestinal conditions can occur, including gastrointestinal foreign bodies, intestinal obstruction or accident, parasitism, and bacterial enteritis (especially salmonellosis).
- Assessment of general body condition and activity levels helps determine the duration and severity of the problem. Some species, such as geckos, store fat in their tails.
- Impacted or obstructed animals may appear bloated, while anorexic animals may seem gaunt with a concave abdominal (coelomic) shape.
- Prolapse of the intestine, bladder, or reproductive tract can occur secondary to diarrhea and/or straining.
- Vomiting is most common in snakes, and may reflect low ambient temperature (autolysis of ingested prey before digestion occurs) or gastric cryptosporidiosis.
- Diarrhea does not necessarily accompany intestinal infection.

Laboratory Evaluation

- Fecal culture and sensitivity are used to identify significant infectious agents and recommend appropriate antibiotic therapy. Many reptiles carry and shed *Salmonella* spp. without having clinical disease.
- Fecal smear and flotation can be used to identify the presence of gastrointestinal parasites, including *Entamoeba invadens* in snakes.
- Complete blood cell count and biochemical profile if possible.
- Plain radiographs may show radiodense foreign objects or the presence of abnormal intestinal outlines and gas patterns.
- A **barium** contrast series is helpful in evaluating motility and the presence of obstruction. **25 mL/kg of a 25 % w/v barium suspension** can be administered by stomach tube. Passage of the barium to the distal colon requires several days. GI motility is slowed under sub-optimal environmental temperature as well as with dehydration and a variety of disease conditions. Ideally, these conditions should be addressed before a barium series is undertaken.

MANAGEMENT

A. Provide general supportive care including antibiotic therapy.

B. Treat enteric parasites as appropriate **(ivermectin should NEVER be administered to turtles or tortoises).**

C. If the reptile is not obstructed, tube feed once daily for nutritional support.

D. Animals with GI foreign bodies and intestinal obstruction or accident, will require exploratory and corrective surgery.

SUGGESTED READING

1. Analgesics/anesthetics for reptiles. Smith DA, Mathews KA. In: PAIN How to Understand, Recognize, Treat and Stop, CD. Jonkar Veterinary Systems Ltd. Guelph, ON, 2003.
2. Exotic Animal Formulary, 2nd edition: Carpenter JW, Mashima TY, Rupiper DJ. WB Saunders, Philadelphia, 2001.
3. Handbook of Veterinary Drugs, 3rd edition: Allen DG, Dowling T, Pasloske K, Smith DA. Lippincott Williams and Wilkins, 2004.
4. Reptile Medicine and Surgery. Mader DR (ed). WB Saunders, Philadephia, 1996.

NOTES

INTRODUCTION

The administration of fluids (crystalloids, synthetic colloids, blood and blood components) is necessary to replace water loss from tissues (dehydration), maintain normal hydration, restore intravascular volume (perfusion) by replenishing blood or fluid loss, increase or maintain colloidal osmotic pressure (COP), administer essential electrolytes and nutrients, and to serve as a vehicle for the administration of intravenous medications. Fluids should be considered as 'drugs' and fluid therapy a 'prescription' because their various compositions will influence many ionic interactions and shifts in plasma. The type of fluid selected will influence resolution of alkalosis or acidosis. Alkalemia and acidemia will affect the pathologic condition experienced by the animal. Selection of fluid type and volume is a major component of the therapeutic plan and should include careful assessment of tissue and intravascular losses, acid-base and electrolyte status, age and species of the animal, nature of illness or injury, acute or chronic history, hematocrit and serum albumin concentration, coagulation status and cardiorespiratory function. The animal's illness or injury is a dynamic event and selection of fluid type and volume may change according to the patient's response to fluid therapy, and with improvement or deterioration of the underlying problem. Therefore, constant monitoring to achieve desired end-points is required. Being aware of associated problems that will necessitate cautious fluid selection, volume and rate of administration is key to **fluid resuscitation** and optimizing recovery.

This author categorizes losses into hemorrhage and non-hemorrhage. With **hemorrhage** it is essential to categorize into compressible (can place a bandage e.g., limbs) or non-compressible (cannot place a bandage .i.e., within the thorax). With **non-hemorrhage,** it is essential to categorize into **capillary leak** (i.e., inflammatory conditions), or non-capillary leak. In **non-capillary leak** conditions it is essential to categorize into assumed or measured **low oncotic pressure** (e.g., hypoalbuminemia), or **normal oncotic pressure.** Selecting the appropriate fluid, volume and rate of administration, for each problem can be considered as the 'prescription' for correcting the hypovolemic state. Capillary leak is due to an alteration in the endothelium in animals with inflammatory conditions which may have a vasculitis or increase in 'endothelial gap' due to action of cytokines. These animals are more predisposed to edema. Patients with inflammatory conditions may be severely hypotensive, especially with a septic process causing distributive and hypovolemic hypotension. These patients frequently require crystalloid, fresh frozen plasma (*Transfusion Therapy p. 667*) and may also benefit from 25% human serum albumin or a cautious titration of synthetic colloid. Appreciating the difference between 'optimal' and 'adequate' end points when treating hypovolemia must be considered until the underlying problem causing the fluid loss is stopped. In situations where attempting to attain 'optimal' systemic blood pressure by aggressive fluid therapy will likely cause pulmonary edema(e.g., pulmonary contusions), or increased blood loss (i.e., ongoing, non-compressible hemorrhage), a reduced rate to attain 'adequate' pressure is advised. The volume of fluid required to correct fluid deficits in all compartments cannot be accurately derived; therefore, therapy is assessed using mathematical formulas based on an estimated percentage of intravascular or tissue loss noted on physical examination and, the history, and laboratory findings. The assessment may not be accurate, therefore the volume of fluid given should be titrated to the patient's needs and the physiological responses to the fluid administered rather than adhering to the 'estimated' requirement. The extent and invasiveness of monitoring utilized to assess these responses are dependent on the severity of illness and stability of the patient, the availability of various monitoring devices, and the level of expertise of the clinician and support staff.

This chapter will focus on **non-hemorrhage hypovolemia.** As fluid therapy in hemorrhage requires specific instruction refer to *p. 619*. For consideration of specific electrolyte problems and therapy, refer to the individual chapters. Complications of fluid therapy and routes of administration of fluids are presented following Diagnosis and Management, followed by discussions on body fluids, and the various types of fluids.

DIAGNOSIS

Hypovolemia, and hypovolemic shock (defined as decreased circulating blood volume in relation to the total vascular capacity, characterized by a reduction of diastolic filling pressures and volume) has many etiologies. Non-hemorrahge fluid losses can be due to:
- Third space sequestration (e.g., peritonitis, pleuritis, vasculitis),
- Vomiting, diarrhea, polyuria and third degree burns.
- Relative hypovolemia due to inadequate circulating volume such as distributive shock (e.g., anaphylaxis, sepsis, hypoadrenocorticism), or capillary leak.

- Occult hemorrhage in veterinary patients is commonly associated with rodenticide toxicity, coagulopathy (e.g., thrombocytopenia, factor deficiency), diseases of the gastrointestinal tract (i.e., ulceration due to non-steroidal anti-inflammatory analgesic ingestion, neoplasia, hypoadrenocorticism, uremia, stress). *See Hemorrhage p. 619.*
- Dehydration.

History/Signalment

A thorough and chronological history should be obtained when determining a fluid therapy regimen in addition to a complete physical examination.
- If diarrhea (*p. 32*) or vomiting (*p. 74*) are present, question the owner regarding duration, frequency and volume, and all events that could precipitate this (i.e., ingestion of foreign body, compost, infectious).
- Vaccination history, especially young animals.
- Determine frequency and volume of urine voided. Frequency itself will not determine polyuria as many animals may only have the opportunity to void 3 – 4 times/day, but the volumes may be very large. Owners may also confuse pollakiuria for polyuria.
- The volume of water consumed may also be a guide to urine volume produced. Third-space losses will also lead to polydipsia with or without polyuria. Ask if the animal has access to the toilet, or other water areas, in addition to designated water bowl.
- Ask appropriate questions regarding potential diabetes mellitus (*p. 263*) and pyometra (*p. 756*).
- Establish known concurrent medical problems (e.g., chronic renal failure, heart failure).
- Environmental situation (i.e., where there is inability to access water or mother's milk, hot weather *p. 291*).

Clinical Signs/Physical Examination

- Shock (*see p. 603*) is generally defined as a mean arterial pressure (MAP) less than 60 mmHg or systolic pressure less than 90 mmHg with accompanied, tachypnea, tachycardia, or bradycardia (end-stage shock or in cold patients), and decreased mentation or depression. However, hypovolemia that is compensated for can be accompanied by near-normal or normal blood pressures; in this instance tachycardia and tachypnea are generally present. In shock, assume ~30% or more, loss in circulating blood volume.
- If the patient's condition appears life-threatening (shock) due to low circulating blood volume i.e., pale, white or grey mucous membrane colour, capillary refill time >2 secs, tachycardia, tachypnea, weak pulses (pulses may appear 'good' in septic shock), mean arterial pressure <60 mmHg, systolic pressure <90 mmHg, cool extremities, obvious blood loss, depression, then institute **emergency phase of fluid therapy** (*Management below p. 351*) immediately.
- Obtain body temperature. Hypothermia is also an indicator of poor perfusion.
- Differentiate between hydration status and circulating blood volume (pressure and volume). Dehydrated patients can have normal blood pressure and circulating volume, while acutely hypotensive, hypovolemic patients can be normally hydrated. Intravascular volume (perfusion) deficits are managed and monitored differently than are tissue water deficits. Unless severe total body water loss is present, the dehydrated animal still has adequate tissue perfusion as indicated by normal acid-base status, normal blood lactate concentration, adequate urine production and appropriate concentrating ability, and normal renal and hepatic function (unless primary problems are known to exist with these organs). Hypoxia, however, due to anemia, may contribute to end-organ dysfunction or injury despite adequate perfusion.
- In all patients, hydration status should be assessed (Tables 1 & 2).
- The physical findings reflect the underlying problem and severity, and its chronicity/acuity. In time, if left untreated, all hypovolemic patients will become dehydrated, and dehydrated patients will become hypovolemic, therefore both dehydration and hypovolemia may be present.
- Look for the underlying cause (i.e., shock due to any cause – *Acute Abdomen p. 21, Trauma p. 682, Sepsis p. 588, Heart Failure p. 149, thoracic pathology p. 555*).
- If the body weight, prior to this illness is known, this information may be useful in estimating degree of fluid loss.

TABLE 1. Estimating Degree of Dehydration (traditional method)

Note: As **loss of water** from the tissues (dehydration) increases to maintain circulating blood volume, a point is reached where both dehydration and hypovolemia (low circulating volume) exists. Therefore, the assessment of hydration given below will include perfusion as the animal enters the >7% dehydration in acute settings and >10% dehydration in the chronic setting. While the underlying illness will affect the clinical signs of a patient which is hypovolemic (cytokine release, fever, anemia, electrolyte and acid-base imbalance) parameters to assist with intravascular volume loss, in general, are presented in Table 3. For parameters associated with hemorrhage *see Hemorrhage p. 619*).

Estimated % Dehydration	Physical Examination Findings
<5	History of fluid loss, but not dehydrated on physical examination.
5	Dry oral mucous membranes, but no panting or pathologic tachycardia.
7	Mild to moderate decreased skin turgor, dry oral mucous membranes, slight tachycardia, normal pulse character.
10	Moderate to marked degree of decreased skin turgor, dry oral mucous membranes, tachycardia, normal pulse pressure, eyes sunken in orbit.
12	Marked loss of skin turgor, dry oral mucous membranes, eyes sunken. Shock depends on the rapidity of the dehydration process. Rapid losses result in rapid perfusion deficits and shock, which is always accompanied by an underlying illness. This is compared to a slowly developing dehydration such as that occurring with 'inadvertent hybernation' of a cat locked in a garage!
12 – 15	Marked loss of skin turgor, dry oral mucous membranes, eyes sunken, weakness, depressed (± moribund, shock). Again, presentation will depend on rapidity of fluid loss.

TABLE 2. Considerations when Assessing Hydration

Aged and cachectic animals	Skin elasticity and body fat is lost. Skin turgor is assessed by pulling and twisting the skin on the lateral thorax with a quick release and noting the time it takes to return to normal. In a non-aged adult or cachectic animal 12% dehydration results in the skin often remaining tented for 5 – 10 seconds. Eyes may be sunken in the orbits. This appearance may exist in the elderly and cachectic animal.
Obese patients, puppies and kittens	May have normal skin resiliency even when dehydrated
Third space losses	Third-space losses are accumulations of fluid in the thoracic or abdominal cavities, intestinal or gastric lumen, in tissues around fracture or trauma sites, or generalized interstitial edema. These losses result in a reduction of circulating (plasma) volume but may not be associated with a reduction in body weight.
Panting	Dries mucous membranes in normal animals.
Nausea	Can cause salivation which will moisten the mucous membranes of a dehydrated animal.
Excitement and anxiety	Increases heart rate.
Body weight	A simple method for assessing fluid volume losses. As 1 mL water is equal to 1 g, an acute weight loss of 100 g (0.1 kg) represents a loss of ~ 100 mL fluid. Losses of lean body mass are never rapid, therefore, acute losses are generally fluid losses and become a quantitative estimator of deficit volumes. An animal deprived of food may lose ~ 0.1 – 0.3 kg BW/day/1000 kcal energy requirement. Any weight loss in excess of this is assumed to be fluid loss. An average illness energy requirement is estimated to be 1.2 – 1.3 x resting energy requirement (1.2 or 1.3 x 70 x BWkg$^{0.75}$ kcals/day) *see Nutrition p. 499*. Generally, 1 mL water is required to excrete the by-products of metabolism of 1 kcal, therefore fluid requirements are similar to energy requirements where no abnormal fluid losses exist.
Serum sodium (*p. 381*)	Not always useful as a measure of hydration status. Isotonic dehydration (normal sodium: 142 – 154 mmol/L, dog; 152 – 163 mmol/L, cat) occurs when water and electrolytes are lost in proportion to their plasma concentration. Hypertonic dehydration (increased sodium) occurs when water loss is in excess of solute. Hypotonic dehydration (low sodium) occurs most commonly with isotonic fluid loss and the animal consumes a lot of water to maintain fluid volume (i.e., peritonitis with excess water intake). This dilutes the sodium. Sodium is also diluted in hypotensive states as anti-diuretic hormone (ADH) contributes to significant water retention at the level of the kidney. Normal sodium or hyponatremia may be associated with hyperglycemia (*Hyperosmolar Syndrome p. 279* and *Diabetic Ketoacidosis p. 263*) and therefore does not necessarily reflect a hypotonic or hypooncotic state.

TABLE 3. Estimating Degree of Intravascular Volume Loss

Clinical Parameter	Mild Hypovolemia ~<10–15% intravascular volume loss	Moderate Hypovolemia ~20–25% intravascular volume	Severe Hypovolemia > 30% intravascular volume loss
Heart rate	130 – 150	150 – 170	170 – 220
Mucous membrane color	Normal to pinker than normal	Pale pink	Gray, white or muddy
Capillary refill time	Rapid (< 1 sec)	Approximately normal (1 – 2 sec)	Prolonged (> 2 sec) or absent
Pulse amplitude	Increased	Mild to moderate decrease	Severe decrease
Pulse duration	Mildly reduced	Moderately reduced	Severely reduced
Metatarsal pulse	Easily palpable	Just palpable	Absent
Mentation is affected by perfusion and the underlying disease	Alert if not associated with serious illness	May be depressed due to underlying illness. Anxious, alert, responsive if hemorrhage only	Depressed, obtunded, stuporous
Mean Arterial Pressure	> 80 mmHg	> 60 mmHg	< 60 mmHg

Modified from Boag AK, Hughes D. Assessment and Treatment of Perfusion Abnormalities in the Emergency Patient Vet Clin NA: Sm Animal Pract. 2005;35(2):319-342.

NOTE: Hypothermia may predispose to hypotension and bradycardia especially in cats.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, TS** are necessary to formulate a fluid plan and assist with underlying diagnosis and severity of illness. PCV and TS may be elevated in free water loss but may be decreased with blood loss. As splenic contraction occurs following a catecholamine surge (i.e., after a traumatic incident or other significant stressful experience), the PCV may be increased even though a significant amount of blood has been lost (*see Hemorrhage p. 619*); the TS, however, will be lower than normal.
- **Stick BUN,** serum urea and creatinine may be increased in pre-renal disease, such as in any illness predisposing to fluid loss. Normally the increase above normal for urea occurs prior to that for creatinine. Urea is also increased with gastrointestinal hemorrhage in the presence of normovolemia. The stick BUN is very sensitive and will be increased above normal range when the serum urea is still within the high normal range.
- **Glucose levels** are increased in diabetes mellitus, which causes excessive urinary fluid losses. Hypoglycemia may indicate sepsis and potential third space fluid losses, increased insensible losses due to fever, or inability to consume water.
- **Serum electrolytes,** predominantly sodium (*p. 381*) but potassium and chloride also, can be increased, decreased or normal with fluid losses. Hypercalcemia also results in polyuria and requires specific fluid requirements.
- **Venous blood gases** (*p. 406*) are extremely helpful in assessing perfusion status. A base deficit > 4 (-4), HCO_3 < 20 mEq/L suggests reduced perfusion, the severity of which is determined by degree of deficit. Non-respiratory alkalosis, base excess > 4 (+4), HCO_3 > 24 mEq/L is frequently present in pure gastric vomiting and over-zealous treatment with furosemide, gastrointestinal mast cell tumour and Zollinger-Ellison syndrome.
- Where **blood gas analysis is not available,** the acid base status (*p. 406*) may be obtained from the biochemical profile and electrolyte analysis. Acidemic patients with HCO_3^- loss can usually be identified as having increased serum Cl^-, decreased total CO_2 (an indirect measure of HCO_3) and normal anion gap. If acidemia is due to the addition of an anion (e.g., lactic acid, glycolic acid) the Cl^- is usually normal but the anion gap is increased. Alkalemic patients are often hypo-chloremic.
- **Lactate** is frequently increased in fluid losses accompanied by poor perfusion.
- **Urine specific gravity** may be extremely concentrated in volume loss with normal renal function; however, where concentrating ability is lost, isosthenuria or hyposthenuria will be present.
- **Systemic arterial (A) blood pressure (BP),** both systolic (SBP) and MAP should be measured where possible.

Extended Laboratory and Imaging Data Base

- **CBC and Serum biochemistry,** while often considered in the extended laboratory data base, are recommended as soon as possible as the results may determine an underlying problem (i.e., sepsis, hypoalbuminemia, liver failure), thereby facilitating early therapeutic intervention to resolve the fluid losses.
- The various diagnostic tests that are relevant to history and physical findings, and stat laboratory data.

Assessment of fluid losses is only an *estimate* and actual losses may be much greater or, even less.

The etiology and severity of the hypovolemic state is an important factor in the type of fluid to select (crystalloid, colloid, blood products), and the volume for resuscitation. Identify those situations where 'optimum' resuscitation to within normal values (CVP 5 mmHg [6 – 7 cmH$_2$O], MAP 80 – 100 mmHg, Systolic BP 100 – 120 mmHg) is the goal and those where 'adequate' resuscitation to a MAP of 60 mmHg and a systolic pressure 90 – 100 mmHg are acceptable (i.e., pulmonary contusions or edema, or continual, non-compressible hemorrhage).

Estimating Fluid Volumes for Replacement Therapy

Of primary concern is the status of the intravascular (blood) volume, and then restoration of total body water and electrolytes. Fluid therapy is divided into three phases: (A) the emergency phase, (B) rehydration phase and (C) maintenance phase. Not all patients require the three-phase therapy.

1. To calculate the volume of fluid required to **correct dehydration** in litres, multiply the percent dehydration assessed by the patients weight, in kilograms. For example. a 10% [10/100 = 0.1] dehydrated 10 kg dog requires 0.1 x 10 = 1 Litre (L). When treating dehydrated patients a general rule to apply is the more rapid the fluid loss (i.e., acute vomiting and diarrhea), the more rapid the replacement (crystalloid solution) should be, especially where pre-renal azotemia exists.

2. To calculate the volume of fluid required in litres to correct perfusion deficits, an estimate of intravascular volume loss is required. To estimate the percent of intravascular fluid losses; assess mentation, mucous membrane colour, capillary refill time and pulse pressure; measure SBP and include pertinent, physical findings and history. This approximation (%) is used in the following equation to estimate volume required to correct perfusion deficits. If hemorrhage is the cause of poor perfusion refer to *Hemorrhage p. 619*. If in shock (*see Physical Examination above and Shock p. 603*), then assume at least a 30% (0.3) circulating intravascular volume depletion.

   a. The approximate blood volume in **dogs** is ~ 8% body weight = 0.08 x BW kg (80 mL/kg).

   b. The approximate blood volume in **cats** is ~ 6.5% body weight = 0.065 x BW kg (65 mL/kg).

   c. 30% intravascular volume loss in the **1 kg dog** = 0.3 x 0.08 x 1 kg = 0.024 L (24 mL/kg). As ~3 times the colloid volume has been recommended for crystalloid replacement, 75 mL/kg may be an estimated requirement. Note, the 90 mL/kg generally recommended is based on an over-estimated blood volume of 10% in the dog.

   d. 30% intravascular volume losses in the **1 kg cat** = 0.3 x 0.065 x 1 kg x 3 = 0.0195 L (19.5 mL/kg). Based on the above for the dog, 3x blood volume lost for crystalloid replacement is 58.5 mL/kg.

3. These calculations are based on estimated findings, therefore, the volumes generated are just estimates. Let the patient's response to therapy guide the fluid regimen.

4. **Adverse effects** of fluid overload are discussed in IV. ANTICIPATED PROBLEMS ASSOCIATED WITH FLUID THERAPY below *p. 357*). Please review these when administering fluids to any patient.

I. EMERGENCY PHASE

The patient is hypotensive and has clinical signs of shock (*see Physical Exam*). Vascular volume must be restored, with the exception of congestive heart failure (*p. 149*). If blood loss due to any cause *see Hemorrhage p. 619*; if cerebral injuries *see Head Trauma p. 691*, if Hyper/Hyponatremic *see p. 381*. It should **not** be assumed that all trauma patients are hypovolemic. There are many situations where these animals do not require fluid therapy, however, this will have to be assessed on an individual basis (*p. 619/555*). **The goal of this phase is to reverse the hypotension and shock,** not to correct dehydration, this is considered in the Rehydration Phase below.

A. Obtain IV access (*see Procedures*) using as large a catheter as possible, and collect blood for laboratory evaluation.

B. IV fluid therapy should be administered according to history, physical examination and laboratory data. See Table 1 – 3 for estimates of intravascular volume deficit. If **Acidemic,** commence a **balanced electrolyte solution (BES)** (Plasma-Lyte® 148 or A, Normosol® R, or lactated Ringer's). If **alkalemic use 0.9% sodium chloride.** Administer 1.5 – 2.0 mL/kg/min (90 – 120 mL/kg/h) dog; 1 mL/kg/min (60 mL/kg/h) cat initially, reassess q5min (*see C below*).

1. If "dying before your eyes" add hypertonic saline 5% (6 – 10 mL/kg max), OR 7.5% (4 – 8 mL/kg max) at 1 mL/kg/min for dogs, **quarter of this for cats,** [respiratory arrest and/or vagoreflex bradycardia may occur, treat with 0.02 mg/kg atropineand/or **synthetic colloid** (pentastarch, hetastarch or dextran-70), **5.0 mL/kg (dog)** to a max of 20 mL/kg, **2.5 mL/kg (cat)** to a max 10 mL/kg boluses. Monitor q5min (*see C below*). Continue with crystalloids.

2. If **hypotensive but not** "dying before your eyes", initially commence with **crystalloid solutions** as in B above. Monitor q5min (*see C below*). If no improvement after 10 min, add an IV bolus of **synthetic colloid 5 mL/kg (dogs), 2.5 mL/kg (cats).** Repeat bolus if indicated as in 1 above.

3. **Hypotensive** with **moderate to severe hypoproteinemia (TS <45 g/L [4.5 g/dL]),** and/or suspect **capillary leak** judicious fluid management is required to avoid pulmonary edema (*see C below*).
   a. Commence a **balanced electrolyte solution (BES)** as in B above. If poorly responsive after 10 min, consider reducing crystalloid volume by ~20 – 40% and ADD aliquots of **synthetic colloids (6% Hetastarch, 6% Pentastarch, dextran 70 at 5 mL/kg (dog) or 2.5 mL/kg (cat),** monitor response to each aliquot [to a maximum of 20 mL/kg (dog), 10 mL/kg (cat)].
   b. If **MAP <60 mmHg** and TS <30 [3.0 mg/dL] (albumin levels assumed to be <15 g/L [1/5 g/dL]) prior to fluid administration, consider **25% Human Serum albumin (HSA) 0.5 mL/kg** (*see Hypoalbuminemia p. 431 and Fluid Therapy Discussion p. 431* for details prior to administration), by slow push while monitoring blood pressure (*see C below*). Repeat if no effect. If pressure increases, reduce rate by 25%. Discontinue bolus dosing and continue as a CRI at 0.3 – 1 mL/kg/h when pressures are adequate or optimal. **Repeat 0.5 mL dose if no effect.** Dosages up to ~ 4 mL/kg in 24 hours have been administerd by the author.
   c. Fresh frozen plasma 10 – 20 mL/kg (dog & cat) is recommended in sepsis, however thawing time precludes its immediate use but should be administered as soon as thawed. Both plasma and 25% HSA may be administered concurrently.
   d. If calculated volume of fluids and colloids are delivered and pressures are still below normal, administer a vasopressor (*see D below p. 353*).

4. **Pediatrics.** Dehydration and hypoglycemia can occur rapidly in puppies and kittens.
   a. Administer 1 mL/30 g Plasma-Lyte® 148 or Normasol® R or lactated Ringer's with dextrose (add 1 mL of 50% dextrose/10 mL crystalloid).
   b. Give as a bolus via jugular vein (easily accessible with 20 gauge peripheral IV catheter), or intraosseous.
   c. Do not administer subcutaneously.
   d. Repeat bolus as needed based on response. Re-check glucose prior to repeat dosing.

5. **Patients requiring surgery** on an emergent basis. An alkalinizing balanced electrolyte solution is recommended in the majority of cases, unless alkalemic, where normal saline is the fluid of choice. The calculated deficit in these patients should be administered, where time permits, before being anesthetized. Blood products and synthetic colloids may also be required and should be assessed on an individual basis. Occult hypoperfusion prior to surgery may contribute to morbidity. Occult hypoperfusion or dehydration may still be present upon completion of the procedure even though the calculated fluid deficit has been administered. Re-assessment with regards to fluid deficit should be made upon completion of the surgical procedure.

6. **Not hypotensive.** Administer a BES based on physical examination and *go to Rehydration Phase p. 355.*

C. **Divide resuscitation volume in 5 min intervals** to assess response to therapy. You may need more or less fluid than estimated. The rate and potentially the volume, **will have to be reduced** in geriatric patients and those with cardiac insufficiency, patients with pulmonary contusions, pre-existing pulmonary edema and aspiration pneumonitis, and frerquently in patients with capillary leak and hypoproteinemia. Fluid administered to '**adequate**' end points is the goal initially for these patients.

End Points of Resuscitation

1. Basic monitoring techniques should be performed and include HR and RR, pulse pressure, CRT, MM colour and improved mentation. Warm, pink digits (unless septic or neurogenic) frequently signal adequate resuscitation (Table 3).

2. A normal SBP, with increased heart rate indicates compensated shock (requires further fluid therapy), or **pain** (administer an opioid, *see Shock p. 603*).

3. Systemic arterial blood pressure (BP), and central venous pressure should be measured where possible.
   a. **Optimum resuscitation** to within normal values, MAP 80 – 100 mmHg, Systolic BP 100 – 120 mmHg, CVP 5 – 8 cm H_2O [3 – 5 mmHg] (Table 4), is the goal.
   b. **Adequate resuscitation** to a MAP of 60 mmHg and a systolic pressure 90 – 100 mmHg is acceptable where indicated.

    c. Signs of hypervolemia may occur with rapid delivery of fluids (Table 5).

    d. Assesment of volume may also be made radiographically (*see* J *below p. 353*).

4. Base deficit or lactate levels can be used to assess perfusion with goals of **base deficit** 0 ± 4, a **lactate concentration** <2.5 mmol/L (dogs), <1.5 mmol/L (cats). Values greater than this are primarily indicative of hypoperfusion (*see Lactate p. 400*) requiring ongoing resuscitation; however, anemia, hypoxemia, or increased activity at the time of collection, as other primary causes must be ruled out.

5. Normothermia or improvement in body temperature. Hypothermia may interfere with attaining resuscitation goals, especially in cats, therefore, warming during resuscitation is necessary.

6. Urine production should be monitored in most instances (goal: 0.5 – 1.5 mL/kg/h with specific gravity within normal range).

7. PCV (>25%) and TS (>45 g/L).

D. Vasopressors & Inotropes are required if hypotension persists after adequate fluid resuscitation (based on calculations above).

1. **Dopamine 5 μg/kg/min (cats and dogs)** and increase by 1 μg/kg/min ~ every 2 min (max 15 μg/kg/min) until **target blood pressure** (MAP 70 – 100 or systolic 100 – 120 mmHg) is reached (*see Dopamine Infusion Chart p. 233*). Stop if tachycardia develops. If vasopressor effects are inadequate at this rate, discontinue and try,

2. **Norepinephrine 0.05 – 0.5 μg/kg/min** increase as for dopamine (i.e., increase by 0.1 μg/kg/min q2min) (*see Norepinephrine Infusion Chart p, 253*), higher dosages may be required. OR

3. **Dobutamine 5 μg/kg/min (dogs), 1 – 2 μg/kg/min (cats)** [CAUTION in cats as seizures may occur] if more inotropic effect is warranted.

4. If only **epinephrine** is available and pressor support is necessary, try **0.1 – 1.0 μg/kg/min** (*see Epinephrine Infusion Chart p. 235*) starting with the low dose and increasing every 2 – 3 min to effect, or the highest dose.

5. Gradually reduce pressor support over several hours, or more rapidly if tachycardia or hypertension develops.

6. If hypotension persists go to E below.

E. If **non-responsive** to adequate fluid and vasopressor therapy, consider the possibility of illness-induced **adrenal crisis p. 274**. Where any patient is non-responsive to all of the above resuscitative efforts, low-dose **methylprednisolone or prednisolone sodium succinate 1 mg/kg IV** may be indicated. Sodium:potassium ratio is freqently normal in this setting. **Dexamethasone 0.1 mg/kg** is recommended if ACTH stimulation is considered. **Corticosteroids are NOT** recommended for routine use in any shock state other than adrenal crisis.

F. **Furosemide 0.25 mg/kg IV** should be administered where pulmonary edema has occurred due to overhydration. A CRI of 0.1 – 0.2 mg/kg/h may be required until resolution.

G. **Monitor PCV and TS q15 – 30 min.**

1. If PCV ≤25% (dog), ≤20% (cat) and /or TS <40 g/L, transfusion with packed cells, whole blood, plasma, or 25% Human Serum albumin, is indicated to avoid further hemodilution (*see Hemorrhage p. 619*).

H. **Electrolytes** are altered during the emergency phase of fluid therapy i.e., hypokalemia may occur due to dilution and diuresis.

I. **Blood glucose** should be assessed periodically, especially if low initially, or when dealing with puppies, kittens or toy breeds.

J. **Radiographic assessment** of the pulmonary vasculature can be used to monitor fluid administration. In animals, the width of the pulmonary vein should be <1.5 times the width of the pulmonary artery, and fluid overload should be considered if the measured difference exceeds this value. The radiographic appearance of pulmonary edema, increased lung sounds such as crackles, and cyanosis indicate a late stage of edema with severe patient compromise.

L. **Post-fluid vs baseline assessment** of the chest should be made by auscultation and thoracic radiography, and gentle ballotment and radiography or ultrasonography can be used to assess the abdomen. With increasing effusion and decreased COP, a colloid + 0.25 mg/kg furosemide should be considered.

TABLE 4. Interpretation of CVP Values in Response to a Rapid Infusion of 20 mL/kg Crystalloid or 5 mL/kg Colloid in a Patient.

NOTE: The first four signs in Table 5 have been noted by the author on occasion with a 20 mL/kg crystalloid fluid bolus administration in dogs. As colloids at this rate are only administered in severe hypovolemic/hypotensive states, these signs of hypervolemia have not been noted by the author.

Response to Infusion	Interpretation of Response
2 – 4 cm H_2O increase from baseline returning to baseline in 15 min.	Euvolemia and normal cardiac function.
An increase in CVP maintained >4 cmH_2O above baseline.	Increased venous blood volume, reduced cardiac compliance, or both.
A prolonged (>30 min) return to baseline.	Increased blood volume relative to cardiac performance.
Minimal to no increase in CVP.	Markedly reduced intravascular volume. Requires further resuscitation.
An increase in CVP with rapid (<5min) return to baseline.	Reduced intravascular volume and accommodation of fluid within the intravascular space and subsequent reduction in vascular tone. Further resuscitation is required.
Raise CVP by 2 – 4 cm H_2O within first few minutes of bolus therapy. If falls rapidly to baseline, repeat bolus therapy until CVP 5 – 10 cm H_2O (3 – 7 mmHg) requiring 10 – 15 minutes to fall. At this point, blood volume and venous return are optimal relative to cardiac performance.	Further resuscitation is required.
CVP should not be pushed higher than 13 – 16 H_2O (10 – 12 mmHg) with normal intra-pleural and intra-abdominal pressures.	Greater than this may predispose to pulmonary edema. Continual resuscitation will likely not improve cardiac output.

TABLE 5. Potential Clinical Signs Associated with Rapid Infusion, Volume Overload and Overhydration.

shivering
nausea (swallowing and licking lips)
vomiting (may be early or late)
restlessness (early)
polyuria (patient dependent)
serous nasal discharge
tachypnea (early or late)
cough (late)
chemosis (late)
dyspnea (late)
diarrhea (late)
ascites (late)
exophthalmous (late)
depressed mentation (late)
tachycardia (followed by bradycardia when severely overloaded)
subcutaneous edema (initially hock joint and intermandibular space then 'jiggly' thorax) (late)
pitting edema
pulmonary crackles and edema (late)
excessive weight gain

II. REHYDRATION PHASE

A. Volume to be administered is total of needs for:

1. **Returning the patient to normal hydration status:** Deficit volume (Litres) = % dehydration x BW(kg). For example a 10 kg dog, 10% dehydrated = 10 x 10/100 = 1.0 L required for rehydration. With chronic loss (i.e., water deprivation, chronic diarrhea), any perfusion deficits (Table 3) should be managed as (estimating fluid volumes for replacement therapy *p. 351*) above to normal blood pressure and urine production; rehydration of the tissue follows to attain normal hydration which should occur within 24 hours. Correction of occult hypoperfusion (lactate >2.5 mmol/L) within 24 hours improves outcome after trauma.

2. **Replacing ongoing losses** which include:
   a. **Normal (insensible)** losses due to water in feces, evaporation through airways, etc. ~ one-third of daily loss (one-third normal **maintenance** requirement).
   b. **Normal urine volume** produced ~ two-thirds of daily loss (two-thirds daily normal **maintenance** requirement).
   c. **Additional ongoing losses** (i.e., vomiting, diarrhea, excessive salivation, excess urine production, third space losses, losses through drains and in bandages) must be estimated and added to the 'normal' maintenance requirements. **Fever** is also considered as an ongoing loss. An additional 10% maintenance fluid should be added to the daily requirement for every 1°C above normal (38.5°C). Fluid loss from full-thickness burned, or other injured skin can be estimated using the formula: *evaporative loss (mL/h) = [25 + % total body surface area (TBSA) burned] x (normal TBSA m²) which continues until healed* (see Burns *p. 682*).

B. **Fluid Selection** will depend on the patient's problem. In most cases a BES, most commonly alkalinizing solution, is selected as ~95% of veterinary patients are acidemic (*see Acid-Base Assessment p. 406*). Normal saline is administered when patients are alkalemic (*see Acid-Base Assessment p. 406*). *See discussion below regarding 'homemade' solutions p. 363.*

C. **Assessment of Requirements and Administration of Fluids**

1. **Neonates and pediatrics.** A volume of 1 mL/30 g body weight orally q15–30min if suckling reflex is good, or subcutaneously (lactated Ringer's solution or 0.9% sodium chloride, at a rate determined by absorption and until hydrated. Note acetate solutions should not be used due to pain upon administration.

2. **Adult.** Rate of administration is determined by rate of loss, degree of dehydration and patient's condition (i.e., underlying cardiac disease, renal disease, pre-renal azotemia/oliguria). Sodium abnormalities (*p. 381*) should be corrected over 24–48h. If surgery is planned, the estimated deficit should be replaced during the time available prior to anesthesia, hydration status should be re-evaluated upon completion of surgery.

3. **Fluid Regimen.** Consider eneteral fluids where possible *(see Routes of Administration below p. 359).*
   a. **Mild dehydration (<5% – 7%)**
      Where there is no evidence of intravascular volume contraction (increased urea, PCV, TS), deliver over 24h with any ongoing losses added. If given IV more rapidly, a diuresis ensues and the tissue dehydration is not corrected. Urine specific gravity >1.040 (dog), >1.060 (cat) alone is not necessarily an indication for a high initial rate of fluid administration.
   b. **Moderate dehydration (8% – 10%)**
      Where there is evidence of intravascular volume contraction (increased urea, PCV, TS) administer a higher fluid rate initially. Divide the calculated volume into two. Aim to give one-half the calculated fluid, including maintenance volume, over four (10% dehydrated) to eight hours (8% dehydrated). The other half is given over the remaining 20 (10% dehydrated) or 16 hours (8% dehydrated). The goal is to more quickly restore the intravascular volume, increase glomerular filtration rate and so prevent further renal injury.

      Example: 10 kg dog, 10% dehydrated: half of the deficit (500 mL) given over four hours (=125 mL/h) plus maintenance (20 mL/h, *see Table 8*) =125 + 20 = 145 mL/h. Give the remaining 500 mL, plus maintenance, over 20 hours (25 +20 = 45 mL/h). If further 'loading' is indicated due to inadequate urine production, then continue. During the first four hours, the patient should be assessed every half an hour and the fluid rate reduced if necessary. Urine output (assess bladder size and/or urine voided) and urine specific gravity are important. As the bladder increases in size reduce the fluid rate. Avoid causing

diuresis. Vital signs, skin resiliency and weight are other major deciding factors in assessing fluid administration rates. Fluid administration during the remainder of the 24 hour period should be adjusted accordingly. It is not always necessary to commence with a high fluid rate in an animal dehydrated to this degree. The decision is based on clinical, laboratory and historical assessment. A rapidly dehydrated patient should be rehydrated more rapidly than a chronically dehydrated patient. If dehydration is chronic and renal function (biochemistry and urinalysis) is normal, the estimated fluid requirement should be delivered evenly over the 24 hour period.

c. **Severe dehydration (>10%)**

This should initially be treated as described in the emergency phase if there is evidence of circulating volume depletion (as occurs with acute diarrhea, third space loss, etc.) and then re-evaluated with respect to the rehydration and maintenance phases (include the ongoing losses). If fluid loss is chronic (no access to water but otherwise healthy, etc.), fluids should be administered over 24–48h as in b above. In this instance, circulating volume is maintained by pulling fluid from the intracellular and insterstitial spaces. Slow rehydration replaces these losses without causing a diuresis.

C. Failure to achieve normal hydration. Base assessment on laboratory findings and weight in combination with physical examination, including mental alertness. Some patients have a normal "appearance of dehydration" (geriatric, emaciated animals)! Weight loss due to lack of food consumption must also be considered. Return to normal hydration takes 24–48h. Reasons for failure to achieve this include:

1. Calculation errors.
2. Underestimation of deficit.
3. Ongoing losses greater than estimated (i.e., polyuria, panting, salivation, fever).
4. Too rapid infusion with consequent diuresis and obligatory loss of fluids.
5. Mechanical problems with fluid delivery (i.e., pump failure).
   If none of the above recognized, increase daily volume by 5% BW and reassess throughout the day.

III. MAINTENANCE PHASE

The maintenance phase begins when the patient's hydration status has returned to normal and the body weight has increased by at least the percentage of dehydration already corrected. Example: 10% dehydrated 10 kg dog would have gained ~ 1 kg (weigh after urination – empty bladder); however, this may not always be the case. Use overall assessment of the patient not just weight.

A. Fluid selection will depend on the acid-base and electrolyte status of the patient (*p. 406*). Specific commercial maintenance solutions are available (Table 7). As the sodium and chloride content of replacement solutions are not always required during the maintenance phase, maintenance-type fluids should be considered. For example, the alkalinizaing maintenance solutions contain only 40 mEq/L of each sodium and chloride, with 13 mEq/L of potassium, which is more than twice that in replacement solutions. Half-strength saline (0.45%) contains 77 mEq/L of sodium and chloride, potassium chloride at 25 mEq/L should be added as a potassium source. It is not always economical to carry all types of fluids, but these can be made in-house. If 5% dextrose is available, this can be added to either 0.9% saline or the Lactated Ringer's, Plasma-Lyte®148 or A solutions at a 1:1 ratio. See Crystalloids in Discussion for preparation instructions (*below p. 362*). Mixing within the bag is necessary to prevent the risk for sterile water, or 5% dextrose accidentally being administered alone. Potassium chloride 20 – 25 mEq/L is added unless contraindicated. Various electrolytes can be added to the maintenance fluids where indicated based on the individual patient needs, and to manipulate changes in acid-base status (*p. 406*).

B. During this phase the **maintenance rate in mL/24h is ~ [30 x BW(Kg) +70], OR 1.2 to 1.3 [70 x BWKg $^{0.75}$]** (the resting energy requirement formula) (Table 8). The 1.2 is more suitable for patients with reduced energy expenditure. The 1.3 is used in the sicker patient where energy expenditure tends to be higher. The difference, however, is small with an increased requirement of 1 – 9 mL/h throughout the whole weight range (Table 8). These equations tend to agree with the calorimetric measurements, whereas the linear equation tends to give a lower volume. Neonates and pediatric patients have a higher fluid requirement (Table 9). Ongoing losses must also be calculated and added to the daily 'maintence' requirement. This volume is in addition to that required to replace ongoing losses (see II Rehydration A2 a–d).

C. Urine output can be measured by free catch when voiding or, in those recumbent or critically ill patients, by placing a urinary catheter and attaching it to a closed system. Bedding can also be weighed prior to placing in the cage and weighed again when wet, the difference is ~ urine voided (1 g = 1 mL). For details see *Acute Renal Failure p. 709.*

D. It is difficult to accurately assess ongoing losses of diarrhea and vomitus. A suggested crude measurement is to estimate these volumes and then double it. Fluid loss into the abdomen or pleural space should also be considered; body weight in this instance will not accurately reflect recovery of hydration.

E. Fluids should be gradually discontinued when hydration is restored. Taper by 25% – 50% per day, depending on the duration of therapy. If more rapid reduction is indicated, decrease by 5%/hour.

IV. ANTICIPATED PROBLEMS ASSOCIATED WITH FLUID THERAPY

A. **Diuresis.** Excessive administration serves no therapeutic benefit and frequently results in patient morbidity. Urine output can double when intravascular volume and pressure rise even a few mm Hg above normal, a response termed pressure diuresis. In addition to water loss, sodium loss also occurs. If this diuresis goes undetected, an excess of all electrolytes is excreted in the urine. In some instances, resultant hypokalemia can be quite profound, especially in cats. Increased medullary blood flow, which can occur with excessive fluid administration, will wash out the hyperosmotic interstitium thereby reducing renal concentrating ability. A vicious cycle then is established in which fluid loss occurs due to lack of concentrating ability. Gradual fluid reduction is required to re-establish the hyperosmotic gradient and maintain hydration.

B. **Electrolyte abnormalities,** especially hypokalemia as above. Occassionally, hypernatremia occurs with longterm replacement solutions, or 0.9% sodium chloride. Hyperchloremia with increased chloride administration (0.9% NaCl, KCl) also occurs.

C. **Concerns for Selection of Fluids**
1. **The type of fluid** selected will influence resolution of alkalosis or acidosis. Alkalemia and acidemia will affect the pathologic condition experienced by the animal (*see Acid-Base Assessment p. 406*). If an inappropriate selection is made such as 0.9% sodium chloride in a patient with hyperchloremia, or another condition resulting in acidosis, acidosis will worsen and has been shown to increase morbidity. Likewise, in a patient with alkalosis, administration of an alkalinizing solution potentially will contribute to morbidity as electrolyte composition of plasma is altered. With alkalosis, a shift of the oxyhemoglobin dissociation curve to the left occurs reducing oxygen offloading to the tissues. Administration of dextrose also can alter the electrolyte composition of plasma. Intracellular shifts of phosphorus and potassium may occur during dextrose infusions, and careful monitoring and supplementation of these ions is required in patients with hypophosphatemia and hypokalemia.
2. **Lactated Ringer's** solution contains lactate as a bicarbonate precursor. Lactate is metabolized in the liver, and it has been suggested that administration of this fluid may increase lactate concentration in animals with severe liver disease. However, the clinical importance of this effect must be determined on an individual basis. Mild hyperlactatemia has been noted in dogs with lymphosarcoma receiving lactated Ringer's solution. Due to the calcium content of lactated Ringer's solution, blood transfusions should not be given through the same fluid administration set. Lactated Ringer's solution will result in microscopic clot formation in blood products.
3. **Acetated polyionic solutions** (Plasma-Lyte®148, Plasma-Lyte®A, Normalsol®R) contain acetate as the alkalinizing component. Acetate is metabolized in muscle cells, and therefore specific organ dysfunction (e.g., kidney disease, liver disease) is not a contraindication for its use. It has been suggested that these solutions not be administered to animals with diabetic ketoacidosis (DKA) because acetate is a ketone precursor and may promote ketone production. This concern appears to be theoretical because concurrent treatment for DKA with insulin prevents further ketone production. Because many patients with DKA are acidemic,

crystalloid solutions containing acetate have been the author's choice for fluid therapy for several years. Rapid administration of polyionic acetate solutions may precipitate vasodilatation and hypotension in animals that already are hypovolemic. Although this is a rare event, monitoring blood pressure during administration of acetated crystalloid solutions is recommended.

4. **Hypertonic saline** solutions have been recommended for various conditions and have several positive attributes. Rate of infusion is important, however, and rapid infusions may result in bronchoconstriction and shallow breathing.

5. **Synthetic Colloid solutions** are recommended for many clinical situations and the commonly used synthetic colloid solutions are formulated in 0.9% sodium chloride. The primary acid-base effect of the colloid solutions on plasma is acidification. Considering the frequency of use of these products in veterinary practice, very little has been published with regard to complications after their administration. A potential complication of colloid administration is hemorrhage, if a pre-existing condition exists in a patient with a moderate coagulopathy. Synthetic colloids are eliminated primarily by renal excretion, and caution must be used when administering these products as rapid volume expanders to patients with oliguria, unless oliguria is determined to be due to hypovolemia or hypotension. These products should not be administered to patients in anuric renal failure or congestive heart failure due to concern about volume overload. Interference with renal function has been reported in human patients receiving synthetic colloids, and most commonly this observation has been associated with use of Dextran-40. A reduction in GFR also has been noted in human surgical and trauma patients receiving synthetic colloids. Another potential complication that may occur is leakage of the small molecules (<50,000 Daltons) into the pulmonary interstitium when administered to animals with capillary leak syndrome.

D. Phlebitis due to hyperosmolar solutions (*see IV Route of Administration below p. 359*).

E. **Overhydration/Hypervolemia.** (*see Table 5*).

1. **Interstitial edema.** Under **normal conditions** there is a slight negative pressure (-3 mmHg) in most loose subcutaneous tissues of the body. This negative pressure holds the tissues together and offers some resistance to fluid flux due to the low compliance of the tissue. With overhydration the interstitial pressure increases facilitating larger volumes of fluid to accumulate in the tissues with little change in interstitial hydrostatic pressure. This effect is called *stress relaxation*. When this occurs, pitting edema is detected by pressing on an area of skin and noting pitting for several seconds until the fluid flows back into the area.

2. Patients with **moderate to severe capillary leak** may develop edema after administration of moderate volumes of crystalloid solutions. Assessing interstitial tissue edema is an essential component of monitoring during fluid administration.

3. **Evaluation of edema** may be conducted by examination of three body regions, these are the hock because non-edematous animals, regardless of the amount of body fat, have a well defined lateral saphenous veins, achilles tendons, and bony prominences; the mandibles and intermanidublar space because these areas also are well defined in most animals; and the movement of the skin and subcutaneous tissues over the torso. With the development of interstitial edema, these anatomical regions become less defined and a 'jelly-like' appearance of the skin develops. If these findings are generalized, overhydration due to excessive fluid administration or capillary leak can be assumed. These regions should always be examined for baseline assessment before fluid administration. Chemosis also may occur with overhydration, but this finding tends to occur later than those previously mentioned.

4. **Edema of internal organs** is likely to occur when edema of subcutaneous tissues is identified. It has been this author's observation at necropsy that edema of the brain, gastrointestinal tract, heart, liver and kidney co-exists with subcutaneous edema. This finding may account for some of the clinical signs observed including depression, vomiting, cardiac arrhythmias, coagulopathy and oliguria

5. **Bandages** placed around the neck to secure a catheter into the jugular vein may cause edema of the head and chemosis after the patient is hydrated, or if over-hydrated. Likewise, edema of a distal limb may occur if it is the dependent limb or a bandage is placed above the hock or carpus.

6. **Effusions,** fluid losses into third spaces (e.g., pleural cavity, pericardial cavity, peritoneal cavity, joint cavities), will also occur with administration of large volumes of fluids, or in moderate volumes if capillary leak is present. This will increase body weight *without* improvement in overall fluid repletion.

7. **Pulmonary edema.** Interstitial fluid dynamics differ from those of other tissues. Pulmonary capillary pressure is lower (approximately 7 mm Hg), and interstitial fluid pressure in the lung is more negative (-8 to -5 mm Hg) than that of peripheral tissue, and the pulmonary capillaries are relatively permeable to protein molecules rendering the COP of the pulmonary interstitial fluid approximately 14 mm Hg. These differences favor fluid

movement from the alveoli into the interstitium and lymphatics. Capillary permeability is increased during systemic inflammatory conditions, endothelial injury, pneumonia and pancreatitis, and capillary leak would be expected to occur with administration of smaller fluid volumes. Monitoring in affected animals must be diligent with even slight changes being a potential warning sign of pulmonary edema. As pulmonary interstitial pressure increases into the positive pressure range and the lymphatics are unable to remove this fluid, it leaks into the alveolar space. In the absence of capillary leak disorders, when the pulmonary capillary pressure exceeds 25 mm Hg (approximately 18 mm Hg above normal) in normal dogs, fluid accumulates in the lungs. This information applies to normal dogs and not dogs with capillary leak conditions or those that are hypoproteinemic. When COP is decreased, as in patients with hypoproteinemia, edema formation may occur even at lower hydrostatic pressures. In experimental models, edema begins to form at 11 mm Hg when COP is decreased (*see colloid osmotic pressure below p. 364*).

8. **Pancreatitis** is a relatively common problem in cats and dogs requiring fluid therapy. Patients with moderate-to-severe pancreatitis will develop acute lung injury and acute respiratory distress syndrome. This complication is due to changes in the pulmonary endothelium associated with the systemic inflammatory process, liberation of pancreatic digestive enzymes (especially elastase) and damage by neutrophils that results in enhanced capillary leak.

9. Hypothermia should be corrected as fluid overload may occur while attempting to correct hypothermia-induced hypotension.

10. **Treatment for edema** is **furosemide 0.25 mg/kg followed by 0.1 – 0.2 mg/kg/h CRI** until edema resolved.

F. Post Surgery

1. Patients who are clinically or sub-clinically dehydrated going into surgery may be prone to continuing dehydration and possibly oliguria several hours following the procedure. Prior to surgery these patients may receive rapid infusions of fluid which increases the intravascular volume, blood pressure and glomerular filtration rate (GFR) but where equilibration between the intravascular and interstitial space may not be reached. Throughout surgery a high fluid rate is continued to maintain normal blood pressure and GFR. An average fluid rate is 5 mL/kg/h, however, volumes well in excess of 10 mL/kg/h may be required during hypotensive episodes. Upon cessation of anesthesia, blood pressure and GFR rises resulting in diuresis. Urinary losses continue for a period following completion of the surgical procedure even though tissue dehydration may still be present. Monitoring with tailoring of adequate fluid therapy is required in these patients. Ideal urine production is 1 – 2 mL/kg/h, (urine specific gravity 1.026) while receiving fluids.

2. Occasionally, surgical fluid rates may not be adequate in those dehydrated patients undergoing open abdomen or chest procedures or major fracture repair. The evaporative losses here can be quite extensive and urine output may be consistently low. Fluid therapy in these patients should be rapid, directed towards renal perfusion and normal urine production, followed by maintenance rates.

3. Excessive surgical fluid rates also result in a relative anemia and hypoproteinemia. In this instance normalization of PCV and TS occurs following diuresis of excess fluids. Should PCV and TS remain <25% (dogs), 20% (cats) and, 45 g/L (cats and dogs) respectively, appropriate therapy should be considered.

V. ROUTES OF ADMINISTRATION OF FLUIDS

The route is selected based on the patient's condition and requirements.

A. Enteral route

1. Use the enteral route when normal hydration status can be maintained, the patient is not vomiting and there is no pre-existing esophageal disease or aspiration pneumonitis. This is ideal for water-deprived patients with or without combination IV fluids.

2. The fluid may be ingested voluntarily or administered through a feeding tube. Electrolyte solutions should be used. For simple, effective and inexpensive delivery of fluids via the enteral route, place a nasoesophageal feeding tube (*see technique Nutrition p. 508*), connect to a delivery set and bag of IV fluids (add dextrose to 5 %) and deliver as a CRI. Fluids can be delivered via gastrostomy and jejunostomy tubes.

3. Potential complications with the enteral route include malpositioning of the tube within the airway with subsequent pneumonia, vomiting if the administration rate is too high, and hyperkalemia if potassium supplementation is excessive.

B. Intravenous

1. The most common route for fluid administration is the intravenous route. Catheters are placed in peripheral veins (e.g., saphenous, cephalic) or a jugular vein. Strict aseptic technique is required. Complications may occur if surgical preparation of the venipuncture site is not performed.

2. The IV route is necessary for correction of moderate to severe dehydration and shock states. It is also recommended, following these states, to proceed into the maintenance phase.

3. Jugular vein catheterization is required for hyperosmolar solutions. Extravasation of fluids can be a serious complication if the fluid is hyperosmolar (e.g., amino acids, ≥5% dextrose in electrolyte solutions), contains vasoconstrictive drugs (e.g., epinephrine, norepinephrine), or contains certain hemotherapeutic agents. To reduce or avoid phlebitis associated with hyperosmolar solutions, a central vein should be used to deliver these solutions. If a central line cannot be obtained and a peripheral vein must be used, a 24 – 22 gauge catheter rather than 20 – 18 gauge catheter should be selected with careful monitoring of the venipuncture site and limb. The exception would be that any drug specifically requiring administration through a central vein, should be administered via this route.

4. If percutaneous catheterization is **difficult,** perform a venous cutdown (*see Rapid IV Access Techniques in Shock p. 609*).

5. Inflammation at the venipuncture site may indicate infection or phlebitis due to movement of the catheter or the rigid material of the catheter (Teflon). In a study in which Violon catheters (Insyte®, Becton-Dickinson) were placed after strict aseptic skin preparation, catheter dwell time could be extended up to 10 days with peripheral catheters and longer with jugular catheters. These catheters become very flexible and soft when warmed to body temperature and catheter replacement every 72 hours is not necessary when using these methods. Reduced inflammation associated with Violon catheters appears to result in minimal discomfort for the animal, and rarely do dogs and cats attempt to remove the catheter. At the Ontario Veterinary College, catheters are only removed when inflammation or fever of unknown origin occurs, or if the catheter is grossly contaminated. Such catheter tips are submitted for culture, and rarely (~ 1 annually) is bacterial contamination identified.

6. Inflammation of the catheter insertion site tends to occur at 72 hours in patients with vasculitis (e.g., immune-mediated hemolytic anemia).

7. Routinely, in all patients, the area of catheter placement should be assessed each time the veterinarian or technician examines the patient. The bandage does not have to be removed, but the limb palpated for heat, swelling and discomfort. If infusion pumps are used and the alarm signals occlusion, the catheter and entry site should be examined carefully.

8. Destruction of the catheter or administration set will occur if the animal bites it, and hemorrhage may be a complication if this event is not witnessed. Serious hemorrhage also may occur if the connector on an arterial catheter becomes dislodged and may require blood transfusion if a large amount of blood loss occurs. It is advised that a colour other than red be used for bandaging catheters as hemorrhage will be detected earlier with other colours.

C. Intramedullary/Intraosseous

1. Should venous access be difficult to obtain, intramedullary administration of fluids may be considered.

2. The bone marrow of the femur and humerus is occasionally more easily accessible than small collapsed veins in neonates and pediatric small animals; although in this author's hospital, the jugular vein is catheterized with a 20 gauge peripheral catheter even in the most moribund of very young patients.

3. The circulation to the bone marrow does not collapse in cases of hypotension and shock.

4. Strict aseptic technique is required to avoid abscessation with potential extension and neurological compromise of the limb.

5. Infiltrate the site with lidocaine as this procedure **IS painful.**

6. A burette should be placed in the fluid line to control the volume of fluid delivered; otherwise, during emergency resuscitation or while unattended in the cage, a large volume of fluid from a 500 mL or 1 L bag could be inadvertently delivered to these small patients.

D. Subcutaneous

1. Subcutaneous fluid administration is contraindicated in patients with moderate to severe dehydration or in shock because peripheral vasoconstriction associated with these conditions results in little if any circulation to the skin; the fluid is not absorbed but gravitates resulting in ventral pooling. Pooling of fluid results in discomfort and lowers body temperature.

2. Subcutaneous fluids are useful for maintenance fluid administration or treatment of mild dehydration.
3. No more than 10 – 20 mL/kg of lactated Ringer's, 0.9% sodium chloride, non-dextrose containing solutions should be administered at any one site. Do not use acetated solutions (painful). The total volume is usually governed by patient comfort.
4. Gravity administration (IV delivery set and bag) is tolerated better than injection under pressure (i.e., butterfly catheter and syringe).
5. Sterile solutions placed aseptically is mandatory to avoid infection. Abscess formation and cellulitis are complications of this route if aseptic technique is not followed carefully.
6. Usually, these fluids are resorbed within six to eight hours. If not, then intravenous administration should be considered.

E. **Intraperitoneal**

1. This route is rarely used, but relatively rapid absorption of crystalloid solutions occurs from this site.
2. Concerns using this route include pathological conditions of the abdomen, and the risk of peritonitis should contamination occur.
3. Solutions containing acetate (e.g., Plasma-Lyte®, Normosol® products) should be avoided as they appear to be very painful when introduced into the abdomen. Lactated Ringer's and 0.9% saline are advised for this route.

DISCUSSION

Body Fluids

Sixty percent of the adult animal's body weight is water (Fig.1), and percentage decreases with increasing body fat and age. In neonates and pediatrics 80% and 75% body weight respectively, is water. In adults total body water is distributed between two major compartments (1) intracellular (ICF) ~67%, and (2) extracelluar (ECF) ~33%. The ECF is further divided into two compartments (1) interstitial (ISF) and intravascular (IVF). Of the 33% ECF, 75% is interstitial (or ~24.75% BW), and ~25% is intravascular (or 8% BW[(~6.5% cats]). The IVF is divided into red blood cells (PCV, Hematocrit) and plasma (Total Solids). When considering total body water, the ICF contains the major amount and it is here that fluid losses result in dehydration. As the IVF is depleted, the extravascular fluid (ISF + ICF) moves into the IV compartment to maintain perfusion. In this setting, hemorrhage for instance, will result in dehydration if there is significant delay in seeking veterinary care.

The approximate ionic composition of body water compartments (Table 6) is important to note as many BES (Table 7) are designed to replenish the intravascular compartment (Table 7). Electrolyte and fluid shifts occur during various clinical situations potentially altering the distribution of the ions.
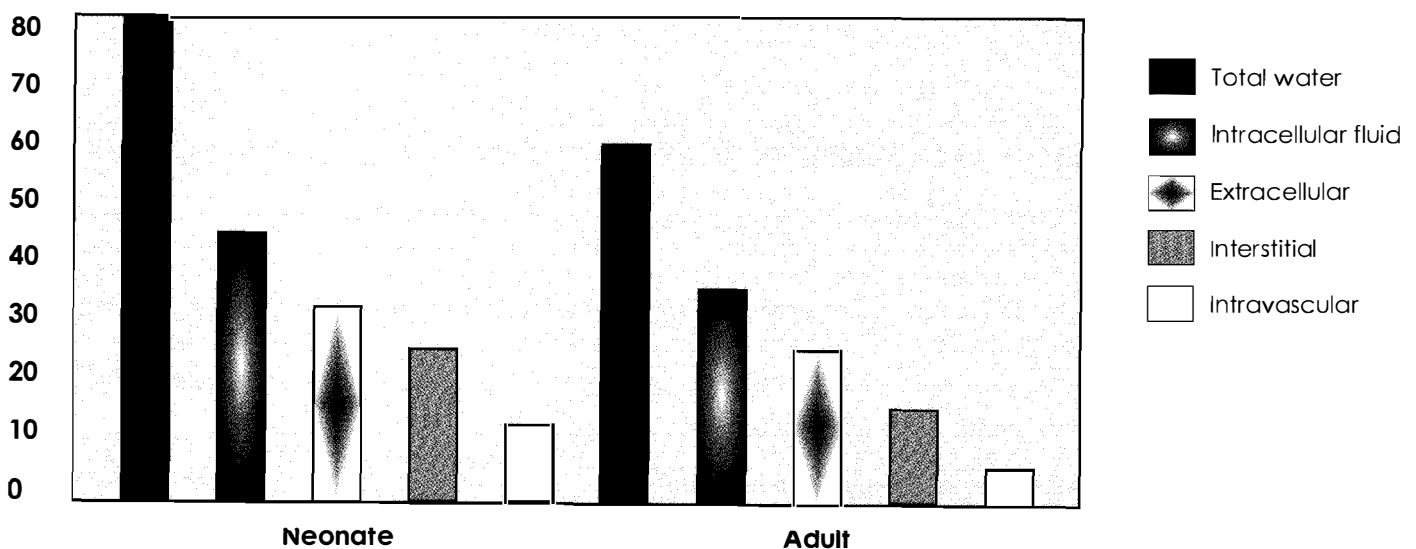
FIGURE 1. Distribution of body water as percentages of body weight.

TABLE 6. Ionic Composition of Body Water Compartments

Ion	Extracellular Fluid Intravascular (mmol/L)	Interstitial (mmol/L)	Intracellular Fluid (mmol/L)
Cations			
Na^+	142.0	45.1	12.0
K^+	4.3	4.4	150.0
Ca_2	2.5	2.4	4.0
Mg_2	1.1	1.1	34.0
TOTAL	149.9	153.0	200.0
Anions			
Cl^-	104.0	117.4	4.0
HCO_3^-	24.0	27.1	12.0
$HPO_4^{2-}, H_2PO_4^-$	2.0	2.3	40.0
Proteins	14.0	0.0	54.0
Other	5.9	6.2	90.0
TOTAL	149.9	153.0	200.0

Water output occurs with losses in the urine and stool, and evaporation from the skin and respiratory tract. Normal ongoing losses are divided into sensible losses, those that can be measured (urine output) and insensible losses which are difficult to quantitate (e.g., sweating, panting, normal feces). One-third of the daily maintenance fluid volume is required to replace insensible losses while two-thirds is required to replace the sensible losses. Water intake is derived primarily from three sources: ingested water, water contained in food and water produced from oxidation of carbohydrates, proteins and fats. AVERAGE daily maintenance fluid need (L/day) of hospitalized animals can be calculated using the standard resting energy expenditure (REE) equation ($70 \times BW^{0.75}$), times a factor of (we use 1.2 or 1.3) for ill animals, where BW is body weight in kg. Measured expenditure (and therefore, requirements) via indirect calorimetry approximates the equation $90.29 \times kg^{0.75}$ which approximates $1.3(70 \times BW^{0.75})$. It is the author's experience that the factor of 1.2 in cats, and 'moderately' ill or recovering dogs is a useful maintenance fluid volume to use. The factor of 1.3 is used where energy expenditure is higher, however, the overall fluid difference is 1 – 9 mL/h over the whole weight range. Additional fluids are factored in based on ongoing losses as described in the Rehydration Phase and Maintenance Phase of management. Where the power function is not at hand, this function ($BW^{0.75}$) can be performed by multiplying $BW \times BW \times BW = Z$ then $2\sqrt{Z}$. The linear equation ($30 \times kg\ BW$) + 70 may also be used, however, this results in a lower estimated volume of fluid.

PARENTERAL SOLUTIONS

Crystalloid Solutions

The commonly used isotonic-sodium based BES used for **resuscitation (replacement)** are Plasma-Lyte® A, Plasma-Lyte®148 (Baxter), Normasol®- R (Abbott), and lactated Ringer's (Hartman's solution). These solutions differ slightly in pH, osmolality, electrolyte composition and buffering capacity; they are alkalinizing solutions (Table 7). The electrolyte composition of these solutions is similar to that of plasma and are therefore considered replacement solutions. These solutions should be used to treat shock and dehydration due to water and solute loss (e.g.,vomiting, diarrhea). Normal saline (0.9% Sodium Chloride) solution is acidifying and not balanced. (Table 7). Replacement crystalloid solutions may also be used as 'maintenance' solutions delivered at maintenance, or higher rates. Dextrose containing solutions should *not* be used as a replacement solution unless the patient is hypoglycemic.

Alkalinizing solutions are selected for their buffering capacity and ability to raise plasma pH, and for specific electrolyte abnormalities (*see Acid-Base Assessment p. 406*). The buffer in lactated Ringer's is lactate and it is metabolized to bicarbonate in the liver. The buffers in Plasma-Lyte® 148, Plasma-Lyte® A, and Normasol® R, are acetate (metabolized in muscle) and gluconate (metabolized in most cells).

Acidifying solutions such as normal saline lower the plasma HCO_3^- by reversing volume contraction (diluting HCO_3^-), removing the stimulus to renal Na^+ retention thereby permitting $NaHCO_3^-$ excretion in the urine, and increasing distal Cl^- delivery which will promote HCO_3^- secretion in the cortical collecting tubule.

To select the best fluid for each individual, it is necessary to examine the patient's acid-base (*p. 406*) and electrolyte status.

1. **Maintenance solutions** are designed for patients who cannot supply their daily needs for water and electrolytes. These solutions are delivered gradually throughout the day and may be hyper, iso- or hypotonic. They usually contain low sodium and chloride, high potassium and may contain dextrose, when compared to replacement solutions. A 'maintenance' fluid is recommended for normovolemic hospitalized patients. The electrolyte composition is quite different from a 'resuscitative fluid (Table 7). As it is not economical for some practices to have commercial maintence fluids in the inventory, 'homemade' solutions can be compounded. Half-strength of the BES solution (1:1 sterile water:BES) as a substitute for Plasma-Lyte® M or Normosol® M (Table 7), or half-strength BES (1:1 5% dextrose in water:BES). Half-strength (0.45%) NaCl can be prepared in a similar manner with either sterile water or 5% dextrose in water. Half the contents of 1 L of 0.9% NaCl or BES is either administered to the patient or discarded. The 500 mL sterile water or 5% dextrose in water (this makes a 2.5% dextrose solution) is then added in a sterile manner to the remaining 500 mL. The fluids should be mixed in the bag and not run individually to avoid the potential problem of sterile water being administered alone in error. Potassium chloride 20 – 25 mEq/L is added unless contraindicated.

2. The clinical situation will determine the type of parenteral fluid to select and will be indicated throughout this manual. In addition to balanced electrolyte solutions mentioned above, various other types of fluids can be administered at a volume and rate tailored to the patient's needs. These consist of hypertonic saline, synthetic colloids, species specific blood products (*see Transfusion Therapy p. 667*), 25% human serum albumin and hemoglobin based oxygen carriers.

Hypertonic Saline (HS)

Hypertonic saline has been recommended for resuscitation in extreme shock states. The role of HS solutions in trauma resuscitation remains somewhat unclear. Although the majority of human prospective studies fail to demonstrate a clear survival benefit over isotonic crystalloid infusion; a potential advantage may be in head injured patients. Recommendations for safe dosing in animals should be adhered to: **maximum dose and rate** for 5% solution is 6 – 10 mL/kg at 1 mL/kg/min, for 7% solutions is 4 – 8 mL/kg at 1 mL/kg/min and 1 – 3% solution is 10 mL/kg at 2 mL/kg/min. The author has experienced respiratory arrest in a cat with rapid administration. Hypertonic saline causes a transient increase in blood pressure (~20 min) buying enough time for resuscitative fluids to be delivered. The potential beneficial effects of HS are many; it has been shown to enhance *in vitro* and *in vivo* cellular immune function potentially due to effects on monocyte/macrophage function and direct stimulation of T-cells. The reversal of hemorrhage-induced immuno-suppression with HS prevented sepsis in a hemorrhage rat model. There is a transient volume expansion following HS administration with selective arteriolar vasodilation and improved microcirculation with decreased leukocyte adhesion. Hypertonic saline has a direct inotropic effect on the heart. Mean arterial pressure, electrocardiogram and electrolytes should be monitored in patients receiving HS. Concerns for coagulopathies precipitated by HS administration have been raised.

Species specific blood products (*see Transfusion Therapy p. 667*) or 25% human serum albumin

These products are required to treat various anemic states, coagulopathies, blood loss, inflammatory, capillary leak, septic and refractory hypotensive and hypoalbuminemic states (*see Hypoalbuminemia p. 431*). **25% human serum albumin** (HSA) (Plasbumin®, Bayer) may be administered to hypoalbuminemic patients, where hypotension is refractory to other fluids and vasopressors. For refractory hypotension the author suggests **2 mL/kg slow push** while monitoring pressures. As pressure increases, the rate is slowed to **0.5 – 1 mL/kg/h as a CRI** for as long as you wish to administer it to maintain albumin levels to 15 – 18 g/L (1.5 – 1.8 g/dL), or assist with maintaining an adequate MAP where other products fail. 25% human serum albumin is also useful to manage edema in hypoalbuminemic patients. Our use for albumin is not as a volume replacement strategy, or to increase albumin levels to those suggested in veterinary patients, (>20 g/L [>2.0 g/dL]), but as an adjunct to current standard therapy where 25% HSA may improve a condition that exists in a critically ill patient (based on individual need), or where standard treatment has failed. Albumin's physiological role in homeostasis supports our reasons for use of albumin in the critically ill patient. A **test dose of** 0.25 mL/kg/h, with an administered volume over 15 minutes, is advised. Very rarely, facial swelling may occur, as with any other blood product. Discontinue and administer diphenhydramine. Repeat administration at a later date is not advised as there is potential for immune-mediated reactions.

Hemoglobin based oxygen carrying solutions (HBOCS)

These solutions pick up and release oxygen in a similar manner to red blood cells, however, the majority of oxygen content of the blood is shifted to the plasma. This fact, coupled with the low viscosity of the solution, facilitates enhanced perfusion of the tissues within a range of PaO_2 40 – 90 mmHg; oxygen uptake and off-loading occurs more readily by HBOC than RBCs. Several human studies indicate that HBOCs may be useful for effective resuscitation after major blood loss or anemia and in head injured patients. Bovine hemoglobin (Oxyglobin®, Biopure) is approved for use in dogs only in the USA. Administration to cats, dogs, ferrets, and some birds improves oxygen delivery compared with crystalloid infusion. This product is stroma-free, reducing the potential for renal injury, and also has minimal nitric oxide scavenging capability, thereby reducing the risks of hypertension. Oxyglobin® requires no cross-matching. It has immediate oxygen carrying capability as there is no requirement for 2 – 3DPG (bovine hemoglobin requires chloride ion to offload oxygen, not 2 – 3DPG). It also contributes to oncotic pressure offering a further advantage in these hypotensive patients. There is a shelf life of three years. **Dosing is 5 – 30 mL/kg, with titration at 5 mL/kg increments, no faster than 10 mL/kg/h,** is advised, depending on the situation at hand (i.e., significant blood loss, immune-mediated hemolytic anemia). **Very slow (≤4.0 mL/kg/h), low dose administration is advised in cats, ferrets and birds to a total dose of <14 mL/kg.** Cats may develop pulmonary edema with rapid administration or dosages of 14 mL/kg or higher; therefore dosages lower than this are advised. To assess adequacy of transfusion, the hemoglobin must be measured (normal range ~10 – 30 g/dL). The packed cell volume (PCV) is of no value as this will be diluted and 'cells' are not transfused. The product is available in 125 mL bags, which only has a 24-hour shelf life once invaded. At the time of writing, this product has limited availability.

Synthetic Colloids

Synthetic colloid solutions; dextran 70, pentastarch and hetastarch contain a wide range of particle sizes, the larger ones of which, do not readily leave the intact vascular space. These particles increase the colloid osmotic pressure in blood thereby expanding vascular volume. They also carry a negative charge which attracts sodium followed by water from the extravascular space increasing the intravascular volume further. Synthetic colloids may be delivered in 5 mL/kg (dogs), 2.5 mL/kg (cats) boluses to effect over a few minutes (shock), or hours (interstitial edema, third space losses, hypoproteinemia etc.) to a maximum of 10 – 20 mL/kg in a 24h period in cats and dogs respectively. Do not deliver maximum volume faster than over 15 minutes in cats as vomiting may occur. Colloids may be selected for volume resuscitation in sepsis, in patients with inflammatory diseases (SIRS), hypoalbuminemia, hypotension of many etiologies including; shock, trauma, and during anesthesia, and in animals with edema and ascites. Colloids can be administered as a slow push in emergent situations, as part of a resuscitative regimen, especially in patients that are hypoalbuminemic or non-responsive to crystalloid therapy. Patients with capillary leak syndrome **may** also benefit from colloid therapy. The larger molecular weight solutions (e.g., hetastartch or pentastarch) are recommended; however, the smaller molecules these products also contain, may leak into the pulmonary interstitium worsening pulmonary edema. Caution is required where pulmonary contusions exist and synthetic colloids should be avoided, or titrated very carefully if deemed necessary.

The crystalloid vs colloid controversy for resuscitation of patients has been a point of discussion in human medicine for many years. Some studies concluded colloids favoured decreased mortality while others favoured crystalloid therapy. Analysis of the available human prospective data indicates that colloid infusions decrease overall fluid requirements and resuscitation time but do not necessarily yield a survival benefit when compared to crystalloid solutions. However, as many of these trials include a variety of illnesses, which were all assessed together, it is difficult to make recommendations for specific causes of hypotension. The administration of crystalloids and colloids should be **individualized** to each patient's needs, based on pathophysiologic rationale, clinical experience and cost. Suggested recommendations in veterinary patients would be to start with crystalloid therapy, introduce colloid therapy when adequate resuscitation and normotension cannot be achieved or maintained, and follow with blood (or packed red cells) or plasma or albumin as the PCV or TS decreases to ≤25% and 45 g/L (dogs), ≤20% and 45 g/L (cats) respectively. Obviously, in the markedly hypotensive individual, crystalloids, colloids and potentially blood products, may have to be administered concurrently. Recommendations and volumes are given with individual problems throughout this manual.

Colloid Osmometry

Under normal conditions, blood volume and extracellular fluid volume are controlled in parallel to each other. However, there are situations in which the distribution of extracellular fluid between the interstitial space and blood can vary. The principal factors that can cause accumulation of fluid in the interstitial space include: 1) increased capillary hydrostatic pressure, 2) decreased plasma COP (colloid osmotic pressure = oncotic pressure), 3) increased permeability of the capillaries, and 4) obstruction of the lymphatic vessels. With the exception of lymphatic obstruction, these conditions frequently are pre-existent in critically ill small animal patients or may develop as a consequence of fluid administration. The endothelium represents a semipermeable membrane which normally prevents loss of proteins. The COP of whole blood obtained from normal dogs is 19.95 ± 2.1 (range, 15.3 – 26.3) mm Hg and for plasma is 17.5 ± 3.0 mm Hg. In whole blood obtained from normal cats COP is 24.7 ± 3.7 (range, 17.6 – 33.1) mm Hg and in plasma 19.8 ± 2.4 mmHg.

TABLE 7. Electrolyte Composition of Commonly used Intravenous Solutions

Solution	Electrolyte Concentration (mmol/L)					Buffer (mEq/L)	Cals/L	pH	mOsm/L
	Na$^+$	K$^+$	Ca$^+$	Cl	Mg$^+$				
Plasma-Lyte®148	140	5		98	1.5	27 acetate 23 gluconate		5.5	294
Plasma-Lyte®A	140	5		98	1.5	27 acetate 23 gluconate		7.4	294
Normasol®R	140	5		98	3.0	27 acetate 23 glutamate			
Lactated Ringer's	130	4	3	109		28 lactate		6.5	273
0.9% NaCl	154			154				5.0	308
Plasma-Lyte®56 (5% dextrose)	40	13		40	1.5	12 acetate 12 glutamate	170	5.5	362
5% dextrose							170	4.0	252
3.3% dextrose + 0.3% NaCl	51			51			113	4.5	269

SUGGESTED READING

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TABLE 8. Suggested Daily Water Requirements for Hospitalized Dogs and Cats $(1.2 \times BWKg^{0.75}) \times 70$

BW (kg)	Total Water (mL/day)	mL/kg/day	mL/h
1	84	84	4
2	141	72	6
3	191	64	8
4	236	59	10
5	281	56	12
6	322	54	13
7	361	52	15
8	400	50	17
9	436	48	18
10	472	47	20
11	507	46	21
12	542	45	23
13	575	44	24
14	608	43	25
15	640	43	27
16	672	42	28
17	703	41	29
18	734	41	31
19	764	40	32
20	794	40	33
25	939	38	39
30	1076	36	45
35	1208	35	50
40	1336	33	56
45	1459	32	61
50	1579	32	66
60	1810	30	75
70	2033	29	86
80	2247	28	94
90	2454	27	102

TABLE 9. Suggested Fluid Requirements for Puppies and Kittens

	Based on the equivalent Daily Caloric requirements for maintenance of average healthy growing puppies and kittens.			
	Weaning to 3 months Daily volume (mL) =		3 – 6 months Daily volume (mL) =	
Body weight (kg)	Daily kcals	mL/h	Daily kcals	mL/h
PUPPIES				
1	268	11	214	9
2	464	19	373	15
3	649	27	520	21
4	808	33	646	27
5	915	38	732	30
7	1167	48	934	40
9	1394	58	1115	46
11	1670	70	1336	55
13	1929	80	1543	64
15	2179	91	1743	72
17	2415	100	1932	80
19	2640	110	2112	88
21	2856	116	2285	95
23	3062	127	2450	100
25			2618	109
27			2785	116
29			2945	122
31			3104	129
33			3250	135
35			3422	142
37			3551	148
KITTENS				
0.5	125	5	65	3
0.75	188	8	98	4
1.0	250	10	130	5
1.5	375	15	195	8
2.0	500	21	260	11
3.0			390	16
4.0			520	21
5.0			650	27

Requirements vary with environmental conditions, activity and temperature. This table is a guide, the caloric intake and volume administered should be adjusted to maintain optimal weight, condition and hydration. One-half to three-quarters should be considered as maintenance for ill animals.

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TECHNIQUES

A LONG CATHETER PLACEMENT INTO A SAPHENOUS VEIN

Indications

1. Delivery of intravenous fluids/medications.
2. Frequent blood sampling.
3. Where jugular catheterization is not possible or should be avoided.
4. Central venous pressure measurements in cats and dogs <4 kg.

Materials

- The length of the catheter depends on the size of the patient. A 12" 19 gauge catheter through a 17 gauge needle is used most often (cats and dogs). The catheter is packaged and protected by a sterile plastic sheath.
- As the needle cannot be removed from the catheter following placement, a guard is provided to protect the needle. The guard hinge is loosened prior to catheterization.
- A luer-lock T-port adapter (T-port, Becton Dickinson, Sandy, Utah) is prefilled with heparinized saline (1 unit/mL).
- Sterile gauze.
- Sterile gloves (optional) — Necessary if catheter not protected.
- Krazy glue, tissue glue, or suture material.
- Tape and bandage.

Technique

- A wide area is clipped (medial saphenous in cats, medial or lateral saphenous in dogs) and prepped as for surgery.
- A through-the-needle catheter is used.
- Hands **must** be washed prior to catheterization. A chlorhexidine soaked gauze square is placed under the needle during placement. The saphenous vein is elevated by compression in the inguinal region for medial saphenous venipuncture, and just below the stifle when the lateral saphenous vein us used.
- If the vein cannot be visualized, it can frequently be palpaged. Pass the needle through the skin, tunnel slightly and then enter the vessel. Do not touch the needle. The catheter should be observed whilst venipuncture is being performed. A flash of blood in the catheter indicates placement of the needle into the vessel lumen. The needle should be stabilized and the catheter fed immediately into the vein. The hub of the catheter is securely placed into the hub of the needle. The sheath and stylet are removed and the T-port attached. The catheter is flushed and the needle guard placed. Blood is withdrawn and the catheter is again flushed to verify catheter placement in the vein prior to fixation. The guard can be sutured to the skin or attached with a small bleb of Krazy glue placed at the guard/catheter insertion site. Sterile ointment and gauze should cover the insertion site. The catheter is taped and bandaged as for jugular catheter placement and bandaged as for cut down onto a peripheral vein.

Maintenance

A new bottle of sterile heparinized saline should be used for flushing. The catheter is in direct communication with the vena cava and sterile materials are necessary to avoid infection. A fluid administration set is attached to the T-port or an adaptor is attached if the catheter is only required for blood sampling.

PERCUTANEOUS PLACEMENT OF A CATHETER INTO A JUGULAR VEIN

Indications
1. Delivery of intravenous fluids/medications.
2. Frequent blood sampling.
3. Measure central venous pressure.

Materials
- The length of the catheter depends on the size of the patient. An 8" 19 gauge catheter through a 17 gauge needle (Intracath, Becton Dickinson, Sandy, Utah) is used for cats and dogs < 10 kg and a 19" catheter for dogs >10 kg. As the needle cannot be removed from the catheter following placement, a guard is provided to protect the needle. The guard hinge is loosened prior to catheterization.
- A luer-lock T-port adapter (T-port, Becton Dickinson, Sandy, Utah) prefilled with heparinized saline (1 unit/mL).
- Sterile gauze.
- Krazy glue or tissue glue, or suture material.
- Sterile gloves (optional) – necessary if catheter not protected.
- Tape and bandage.

Technique
- A wide clip. Shorten the hair in longhaired dogs under the mandible and opposite side of the neck to avoid contact with the venipuncture site during taping. The skin should be prepped as for surgery. Wash hands.
- The vein is elevated by applying digital pressure at the thoracic inlet. If the vein cannot be visualized, it can frequently be palpated.
- A chlorhexidine soaked gauze square placed under the needle protects the needle from contamination. Pass the needle through the skin, tunnel slightly and then enter the vessel. Do not touch the needle. The catheter is protected by a sterile plastic sheath. The catheter should be observed whilst venipuncture is being performed. A flash of blood in the catheter indicates placement of the needle into the vessel lumen. The needle should be stabilized and the catheter fed immediately into the vein. The front legs are pulled caudally during passage to ensure that the catheter passes into the anterior vena cava. The hub of the catheter is securely placed into the hub of the needle. The sheath and stylet are removed and the T-port attached. The catheter is flushed and the needle guard placed. Blood is withdrawn and the catheter is again flushed to verify catheter placement in the vein prior to fixation. The guard can be sutured to the skin or attached with a **small** bleb of krazy glue, or tissue glue placed at the guard/catheter insertion site.
- Sterile gauze should cover the insertion site. The hub of the catheter is taped securely to the hub of the needle within the guard. Tape should also pass over the guard and around the catheter hub. Failure to do this will result in the catheter being pulled out. The catheter is taped to the neck of the patient by passing tape around the neck, over the catheter insertion site and over the guard as well as under the catheter more proximally. Don't tape too tight, if the patient is dehydrated, facial swelling may occur as rehydration takes place.

Maintenance

A new bottle of sterile heparinized saline should be used for flushing. The catheter is in direct communication with the heart (i.e. in the anterior vena cava) or in the right atrium. Sterile materials are necessary to avoid infection.

A fluid administration set is attached to the T-port. A loop is made in the fluid line and taped to the bandage around the neck. An adapter is attached to the T-port if the catheter is only required for blood sampling.

CENTRAL VENOUS CATHETER PLACEMENT USING THE SELDINGER TECHNIQUE (J. Ball RVT)

Indications

1. Delivery of intravenous fluids/medications.
2. Frequent blood sampling.
3. Measurement of Central Venous Pressure.

Materials

- The length of the catheter depends on the size of the patient. A 4 Fr. x 13 cm pediatric catheter is used for cats and small dogs (Arrow Pediatric single, double and triple lumen catheters are available). A 7 Fr. x 20 cm or 30 cm adult catheter is used for medium to large size dogs (Mila International Inc. Single, double and triple lumen catheters are available). Some of the supplies noted are included in the pediatric double lumen catheter kit.
- A 22 gauge x 1inch catheter is required for placement of a pediatric catheter, and a 20 gauge x 1-inch catheter is required for placement of the adult catheter. These catheters are "through the needle" catheters.
- Suture material
- Sterile gauze
- opSite – transparent adhesive film (Smith and Nephew)
- Sterile gloves
- Sterile eye drape
- Bandage material
- A bottle of sterile heparinized saline (dedicated to this patient only)

Technique

- Clip a wide area followed with a surgical prep.
- Open the catheter kit carefully and use the inside of the protective wrap as a sterile field.
- Wash hands thoroughly and put on sterile gloves.
- Flush both ports of the jugular catheter with sterile heparinized saline to remove air.
- Place the eye drape over the prepped area. Elevate the vein using digital pressure at the thoracic inlet. If the vein cannot be visualized, it is usually palpable; apply pressure to both veins.
- Place the "through the needle" catheter into the jugular vein. A flash of blood in the catheter indicates placement into the vein. Feed the catheter into the vein. Do not remove the stylet until you are prepared to introduce the guide wire.
- Remove the stylet and insert the guide wire quickly into the catheter. Take care not to insert the guide wire any further than the thoracic inlet (eyeball/guestimate). Remove the catheter with the guide wire still in place. The sterile gauze can now be used to stop any bleeding at the insertion site.
- Feed the dilator over the guide wire. It is important that the dilator is inserted all the way to ensure the jugular catheter inserts smoothly. Make a small scalpel cut in the skin to facilitate insertion of the entire dilator. Remove the dilator and insert the jugular catheter over the guide wire. The guide wire may need to be backed out slightly while the catheter is inserted. Remove one of the adaptors on the end of the pediatric catheter to enable the wire to go through the port. Once the catheter is in place the entire guide wire can be removed.
- Place an injection adaptor on each port. Pull back on your syringe to remove air from within the catheter and to make sure that you have a flash of blood indicating that the catheter is inserted properly in the vein. Flush both ports of the catheter with heparinzed saline. Suture the catheter to the skin.
- Cut a piece of sterile OpSite™ transparent adhesive dressing to size and place over the insertion site and the immediate surrounding area, incorporating the catheter.
- Bandage the patient's neck. It is recommended that a light colour bandage material is used so hemorrhage from the catheter site is readily visible.

Maintenance

A new dedicated bottle of sterile heparinized saline (1U/mL) should be assigned to each patient for flushing the catheter. The injection port of the bottle is swabbed with alcohol prior to each insertion of the needle. The catheter is in direct communication with the heart (i.e., in the anterior vena cava or in the right atrium). Sterile materials are absolutely essential to avoid infection. The site ventral to the bandage should be checked q8h. The bandage should be changed every 3 days or sooner, if a problem is suspected.

ADDITIONAL INDICATIONS FOR JUGULAR CATHETER PLACEMENT

A.   BLOOD COLLECTION

Indications

A catheter can be placed specifically for blood collection i.e., establishing glucose or insulin curves, frequent electrolyte monitoring. Or, blood samples can be collected any time during intravenous fluid infusion.

Technique

- Strict sterile technique should be adhered to. Always wipe the injection port with alcohol prior to sampling. Flush 2 or 3 mL heparinized saline into catheter and pull back 4 mL of blood. Cap needle and put aside; keep sterile.
- Remove desired volume of blood for tests.
- Replace blood and saline from above.
- Flush with 3 or 5 mL of heparinized saline.

B.   MEASUREMENT OF CENTRAL VENOUS PRESSURE

Indications

Monitoring CVP during fluid administration in patients with:

1. Oliguric/anuric renal failure
2. Heart failure
3. Pulmonary edema
4. Pulmonary thromboemboli

Materials

- The length of the catheter depends on the size of the patient. An 8", 19 gauge catheter through a 17 gauge needle is used for cats and dogs <10 kg and a 12" catheter for dogs > 10 kg (a longer catheter may be required for large to giant breed dogs). As the needle cannot be removed from the catheter following placement, a guard is provided to protect the needle. The guard hinge is loosened prior to catheterization.
- Catheter and supplies as for those mentioned for Jugular Catheter Placement above.
- Water manometer intravenous fluids and delivery set.

Technique

- The catheter is positioned via the external jugular vein into the anterior vena cava. Verification of a well-placed, unobstructed catheter can be ascertained by small fluctuations of the fluid meniscus, within the manometer, synchronous with the heart beat and larger excursions with ventilation. Also radiographic confirmation.
- The zero reference point on the manometer is at the level of the right atrium. The difference between the "zero" level and the equilibrated fluid level in the manometer is considered to be the central venous pressure. This is the luminal pressure of the anterior vena cava and is a measure of the relative ability of the right side of the heart to pump the quantity of fluids being returned to it.
- Factors that influence CVP include circulating blood volume, venous tone, distensibility and contractility of the chambers of the heart and intrathoracic pressure (pneumothorax, pleural effusion, pericardial effusion).
- Normal CVP is 0 – 5 cm H_2O. Low values suggest hypovolemia/hypotension. Values up to 10 cm H_2O can be tolerated, however pressures higher than this should be avoided.

CUT DOWN ONTO A PERIPHERAL VEIN

Indications

Where percutaneous placement of an intravenous catheter is not possible:

1. Hypovolemia/Hypotension
2. Edematous State
3. Obesity
4. Unable to visualize vessel

Materials

- Over-the-needle catheter
- PRN (injection) adaptor
- Tape
- Sterile gauze
- Bandage material

Technique

See Vascular Access Techniques for diagram p. 610.

- Perform as a sterile procedure. A wide area should be clipped and prepped as for surgery. The foot should be wrapped in a sterile drape. Sterile gloves should be worn and sterile instruments used.
- The skin should be mobilized medial or lateral to the vein and the skin incision made parallel and adjacent to the vein on the lateral or medial side with the direction of skin mobilization (Fig. 1). This avoids incising directly onto the vein. The skin is released and the incision should lie directly over the vessel. Subcutaneous tissue and adventitia are dissected off the vein in edematous patients to directly visualize the vessel. If this step is not performed, the catheter may be inadvertently placed between the adventitia and the vessel wall. The vessel is isolated and the catheter fed into the vein. The catheter is secured and the skin incision closed with simple interrupted sutures.
- Following catheter placement, the catheter should be flushed with sterile heparinized saline (1 unit/mL). The limb should be bandaged from the toe to proximally beyond the venipuncture site to avoid swelling of the distal limb. Bandaging also protects the catheter insertion site from contamination and infection. If not soiled, and no heat or swelling is noted in the limb under the proximal or distal ends of the bandage and no pain is elicited on palpation over the veni-puncture site, the bandage need not be changed for 72 hours.
- IN AN EMERGENCY, the sterile draping may be eliminated. If there is any contamination during this procedure, another catheter should be placed in another area, once the animal is stabilized, and the emergency catheter removed. This will avoid infection.

INTRODUCTION

Hypercalcemia has many etiologies and is more common in dogs than cats. The most common cause of hypercalcemia in both dogs and cats is secondary to neoplasia. Hypercalcemia is the most common metabolic emergency seen in veterinary patients with cancer and has been associated with lymphoma, anal sac apocrine gland adenocarcinoma, mammary gland and prostatic adenocarcinoma, multiple myeloma and other malignancies. Acute renal failure caused by grape/raisin ingestion in the dog can also cause hypercalcemia. Hypervitaminosis D is caused by the ingestion of cholecalciferol-containing rodenticides, calcipotriene/calcipotriol (human medication for treatment of plaque psoriasis), toxic plants containing glycosides of calcitriol, and may also be iatrogenic due to over-supplementation. Primary hyperparathyroidism is an uncommon cause of hypercalcemia and may be secondary to an adenoma, adenocarcinoma or hyperplasia of the parathyroid gland(s). Non-malignant skeletal lesions causing hypercalcemia (osteomyelitis [bacterial or fungal], hypertrophic osteodystrophy) are usually not of clinical significance. Although hypoadrenocorticism and chronic renal failure are also common causes of elevated serum calcium, they are rarely associated with clinical signs. Nutritional secondary hyperparathyroidism can cause hypercalcemia or hypocalcemia.

The severity of the clinical signs associated with hypercalcemia is related to the magnitude, duration and the rate of onset of hypercalcemia. Acid-base and electrolyte imbalances, as well as renal dysfunction, may contribute to the severity of the clinical signs. Because hypercalcemia is often secondary, the finding of this abnormality is an indication to pursue a wide variety of etiologies. This protocol is designed for the patient that has clinical manifestations of hypercalcemia.

DIAGNOSIS

History

- An underlying cause of hypercalcemia should be thoroughly investigated through history and physical examination.
- Hypercalcemia caused by ingestion of toxins, diet-related or iatrogenic causes can be ruled out with historical information.
- A breed predisposition for primary hyperparathyroidism is suspected in the Keeshond.
- The history of a hypercalcemic pet is not specific and may include changes such as lethargy, decreased appetite, vomiting, constipation, weakness or polyuria/polydipsia (PU/PD).
- In hypercalcemic cats PU/PD and constipation are infrequently reported by owners.
- The duration of PU/PD may assist the clinician in determining the duration of hypercalcemia.
- Anorexia and vomiting are due to decreased gastrointestinal motility (also constipation) and increased gastric acid secretion.

Clinical Signs/Physical Examination

- Many patients with hypercalcemia are asymptomatic. The physical examination, in cases of primary hyperparathyroidism, is usually normal in dogs.
- Most dogs with neoplasia tend to be older at presentation. In a young hypercalcemic dog, differentials include lymphoma, hypoadrenocorticism, renal failure or hypervitaminosis D.
- A nodule may be palpated in the area of the thyroid gland in some cats with hyperparathyroidism.
- Lymph nodes should be palpated to assess size, and a thorough rectal examination should be performed to evaluate the size and symmetry of the prostate and rule out a perianal mass.
- Muffled heart or lung sounds may be indicative of a cranial mediastinal mass.
- Bone pain may be present in cases of multiple myeloma, acute lymphocytic leukemia or skeletal metastasis.
- Mammary gland chains should be carefully palpated for masses.
- Neuromuscular abnormalities include lethargy, depression, muscle weakness and twitching, depressed deep tendon reflexes, seizures and coma.
- PU/PD may result in mild to severe dehydration. Hypercalcemia and dehydration can lead to decreased GFR, decreased renal blood flow, nephrocalcinosis and interstitial nephritis.
- Cardiac arrhythmias and hypertension may be detected (rare).
- Abdominal pain may be present and can be secondary to pancreatitis or gastric or duodenal ulceration.
- Renal failure frequently occurs with vitamin D toxicity; therefore the presenting signs will most likely be consistent with acute renal failure (*see Renal Failure p. 709*).

Laboratory Evaluation/Diagnostic Imaging

Stat

The diagnosis of hypercalcemia is defined as a fasting serum calcium greater than 3.0 mmol/L (12 mg/dl) for dogs and cats. This should be a repeatable finding in a non-lipemic, non-hemolyzed blood sample. The work-up for hypercalcemia should rule-out neoplasia first. If a neoplastic lesion is not identified, and there is no history of toxin ingestion (rat poison or cholecalciferol), a diagnosis of hyperparathyroidism should be sought.

- **PCV, TS** to obtain a baseline, rule out abnormalities and to assess hydration status.
- **Stick BUN** to assess renal dysfunction (cholecalciferol toxicity) or dehydration (pre-renal).
- **Urine specific gravity** tends to be low with hypercalcemia due to calciuresis or primary renal injury secondary to nephrocalcinosis.
- **Glucose** to document abnormalities.
- **Body weight** to assess hydration and renal concentrating ability and as a baseline prior to fluid therapy.
- **Electrolytes** including calcium and phosphorous. Phosphorus may be normal or decreased with primary hyperparathyroidism or hypercalcemia of malignancy. In contrast, phosphorus is likely to be increased in cases of acute or chronic renal failure, vitamin D toxicity (due to renal failure), hypoadrenocorticism and nutritional secondary hyperparathyroidism. If calcium is increased, it is suggested that this be repeated on a different blood sample for confirmation. If hypoadrenocorticism is present, the patient may be hyponatremic and hyperkalemic (*see Hypoadrenocorticism p. 274*).
- **Urea, creatinine** to assess renal status or dehydration. Azotemia is a common laboratory finding and may be either pre-renal or renal in origin.
- **Amylase and lipase** to assess for pancreatitis.
- **Venous blood gases** or serum total CO_2. Metabolic acidosis may be secondary to hypovolemia or renal failure and worsens the signs of hypercalcemia by increasing the ionized fraction of calcium.
- **ECG.** Monitor for a prolonged PR interval, shortened QT interval or ventricular fibrillation.
- **Blood pressure.** Hypertension may rarely occur with hypercalcemia.
- **Abdominal and thoracic radiographs** if there is no history of toxin ingestion and abdominal ultrasound. Radiographs/ultrasound may identify neoplasia in the chest, abdomen or skeletal system. Abnormal renal structure may be cause, or result, of renal failure. Hypercalcemia and hypercalciuria may result in calcium oxalate urolithiasis.
- **Ultrasound** of the parathyroid glands has been reported to be useful in identifying a mass or hyperplasia of the gland(s).

Laboratory Evaluation/Diagnostic Imaging

- If all causes of hypercalcemia have been ruled out, serum for ionized calcium, PTH and PTH-rp levels should be submitted to a diagnostic laboratory. The presence of a normal to increased serum PTH, and increased ionized calcium with normal renal function is diagnostic for primary hyperparathyroidism. PTH-rp is a peptide that is produced by some neoplastic cells and will be elevated if hypercalcemia of malignancy is present.
- **Blood** collected for ionized calcium must be kept in an anaerobic environment for accurate results. Recommendations are to collect blood using a vacutainer and red top tube. Heparinized tubes and tubes with silicone gel are not recommended. After the blood clots, the serum should be collected through the top (do not open the tube) and placed directly into a second sealed tube (through the top). The anaerobically collected serum is stable for 72 hours at 23°C or 7 days at 4°C. Serum for PTH is not stable and should be shipped frozen overnight.
- **CBC** may be normal; abnormalities will depend on the underlying disease.
- **Serum biochemistry profile.** Changes depend on the underlying disease (i.e., acute/chronic renal failure, hypoadrenocorticism). Calcium levels will be increased.
- **Urinalysis with culture** (obtained by cystocentesis). Infection is frequently associated with dilute urine.
- **ACTH** stimulation test if hypoadrenocorticism is suspected (*see p. 274*).

MANAGEMENT

Specific treatment for laboratory identified hypercalcemia without clinical manifestations is not necessary. If clinical manifestations of hypercalcemia are severe, regardless of etiology, treat immediately (*see A & B below*). Definitive treatment of hypercalcemia is dependent upon treatment of the underlying cause (i.e., neoplasia). Definitive therapy of primary hyperparathyroidism typically involves surgical removal of the gland(s). If a toxin has been ingested (*see p. 630*). If lymphoma is suspected, a sample must be obtained for histopathology prior to initiating therapy (if glucocorticoids are to be used).

A. If the patient is seizuring, give diazepam IV, or rectally: < 10 kg 1 – 10 mg; 11 – 25 kg 5 – 15 mg; >25 kg 15 – 25 mg. (*see Seizures Dogs p. 460, Seizures Cats p. 456*).

B. Place a large bore intravenous catheter. If the patient has underlying cardiac disease and/or is severely azotemic a jugular catheter may be warranted to monitor CVP during rehydration.

C. Fluid therapy of choice is isotonic saline, as most patients are hypovolemic and hyponatremic and saline enhances calciuresis. Calculate fluid volume replacement (*see p. 351*) and administer over 1 – 24 hours, depending on the severity of the signs and the patients' clinical condition. Once replacement fluids are administered, continue at 2 – 3 times maintenance. Fluid therapy alone may be sufficient to reduce calcium levels. It is advised that the high maintenance rate only be established in animals with clinical signs of hypercalcemia. Otherwise, only administer to maintain hydration and, note inconsistency: '1 – 24 hours' above 4 and '4 – 6 hours' below normal urine production. Medullary washout will occur and polyuria may be difficult to manage.

D. Electrolytes should be monitored as potassium supplementation will be necessary in most cases. Calculation of administered potassium is mandatory (*see Hypokalemia p. 394*). Potassium levels will change quickly as metabolic acidosis and hypovolemia are corrected, so monitor every **4 – 6 hours.** Sodium will be decreased in most cases and should be closely monitored (*see Hyponatremia p. 386*).

E. **Phosphorus binding agent** aluminum hydroxide 30 – 90 mg/kg/day or sucralfate 1 g/30 kg with meals (reduced protein diet if in renal failure) should be administered in conjunction with fluid therapy due to the possibility of soft tissue mineralization (if Ca (mg/dL) x Phos (mg/dL) > 60) [S.I. Units: Ca $\underline{(mmol/L)}$ x Phos $\underline{(mmol/L)}$ > 60].

$$\frac{}{0.2495} \qquad \frac{}{0.3229}$$

Serum calcium should be reassessed every 8 to 12 hours.

F. **Furosemide 2 – 4 mg/kg PO, SC, IM, IV q8–12h** after the patient has been volume expanded and calcium reduction is still necessary (clinical manifestation of hypercalcemia). Do not treat with furosemide if clinical signs are not present because medullary washout may occur. Furosemide therapy should be continued until the serum calcium is within normal limits. Thiazide diuretics are contraindicated.

G. **Monitor urine output** (an indwelling catheter may be necessary) and body weight during rehydration and diuretic therapy. It is important to match the parenteral fluid intake with the urine output to prevent dehydration and to maintain calciuresis.

H. **Prednisone 1 – 2 mg/kg PO, IV q12h or dexamethasone 0.1 – 2 mg/kg SC, IV q12h.** Glucocortcoids will decrease hypercalcemia in cases of malignancy, hypervitaminosis D or hypoadrenocorticism only, but should not be administered when a diagnosis has not been made.

I. **Salmon calcitonin 4 U/kg IV initially, followed by 4 – 8 U/kg SC once to twice daily** may be used to maintain normocalcemia if hypercalcemia is due to cholecalciferol-containing rodenticide intoxication.

J. Cardiac arrhythmias (*see specific chapter p. 164–179*) or hypertension (*see Hypertension p. 205*).

K. **Sodium bicarbonate** can be used to lower ionized calcium levels, and is useful if the patient has a persistent metabolic acidosis after rehydration (*see Acid-Base abnormalities p. 406*).

Bisphosphonates (Etidronate and others) have not been well investigated in veterinary patients and have a slow onset of action. They are therefore are not recommended in an emergency situation.

Plicamycin (Mithramycin) lowers serum calcium in 24 – 48 hours. It is, however, associated with multiple side effects and is also not recommended.

PHARMACOLOGY

1) **Furosemide** is a loop diuretic which will block calcium reabsorption in the thick ascending limb of the loop of Henle. This action is dependent upon an abundance of sodium ions, therefore, volume expansion with normal saline is essential.

2) **Glucocorticoids** decrease calcium by inhibiting osteoclastic bone reabsorption and vitamin D-mediated gastrointestinal calcium uptake and by increasing urinary calcium excretion.

3) **Salmon calcitonin** is a natural peptide hormone that is used as an antidote for cholecalciferol rat poison. It inhibits bone resorption of calcium and also increases urinary calcium excretion. The drug is expensive, can cause vomiting and has short-lived and unpredictable effects. Resistance can develop and may be delayed by the co-administration of glucocorticoids.

4) **Sodium bicarbonate** can be used to treat severe signs of hypercalcemia if the patient has a metabolic acidosis. As the acidosis is corrected, calcium becomes protein bound and less is ionized (ionized calcium is responsible for the toxic effects).

5) **Plicamycin (Mithramycin)** is a cytotoxic antibiotic that decreases calcium by inhibiting bone resorption and decreasing bone turnover. Significant toxicity has been associated with the use of this drug.

6) **Bisphosphonates** are synthetic metal-complexing compounds that inhibit osteoclastic bone resorption and have other effects on bone remodeling. In addition, they decrease the activity of renal 1-alpha-hydoxylase and therefore reduce calcitriol synthesis. Clinical reports involving veterinary patients are sparse; the drugs are not widely available and are expensive.

SUGGESTED READING

1. Canine and Feline Endocrinology and Reproduction 3rd edition, Feldman and Nelson (eds). Saunders, St. Louis, MO. 2003:661-715.
2. Kirk's Current Veterinary Therapy XIII, Bonagura (ed). W B Saunders, Philadelphia, PA. 2000:345-347.
3. Small Animal Internal Medicine, 3rd edition, Nelson and Couto (eds). Mosby, St. Louis, MO. 2003:836-839, 681-686

NOTES

INTRODUCTION

Hypocalcemia is a relatively common laboratory abnormality in both dogs and cats and may be caused by parathyroid disorders, redistribution or vitamin D disorders, or may be associated with a low serum albumin. Primary parathyroid disorders include hypoparathyroidism caused by atrophy or lymphocytic inflitrate of the gland, or infarction of an adenoma. Secondary hypoparathyroidism is most often due to thyroidectomy, but may also be caused by parathyroidectomy (for treatment of hyperparathyroidism) and cervical trauma. Disorders of redistribution are numerous and include puerperal tetany (eclamspia), feline urinary tract obstruction, sodium phosphate (Fleet) enemas used in small dogs or cats, alkalinizing therapy, massive blood transfusion (using citrated products), furosemide administration, ethylene glycol intoxication or pancreatitis (causing saponification of peripancreatic fat). Vitamin D disorders that cause hypocalcemia include acute and chronic renal failure and nutritional secondary hyperparathyroidism, seen in young animals fed diets with an inappropriate calcium to phosphorous ratio (including all meat and raw meat-type diets). Hypocalcemia associated with renal failure, urethral obstruction and pancreatitis is rarely of clinical significance. The severity of clinical signs associated with hypocalcemia are related to the magnitude and duration of onset and may be intermittent or absent. Calcium and magnesium can be concurrently decreased in critically ill patients. This protocol is designed for the hypocalcemic patient with signs of disease and will most often include cases of eclampsia and primary and secondary hypoparathyroidism, and rarely, massive infusion of blood products. While typical signs of hypocalcemia may not be present after greater than 40 mL/kg of blood products have been administered, evidence of coagulopathy may manifest.

DIAGNOSIS

History

- A thorough history will identify cases of eclampsia, commonly seen in small breed dogs (rarely cats) often within 21 days of whelping (range 1 week pre-partum to 45 days postpartum). Post-surgical hypocalcemia often occurs within 1 – 5 days after thyroidectomy or parathyroidectomy. Blood product transfusion results in immediate clinical signs, as does phosphate-enema toxicity. Diet-induced hypocalcemia will have a slower onset of signs.
- Drug administration such as furosemide or sodium bicarbonate infusion may precipitate hypocalcemia and the time of onset is dependent on dose and associated protein and metabolic abnormalities.
- A diagnosis of acute (*see Acute Renal Failure p. 709*) or chronic renal failure, urethral obstruction (*see Urethral Obstruction p. 745*) or ethylene glycol toxicity (*see Ethylene Glycol Toxicity p. 655*) can be ruled in or out using historical, physical and laboratory findings.
- Primary hypoparathyroidism should be considered when history and physical exam rule out all other causes, and renal function is assessed as normal.

Clinical Signs/Physical Examination

- Any patient that presents for an acute onset of tetany, or seizures, should be evaluated for hypocalcemia. Clinical signs of hypocalcemia are mostly related to its effects on neuromuscular excitability.
- Hyperthermia is common due to increased muscle activity.
- Increased muscle activity can cause muscle fasiculations/tremors, facial rubbing, ear twitching, stiffened gait, rear leg muscle cramping/pain and/or seizures. These changes may worsen with excitement.
- Signs of hypocalcemia may be <u>intermittent</u> or <u>absent</u>.
- Nonspecific signs including lethargy, inappetance, vomiting and diarrhea (rare) may be present.
- Behavioral changes such as restlessness, hyperexciteability, aggression, disorientation or increased sensitivity to external stimuli may also be seen.
- Panting may be seen in dogs, and prolapse of the third eyelid or salivation in cats.
- Cardiovascular manifestations of hypocalcemia include tachycardia or other arrhythmias.
- Chronic findings may include polyuria/polydipsia and posterior lenticular cataracts (with primary hypoparathyroidism).

Laboratory Evaluation/Diagnostic Imaging

Stat

- **Serum calcium.** The diagnosis of hypocalcemia is defined as a serum calcium less than 2.0 mmol/L (8 mg/dL) in dogs and cats. This should be a repeatable finding. Normal ionized calcium value is generally 50% of normal total serum calcium
- **Total Protein or Albumin.** Hypoalbuminemia, although commonly associated with low calcium, does not cause clinical signs of hypocalcemia as the ionized fraction of calcium is usually normal. Where ionized calcium cannot be measured, the formulas below adjust calcium levels with decreased total protein or albumin, but are not very accurate, and abnormalities should be confirmed using ionized calcium. These formulas should not be used in the cat. **Adjusted Ca:**

    1. (mg/dL) = measured Ca (mg/dL) – albumin (g/dL) + 3.5 **OR**
    2. (mg/dL) = measured Ca (mg/dL) – [0.4*total protein (g/dL)] + 3.5 **OR**
    3. Where calcium is in mmol/L and total protein (TP) in g/L, the following equation should be used

    $$[24 * Ca - (TP/30)] / [(TP/10) + 6] / 4 = mmol/L$$

- **PCV** as an estimate of hydration status or further requirement for blood transfusion.
- **TS** as an estimate of hydration status if high or as a potential reflection of hypoalbuminemia.
- **ACT** to assess coagulation if large volume blood products have been administered.
- **BUN** as an increase may indicate pre-renal azotemia or primary renal disease.
- **Glucose** as part of a systemic assessment overall.
- **Urine specific gravity** as part of renal assessment and concentrating ability.
- **Electrolytes, (Na^+, K^+, Cl)** including calcium, phosphorous and magnesium (if available). Hypernatremia and hyperphosphatemia can be seen in cases of sodium phosphate enema toxicity. Hyperphosphatemia may be seen in cases of primary hypoparathyroidism, renal failure and urethral obstruction. Hypochloremia and hypokalemia may be associated with furosemide overdose.
- **Venous blood gases** to assess acid-base and perfusion status.
- **Urea, creatinine** is increased in pre-renal, primary renal and post-renal abnormalities. (*see Acute Renal Failure p. 709*).
- **Lipase, amylase** may both be increased in pancreatitis and up to twice normal values in renal insufficiency/failure.
- **ECG** typically reveals a tachycardia and a prolonged QT interval with severe hypocalcemia.

Extended Laboratory Data Base

- **CBC** may be normal or reflect other aspects of patient's condition.
- **Serum biochemical profile** to document hypoalbuminemia, renal and liver disease, electrolyte abnormalities or an etiology for potential metabolic disturbances.
- **Urinalysis** to establish specific gravity, concentrating ability and existence of inflammation.
- **Abdominal radiographs/ultrasonographic** evaluation to assess size and structure of kidneys and pancreas.
- **Skeletal radiographic** assessment may identify orthopedic abnormalities if nutritional secondary hyperparathyroidism is suspected.
- **Ophthalmological examination** may identify posterior lenticular opacities, if primary hypoparathyroidism is suspected.
- **Serum ionized calcium and PTH levels** should be measured if hyper-or hypoparathyroidism is suspected and if no underlying cause of hypocalcemia is identified and renal function is normal. Blood collected for ionized calcium must be kept in an anaerobic environment for accurate results. Recommendations are to collect blood using a vacutainer and red top tube. Heparinized tubes and tubes with silicone gel are not recommended. After the blood clots, the serum should be collected through the top (do not open the tube) and placed directly into a second sealed tube (through the top). The anaerobically collected serum is stable for 72 hours at 23°C or 7 days at 4°C. Serum for PTH is not stable and should be shipped frozen overnight.

MANAGEMENT

Therapeutic intervention is only recommended if clinical signs of hypocalcemia are present. Therapy is not recommended in cases where the ionized fraction of calcium is likely to be normal (hypoalbuminemia, hypoproteinemia or renal failure). However, where hypocalcemia exists, clinical signs of hypocalcemia may develop if an existing metabolic acidosis is corrected as the ionized fraction decreases.

A. **IV peripheral** catheter must be placed in emergent situations.

B. **Body temperature > 41°C** (muscle fasciculations/seizures) requires immediate cooling with cold wet towels, fan and cool fluids, simultaneously with **A and C.** Hyperthermia should resolve as the muscle fasiculations cease.

C. **Calcium supplementation.** Note: Calcium gluconate is available in two forms, 10 mL ampule 10% solution = 9.3 mg elemental calcium/mL and a vial with concentration of 94 mg elemental calcium/mL.

  1. **Calcium gluconate** should be administered IV **immediately** to patients exhibiting tetany, severe muscle fasiculations or seizures, or clinical coagulopathy after massive transfusions. Calcium gluconate 10% delivers 5 – 15 mg/kg elemental calcium at a dose of 0.5 – 1.5 mL/kg IV is the preferred supplementation (less caustic); however, other solutions can be used (calcium chloride) and should be dosed at 5 – 15 mg/kg elemental calcium **IV.**
     a. Calcium solutions must be infused IV slowly over 10 – 30 minutes with continuous ECG monitoring. If bradycardia, shortened QT interval, or vomiting is noticed, the infusion should be slowed or discontinued, as cardiac arrest can occur!
     b. Although most clinical signs resolve immediately it may take 2 – 6h before all signs abate (especially nervous changes like restlessness and panting).

  2. A **maintenance CRI calcium gluconate** solution **1 – 5 + mg elemental calcium/kg/h in 0.9% saline** may be indicated in patients who are critically ill, vomiting or anorectic, or where the underlying cause of hypocalcemia is unknown. Calcium > than 10 mL of 10% calcium gluconate/L for constant infusion should not be added to fluids containing acetate or lactate anions (Plasma-Lyte®, Normasol®, Lactated Ringers solutions) because precipitation may occur. Calcium and bicarbonate should not be mixed at all. Alternatively, a 1:1 calcium gluconate 10% and normal saline solution can be administered subcutaneously, although severe cutaneous reactions have been reported.

  3. Calcium levels should be monitored q8–12h and should be corrected to just below normal.

D. **Fluid therapy:** Normal saline for infusion of calcium, and where alkalosis exists. However, a balanced electrolyte solution (BES) Plasma-Lyte® 148, Normasol® R or Lactated Ringers is preferred if fluid replacement is required and the patient is acidemic. Also, normal saline induces calciuresis. A separate line is recommended if these fluids are required (*see C above*). Estimate hydration and perfusion status and administer fluid therapy accordingly. *See Fluid Therapy p.* for guidelines. Ongoing fluid therapy will depend on the patients' clinical condition [vomiting, anorexia, renal failure (*see Renal Failure p. 709*), pancreatitis (*see Pancreatitis p. 45*)].

E. **Electrolytes.** Hypernatremia may be seen with cases of sodium-phosphate enema toxicity (*see Hypernatremia p. 382* for guidelines on correction). Potassium supplementation (20 – 40 mEq/L) may be indicated depending on the serum potassium (*see Hypo/Hyperkalemia p. 394*). Phosphorus levels must be determined prior to calcium supplementation, as calcification of soft tissues is possible if concurrent increases in phosphorus and calcium exist. Calcium supplementation should be administered with caution in patients that are hyperphosphatemic (renal failure or phosphate-enema toxicity). Oral phosphorous binding agents (aluminum hydroxide 30 – 90 mg/kg/day or sucralfate 1 g/30 kg) given with food, and fluid therapy at twice maintenance rate, should be initiated in these patients. Hypocalcemia may be refractory to treatment in critically ill patients that have concurrent hypomagnesemia. Magnesium supplementation is discussed on *p. 403*.

F. **Jugular catheter** placement is recommended in patients with pancreatitis or renal failure.

G. Maintenance Therapy.

1. **Oral calcium** maintenance therapy, in the form of vitamin D supplementation, is usually only required in cases of primary or secondary hypoparathyroidism (rarely). Supplements that can be used include vitamin D2 (ergocalciferol) 4000 – 6000 U/kg/day as an induction dose, then 1000 – 2000 U/kg/day for maintenance, vitamin D3 (dihydrotachysterol) 0.02 – 0.03 mg/kg/day as an induction dose, then 0.01 – 0.02 mg/kg/day for maintenance, or vitamin D3 (calcitriol) at 0.02 – 0.03 μg/kg/day (see pharmacology section for details). In addition, oral calcium supplementation (calcium salts of carbonate, acetate or lactate dosed as elemental calcium at 25 mg/kg/day every 8 – 12 hours) may be indicated depending on the underlying disease and onset of action of the vitamin D supplement. Caution must be taken to avoid oversupplementaion and hypercalcemia when using oral calcium and vitamin D concurrently.

2. A **high quality commercial diet** should be fed once the patient is willing and able to eat and further calcium supplementation is not necessary.

PHARMACOLOGY

1) **Calcium salt solutions** are indicated for the treatment of clinical hypocalcemia. Calcium chloride is irritating if injected perivascularly and can cause hypotension.

2) **Vitamin D2 (ergocalciferol)** has a late onset of action (5 – 20 days) and is stored extensively in the body. Because of these effects, hypercalcemia due to overdosage is a severe complication and frequent monitoring of calcium levels are essential.

3) **Vitamin D3 (dihydrotachysterol)** is a synthetic formulation and has a relatively short onset of action (1 – 7 days) and a short duration (1 – 3 weeks). It requires close monitoring to prevent toxicity and is difficult to dose because of available pill sizes.

4) **Calcitriol** is the active form of vitamin D3 and is administered in physiological doses. Because the onset of action is rapid (1 – 4 days) and the duration is short because it is not stored in the body, it is the preferred treatment. Toxicity (hypercalcemia) is possible is spite of appropriate monitoring, but is less likely. The drug is expensive and difficult to dose because of large pill sizes, however, an oral liquid form may be available. The maintenance dose is 0.005 – 0.015 μg/kg/day.

5) **Oral calcium** supplements are dosed according to the amount of elemental calcium in the formulation. Extreme caution and careful monitoring must be maintained to avoid hypercalcemia when giving oral vitamin D and calcium supplements together. If the patient is normocalcemic, oral calcium supplementation may not be required in combination with vitamin D if a high-quality diet is fed.

SUGGESTED READING

1. Kirk's Current Veterinary Therapy XIII, Bonagura (ed). WB Saunders, Philadelphia, PA :340-345.
2. Small Animal Internal Medicine, 3rd edition, Nelson and Couto (eds). Mosby, St. Louis, MO :686-689, 840-841.

NOTES

INTRODUCTION

Disorders of serum sodium are frequently mild and secondary to the primary problem for which the animal is presented. However, sodium concentrations which markedly deviate from normal will have severe clinical consequences. Identifying and treating the underlying problem is essential to prevent continuing sodium derangements; however, treating the sodium abnormality itself becomes a priority. As hyper/hyponatremia are frequently identified on laboratory work-up and not as a presenting complaint (rarely suspected), it is essential that serum electrolytes be performed on all animals presented on an emergency basis and those being cared for in hospital. The serum sodium concentration is an indication of the amount of sodium relative to the amount of water in the ECF and provides no direct information about total body sodium content. Patients with hyper- or hyponatremia may have a decreased, normal or increased total body sodium content. Normal serum sodium concentrations do not always represent normal total body sodium as volume contraction due to concurrent water and sodium loss is frequently iso-osmotic (e.g., vomiting or diarrhea). Individual laboratories provide serum sodium concentrations based on normal values obtained on their analyzers, however reported ranges are 142 – 154 mEq/L in dogs and 150 – 160 mEq/L in cats. The serum sodium concentration (serum osmolarity) is tightly controlled by water homeostasis which is mediated by thirst, antidiuretic hormone ([ADH], also known as argenine vasopressin, and volume regulation mediated by the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system (SNS), atrial natruretic peptide (ANP), and 'pressure natriuresis'. It is important to keep in mind that these mechanisms are very powerful in maintaining normovolemia and it is highly unlikely that a conscious animal with an intact thirst mechanism and access to water, will present with hypertonicity caused strictly by water loss, unless the water loss is excessive (e.g., diabetes insipidus). The normal physiology of sodium and water homeostasis is vast and beyond the scope of this chapter; however relevant points will be presented. The reader is referred to Suggested Reading 1 below for an in-depth review of this topic. Refer to *Hyperosmolar Syndrome p. 279* for animals with hypernatremia and hyperglycemia.

*When managing dysnatremias, serum sodium should not change more than 0.5 mEq/L/h **(12 mEq/L/24h) if duration of abnormality is >24 hours** to avoid irreversible CNS injury.* **Note:** the **change** is mEq/L/h for all size animals and is not related to body weight. Take 24–48h to correct dehydration in patients with sodium abnormalities. Rapid correction will cause permanent neurological damage due to myelinolysis, which is usually evident 2 – 4 days following resuscitation. The primary area of injury is the thalamus in dogs, not the area of the pons as occurs in humans. If in doubt as to duration of sodium abnormality, assume longer than 24 hours. Other risk factors for the development of myelinolysis include concomitant hypokalemia and malnutrition.

Total body water is distributed between the various body compartments; the extracellular (ECF) (intravascular and interstitial) and the intracellular (ICF). Normal distribution within these compartments is maintained by osmotic forces; sodium in the extracellular compartment, and potassium in the intracellular compartment. As sodium is the most abundant electrolyte within the intravascular space, the contribution of sodium to serum osmolality is demonstrated in the following equations:

Serum osmolality (mOsm/kg):
 SI Units: mOsm/kg = $[1.86 \times (Na^+ + K^+)]$ + glucose + urea + 9, all units in mmol/L.
 Effective serum osmolality (mOsm/kg) [equivalent to tonicity] = $[1.86 \times (Na^+ + K^+)]$ + glucose + 9, all units in mmol/L; (i.e., calculated serum osmolality minus urea).
 Traditional units: mOsm/kg = $[1.86 \times (Na^+ + K^+)(mEq/L)]$ + [glucose (mg/dL)/18] + urea/2.8.
 Effective serum osmolality (mOsm/kg) = $[1.86 \times (Na^+ + K^+)(mEq/L)]$ + [glucose (mg/dL)/18]; (i.e., calculated serum osmolality minus BUN).

Consider **hyperosmolar** if serum osmolality >350 mOsm/kg or **effective serum osmolality** >320 mOsm/kg in **dogs** (normal 290 – 310), or >330 mOsm/kg in **cats** (290 – 330). The serum osmolality may be increased due to the presence of unmeasured substances such as ethylene glycol, salicylates, uremic toxins, lactate, sulfates, radioconstrast solutions, mannitol and others. The concentration of these potential substances can be estimated by subtracting the calculated serum osmolality above from the measured osmolality performed in the lab by osmometry freezing point. The difference, **the osmolar gap, is normally 10 mOsm/kg,** a gap larger than this implies the presence of an unknown substance contributing to the osmolality.

Plasma osmolality **<260 mOsm/kg is considered hypoosmolar.** Where hyponatremia is identified, serum osmolality should be measured as hyperosmolality due to other substances may be present (e.g., hyperglycemia). The

hyperosmolar state results in a shift of intracellular fluid into the intravascular space reducing serum sodium concentration. This is important to recognize as this will influence patient management (*see Diabetic Ketoacidosis p 263. and Hyperglycemic Hyperosmolar Syndrome p. 279*).

Urine osmolality (mOsm/kg) can be measured directly and can be used to detect renal (200 – 1500) or extra-renal (>1500 dog, >1800 cat) fluid losses, or central or nephrogenic diabetes insipidus (<100). Intermediate values indicate 'partial' disease processes. A comparison to serum osmolality will also assess the degree of renal free water loss i.e., high serum osmolality compared to a low urine osmolality. Where osmolality cannot be measured, urine specific gravity may be used instead providing other confounding conditions do not exist such as glucosuria, proteinuria, or ethylene glycol toxicity. Under homeostatic conditions specific gravity and osmolality closely correlate. However, proteinuria or glucosuria will affect osmolality much more than specific gravity. Therefore, a correlation of low urine sodium concentration with low specific gravity, and vice versa should not always be assumed. In general, however, because there is a good correlation (R = 0.91) between USG and osmolality in both cats and dogs, the following may be used:

USG   ~ osmolality (mOsm/kg)
1.025 ~ 1,000
1.030 ~ 1,200
1.035 ~ 1,400
1.040 ~ 1,600
1.045 ~ 1,800

Note: The equipment used to measure osmolality may also affect results, as an example, some solutes such as ethylene glycol affect freezing point osmometers, but not vapour pressure osmometers.

Fractional excretion of sodium (FE_{NA}) (**spot check**) is calculated to determine renal sodium losses which are associated with renal injury (P = plasma, U = urine).

FE_{NA} =
$[(U_{sodium}/P_{sodium}) \times (P_{creatinine}/U_{creatinine})] \times 100$
<1% = pre-renal
>2% = acute tubular necrosis (ATN)

A combination of pre-renal plus ATN may result in <2% FE_{NA}. However, a severe pre-renal insult causing ATN may result in >2% FE_{NA}.

HYPERNATREMIA

Serum sodium concentrations >155 mEq/L in dogs and >162 mEq/L in cats is considered hypernatremia, with upper ranges reported from 155 – 165 mEq/L. Water loss or sodium gain is elucidated from the history and physical findings. Hypernatremia may be present upon admission to hospital or occur during the hospital stay. An increase in serum sodium concentration **≥170 mEq/L** results in early signs of toxicity with severe signs occurring at ≥180 mEq/L. The central nervous system (CNS) is the most vulnerable as water moves from the brain into the intravascular space resulting in shrinkage of the brain. Hemorrhage and infarction occur producing neurological signs. Sodium passively crosses the blood-brain barrier into the CSF subsequently affecting neuronal function.

DIAGNOSIS

History/Signalment

- Miniature Schnauzers may be genetically predisposed to hypodipsic hypernatremia.
- Question the owner regarding exposure to potential **exogenous sources** of sodium chloride, such as recent ingestion of homemade play dough made from salt and flour, excessive salt used as an emetic, improperly mixed feed, seawater, or hypertonic saline enemas.
- As water loss may also result in hypernatremia, medical conditions associated with this should be considered (Table 1). Question the owner as to the duration of clinical signs noted below, should they be present.
- Question the owner as to the availability of water, especially if housed outside in hot weather, or confined in a car.
- A recent history of head trauma, which may have been mild, can potentially interfere with antidiuretic hormone (ADH) production/secretion/function.

TABLE 1. Causes of Hypernatremia

Exogenous sources of sodium gain	Endogenous sources of sodium gain
Homemade play dough ingestion	Cushing's syndrome
Excessive salt used as an emetic	Primary hyperaldosteronism (rare in animals)
Improperly mixed feed	Hepatic insufficiency
Seawater ingestion	Hyperthyroidism
Hypertonic saline enemas	
Hypertonic sodium bicarbonate infusion	
Hypertonic saline infusion	
Normal saline for a prolonged period	
Hypertonic feeding preparation	
Hypertonic dialysis	
Exogenous mineralocorticoids	

Pure water loss	Hypotonic fluid loss (water & some sodium loss)
Decreased water intake:	Vomiting
Lack of access to water	Diarrhea
Depression	Gastric suction
Hospitalization – drugs	Loop diuretics (hypo- or hypernatremia)
Primary hypodipsia	Osmotic diuresis (Diabetes mellitus, mannitol)
Neurologic disease	Small intestinal obstruction
Meningitis, encephalitis	Post-obstructive diuresis
Hypothalamic disorders	Polyuric phase of acute tubular necrosis
Resetting of osmostat	Intrinsic renal disease
Central diabetes insipidus	Lactulose enema
Head trauma	Third-space losses (peritonitis, pancreatitis may cause
Neoplasia	hypo- or hypernatremia)
Amphotericin B	Burns
Hypercalcemia, hypokalemia	
Nephrogenic diabetes insipidus	
Dexamethasone	
Hyperglycemia	
Ethylene glycol, or ethanol intoxication	
Insensible respiratory losses (fever, environment)	

Physical Examination/Clinical Signs

- Those associated with fluid loss such as vomiting, diarrhea, polydipsia, polyuria
- Abdominal pain
- Neurological signs such as muscle fasciculations, tremors, seizures
- Hyperthermia associated with neurological signs above
- Signs associated with low circulating blood volume such as tachycardia, dehydration, and recumbency due to shock.
- Dehydration is usually associated with fluid loss, whereas extracellular fluid volume is increased in sodium gain situations; therefore, weight gain and edema may be noted.
- Numerous physical findings associated with the conditions listed in Table 1.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **Baseline PCV/TS, stick BUN and glucose.** Confirm abnormalities with chemical analyzers.
- **Serum electrolytes.** Serum sodium >170mEq/L is associated with clinical signs. All other electrolytes must be measured as these may also be abnormal.

- **Serum osmolality** may be useful in identifying defects in antidiuretic hormone (ADH) secretion/function. A high serum osmolality with a low urine osmolality is highly suggestive of central or nephrogenic diabetes insipidus.
- **Urinalysis** to assess the presence of infection, measure specific gravity and osmolality. If a **dehydrated patient** has a urine osmolarity of >1500 mOsm/kg (dog) or >1800 mOsm/kg (cat) then extra-renal water loss is the cause of hypernatremia. If <100 mOsm/kg, then central or nephrogenic diabetes insipidus is the likely cause of hypernatremia. If urine osmolarity is 200 – 1500 mOsm/kg, diagnosis is more difficult as many of the causes listed in Table 1 should be considered.
- **Systemic blood pressure** measurement is advised as dehydration may be associated with intravascular volume loss and hypotension.

Extended Laboratory Data Base

- Tests will vary depending on history and clinical signs
- **CBC** and **biochemical profile** are essential in diagnosing a potential etiology for hypernatremia and obtaining baseline values.
- **Aldosterone** levels (very specific handling methods required therefore consult your laboratory prior to collection and submission) where other causes of hypernatremia are ruled out.

MANAGEMENT

Therapy for hypernatremia must also include correction of the underlying problem. However, this may not always be known upon initial presentation. Recommendations here will be restricted to correction of hypernatremia.

When managing dysnatremias, serum sodium should not change more than 0.5 mEq/L/h (12 mEq/L/24h) to avoid irreversible CNS injury. The 0.5 mEq/L/h is applicable to all animals and is not associated with body weight. Take 24–48h to correct dehydration in patients with sodium abnormalities. Rapid correction will cause permanent neurological damage due to myelinolysis, which is usually evident 2 – 4 days following resuscitation.

A. Hypernatremia secondary to fluid loss

The type and rate of fluids administered are by 'prescription' as no 'standard' therapy can be recommended or safe. The individual patient's problem and response to therapy will dictate ongoing management. The suggestions are offered as a guide.

1. If *pure water loss* is diagnosed fluid requirements may be estimated as follows:
   a. If body weight is **known** prior to an acute period of fluid loss, the estimated fluid loss is
   $$\text{Litres} = \text{BWkg}_{before} - \text{BWkg}_{after}$$
   b. If body weight prior to loss **is not known** the estimated potential fluid deficit may be calculated using the following published equations:

   i. $\text{Litres} = \text{BWkg}_{present} \times \left(\left[\dfrac{\text{Serum Na}^+}{150} \right] - 1 \right)$

   OR

   ii. $\text{Litres} = 0.6 \times \text{BWkg} \times \left(1 - \left[\dfrac{150}{\text{Serum Na}^+} \right] \right)$

2. In *all situations* (pure water loss, hypotonic water loss, hypovolemic shock) this author prefers to **calculate the fluid volume** required to achieve normovolemia based on degree of dehydration and loss of circulating volume (*see Fluid Therapy p. 347*). Formulas in 1b above are not suitable for calculating hypotonic fluid loss or losses associated with shock. Above all, serum sodium should be used to guide therapy.

3. Serum sodium **>169 mEq/L associated with shock,** regardless of duration of hypernatremia, should receive fluid therapy to **correct the shock state as quickly as possible** (*see Shock p. 603*).
   a. This author usually starts with 0.9% sodium chloride or Plasma-Lyte® A, 148 or Normosol® R. Serum sodium is measured after one-third of estimated fluid is administered. Hypotonic solutions are not advised as these will leave the intravascular space more quickly than isotonic solutions.
   b. If sodium is unchanged or higher, change fluids to lactated Ringer's solution.
   c. If the patient has not recovered from the shock state, administer a second one-third of estimated fluid requirement and re-check serum sodium.
   d. If serum sodium has increased, change to 0.45% sodium chloride or half-strength balanced electrolyte solution with careful monitoring of serum sodium. Synthetic colloids may be required if hypotension persists.
   e. After resolution of the shock state, slow correction of serum sodium by <0.5 mEq/L/h is then followed for 48 –60h.

  f. The patient may be very thirsty but caution is required when offering water as this may lower sodium too quickly. Crushed ice or very small volumes of water should be given to relieve the anxiety of thirst.

  g. Measure electrolytes at 1–2h to establish a trend and ensure that serum sodium does not fall faster than 0.5 mEq/h. Reduce frequency of monitoring as appropriate (q4h). The fluid selected will depend on the patient's response to the resuscitation fluid and serum sodium concentration.

  h. In addition to the fluids mentioned, 5% dextrose in water may also be considered if the patient cannot drink.

  i. **Should correction occur too quickly, add 0.5 – 1.0 mL/kg/h 5% sodium chloride** to maintenance fluids until serum sodium concentration is corrected to that desired, then discontinue. This usually raises serum sodium by 1 – 1.5 mEq/h.

4. Serum sodium **>169 mEq/L for <24h** may be corrected as rapidly as required by the patient's condition. If hypovolemic, consider 0.45% sodium chloride and offer water if able to drink. If (or when) normovolemic offer water primarily; if unable to drink continue with 0.45% sodium chloride, half-strength balanced electrolyte solution, 5% dextrose in water, or one-third dextrose/two-thirds sodium chloride. The rate of drop of serum sodium can be 6 – 8 mEq/L in 3--4h, then continue to drop at 1 mEq/L/h to correct to 160 mmol/L. At this point, resume a balanced electrolyte solution if the patient is acidemic or normal; continue with saline if alkalemic. Most importantly, allow the patient to drink.

5. Serum sodium **>169 mEq/L for >24 hours in normovolemic, asymptomatic patient** requires slow correction, **no faster than 0.5 mEq/L/h** change in serum sodium, over 48–60h.

  a. Start with 0.9% sodium chloride, Plasma-Lyte® A or 148, or Normasol® R depending on acid-base status.

  b. Change to 0.45% sodium chloride, half-strength balanced electrolyte solution (equal volumes 5% dextrose in water and balanced electrolyte solution), or Plasma-Lyte® 56 or Normasol® M, as required following assessment of electrolytes at 2 hour intervals to assess trend, followed by 4 hour trending once the rate of drop is established.

  c. CAUTION: consumption of water can reduce serum sodium concentration very quickly. If a patient is desperately looking for water, maintain on fluids in 5a above or 0.9% sodium chloride and offer crushed ice, or very small volumes of water, to relieve the anxiety of thirst.

6. Serum sodium **>169 mEq/L for >24h in normovolemic, neurologically impaired** (frequently >175 mEq/L), may require 5% dextrose in water until neurological signs subside or serum sodium is reduced to 169 mEq/L whichever occurs first. Reassess at this point and treat as 5 above. Reducing serum sodium more rapidly initially here is necessary due to the neurological abnormalities.

7. **Maintenance losses** (*sensible and insensible see Maintenance Fluid chart p. 366*) must be included in the correction. Further ongoing losses (e.g., polyuria, vomiting, diarrhea) are also included. A mixture of fluids may be administered, 0.45% saline, or 5% dextrose in water as the correction solution and for ongoing water losses; and a balanced electrolyte solution (preferably Lactated Ringers) if the patient is very acidemic for maintenance, or 0.45% sodium chloride if alkalemic, until the underlying problem is managed. Again, the 'prescription' approach is required.

8. **Where the animals are able to drink,** offer water. **Caution** is still required as water is rapidly absorbed and will cause a rapid reduction in serum sodium.

9. **Where diabetes insipidus** is suspected, **desmopressin (DDAVP nasal spray) one drop** (1.5 – 4 µg) placed in the conjunctival sac q12h should reduce/resolve the polyuria associated with free water loss. The effect lasts from 8–24h. Ongoing dosing and frequency is based on patient response.

10. Measurements of serum electrolytes q1–4h to establish and confirm appropriate reduction in sodium and correct other electrolyte abnormalities. Once the acute phase is resolved, q8h measurements are recommended.

B. **Hypernatremia due to sodium gain**

These patients tend to be hypervolemic and hypernatremic. Systemic blood pressure is elevated and peripheral edema may be present. In this instance the excess sodium and water must be excreted.

1. **If fluid overload is not present, furosemide 0.2 mg/kg IV** to facilitate sodium loss and 5% dextrose in water to replace ongoing losses. Change to 0.45% saline should serum sodium decrease >0.5 mEq/L/h in a >24h situation. If the problem is acute (<24h) correction to high normal within 3–6h is acceptable.

2. **If fluid overload is present, furosemide 0.2 mg/kg IV** initially with repeat dosing as required depending on the patient's response, degree of fluid excess, and serum sodium. If renal insufficiency is present, **1 – 2 mg/kg** may be required to produce a diuresis. 5% dextrose in water is administered at maintenance rate to reduce serum sodium. **Avoid rapid changes in volume and serum sodium.** The same principles as 4 – 7 above apply. Careful titration of furosemide and fluids based on frequent (q2--4h) monitoring of serum electrolytes is required to formulate a 'prescription' for the individual patient.

3. Hypokalemia and hypochloremia may occur with furosemide administration.

4. Frequent measurement of urine voided and body weight is advised.

HYPONATREMIA

Hyponatremia is defined as serum sodium concentrations <140 mEq/L in dogs and <149 mEq/L in cats. In the presence of normal serum sodium a relative hyponatremia may occur due to fluid shifts from the intracellular to the extracellular compartment if the extracellular space is hyperosmolar when compared to the intracellular space (e.g., mannitol administration, hyperglycemia). This fluid translocation temporarily dilutes the serum sodium. Other etiologies of 'dilutional' hyponatremia are listed in Table 2 (water retention). Where fluid loss is experienced, preservation of intravascular volume is maintained through reduced renal excretion of water, ADH release, and the patient's thirst mechanism resulting in increased water consumption. These three mechanisms dilute sodium in excess of that retained by aldosterone at the level of the kidney. The syndrome of inappropriate ADH (SIADH) also results in retention of water with subsequent dilution of sodium. In **SIADH,** aldosterone action is not increased; therefore, **renal excretion of sodium is normal.** Where ADH release is in response to hypovolemia, sodium is also retained through the action of aldosterone and **urine sodium will be low.** To further differentiate between the two conditions, renal excretion of sodium will increase following administration of 0.9% sodium chloride in SIADH but not where there is a decrease in effective circulating volume.

Hyponatremia may be present upon admission to hospital or occur during the hospital stay. Serum sodium concentration <125 mEq/L results in early signs of toxicity with severe signs occurring at <120 mEq/L. However, the more rapid the lowering of the sodium concentration (>0.5 mEq/L/h), the more likely cerebral edema and water intoxication will occur. Clinical signs are usually absent in the chronic hyponatremic patient as there is time for brain adjustments to occur such as shifts of potassium and organic osmolytes out of the cells.

DIAGNOSIS

History/Signalment

- Questions for the owner should be directed to the most applicable problems listed in Table 2.
- Duration of illness should also be determined as acute vs chronic changes in serum sodium concentration will influence therapy.
- As hyponatremia can be associated with adrenal insufficiency, does the history fit (*see Hypoadrenocorticism p. 274*)?
- Loop diuretics (e.g., furosemide) if administered inappropriately, can cause severe hyponatremia and hypovolemia.
- Question the owner regarding drinking of large volumes of water (i.e., toilet bowl, emptying water bowl quickly) as hypovolemia due to blood loss (e.g., ruptured hemangiosarcoma) or third space loss (e.g., peritonitis, pleural effusion) will enhance low serum sodium by dilution.
- Larger breed dogs tend to be psychogenic water drinkers.

Table 2. Causes of Hyponatremia (rule out pseudohyponatremia in the presence of lipemic serum)

Water retention (normovolemia/ hypervolemia)	
Congestive heart failure (*p. 149*)	Hypothyroidism (*p. 285*)
Advanced Renal failure (*p. 709*)	SIADH
Pregnancy	*Cancer*
Liver failure (*p. 37*)	pulmonary/thoracic tumours
Drugs	extra-thoracic tumours
DDAVP overdose	*CNS disorders*
ADH mechanism (inappropriate)	head trauma (*p. 691*)
Opioids	mass lesions
Oxytocin	inflammatory and demyelinating disease
Non-steroidal antiinflammatory drugs	cerebrovascular accident
Phenothiazines	*Pulmonary disorders (p. 555)*
Tricyclic antidepressants	pneumonia
Serotonin re-uptake inhibitors	acute respiratory failure
Chlorpromazine	positive pressure ventilation
Carbamazzine	*Post-surgery (p. 12)*
Cyclophosphamide	*Pain (p. 117)*
Vincristine	Potassium sparing diuretics (*p. 161*)

Sodium loss ± hypovolemia	Water intake in excess of solute (normovolemia)

Renal (p. 709)
    Loop diuretics
    Osmotic diuresis
    Adrenal insufficiency (p. 274)
    Salt-wasting nephropathy
    Bicarbonaturia (renal tubular acidosis)
    Ketonuria (p. 263)
Extra-renal
    Diarrhea (p. 32)
    Vomiting (p. 74)
    Severe gastrointestinal disease of all categories
        i.e., parasitic, viral, bacterial, hepatic encephalopathy
        Blood loss (± ADH secretion ± water consumption)
        (p. 619)
    Third space losses (± ADH secretion ± water
        consumption) peritonitis, pleural effusion,
        ileus/obstruction
    Brain injury and salt-wasting
	Psychogenic polydipsia
	Hypoosmolar fluids
	Low sodium diets

Physical Examination/Clinical Signs

- Clinical signs and physical examination will vary according to the underlying problem listed in Table 2.
- Assessment of hydration and volume status will indicate the degree of fluid loss (*see Fluid Therapy p. 347*).
- Signs associated with serum sodium ~125 mEq/L are nausea and lethargy, progressing to vomiting, weakness and rarely pulmonary edema (~120 mEq/L) with neurological signs such as depression, fasciculations, tremors, seizures and coma developing with severe hyponatremia (<120 mEq/L). **Of note,** neurological examination may reveal assymetric abnormalities.
- Hyperthermia may be associated with neurological signs above.
- Peripheral edema may be present.
- Patients with sodium loss states may be hypervolemic, normovolemic, or dehydrated, with a low circulating volume.
- Note if diarrhea is present, and if associated with Trichuris parasitic infection.

Laboratory Evaluation/Diagnostic Imaging

It is essential to distinguish between hyponatremia with hyposmolality and hyponatremia with normal or hyperosmolality. Also, pseudohyponatremia must be ruled out.

Stat

- **Baseline PCV/TS, stick BUN** and **glucose.** Confirm abnormalities with chemical analyzers. If total solids are very high (hyperproteinemia), a low sodium concentration may not be real. Hyperproteinemia may cause pseudohyponatremia. High blood glucose and ketonemia (*see Diabetic Ketoacidosis p. 263*) will reduce serum sodium as the increased osmolality results in translocation of intracellular water to the intravascular compartment.
- **Plasma appearance** must be evaluated, as a low sodium (measured by flame photometry) in the presence of lipemia suggests psuedohyponatremia, which does not require therapy. In this setting serum osmolality is normal. If sodium measurements are obtained by direct potentiometry using an ion selective electrode, lipid in the sample does not affect the measured serum sodium concentration
- **Serum electrolytes.** Serum sodium ≤125 mEq/L is associated with clinical signs. All other electrolytes must be measured as these may also be abnormal.
- **Serum osmolality** is useful in identifying hypo-, iso- or hyperosmolar states associated with hyponatremia. A low serum osmolality with a high urine specific gravity is highly suggestive of ADH secretion, which may be appropriate (low circulating volume), or inappropriate (*see Table 2 for list*). Hyponatremia with hyperosmolality is usually due to hyperglycemia (diabetes mellitus, or presence of other effective osmole e.g., ethylene glycol.
- **Urinalysis** to assess the presence of urinary tract infection, to measure specific gravity and sodium concentration.

    a. If a **dehydrated patient** has a urine sodium <10 mEq/L then there is non-renal sodium loss (extra-renal water loss is the cause of hyponatremia, i.e., potential gastrointestinal lossese). If urine sodium is >20mEq/L, proximal renal dysfunction, hypoadrenocorticism or loop diuretics are likely causes of hyponatremia.

    b. If the patient is **not dehydrated** and urine sodium is <10 mEq/L, then appropriate ADH release has occurred if hypothyroidism, congestive heart failure, non-renal losses, or hypoalbuminemia is identified. However, if urine sodium is >20 mEq/L, SIADH or a reset hypothalmic osmostat should be considered.

- **Systemic blood pressure** should be measured to assess intravascular volume and perfusion.

Extended Laboratory Data Base

- **CBC** is essential to rule out any infectious process
- **Biochemical profile** should be performed to identify organ dysfunction as a cause of hyponatremia and overall health of the patient.
- **Fecal analysis** to rule out *Trichuris* infection.
- **Specific tests** to pursue will be dependent on differential diagnoses (Table 2). If SIADH is suspected and the patient is not receiving drugs that cause this, tests should include searching for neoplasia.

MANAGEMENT

Management of the underlying problem must be pursued. The following guidelines relate to management of hyponatremia only. The presence of symptoms and their severity will determine the pace of correction.

A. **Neurologic deficits with hypotonic hyponatremia (sodium loss Table 2) and hypovolemia.**

    1. **Reversing neurologic deficits due to hyponatremia, and shock** due to low circulating volume, are the immediate goals. Serum sodium should only be increased to the level required to reverse neurological signs.

    2. Calculate volume deficit based on history and physical examination (*see Fluid Therapy p. 347*). **Administer 0.9% sodium chloride** to reverse the shock state.

        a. Fluid reduction is based on return to adequate circulating volume (systolic blood pressure 100 mmHg, mean arterial pressure 60 – 70 mmHg).

        b. Measure serum sodium; aim for 120 mEq/L, OR 125 mEq/L if neurologic dysfunction is present at 120 mEq/L. Depression due to poor perfusion should **not be** considered as neurological dysfunction.

        c. If there is no change half way through resuscitation, in addition to calculated fluids, administer hypertonic saline (1.5% solution = 256 mEq/L, 5% solution = 856 mEq/L) to raise sodium by 1 mEq/h until asymptomatic. In the author's experience 0.5 – 1mL/kg/h of 5% sodium chloride has raised serum sodium by 1 – 1.5 mEq/L/h. Hypertonic saline is recommended only in significantly symptomatic patients with acute hyponatremia. The target sodium level should be 125 mEq/L. The rate of correction of hyponatremia depends on the severity of neurological dysfunction, which is related to the acuteness and degree of hyponatremia. In patients with severe symptoms, it is recommended that the rate of correction should be 1 – 2 mEq/L/h for several hours, not exceeding 8 mEq/L on any day of treatment.

        d. Addition of 2 – 5 mL/kg synthetic colloid may be required in refractory hypotension. Repeat as needed.

        e. As soon as neurological abnormalities abate, go to B 1 and 2 below.

    3. If the patient is **seizing administer diazepam 0.5 mg/kg IV** (*see Seizures in Dogs p. 460, Seizures in Cats p. 456*). Seizures should stop once the serum sodium levels are increased to 120 – 125 mEq/L, therefore continuing diazepam should not be necessary.

B. **No neurologic deficits with hypotonic hyponatremia (sodium loss Table 2) and hypovolemia.**

    1. Immediate goal is to **return to normal circulating volume** without increasing serum sodium more than 0.5 mEq/L/h, preferably no more than 8 mEq/L/day in animals with a **chronic (>24h)** history of hyponatremia. If hyponatremia is documented to be **acute (<24h),** a more rapid return to serum sodium of 130 mEq/L should have no detrimental effect.

    2. Manage as A2 a and b above with **lactated Ringer's solution** (preferred as has lower sodium), or Plasma-Lyte® A, 148 or Normasol® R.

    3. **Monitoring serum electrolytes** is required q1–2h until a trend is noted and the rate of rise of sodium is approaching 120 mEq/L, or 125 mEq/L. A further period of trending is required to ensure that a rise not greater than **0.5 mEq/h outlined in A & B above** is occurring; if it is, change to 0.45% sodium chloride.

    4. Once volume has been restored, the stimulus for ADH secretion is reduced allowing the animal to excrete the excess water. This will correct hyponatremia to some degree, and treating the underlying problem (e.g., vomiting, diarrhea, third space losses), will correct the problem further. Therefore, caution is required from this aspect to avoid over-shoot of sodium correction.

C. Hyponatremic (water retention Table 2), normovolemic or hypervolemic.

1. Refer to appropriate chapters for specific management of problems listed in Table 2.
2. It is the author's experience that drug-induced SIADH can be managed with **furosemide 0.2 mg/kg IV** when oliguria and high specific gravity, or peripheral edema develop. This is a common occurrence with the administration of opioid analgesics, especially for > 12 hours. It is the ADH action and retention of water that is the primary cause. In these cases serum sodium has not been noted to be critically low. Hypovolemia as a cause of oliguria must be ruled-out prior to furosemide administration. Furosemide will cause a diuresis, however, sodium may also be lost.
3. Removing the underlying cause will reverse the problem, however, it may be necessary to continue with the drug causing the problem (e.g., opioids); therefore, intermittent (~q12h) furosemide administration is required based on the patient's condition.
4. Ongoing fluid therapy will have to be adjusted to the patient's needs (*see Fluid Therapy p. 347*).

D. Water intake in excess of solutes

1. Correct underlying cause.
2. Cautious administration of 0.9% sodium chloride.

SUGGESTED READING

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NOTES

INTRODUCTION

In critically ill patients phosphorous levels should be noted and treated when low. Normal values for phosphorous are (3.0 – 6.2 mg/dL]), 0.8 – 2.6 mmol/L in dogs and 1.03 – 2.82 mmol/L in cats but are normally higher in young animals and if lipemia is present. Phosphorous is vital in energy dependent physiologic processes being an important component of adenine triphosphate (ATP). Phosphorous is also a component of the phospholipid layer of cell membranes. Of primary concern in hypophosphatemia (phosphorous [0.8 mmol/L in dogs, <1.00 mmol/L in cats [<2.5 mg/dL])are affects on cells that are high energy users, such as red blood cells, skeletal muscle cells and cerebral cells. Cats are more susceptible to hypophosphatemia than dogs. Hyperthyroidism in cats increases phosphorous serum concentration. Hypophosphatemia results from decreased intestinal absorption, increased urinary loss, and shift from the extracellular to the intracellular space for utilization in the production of ATP. Serum phosphorous concentration should always be evaluated relative to serum calcium concentration and renal function.

HYPOPHOSPHATEMIA

DIAGNOSIS

History/Signalment

The following may be associated with hypophosphatemia:
- A history of very recent blood transfusion with stored blood (depletion of 2,3DPG) causing a massive drain of phosphorous.
- Recently instituted glucose therapy.
- Recent administration of high volumes parenteral fluid therapy.
- Enteral or parenteral nutritional support in an energy depleted patient.
- Administration of intestinal binding agents.
- Clinical picture associated with nutritional secondary hyperparathyroidsim (*see Hypocalcemia p. 377*).
- Ingestion of face cream containing calcipotriene.
- History of chronic diarrhea, especially steatorrhea
- History of polyuria and polydipsia
- Insulin therapy in a diabetic patient.
- After correction of non-respiratory acidosis.
- Starvation.
- Cats with a recent illness that would predispose them to hepatic lipidosis.
- Dialysis therapy.
- General malaise due to decreased oxygen release from red blood cells (deceased 2,3 DPG) to the tissue, including the heart muscle.

Cinical Signs/Physical Examination

Signs are usually related to the organs most affected by hypophosphatemia and those resulting in loss of phosphorous .
- A decrease in cerebral function (i.e., depression, obtundation, stupor and coma), seizures.
- Rapid hemolysis and anemia, especially 24 hours after institution of therapy for diabetic ketoacidosis in both cats and dogs.
- Muscle weakness or rhabdomyolysis with myoglobinuria.
- Leukocyte and platelet function is reduced resulting in associated problems.
- Anorexia, nausea and vomiting due to ileus caused by hypophosphatemia.
- Physical findings associated with hepatic lipidosis in cats may be present.
- Eclampsia, commonly seen in small breed dogs (rarely cats) often within 21 days of whelping (range 1 week pre-partum to 45 days postpartum).
- Thyroidectomy or parathyroidectomy within 1 to 5 days after surgery.
- Alkalemia and bicarbonate therapy can promote intracellular shift of phosphate.
- Non-respiratory acidosis may maintain a normal serum phosphate due to ionic shifts. However, with correction of acid-base status, hypophosphatemia may occur.
- Diarrhea and malabsorption can lead to loss of phosphorous.
- Polyuria and renal loss of phosphorous.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV** is decreased due to hemolysis and is common following treatment for DKA if hypophosphatemia is not contemplated and prophylactically treated.
- **TS** may be increased due to fluid losses or decreased with gastrointestinal problems or starvation.
- **Stick BUN** may be increased with renal disease, or pre-renal dehydration.
- **Urinalysis** to identify lower urinary tract pathology, and urine specific gravity which may be low with renal tubular dysfunction or glucosuria.
- **Blood glucose** is increased with diabetes mellitus but may be low or normal with insulin therapy.
- **Venous blood gases** are indicated to identify respiratory or non-respiratory alkalosis. If acidosis is identified and phosphorous levels low normal or low, phosphorous levels may drop further with correction of acidosis; diabetic ketoacidosis is a classic example.
- **Serum electrolytes,** in addition to phosphorous, should be measured as the underlying problem (e.g, hyperaldosteronism) may also be associated with abnormalites in sodium, chloride, potassium.
- **Buccal mucosal bleeding time** if platelet function is questionable.
- Obtain samples for **culture and sensitivity** from any infectious focus.

Extended Data Base

- **CBC** may reveal abnormalities across all cell lines due to loss of integrity of cell membranes. However, cell function may be affected even if cell counts are within normal.
- **Biochemical profile** will identify the low phosphorous and other problems potentially associated with hypophosphatemia i.e., increased alanine aminotransferase and increased alkaline phosphatase associated with hepatic lipidosis in cats; alterations in urea and creatinine associated with renal failure, and hyperglycemia, hypercalcemia in malignancy, or hyperglycemia in diabetes mellitus.
- **Parathyroid hormone levels** to rule out primary or secondary hyperparathyroidism (*see Hypocalcemia p. 377*).
- **Aldosterone levels** if indicated.

MANAGEMENT

A. If not already present, place an **IV catheter and commence fluid therapy,** without calcium (no, lactated Ringer's or Hartman's solution) appropriate for the underlying problem **alkalinizing solution** (Plasma-Lyte® or Normasol®) for acidemic, and **0.9% sodium chloride for alkalemic patients**) and hydration status (*see Fluid Therapy p. 347*). If myoglobinuria is present, diurese the patient to prevent, or treat renal injury (*see Acute Renal Failure p. 709*).

B. The **dose of phosphate** needed to correct hypophosphatemia is variable, ranging from 0.01 – 0.03 mmol/kg/h 6 – 24h to a rare extreme in emergent settings of 0.12 mmol/kg/h, for 1 – 2h, then reduce to previous dosing. Phosphate supplements are either **Potassium Phosphate** or **Sodium Phosphate;** check the **concentration (mmol/mL, mEq/mL and mg/mL)** on the product you have and calculate accordingly (*see Pharmacology below*).

C. Measure serum phosphorus q6h and reduce or increase the dose accordingly.

D. **Serum potassium** must be monitored if potassium phosphate is used. Calculate and adjust potassium supplementation based on the dose of phosphate used. If potassium is contraindicated, use sodium phosphate. If hyperkalemia and hypernatremia may be a problem, both formulations, in half volumes, can be used. Do not use excessive doses of phosphorous to supplement potassium. Do not exceed 0.5 mEq/kg/h K⁺, unless severely hypokalemic and closely monitored.

E. Treat the underlying problem.

F. A packed red cell transfusion may be required if PCV is <25 (dogs), or <20 (cats). Use cells that have been stored for less than 12 days. Stored red blood cells are ATP depleted and consume blood phosphate to remake ATP.

G. In severely energy depleted patients, **institute re-feeding very gradually over 5 – 7 days** (especially tube or parenteral feeding where the animal has no control over volume received). With re-feeding, the provision of energy and calories to a severely energy depleted patient leads to reformation of ATP in a variety of body tissues, thereby causing an acute depletion of limited amount of serum phosphate. The correction of hypophosphatemia is necessary prior to institution of adequate nutrition.

H. If hypophasphatemia is anticipated (diabetic ketoacidosis, re-feeding severely energy depleted animal or hepatic lipidosis), supplementation with low dose phosphate, with monitoring, may prevent the clinical signs of hypophosphatemia.

HYPERPHOSPHATEMIA

DIAGNOSIS

History/Signalment

- Recent chemotherapy for large tumour burden may lead to tumour lysis syndrome.
- Recent history of trauma.
  - massive tissue injury results in release of intracellular phosphorous
  - trauma to the urinary tract with urine leakage
- Behaviour associated with urethral obstruction.
- Hemolysis.
- History of events leading to rhabdomyolysis.
- Snakebite.
- Question the owner regarding any incident precipitating acute renal failure, or if chronic renal failure has been diagnosed.
- Exposure to vitamin D rodenticides.
- Use of phosphate enemas.

Clinical Signs/Physical Examination

- Typical of those associated with the above
- Diarrhea
- Tetany
- Metastatic soft tissue calcification
- Acromegaly

Laboratory/Diagnostic Imaging Data Base

- **CBC, TS** will reflect changes occurring in the above situations.
- **Electrolytes** may be altered, especially sodium which may be increased.
- **Glucose** may be increased or decreased based on association with above.
- **Stick BUN, urea, creatinine** to identify renal failure.
- **Venous Blood gases** may identify a non-respiratory acidosis, the cause of which should also be identified.

Extended Data Base

- **Biochemical Profile** to confirm hyperphosphatemia and identify any of the above a potential causes.
- **PTH** levels to rule out hypoparathyroidism.

MANAGEMENT

A. Place IV catheter and administer alkalinizing fluids (Plasma-Lyte®, Normosol®, lactated Ringer's), administer at appropriate rate, in excess of that to correct intravascular volume loss and dehydration (*see Fluid Therapy p. 347*) in order to promote diuresis. Until underlying cause removed.

B. **Dextrose** added to the fluids will promote intracellular movement of phosphorous if levels are high. Dextrose may also promote diuresis.

C. **Of utmost importance is removal of the underlying cause.** Diuresis is treating the symptom not the problem. Caution with diuresis is warranted as this may promote loss of concentrating ability with resultant polyuria, even after the underlying problem is removed (i.e., non-respiratory acidosis corrected, relief of urethral obstruction).

D. **Intestinal phosphate binders,** while treating renal failure.

1. **Sucralfate 0.5 – 1 g/25 kg** (preferrrably emulsion) in hospital if anorectic.
2. **Aluminum hydroxide or calcium** acetate/carbonate **30 – 180 mg/kg/day** with meals.

PHARMACOLOGY

1) Sodium phosphate contains 4.0 mmol of sodium and 3 mmol phosphate/mL.

2) Potassium phosphate contains 4.4 mEq potassium and 3 mmol phosphate/mL.

3) Please check the concentration you are using.

SUGGESTED READING

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2. Nelson RW. Metabolic and Electrolyte Disorders. In: Nelson RW, Couto CG (eds) Small Animal Internal Medicine 3rd ed. Mosby. St. Louis. MO. 2003:816-846.

NOTES

INTRODUCTION

Alterations in serum potassium (K^+) can occur with many conditions resulting in K^+ loss or gain. Serum K^+ concentration is also influenced by the acid-base status of the patient. Potassium is the major intracellular cation. At least 95% of body potassium is located within the cell and 5% in extracellular fluid. Potassium translocates in and out of cells with changes in pH. **Acidemia** is associated with outward translocation of K^+, and **alkalemia** with inward movement in exchange for hydrogen (H^+) in an attempt to maintain normal pH. However, this does not always result in hyperkalemia as total body K^+ stores may be low. As the acidosis is corrected, pH rises and the reverse occurs. Sodium ions move with K^+ in the hydrogen exchange. Therapy to correct the pH will alter serum K^+, and therapy to correct K^+ levels alters pH. Serum K^+ measurments are highest during acidemia.

Hypokalemia is present when the K^+ is <3.6 mEq/L. Hypokalemia is more common in cats than dogs. Hyperkalemia is present when the serum K^+ concentration exceeds 5.5 mEq/L in the dog and 5.0 mEq/L in the cat. Hyperkalemia is less common than hypo-, but is associated with several disorders in both cats and dogs.

HYPOKALEMIA

DIAGNOSIS

History/Signalment
- **Hypokalemia** can occur with many illnesses and acid-base disturbances. Especially alkalemia, therefore a thorough history must be obtained. Consider the following:
- Cats fed diets marginally replete in K^+ and containing urinary acidifiers, cause hypokalemic nephropathy.
- Burmese cats may be predisposed.
- Medications, especially furosemide, amphotericin B and beta$_2$-agonists decrease K^+. Hypokalemia due to albuterol intoxication has been reported in dogs, therefore, question the owner regarding potential exposure to a 'puffer'. Hypokalemia predisposes to digitalis toxicity (*p. 672*).
- Potassium losses occur with diarrhea .
- Anorectic patients have reduced intake of K^+; although rarely the cause of hypokalemia, this may contribute to maintaining it.
- Anorexia may be due to hypokalemic ileus and gastric atony.
- Detrusor muscle atony may result in urinary retention
- Hypokalemia causes progressive generalized weakness (*p. 492*) in geriatric cats.
- Polydipsia and polyuria, potentially as a result of chronic renal failure, diabetes mellitus, or hyperadrenocorticism can cause hypokalemia.
- Question regarding insulin dosage if diabetic.
- May have a history associated with hyperadrenocorticism (*p. 270*) and hyperaldosteronism or phaeochromocytoma (*p. 206*).

- **In hospital potential** causes of hypokalemia
    - Glucose-containing fluids causing diuresis
    - Insulin therapy, especially during treatment for DKA
    - Stress of illness with subsequent epinephrine release
    - Infusions of epinephrine, norephinephrine, dopamine
    - Hypothermia (resultant 'cold' diuresis)
    - Post-obstructive diuresis
    - High volume fluid diuresis
    - Mannitol diuresis
    - Furosemide and thiazide diuretics
    - Penicillin
    - Peritoneal dialysis

Clinical Signs/Physical Examination

A thorough physical examination to detect underlying causes of hypokalemia, as well as abnormalities resulting from the low K^+, must be performed.

Sub-normal serum K^+ levels can lead to:
- Generalized muscle weakness progressing to inability to stand and expand the chest wall (rapid shallow respiratory pattern)
- Ventroflexion of the neck in cats
- Gastrointestinal weakness (i.e., gastroparesis, ileus)
- Large bladder secondary to detrusor dysfunction and urine retention
- Reduced renal water conservation resulting in polyuria
- Reduced cardiovascular function
- Possibly cause, or sustains cardiac arrhythmias such as supraventricular (*p. 170*) and ventricular arrhythmias (*p. 179*)
- Physical findings of hyperadrenocorticism (*p. 270*)

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV and TS.** PCV may be low with anemia of renal failure, or normal-to increased if the patient is dehydrated. TS may be normal-to increased depending on state of hydration, or decreased depending on the underlying problem (e.g., diarrhea, peritonitis).
- **Serum electrolytes** are important to identify hypokalemia and other associated electrolyte disturbances. K^+ <3.0 mEq/L may lead to muscle weakness. As the K^+ decreases further, manifestations of the above clinical signs progressively worsen. **Hyperaldosteronism** will result in hypokalemia and hypernatremia. Dehydration may result in hypernatremia and normal K^+. **Hypomagnesemia** may also result in hypokalemia.
- **Venous blood gases** are useful in identifying the metabolic status of the patient and to evaluate the association of hypokalemia with an acid-base disorder. If the patient is acidemic (base deficit >4, pH <7.35), the serum K^+ will increase with intracellular H^+ shift but K^+ may still be low or normal due to the underlying problem, or normal. The K^+ will decrease as acidosis improves. Alkalosis may be associated with hypokalemia. The alkalosis may not resolve until hypokalemia is treated (*see Acid-Base p. 406*).
- **Glucose** is increased with diabetes mellitus and DKA. May also be increased as a stress response, especially in cats.
- Stick **BUN, or creatinine** will ascertain whether renal failure may be the etiology of polyuria in cats.
- **ECG** should be performed to identify any associated cardiac arrhythmias (e.g., *supraventricular p. 170, ventricular p. 179*).

Extended Laboratory Data Base

- **Biochemical profile** is necessary to identify other organ dysfunction. Serum creatinine will confirm degree of renal failure, elevated creatine phosphokinase is associated with hypokalmic polymyopathy; increased ALP may indicate hyperadrenocorticism.
- **CBC** will identify degree of anemia and identify the presence of leukocytosis and underlying infection.
- **Diagnostic imaging** is not generally useful, but is of value in identifying certain underlying problems.
- **Fractional Excretion of Potassium (FE_k) (spot check) U = Urine, P = Plasma.**
  $[(U_{potassium}/P_{potassium}) \times P_{creatinine}/U_{creatinine}] \times 100$ if > 4–6% indicates excessive renal losses

  Note: When SI units are used, the urine creatinine should be reported in μmol/L.

MANAGEMENT

A. Potassium supplementation of intravenous fluids (delivered at maintenance rate)
A maximum of 80mEq/L is recommended due to increased osmolality.

Serum Potassium (mEq/L)	Total mEq KCl required per 1L fluid K^+ content of fluid must be factored in
3.5 – 5.5	20
3.0 – 3.5	30
2.5 – 3.0	40
2.0 – 2.5	60
<2.0	80

When adding K^+ to the fluid bag, **hold the 'spiked' area of the bag closed** to avoid some getting into the drip chamber prior to mixing well in the bag.

DO NOT ADMINISTER K^+ AT A RATE FASTER THAN 0.5 mEq/kg/h UNLESS CRITICAL (i.e., serum K^+ <3.0 mEq/L when correcting acidemia or ≤ 2.7 mEq/L otherwise). Under careful supervision, K^+ can be delivered at 1.0 mEq/kg/h, especially when severe hypokalemia and acidemia are being concurrently corrected. In the author's experience, a four-hour infusion of 1.0 mEq/kg/h is usually adequate at this dose to raise K^+ to the lower limits of normal. Re-check K^+ at this time. Continue if necessary, re-checking in 2 – 4 hours depending on the level reached. **At 0.5 – 1.0 mEq/kg/h the concentration of K^+ in the fluids is very high** as is the osmolality. Pain on adminstration has not been noted by the author at this concentration but may be noted at higher concentrations. Administration through a central line will reduce the discomfort. ECG monitoring is essential during high K^+ infusions. Tachycardia may precede spiked T waves and bradycardia.

B. Occasionally a **cat** that is dehydrated and being volume expanded will become severely hypokalemic despite addition of K^+ to IV fluids. These cats must be volume expanded slowly, at least over 24 hours (unless in shock), to minimize the potential worsening of the hypokalemia.

C. **Potassium supplementation via the Enteral route.** Where serum K^+ is <3.0 mEq/L, and the patient can take oral fluids, give oral K^+ [Potassium gluconate diluted 1:1 with water or Kaon elixir (20 mEq/15 mL)] divided over 12 hours while receiving maintenance IV fluids. Volume expansion should be completed over the following 12 hours.

1. Ideally, a nasoesophageal (NE) feeding tube (*see Nutritional Support p. 508*) is placed and the fluid deficit can be given with the K^+ supplementation via the enteral route. Plasma-Lyte® 56 (13 mEq/L K^+ in the bag but an additional 10 mEq/L may be added), lactated Ringer's or Plasma-Lyte® 148 can be delivered via the NE tube at an hourly rate with additional 10 – 20 mEq/L K^+ added. CAUTION: Iatrogenic hyperkalemia can occur with K^+ administration via the oral route, therefore, supplemenation via the oral route requires careful assessment and calculation. Recommendations for K^+ supplementation:
2. **Acute rescue:** 5 – 10 mEq/cat/day divided q8h.
3. **Sub-acute rescue:** 3 – 8 mEq/cat/day divided q8h.
4. **Maintenance:** 2 – 4 mEq/cat/day divided q8h.
5. It is important to **note the K^+ content of all fluids** being administered when calculating requirements.

D. **Cardiac arrhythmias** may be maintained by low K^+ levels. Addition of K^+ to maintenance fluids may enhance recovery. Addition of K^+ should be reduced if magnesium (*p. 403*) is also added.

E. Frequently, hypokalemia may not resolve unless hypomagnesemia is resolved (*see Magnesium p. 403*).

HYPERKALEMIA

DIAGNOSIS

History/Signalment

- Question the owner regarding oliguric/anuric renal failure (*see p. 709*), or urethral obstruction or, ruptured bladder (*see p. 727*) as these are the most common problems associated with severe hyperkalemia.
- Massive **tissue breakdown** due to extensive trauma or snakebites, or **heat stroke, severe exercise** (transient) and hypothermia cause release of K^+.
- Reperfusion of thrombosed areas (i.e., cats with thromboembolic disease) increase K^+ significantly.
- Question owner regarding aspects of the differential diagnoses below, and recent medications (e.g., prostaglandin inhibitors [Non-steroidal anti-inflammatory analgesics], beta blockers, ACE inhibitors, potassium-sparing diuretics spironolactone, triamterene and amiloride).
- Question owner regarding diet as an increased intake of K^+ in renal insufficiency may cause hyperkalemia.
- Direct questions towards hypoadrenocorticism, GI disease due to Trichuris, salmonellosis, perforated duodenal ulcer. Each lead to hyperkalemia-hyponatremia (Na-to-K <27:1).
- In diabetes mellitus and hyperosmolality total body potassium may be normal or low (*see DKA p. 263*).

- **If in hospital,**
  - **Consider heparin** therapy as a cause as heparin reduces aldosterone secretion and may cause hyperkalemia.
  - **Reperfusion** of ischemic areas, especially after **thrombolysis** therapy
- Consider causes of **PSEUDOHYPERKALEMIA** secondary to thrombocytosis where K^+ leaks into the serum from platelets. This can also occur if blood for K^+ measurement was collected in EDTA. **Akitas and Shiba Inu** with thrombocytosis and hemolysis have increased K^+ due to leakage into serum from platelets and red blood cells.
- Massive **tissue breakdown** due to extensive trauma or snakebites, or **heat stroke** and **severe exercise** (transient) and release of K^+.
- **Chylous effusion** with frequent drainage may result in hyperkalemia.
- Recent **chemotherapy** may lead to acute tumour lysis syndrome (K^+ leakage from cells) with renal insufficiency (reduced excretion of K^+).
- **Iatrogenic** administration of K^+ either over-dosing or inadequate mixing of K^+ added to fluids.

Clinical Signs/Physical Examination

- Severe hyperkalemic patients are moribund, and suffering from circulatory collapse, and is most commonly associated with abnormalities of the urinary system.
- Bradycardia or irregular rhythm may be detected on physical examination.
- Hyperkalemia may cause muscle weakness or periodic paralysis.

Laboratory Evaluation/Diagnostic Imaging

Stat

- Based on history and physical findings, serum electrolytes must be performed. **Life-threatening hyperkalemia (>8 mEq/L),** and serum potassium **>6.5 mEq/L** should be treated promptly; while those between 5.5 – 6.5 mEq/L may not require immediate treatment. The underlying cause of hyperkalemia should always be sought and treated. Fluid depleted states, third space losses and primary hypoadrenocorticism usually results in hyperkalemia and hyponatremia. Normally, serum (red top tube) K^+ concentrations exceed plasma (purple top tube) concentrations because K^+ is released from platelets during the clotting process.
- **Venous blood gases** are required to assess metabolic status. Frequently, metabolic acidosis results in an increased K^+; the degree to which is variable.
- **Blood glucose** is necessary to assess baseline glucose prior to dextrose/insulin or sodium bicarbonate therapy. See Management A & D.
- **BUN, urea, creatinine** is increased in renal failure and renal obstruction. Oliguria/anuria result in hyperkalemia which is the most common presenting problem.
- **PCV and TS** may be increased in dehydration or PCV may be decreased in anemia of renal failure. TS may be decreased in third space losses (e.g., peritonitis) and may be associated with uroperitoneum.
- **ECG findings.** Loss of P waves, spiked T waves, shortened Q-T interval are classical findings of hyperkalemia; however, in early acute hyperkalemia, tachycardia may be noted. Often there may be no ECG abnormalities even though the K^+ may be markedly increased. Hyperkalemia cannot be ruled out on ECG findings alone. Wide-complex tachycardia as well as ventricular tachycardia may be present. **DO NOT USE LIDOCAINE TO TREAT THESE** as ventricular fibrillation or asystole may result. *See Pharmacology of lidocaine below.*

Extended Laboratory Data Base/Diagnostic Imaging

- Biochemical profile and hematology directed toward identifying the underlying etiology of hyperkalemia.
- Radiographic imaging based on physical findings and differential diagnoses, especially with trauma to the urinary tract.

MANAGEMENT

A. **Life-threatening hyperkalemia.** Potassium >8mEq/L with severe cardiac arrhythmia: Do not use antiarrhythmic drugs prior to lowering the potassium.
   1. Discontinue all medications that may contribute to hyperkalemia.
   2. Obtain IV access if not already present.
   3. Rapid infusion of crystalloid fluids (1.5 – 2.0 mL/kg/min to effect) if circulatory collapse. (*See Urethral Obstruction p. 745*) for guidance if this is the cause of the hyperkalemia). Lower rates to be administered based on clinical findings, especially geriatric and cardiac insufficiency patients (*see Fluid Therapy p. 347*).

a. 0.9% saline is an **acidifying solution** and is recommended for **alkalemic patients.** It is also a potassium-free solution.

b. Plasma-Lyte® 148 or A, Normosol® R, OR lactated Ringer's are **alkalinizing solutions** and will facilitate translocation of potassium intracellularly and enhance urinary excretion. Although potassium-containing (4 mEq/L) they will have a dilutional effect. As most hyperkalemic patients are acidemic, an alkalinization solution is appropriate. The author has used Plasma-Lyte® 148 and A resulting in a reduction in potassium.

4. Administer **10% calcium gluconate 50 – 100 mg/kg (0.5 – 1.0 mL/kg) IV over 2 – 5** min with continuous ECG evaluation. This will decrease the membrane threshold potential for approximately 20 min. Avoiding a fatal arrhythmia until the K^+ is lowered by **5 below.** Stop the infusion should an arrhythmia appear.

5. It is the author's preference to follow the **dextrose/insulin protocol.** Blood glucose must be obtained prior to therapy.
   a. **Regular insulin 0.25 – 0.5 U/kg IV plus 1 – 2 g dextrose (4 mL of 50% dextrose) per unit of insulin administered.** Dilute dextrose 1:1 in sterile water or 0.45% saline and administer one-quarter, then administer regular insulin, continue with remainder of dextrose. Establish a 2.5% dextrose (50 mL of 50% dextrose/L of administered fluids) CRI. Monitor blood glucose and K^+ (q1 h) initially, for several hours after administration of the insulin to avoid hypoglycemia. Should hyperglycemia persist and K^+ still increased, repeat low insulin dose. If K^+ normalizing, and not hypoglycemic, reduce dextrose infusion. Frequency and duration of monitoring is patient dependent.
   b. **B1 below** is an alternative approach.

B. Hyperkalemia with cardiac arrhythmia but not critical

1. **Potassium 6.5 mEq/L≤ 8 mEq/L**
   a. **50% Dextrose IV 1.0 – 2.0 mL/kg,** dilute as 5a above in small patients, **slow push over** 10 min to effect.
   OR
   b. **5 – 10% dextrose** (100 or 200 mL of 50% dextrose/L fluids) CRI. Not suitable for diabetics.
2. **Potassium 5 mEq/L≤ 6.5 mEq/L**
   a. IV crystalloid alkalinizing solution at a rate appropriate for the clinical findings and underlying etiology (*see Fluid Therapy p. 347*).

C. Hyperkalemia without clinical signs or cardiac arrhythmia

1. Potassium **5 mEq/L≤ 6.5 mEq/L**
   a. IV crystalloid alkalinizing solution at a rate and type appropriate for the clinical findings and underlying etiology (*see Fluid Therapy p. 347*).

D. For all patients, CONSIDER:

a. **Sodium bicarbonate** if venous pH <7.2 or adjusted base excess > -12 (base deficit >12), or if HCO_3^- or total CO_2 <12 mmol/L. (Note: Total CO_2 levels may be low if tubes are transported or allowed to sit open prior to test). **Contraindicated** if encephalopathic, liver disease or if hyperosmolar [*see b below*]). Do not administer with calcium gluconate.
   i. Calculated dose:
       HCO_3^- (mmol/L[mEq/L]) = body weight (kg) x (12 – patient HCO_3^-) x 0.3.
   ii. Empirical dose: $HCO_3^- = 0.5 – 2.0$ mEq/kg.
b. Measure or calculate **serum osmolality** (mOsm/kg) prior to administration of $NaHCO_3$ or dextrose:
   i.   mmol/L: [1.86 (2Na^+ + K^+)] + glucose + urea], OR
   ii. mg/dL: 2[Na^+] + [glucose (mg/dL)]/ 18 + BUN (mg/dL)/2.8 (results in mmol/L).
   iii. If >320 mmol/L in dog (normal 290 – 310) or >330 mmol/L in the cat (290 – 330) in euvolemic animals, refrain from using $NaHCO_3$ or dextrose unless absolutely necessary. If still dehydrated, increase the fluid rate. This is necesary to avoid the hyperosmolar syndrome.
c. Administer **half** $NaHCO_3$ over 5 min (monitor ECG and pulses for ventricular arrhythmias and pulse deficits) and reassess, repeat if necessary over 10 minutes to effect.

E. **Furosemide 2 – 4 mg/kg** may be considered where applicable (non-obstructive anuria, oliguria, fluid overload) as this enhances potassium excretion.

F. If not successful with any of the above, consider **peritoneal dialysis** *p. 723* in those with reversible disease.

G. Treat underlying disease.

H. Serum potassium should be monitored at least q2h initially to evaluate therapy. If trending in the right direction, this can be reduced to q4h and then to q6h.

I. Where possible measure **venous blood gases** and pH; attempt to maintain venous pH 7.35 – 7.4 or total CO_2 18 – 30 mmol/L (dog), 14 – 26 (cat) as alkalemia and acidemia should be avoided.

J. Monitor **blood glucose** if the dextrose protocol is used.

K. Monitor **urine production** and calculate fluid 'in' and urine 'out' to avoid dehydration or overhydration (*see Acute Renal Failure p. 709*).

PHARMACOLOGY

1) **Dextrose** stimulates insulin secretion which promotes the intracellular shift of glucose and potassium thus reducing the serum potassium level.

2) **Insulin** administration will promote glucose shift without having to rely on endogenous secretion of insulin.

3) **Sodium bicarbonate** should only be used in acidemic states. With low serum pH, hydrogen ions translocate intracellular in exchange for potassium (and sodium) in an attempt to minimize acidemia. Sodium bicarbonate will raise the pH of blood facilitating the opposite action. Careful monitoring of acid-base status is required with sodium bicarbonate administration.

4) **Calcium gluconate** will antagonize the membrane effects of potassium by increasing the threshold potential reducing the potential for fatal arrhythmias.

5) **Lidocaine** is contraindicated in treatment of potassium induced wide-complex and ventricular tachycardia because hyperkalemia potentiates the sodium channel blocking effect of lidocaine, and therefore, the combination of hyperkalemia and lidocaine can produce severe depression of conduction and asystole.

SUGGESTED READING

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NOTES

INTRODUCTION

In critical injury and illness assessment of perfusion and oxygen delivery is extremely important. Blood lactate concentration, as a measure of lactic acidosis, is a very good indicator of degree of systemic hypoperfusion and tissue hypoxia. Lactate rises proportionally to the severity of hypoperfusion and severity of illness in dogs, and presumably, cats. However, reversibility of tissue injury cannot be predicted based on level of blood lactate as patients with extremely high levels of lactate have been successfully resuscitated. Values above normal (2.5 mmol/L in dogs and 1.4 mmol/L in cats) in association with hypoperfusion should prompt the clinician to pursue aggressive management to restore tissue perfusion (*see Fluid Therapy p. 347, Shock p. 603, Hemorrhage p. 619, Sepsis/Septic Shock p. 588, Congestive Heart Failure p. 149*). Trending lactate concentration also provides a guide for ongoing therapy. Where appropriate therapy is pursued, trending lactate concentration will reveal those patients unlikely to recover. In a recent, as yet unpublished retrospective pilot study, mortality was 97% where eulactatemia was not achieved (Dez Hughes personal communication). Serum lactate concentration has been shown to be predictive of survival in dogs with gastric dilatation volvulus, where 99% of dogs with plasma lactate concentration <6.0 mmol/L survived, compared with 58% dogs with plasma lactate concentration >6.0 mmol/L; median plasma lactate concentration in dogs with gastric necrosis was 6.6 mmol/L compared to 3.3 mmol/L in dogs without gastric necrosis. Similar findings were associated with groups of dogs in an intensive care unit, dogs with heartworm caval syndrome, and in horses with acute abdominal crises. Lactate concentrations have also been used by the author to assess re-perfusion of limbs in cases of feline and canine thromboembolic disease.

TABLE 1. Causes of Lactic Acidosis

TYPE A (clinical evidence of absolute or relative tissue hypoxia)	TYPE B (no clinical evidence of tissue hypoxia)
Shock (systemic hypoperfusion) Hypovolemic Cardiogenic Septic	**B₁ (in association with an underlying disease)** Diabetes mellitus Severe liver disease Malignancy Sepsis Pheochromocytoma Thiamine deficiency
Local hypoperfusion Gastric necrosis and other causes of splanchnic ischemia Aortic thromboembolism	
Other causes of tissue hypoxia Severe hypoxemia ($P_aO_2 < 30 – 40$ mmHg) Severe euvolemic anemia (packed cell volume <15%) Carbon monoxide toxicity Severe asthma	**B₂ (due to drugs or toxins)** Acetaminophen Cyanide Epinephrine Insulin Ethanol Ethylene glycol Methanol Propylene glycol Morphine Nitroprusside Salicylates Terbutaline Sorbitol Xylitol
Increased glycolysis Excessive muscular activity Exercise Trembling Seizures	
	B₃ (due to congenital metabolic defects) Mitochondrial myopathy **Miscellaneous** Alkalosis/hyperventilation Hypoglycemia

Personal communication Dez Hughs, Royal Veterinary College, London, England.

Lactic acid, $CH_3CH(OH)COOH$, is a strong acid that, at physiological pH, is almost completely ionized to lactate, $CH_3CH(OH)COO^-$, and H^+. Elevated blood lactate concentration is termed hyperlactatemia, however, this may or may not be associated with acidemia (blood pH lower than 7.35) depending upon buffer reserves and concurrent acid/base disturbances. Lactic acidosis is a situation where lactate production exceeds lactate clearance, i.e., a state where lactic acid causes a fall in pH. Lactic acidemia refers to an acidemic blood pH and increased lactate levels. A plasma lactate concentration over 5 mmol/L is usually associated with acidemia. Lactic acidosis is divided into two categories; type A, which is associated with clinical signs associated with hypoperfusion and subsequent reduction in oxygen delivery to the tissues, and type B which may be unassociated with hypoperfusion (Table 1). The distinction therefore, is based on the absence or presence of clinical evidence of inadequate oxygen delivery to tissues (Table 1). **Type A lactic acidosis,** with reduced oxygen delivery such as that occurring in shock, is the predominant form of lactic acidosis in veterinary patients, rather than increased demand such as that occurring during excessive motor activity for example. However, occult or clinical evidence of hypoperfusion may still exist in type B lactic acidosis which requires the same attention as the type A. Once hypoxia is reversed, lactic acidosis is corrected. Therefore, sodium bicarbonate should not be administrered to correct lactic acidosis as correction of hypoperfusion reverses the acidosis. **Type B lactic acidosis** associated with conditions listed in Table 1 remains largely **undocumented in veterinary medicine.** However, lymphoma in dogs is associated with elevated resting lactate levels and a mild increase in hyperlactataemia may occur following a glucose challenge. Hyperlactataemia following intravenous fluid therapy with lactate-containing crystalloids has also been reported in dogs with lymphoma.

Hyperlactatemia must be considered in association with the patient's clinical picture as hypoperfusion does not always have to be the primary cause. Because glycolysis can proceed more rapidly than the oxidation of pyruvate, hyperlactataemia can occur in the absence of tissue hypoxia when glycolysis and lactate production are increased (e.g., alkalosis, glucose infusion, and sepsis without hypoperfusion). **Hyperlactataemia also occurs due to relative, rather than absolute, tissue hypoxia when energy requirements exceed the capacity of aerobic metabolism.** Exercising greyhounds may generate lactate levels of 30 mmol/L and a trembling or seizing patient may generate levels up to 8 mmol/L. **Lactate levels revert to normal within 30 minutes in these patients. Hyperlactataemia from tissue hypoxia can occur due to severe reductions in arterial oxygen content, such as in patients with severe pulmonary disease or anemia, or rarely due to cellular inability to utilize oxygen.**

Lactic acidosis due to hemorrhage or other fluid losses, when timely and appropriately treated, is reversible. **Lactic acidosis associated with cardiac disease may not respond as rapidly if correction of the underlying disease is poorly responsive resulting in continual poor cardiac output. Septic shock patients may have lower lactate levels than those with hemorrhagic shock, even though generation is as high** or higher, as initially hepatic perfusion may be better in the septic patient and therefore lactate elimination (utilization) is faster. However, with severe hepatic dysfunction that may occur in severe sepsis, the liver becomes a net producer of lactate. Also, while the septic patient may respond well to fluid resuscitation and perfusion is improved, there may be a tendency for lactate levels to remain high or trend down more slowly than a patient with hemorrhage. This is due to a hypermetabolic state seen with sepsis, usually associated with muscle metabolism and increased glycolysis and pyruvate production. In this instance lactate levels may be mildly increased, however where hypoperfusion still exists, hyperlactatemia is much higher. The clinical evaluation will identify those patients requiring further resuscitation. **Trending the lactate concentration and clinical signs will be of great value in assessing the success of recovery of adequate perfusion. In dogs, clinical experience suggests that mild systemic hypoperfusion is associated with a plasma lactate concentration of 3 – 5 mmol/L, moderate hypoperfusion with a lactate of 5 – 7 mmol/L, and in severe hypoperfusion, lactate levels exceed 7 mmol/L. As normal values for lactate are <1.5 mmol/L in cats, similar extrapolation, but with lower values than those in dogs may be used.**

Lactate quantitation in **fluids other than blood may be useful as a predictor of bacterial infection, as an indicator of a successful response to antibiotic therapy, and as a means of assessing the degree of tissue injury and therefore prognosis. Abdominal fluid lactate concentration in dogs and cats with bacterial peritonitis was 8.4 ± 4.2 mmol/L compared to 4.2 ± 2.9 in non-bacterial causes of abdominal effusion.** The gradient between venous and abdominal fluid lactate concentration may be a more accurate predictor of bacterial peritonitis than the absolute concentration with lactate values being higher in abdominal fluid when compared to the venous values (*see Acute Abdomen p. 21*). The converse is true for glucose where levels are higher in venous blood compared to abdominal effusion. Lactate concentration in cerebrospinal fluid has been used in people to detect bacterial meningitis and correlates with the severity of central nervous system damage and prognosis. Similarly, synovial fluid lactate concentration may also be helpful in the diagnosis of bacterial arthritis.

Blood sampling site, arterial vs venous, is of no consequence. Frequently, venous samples are obtained. Blood samples with a normal plasma lactate concentration held on ice, or plasma or serum samples separated from red blood cells kept at room temperature, no major elevation of lactate concentration was noted if the sample was analyzed within half an hour. However, **blood samples kept at room temperature, the lactate concentration increases by approximately 0.2**

mmol/L after 30 minutes, mainly due to glycolytic activity in red blood cells. However, to avoid **pseudohyperlactatemia** the following is recommended for **optimal** results:

1. Occlusion of the sampling site should be less than one minute during sampling to avoid an anaerobic environment.
2. Avoid air in the syringe as it may have an affect.
3. Waiting too long prior to test may increase lactate as glycolysis within red blood cells rapidly produces lactate, thus it is generally recommended that lactate in whole blood be measured within less than 5 min after collection. This would not apply to serum samples following rapid separation from red blood cells.
4. Other known interferents with the amperometric assay are oxyglobin and bromide.
5. Patient trembling prior to and during sampling may show an increase in lactate. However this is a 'true' increase but non-pathologic.

TREATMENT

Because hyperlactatemia is frequently a manifestation of an underlying disease process resulting in hypoperfusion, treatment comprises intravenous fluid resuscitation, and the diagnosis and correction of the specific cause. Aggressive intravenous fluid therapy using crystalloids, colloids, or blood products is usually necessary in the patient with lactic acidosis due to hypovolemia in the absence of cardiopulmonary disease. Maintaining a packed cell volume of >20% is suggested based on the effects of anemia on arterial oxygen content and hyperlactatemia. The use of intravenous sodium bicarbonate should only be considered in patients with severe hemodynamic compromise and acidosis (pH <7.10) that are refractory to intravenous volume loading and provided that pulmonary ventilation is adequate. Thiamine treatment may also be rational in the treatment of lactic acidosis because it is an essential cofactor in the oxidation of pyruvate.

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NOTES

INTRODUCTION

Magnesium participates in many intracellular biological functions; it serves as a **cofactor** for many intracellular enzymes such as those involved with generation and storage of energy, enzymatic processes involving DNA synthesis and transcription, nucleic acid polymerization, binding of ribosomes to RNA, phosphorylaton of glucose, and indirectly involved in mitochondrial oxidative metabolism; and **cell membrane enzymes** such as Na^+, K^+-ATPase. From these essential cellular functions, hypomagnesemia is of concern in critical illness. The majority of magnesium resides within bone and the cell with only ~2% of total body in extracellular fluid. With magnesium depletion, however, early changes are noted with a reduction in the extracellular concentration. In addition to decreased dietary intake, hypomagnesemia is due to losses and redistribution (Table 1). **Normal serum levels for cats and dogs 0.7 –1.2 mmol/L (1.8 – 3.0 mg/dL).**

HYPOMAGNESEMIA

TABLE 1. Causes of Magnesium Depletion

Losses	Redistribution
Gastrointestinal disorders	Pancreatitis
malabsorption syndromes	Hyperadrenergic states
extensive small bowel resection	Massive blood transfusion
inflammatory bowel disease	Acute insulin therapy
cholestatic liver disease	Refeeding
Renal losses	Acute administration of glucose and amino acids
glomerulonephritis	Hypothermia
acute tubular necrosis	Acute respiratory alkalosis
post-obstructive diuresis	Sepsis
diuretic-induced diuresis	Cardiopulmonary by-pass
nephrotoxic drugs	
Metabolic disorders	
hypercalcemia	
hypokalemia	
hypophosphatemia	
Endocrine disoders	
diabetes mellitus/ketoacidosis	
hyperthyroidism	
primary hyperparathyroidism	
hyperadrenocorticism	
inappropriate secretion of antidiuretic hormone	
Drug-induced SIADH	
Severe burns	
Heavy lactation	

Manifestations of magnesium depletion

Hypocalcemia has been observed in hypomagnesemic critically ill patients and hypocalcemia, such as that associated with eclampsia can be worsened with hypomagnesemia; seizures may occur in these patients. Frequently hypocalcemia cannot be corrected unless the hypomagnesemia is corrected. Refer to Hypocalcemia (*p. 377*) for clinical signs and therapy (in addition to magnesium), associated with hypocalcemia.

Hypokalemia is similarly observed in hypomagnesemic patients. Magnesium deficiency has been associated with loss of cellular potassium in many tissues due to impairment of cell membrane Na^+ K^+-ATPase enzyme regulation of potassium transport across cell membranes. Magnesium also has a direct effect on potassium channels and favours net inward movement of potassium. Hypomagnesemia may be suspected when potassium supplementation fails to correct hypokalemia. Magnesium supplementation is required to restore normal plasma concentrations of potassium. Refer to Hypokalemia (*p. 394*) for clinical signs and therapy (in addition to magnesium), associated with hypokalemia. However,

as both hypokalemia and hypomagnesemia have deleterious affects on electrical and mechanical cardiac function, co-morbid conditions, such as traumatic myocarditis, abnormal acid-base status, hypovolemia, and re-perfusion injury may predispose the patient to worsening of the cardiac arrhythmias and function. Hypomagnesemia has been associated with hypertension, coronary artery spasm and platelet aggregation.

Cardiac electrical changes associated with hypomagnesemia usually occur at serum concentrations ~ 0.35 mmol/L (0.8 mg/dL) with ECG changes of peaked T waves and mild ST segment depression, similar to that occuring with hypokalemia. Arrhythmias were not a major problem when hypomagnesemia was experimentally induced, however, premature beats occurred with serum magnesium concentrations of less than 0.4 mmol/L (1 mg/dL). In the clinical setting however, arrhythmias are maintained or worsened with low or low normal serum magnesium or potassium concentration.

Neuromuscular and nervous system signs associated with experimentally induced hypomagnesemia include hyperexcitability, restlessness, collapse, extensor rigidity, opisthotonus progressing to generalized tonic-clonic seizures. Respiration ceases during these episodes. Many dogs die at this stage. Magnesium decreases acetylcholine release from nerve terminals and depresses the excitability of nerve and muscle membranes. Neuromuscular signs may also develop with concurrent hypocalcemia, hypokalemia and hypomagnesemia. Interestingly, the spasms associated with **tetanus** may be managed with intravenous magnesium (*see Tetanus p. 486*).

INDICATIONS FOR MAGNESIUM TREATMENT

NOTE: When dosing is given in milligrams this is the dose of the salt (i.e., magnesium + sulphate) and not elemental magnesium. The mg/mL is the concentration of the salt in the vial which is used for dosing when mg/kg is used. Millimoles (mmole)/mL or milliequivalents (mEq)/mL noted on the vial, is the elemental magnesium which is used in dosing when these units are used. When a 20%, or 200 mg/mL (0.8 mmol or 1.6 mEq/mL) solution is used, and 30 mg is required, this = 0.15 mL.

A. **Cardiac arrest with ventricular fibrillation. If no response to defibrillation, give magnesium sulphate (≤ 200 mg/mL) 30 mg/kg (0.12 mmol/kg [0.25 mEq/kg])** with counter shock. **If countershock not** available magnesium 1 – 2 g total IV over 2 min has been recommended. **CAUTION:** if hypocalcemic administer **calcium chloride** 10% **0.1 – 0.3 mL/kg or calcium gluconate 10% 0.5 – 1.0 mL/kg** when magnesium is administered.

B. **Life-threatening cardiac arrhythmias** in cats or dogs 0.075 – 0.15 mmol/kg (20 – 40 mg/kg, 0.15 – 0.3 mEq/kg) **diluted to at least 20% (200 mg/mL), administered over 5 – 15 min** has been recommended but could result in severe hypocalcemia in a calcium-depleted patient.

C. Early administration of magnesium may prevent **ventricular tachycardia** (V tach) and the requirement for lidocaine therapy where serum magnesium concentrations are below normal and ventricular premature ventricular contractions (VPCs) are present at any rate. The dose is empirical, but current recommendations are **0.075 – 0.15 mmol/kg (20 – 40 mg/kg, 0.15 – 0.3 mEq/kg) diluted to at least 20% (200 mg/mL), administered over 2 – 4 hours in a burette with the hourly fluids.** Again, ensure serum calcium levels are normal. Serum calcium levels should be monitored in this setting. Magnesium may be repeated to a **maximum of 0.5 mmol/kg/day (125 mg/kg/day, 1 mEq/kg/day) as a CRI.** Do not expect to eliminate the V tach. A satisfactory reduction in heart rate is < 150/min. (lower if multiform V tach or continued poor pulse pressure). Magnesium sulfate should be **reduced by 50% – 75% if the patient is azotemic** after fluid resuscitation, as magnesium is cleared by the kidneys. **Excessive magnesium** administration will cause a diuresis and potential dehydration. **If V tach is non-responsive to magnesium sulfate,** try lidocaine.

C. **Supplemental magnesium** to a **maximum of 0.5 mmol/kg/day (125 mg/kg/day, 1 mEq/kg/day)** as a CRI in **hypomagnesemia** may be beneficial especially when **hypokalemia** is also present in the critically ill patient.

D. **Tetanus** patients may have a reduced requirement for sedation and neuromuscular junction blockade with magnesium supplementation (*see Tetanus p. 486*).

E. **Acute severe asthma** inhaled magnesium appears to have benefit in human patients.

F. **Monitor** deep tendon reflexes and systemic blood pressure, which are reduced with hypermagnesemia. ECG abnormalities include prolongation of the PR interval and QRS duration. Respiratory and CNS depression may also occur warranting ongoing assessment. Should abnormalities occur and magnesium overdose suspected, administer **calcium gluconate 10% 0.5 – 1.0 mL/kg or calcium chloride 10% 0.15 – 0.5 mL slowly IV** until adverse effects are reversed. Monitor serum magnesium levels during therapy. Potentiation of muscle relaxants can occur.

HYPERMAGNESEMIA

Hypermagnesemia is rare in veterinary patients but may be associated with renal failure. Clinical signs potentially observed are those in F above. Hypermagnesemia is rarely suspected as a presenting sign but is detected on biochemical profile.

MANAGEMENT

Only treat if clinical signs are noted and of concern.

A. Discontinue magnesium supplementation.

B. If signs are severe (*see F above*)

1. Titrate **calcium gluconate 10% 0.5 – 1.0 mL/kg kg or calcium chloride 10% 0.15 – 0.5 mL slowly IV** until the patient improves.
2. Enhance renal excretion with 0.9% sodium chloride and furosemide 1 mg/kg.
3. Measure potassium levels as these will drop with diuretic therapy.

C. If magnesium is required for therapy of other problems (*e.g., Tetanus p. 486*), reinstitute at a lower dose.

PHARMACOLOGY

1) Elemental magnesium has an atomic weight of 24.32 mg = 1.0 mmole (2 mEq). The concentration of magnesium in a prepared solution is usually given as mg/mL, which is the total weight of the salt (e.g., magnesium sulphate or magnesium chloride) and not just elemental magnesium. Dosage in the literature, when given as mg/dL, indicates the dosage as the salt unless stated as that of elemental magnesium only. The content/mL is also given as mEq or mmole. Administration is recommended at no higher than a 20% solution, which is 200 mg/mL of the salt (magnesium sulphate or magnesium chloride).

2) **Magnesium infusion is compatible with** dextrose 5% in water, 0.9% sodium chloride and lactated Ringer's solution. Compatibility at the 'Y' site for gentamicin, cefazolin, metronidazole

3) **Magnesium is incompatible with** fat emulsions 10% w/v, amphotericin, calcium gluconate, cefepime, ciprofloxacin, clindamycin, cyclosporin, dobutamine, hydrocortisone sodium phosphate, polymyxin, procaine, potassium phosphate, sodium phosphate.

4) **Administration.** Dilute in 500 to 1000 mL. Maximum concentration 200 mg per 1 mL.

5) **Adverse Effects.** Hypotension, bradycardia, depression of reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac function depression, CNS depression, respiratory depression or paralysis. Administration of 0.06 mmol/kg/min (0.12 mEq/kg/min) caused hemodynamic alterations after 0.1 mmol/kg/min (0.2 mEq/kg/min) and death when the cumulative dose exceeded 0.3 mmol/kg (5.9 mEq/kg).

6) **Precautions.** Monitor vital signs during bolus administration. Intravenous calcium should be readily available to reverse the respiratory depression or heart block caused by magnesium intoxication. Use with caution in patients with renal dysfunction.

7) **Contraindicated** in patients with heart block or myocardial damage, hepatitis or hypoadrenocorticism.

SUGGESTED READING

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NOTES

INTRODUCTION

The history and physical examination is an important part of the 'equation' when assessing the acid-base status of the patient. Many conditions are associated with alterations in the metabolic status of a patient, for example, diabetic ketoacidosis may result in profound acidosis, while upper gastrointestinal vomiting is frequently associated with alkalosis. Assessment of the acid-base status of a patient in the emergent and critical care setting is one of the most valuable tools a clinician can use to evaluate the severity of illness or injury, the pre- and post-operative condition of the patient, the success of therapy, to assist in diagnosis, to select and formulate the 'prescription' for fluid therapy, and to influence many other therapies, especially the delivery of electrolytes. As you review the remainder of this manual you will see how frequently the acid-base status of the patient is considered when directing therapy.

The *non-respiratory* (**metabolic**) status of patients can be derived from information that all clinics are able to obtain on a biochemical profile as a blood gas machine is not required for a 'ballpark' assessment. Abnormalities relating to the *non-respiratory* component is more common than the *respiratory* component of acid-base disorders in veterinary practice. To assess the *respiratory* component contributing to the acid-base status, and a more thorough evaluation of the *non-respiratory* component, $PaCO_2$ or $PvCO_2$ is required and therefore, a blood gas machine is necessary. In addition to a primary abnormality in either the *respiratory* or *non-respiratory* component, a secondary affect occurs as the body attempts to maintain a neutral pH so the *respiratory* and *non-respiratory* components will respond (change) to an abnormality in the other compartment to approach this neutrality. In addition, electrical neutrality has to be maintained and it is on this basis that one can use electrolytes and weak anions (plasma proteins, HCO_3^-, phosphate) to assess the acid-base disorder. Only the essentials will be presented here. The elements of the equations will be used to illustrate various aspects rather than the lengthy, but fascintating, physiological reasons for these alterations. As you can imagine the topic is a very complex one and you are referred to the suggested reading for more details. The values given here will vary from laboratory to laboratory and with different analyzers, as are published normals, but the information will be able to give a 'ballpark' assessment. As a day-to-day tool for assessing the patient's condition, a very simplified version is also presented that does not require a blood gas analyzer and is presented below. However, even if you do not possess a blood gas analyzer, the first part of the discussion will help in understanding the 'biochemical profile-only' approach.

The terms acidosis and alkalosis refer to the pathophysiologic process that causes a net accumulation of an acid or alkali in the body. The terms acidemia and alkalemia refer to to the pH of the blood. The patient would be acidemic (not acidotic) if the underlying problem resulted in acidosis due to H^+ gain or HCO_3^- loss.

Assessment of acid-base status using blood gas information

When assessing the acid-base status of the patient, venous blood gases are more commonly used as venous blood is easier to collect than arterial blood, and is a better reflection of the metabolic status of the body. As much of the earlier research was performed on arterial blood, normal values may differ by a small number, except PO_2 which is dramatically different between the two samples. Arterial blood gases are discussed in *Oxygen Supplementation p. 577*. First, identify if the patient is normal and if not, what is the primary disturbance? Is the patient acidemic (decreased pH of blood) or alkalemic (increased pH of blood), normal values ~ 7.33 – 7.38? If acidemic or alkalemic look at the $PvCO_2$ to see if it is within normal range, ~38 – 46 depending on sampling site. If pH is high and PCO_2 low, there is a respiratory alkalosis, if pH is low and PCO_2 high, there is a respiratory acidosis. If the base excess (BE) or adjusted base excess (ABE) is less than normal (0±4) i.e., has a negative value, or otherwise stated, a base deficit exists, and the pH is less than normal, there is a *non-respiraotry acidosis*; if the BE or ABE has a positive value, or a base excess, with a higher than normal pH, there is a *non-respiratory alkalosis*. The normal $[HCO_3^-]$ is 20±4, if higher with an increased pH then there is a *non-respiratory alkalosis*, if lower with a decreased pH, a *non-respiratory acidosis* is present. Where a high PCO_2 exists, the $[HCO_3^-]$ will be increased as CO_2 is carried as H_2CO_3 (i.e., increased CO_2 shifts the equilibrium to yield more HCO_3 and H^+). In this setting the pH is usually low with *respiratory* acidosis. A normal pH does not imply the patient is normal. As an example, a mixed acid-base picture may exist where a primary *respiratory alkalosis* will raise the pH of a patient with a *non-respiratory acidosis*, the two abnormal pH's average out to a normal pH, therefore, a pH within normal range requires further investigation to rule out a mixed acid-base disorder. When the abnormality is identified as *respiratory* or *non-respiratory*, identify whether the secondary response is appropriate. In this situation the pH is not normal but approaching normal. An example would be a patient with diabetic ketoacidosis $[HCO_3^-]$ is low due to an increase in unmeasured anions (ketoacids) and the PCO_2 is decreased via a hyperpneic respiratory pattern

(Kuhsmal) in an attempt to raise the blood pH. This secondary, or compensatory, response is a change in the PCO_2 in the same direction as the HCO_3^- is shifting i.e., when the pH is decreased in ***non-respiratory acidosis*** there is a 0.7 mmHg decrease in PCO_2 for each 1.0 mEq/L decrease in plasma $[HCO_3^-]$; or the converse when the pH is increased in ***non-respiratory alkalosis***. During ***respiratory acidosis***, the pH is decreased but the PCO_2 is increased; the HCO_3^- also increases, but by 0.15 mEq/L within 24h and 0.35 mEq/L >48h. In respiratory alkalosis the pH is increased but the PCO_2 is decreased and an appropriate response is a decrease in HCO_3^- by 0.25 mEq/L for each mmHg PCO_2 decrease. However, the HCO_3^- shift decreases by 0.55 mEq/L after 48 hours. The reason for the delayed response is that HCO_3^- shift requires renal excretion which commences within hours of the alteration in PCO_2 but may take up to 5 days (potentially longer) to be complete. Where the secondary response is appropriate, this is referred to as a ***simple disorder*** as it is limited to the primary abnormaltiy. However, more than one ***primary*** acid-base disorder may coexist and the pH may be normal or abnormal; this is a ***mixed disorder***.

A common situation is a sick animal with a ***non-respiratory acidosis*** but is anxious and panting resulting in a ***respiratory alkalosis***; here the pH may be normal, or increased if the anxiety and panting are severe. As an example of the effect hyperventilation may have on acid-base, this author recalls a healthy dog with a pH 7.55 due to a $PvCO_2$ of 19 mmHg and was obviously very stressed based on behaviour. Administration of 0.3 mg/kg acepromazine eased the anxiety resulting in a return towards a normal respiratory pattern and a subsequent rise in the $PvCO_2$ to 30 mmHg thus lowering the pH. A similar respiratory effect may be seen when a hypovolemic (***non-respiratory acidosis***) animal is tachypneic (***respiratory alkalosis***) as a normal response to low volume state. The pH may be normal but this is due to the low CO_2 (***respiratory alkalosis***) 'masking' the hypovolemic lactic acidosis. In this instance the ***mixed disorder*** is detected because the expected compensatory response to ***non-respiratory acidosis*** exceeds the magnitude of change expected for jusrt compensation. If the CO_2 had been normal, or increased then the magnitude of change for compensation would fall short of that expected indicating the presence of a ***primary respiratory acidosis***; respiratory depression (e.g., head injury) or lung injury (e.g., pulmonary contusions) should then be considered. It is important to identify the primary disorder as this influences treatment; again, history and physical examination should be considered in the evaluation. Where ***non-respiratory acidosis*** is detected, a balanced electrolyte (BES) alkalinizing solution should be selected. If this is associated with a ***primary respiratory alkalosis***, as could be present in the anxious, and the pH is normal or slightly increased, therapy to correct this primary disorder should be given (i.e., analgesia for pain, sedative for anxiety) and not treatment with 0.9% sodium chloride as an acidifying solution. Likewise, a ***non-respiratory alkalosis*** due to loss of chloride as a primary problem, with a ***primary respiratory acidosis*** i.e., drug-induced bradypnea, or over-zealous furosemide administration and associated hyponatremic neurological disorder lowering the pH, should not be given an alkalinizing solution as the sodium chloride deficit must be corrected to correct the ***primary non-respiratory disorder***.

While it has been said that a PO_2 value in a venous sample cannot be used to assess oxygenation, this is not entirely so. A PO_2 value <75 mmHg from a central (jugular vein catheter) suggests low oxygenation (i.e., inadequate oxygenation due to lung pathology or oxygen availability), or increased extraction (e.g., sepsis, inflammation). A jugular venous blood sample with a PO_2 value <30 mmHg, and saturation <50%, suggests a significant lack of oxygen. The history and physical examination will identify the primary problem causing this. In addition, one would expect to see a ***non-respiratory acidosis*** as the reduced oxygen delivery to tissues, or increased requirement, would cause a lactic acidosis. A primary or secondary (compensatory) ***respiratory alkalosis*** would accompany this finding if there was no lung pathology.

Blood gases are useful in identifying the acid-base disturbance as that resulting from a ***respiratory*** or ***metabolic (non-respiratory)*** problem, the secondary or compensatory response, and whether a mixed disturbance is present. The *traditional approach* to acid-base evaluation focuses on the relationship between pH, PCO_2 and HCO_3^- as described by Henderson-Hasselbalch equation where pH is shown to be a function of $[HCO_3^-]$ and PCO_2. The PCO_2 being the respiratory component determined by alveolar ventilation, and the $[HCO_3^-]$ being the non-respiratory component controlled by the kidneys. The implication is that both are independent variables, that is, their changes are not influenced by other aspects considered in acid-base assessment. In fact $[HCO_3^-]$ is dependent on many other aspects of acid-base balance i.e., a primary increase in PCO_2 results in H_2CO_3 (carbonic acid) which dissociates into H^+ and HCO_3^-; here HCO_3^- is dependent on PCO_2. Serum electrolytes and plasma proteins also contribute to alterations in acid-base status as their concentrations influence the $[HCO_3^-]$. The *non-traditional approach (Stewart's Theory)* where consideration is given to the maintenance of electrical neutrality (cations must equal anions), conservation of mass, and satisfaction of dissociation equilibria for incompletely dissociated solutes, also considers the role of electrolytes, the total concentration of weak acids (i.e., proteins, especially albumin and phosphates). With this information assessment of the ***non-respiratory*** acid-base status can be better differentiated with information from the biochemical profile. It should be understood that there is variation in data obtained from the different analyzers used, and the various normal values published so a definitive, or totally correct, answer may not be obtained in some cases. However, in most instances assessing the acid-base status of your patient will be helpful in case management.

Assessment of acid-base status using biochemical profile information

From a clinical standpoint it is important to ask: Is the patient acidemic or alkalemic? Is the pH within normal range? To answer these questions one needs to know the pH. However, this is not given specifically on a biochemical profile but can be elucidated. The question: is the acid-base status normal? can be answered using information from the biochemical profile. The anion gap [AG] equations (1) and (2) and the strong ion difference [SID] equations (3) and (4) will give us this information. Using this information and equation (5), the base excess can also be estimated using equation (6). Starting with the AG it is important to note, there is no 'gap' , this term represents anions that can (albumin- and inorganic phosphate-), and cannot (e.g., uremic toxins, ketoacids, ethylene glycol) be measured in the most part in pathologic states. As electroneutrality and mass have to be conserved the 'gap' represents unmeasured anion(s), and in humans has been estimated at approximately 2 x total protein (g/dL); however this is a crude estimate as the gap is greater in dogs due to the higher protein charge. From the biochemical profile; the total CO_2 ($tCO_2 = 13 - 24$ mmol/L) is a good estimate of the [HCO_3^-] for use in the formula below, while the Na^+, K^+, Cl^- are easily obtained. The low value here may be due to handling (*see Technical Aspects below*).

Equations 1 & 2 define a *non-respiratory* disorder due to an unmeasured anion imbalance.

1. **The AG** $= (Na^+ + K^+) - (Cl^- + HCO_3^-) = 12 - 24$ mEq/L in dogs and $13 - 27$ mEq/L in cats.
   As there are many other unmeasured anions, especially during illness or injury, the equation is better utilized by manipulation to:

   $(Na^+ + K^+ + $ Unmeasured Cations$) = (Cl^- + HCO_3^- + $ Unmeasured Anions$)$. As the change in UC (magnesium, calcium) would have to be small to be compatible with life, the equation is essentially:
   $Na^+ + K^+ = Cl^- + HCO_3^- + UA^-$, which is:

2. **UA-** $= (Na^+ + K^+) - (Cl^- + HCO_3^-)$.

When the patient's values (these are values for dogs, extrapolated to cats, as values are not available for cats) are plugged into this equation the UA^- (or gap) will be lower, higher or the same as the values given in equation (1) above. A low anion gap is very rare and is commonly associated with hypoalbuminemia (each decrease of 10 g/L [1 g/dL] in albumin is associated with a decreases of 4.1 mEq/L in the AG, whereas each decrease of 1 g/dL total protein is associated with a decrease of 2.5 mEq/L in AG which will be discussed later. The AG differentiates between hyperchloremic and high-AG metabolic acidosis (HCO_3^- is decreased in both situations). To maintain electrical neutrality, the decrease in HCO_3^- may be associated with an increase in Cl^-, which results in a normal AG, or an increase in UA, which results in a high AG. The increased UA^- contributes to acidosis as does the high Cl^-. Plasma [Cl^-] and [HCO_3^-] move in opposite directions in non-respiratory acidosis and alkalosis where UA^- are unchanged. For example, the mechanism for alkalosis following administration of furosemide or gastric vomiting, where Cl^- is lost, results in an increase in [HCO_3^-]. Sodium concentration tends to stay within normal limits in acid-base disorders, unless the primary problem also affects sodium. The cations rarely contribute to changes unless sodium is lost or gained in excess of Cl^-. This is where the SID comes in.

Equation 3 calculates the SID which defines a non-respiratory disorder due to an electrolyte imbalance.

3. **SID** $= (Na^+ + K^+ + Ca^{2+} Mg^{2+}) - Cl^-$ is referred to as the *apparent* SID. For clinical purposes this $SID_{app} = Na^+ - Cl^- = 32 - 40$ mEq/L (36 mEq/L frequently used).

   As the main components are Na+ and Cl- the difference ($Na^+ - Cl^-$) can be used as a clue to the problem.

   Obtaining the difference between the [Na^+] and [Cl^-] is useful in assessment of mixed disorders, or metabolic disturbances not associated with an increase in UA^-. Changes in [Na^+] occur with changes in water balance, contraction or dilution of the plasma volume. However, Cl- can change for reasons independent of water balance. To identify this and removing the water component, the correction for [Cl^-] must be made in conjunction with measurement of [Na^+].

4. **Dogs: [Cl]$_{corrected}$** $= [Cl^-_{patient}] \times 146/[Na^+_{patient}]$ and for **cats: [Cl]$_{corrected}$** $= [Cl^-_{patient}] \times 156/[Na^+_{patient}]$

   Normal [Na^+] for dogs is 146 mEq/L and for cats [Na^+] is 156 mEq/L. [Cl^-]$_{corrected}$ for dogs is $107 - 113$ mEq/L and for cats $117 - 123$ mEq/L. Where [Na^+] is normal and [Cl^-] is low, the SID is increased above 36 mEq/L representing a non-respiratory alkalosis; if the SID is decreased due to an increased [Cl^-], a non-respiratory acidosis exists. If the SID is normal, with normal [Na^+] and [Cl^-] and the AG is normal, the metabolic status

of the patient is normal; however, if the AG is increased, a non-respiratory acidosis is present due to UA$^-$. The UA$^-$ are likely lactate, ketoacids, sulfate, phosphate, or very rarely increased protein. Sometimes the SID can be normal because the [Na$^+$] and [Cl$^-$] are both low but the difference is still close to 36 mEq/L. This can occur in large volume, high gastric vomiting with loss of chloride and the effect of anti-diuretic hormone conserving water (volume) with dilution of sodium, or the patient drinking a lot of water. So looking at the SID alone may not help with assessing the acid base status if sodium is abnormal. However, when one looks at the AG equation, the Cl$^-$ will be low, and the HCO$_3^-$ may be reciprocally high (normal AG) (in the early stages) indicating a *non-respiratory alkalosis.* In this case 0.9% sodium chloride would be the fluid of choice to increase both Na$^+$ and Cl$^-$; the Cl$^-$ in this solution is in excess of Na$^+$ which would then replace the Cl$^-$ debt, reduce the [HCO$_3^-$] and correct the alkalosis.

While this is simplified into two categories either a problem with the SID or a problem with the AG, both may be used to identify a *mixed non-respiratory disorder.* Using our vomiting patient above, if the HCO$_3^-$ is lower than expected, the AG will be increased indicating an excess of UA$^-$ which would suggest lactic acidosis if the patient was hypovolemic/hypotensive due to fluid loss through vomitus (later stage). In this case 0.9% sodium chloride would still be indicated to replace the losses, but a larger volume of fluid would be required as there is indication of hypovolemia with perfusion deficits in this instance whereas the patient in the previous example may not require such a large volume of fluid as it is in the earlier stages of fluid losses.

If the SID is low the [Na$^+$] may be low due to losses in excess of Cl$^-$ such as in diarrhea. If the [Cl$^-$] is normal and volume loss is minimal the AG may be normal as a minimal drop in [HCO$_3^-$] may offset the low [Na$^+$] in the calculation. With large volume small bowel diarrhea, Na$^+$ and HCO$_3^-$ losses may be severe resulting in a hyperchloremic acidosis. If volume loss is enough to reduce perfusion, then the AG may be high due to lactic acidosis increasing the UA$^-$. This combination results in a severe non-respiratory acidosis. This situation may be managed by fluid selection (*see #7 in Selection of Fluid below*) and adding 5% sodium chloride at 0.5 – 1.0 mEq/kg/h. The SID may also be decreased due to an increase in [Cl$^-$] with normal [Na$^+$]. This may occur when 0.9% sodium chloride is used as the [Na$^+$] and [Cl$^-$] are equal, raising the serum [Cl$^-$] relative to [Na$^+$] resulting in a non-respiratory, normal AG, acidosis. The addition of potassium chloride (KCl) to intravenous fluids is routine. If a high [KCl] is required to maintain K$^+$ within normal range, the [Cl$^-$] can increase enough to cause a non-respiratory acidosis. Lowering the administered Cl$^-$ is necessary to correct the acidosis and this can be achieved by using potassium phosphate (this will have only a minimal effect on the anion gap) instead of potassium chloride.

Other changes in SID

Aside from changes in our typical calculated SID due to electrolyte abnormalities ([Na] + [K] – [Cl],) free water abnormalities also change the true SID. A deficit of free water will proportionally increase all strong cations and anions and therefore, SID (the so-called concentration alkalosis). SID increases 1 mEq/L for each 4 mEq/L (4.4 mEq/L in cats) increase in Na$^+$ concentration. Dilutional acidosis occurs during hyponatremia where a decrease in 4 mEq/L in sodium concentration is associated with a 1 mEq/L decrease in SID.

Plasma Proteins$^-$ and Phosphate$^-$ [A$_{TOT}$]

Plasma proteins$^-$ and phosphate$^-$ also influence the acid-base status as they are weak anions and are included in the UA$^-$ part of the equation where they are referred to as ATOT. Proteins- contribute a charge of approximately 12 (cats) or 16 (dogs) to the UA$^-$ part of the equation in normal individuals. As one can see from equations (1) and (2) as plasma proteins decrease, such as in hypoalbuminemia, which is quite common in really ill animals, the anions in the equation have to increase to maintain electrical neutrality. The [HCO$_3^-$] frequently increases causing a *non-respiratory alkalosis.* If hypoalbuminemia is accompanied by a situation that results in generation of UA$^-$ (i.e., lactate due to poor perfusion), then the AG could be unchanged, or increased (although not to the extent typically seen in situations of lactic acidosis where albumin is normal) if the UA$^-$ caused a reduction in [HCO$_3^-$] as it is used as a buffer. Hypoalbuminemia, therefore, can mask the severity of an acidosis. As other buffers, such as hemoglobin, can also buffer the UA-, a reduction in [HCO$_3^-$] may not occur early in the disease process. As phosphate is considered in the [A$_{TOT}$], **severe** hyperphosphatemia can cause a *non-respiratory acidosis* due to decrease in [HCO$_3^-$].

*To identify the **true base excess or deficit** and the existence of unmeasured anions, the changes in SID influence [A$_{TOT}$] must be considered.* **To calculate the change in [A$_{TOT}$], the following calculations can be used:**

5. **Other changes in [A$_{TOT}$]**

    Changes in the components of A$_{TOT}$ will impact the AG. A decrease of 10 g/L [1 g/dL] in albumin will increase AG roughly 4 mEq/L, whereas a change of 10 g/L [1 g/dL] in TP will change the AG, in the same direction, by 2.5 mEq/L. For example, if the TP is decreased by 20 g/L [2 g/dL], the AG is expected to be 5 mEq/L less than normal. If the AG is normal, this may represent an increase in UA$^-$ of 5 mEq/L. An increase in phosphate can also increase the AG (e.g., toxicity following the use of a hypertonic sodium phosphate enema in cats).

Since many patients with increased unmeasured strong anions also have hypoalbuminemia (typical of critical illness), the AG may be artificially normal because of the decrease in [UA⁻] resulting from hypoalbuminemia. The AG can be corrected for changes in protein concentration in dogs by using the following formulas.

$$AG_{Alb\text{-}adjusted} = AG + 4.2 \star (3.77 - [alb])$$

OR

$$AG_{TP\text{-}adjusted} = AG + 2.5 \star (6.37 - [TP])$$

where [alb] is albumin concentration in g/dL and [TP] is total protein concentration in g/dL.

Although contribution of phosphate concentration to the AG is negligible in normal dogs and cats, hyperphosphatemia can also increase the AG in the absence of an increase in strong unmeasured anions. The AG can be adjusted to increase in phosphate concentration by expressing phosphate in mEq/L and assuming plasma pH to be 7.4 as:

$$AG_{alb\text{-}phosph\text{-}adjusted} = AG + 4.2 \star (3.77 - [alb]) + (2.52 - 0.58 \star [Phosph])$$

OR

$$AG_{TP\text{-}phosph\text{-}adjusted} = AG + 0.25 \star (63.7 - [TP]) + (2.52 - 0.58 \star [Phosph])$$

where [Phosph] is the concentration of phosphorus in mg/dL.

6. **Base excess (BE)** can be crudely estimated by considering all the changes in the metabolic state discussed above using the equation:

BE = change in SID due to electrolyte abnormalities – change in AG (since a rise in AG is acidosis) + change in SID from free water abnormalities. Note that the change in AG accounts for protein abnormalities.

Selection of fluids to correct acid-base disturbances (*see Fluid Therapy p. 347*)

Crystalloids available are:

1. Balanced electrolyte solutions (BES), which are sodium based with a similar composition of electrolytes to that of plasma. Most have acetate + gluconate, or lactate as bicarbonate precursors and are therefore, alkalinizing solutions. These solutions are recommended for treating *non-respiratory acidosis*.
2. Sodium chloride (NaCl) 0.9%, which has 154 mEq/L Na⁺ and 154 mEq/L Cl⁻. This is an acidifying solution as the SID = 0 and an increase in Cl⁻ will require the loss of another anion, which is usually HCO_3^-. The administration of 0.9% sodium chloride has been reported to be a common reason for acidosis in humans as it is used as a standard treatment rather than specifically for treating *non-respiratory alkalosis*. The addition of KCl to fluids also increases the [Cl⁻], contributing to acidosis. 0.9% NaCl is recommended for treating *non-respiratory alkalosis* as both Na⁺ and Cl⁻ may be low, or the SID is increased due to hypochloremia.
3. Maintenance alkalinizing solutions contain 40 mEq/L Na⁺ and Cl⁻ and acetate + gluconate, with or without 5% dextrose. These may be used if a reduction in Cl⁻ is desired and an alkalinizing solution is indicated.
4. Half-strength of the BES solution (1:1 sterile water BES) may be administered as a substitute for (3) above if this is not available, or if 5% dextrose is not wanted.
5. Half-strength (0.45%) NaCl may be indicated in hypernatremia and water loss (*see Hyper/Hyponatremia p. 381/386*), or as a maintenance solution.
6. Most synthetic colloid solutions have a 0.9% NaCl base and are, therefore acidifying solutions.
7. Where a reduction in [Cl⁻] is required but supplementation with K⁺ is necessary, potassium phosphate may be used as a substitute for KCl. Volumes and rate of administration of the various fluids should also be considered in the fluid plan, as well as alterations in electrolytes, especially potassium, as acid-base status is improved (*see Fluid Therapy p. 347, Hypokalemia/Hyperkalemia p. 394/396*).

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INTRODUCTION

Immune-mediated hemolytic anemia (IMHA) results from antibodies binding to red cells. Hemolysis is most often extravascular, where red cells are destroyed by the mononuclear phagocyte system. Antibodies may be present in a sufficiently high titre to cause agglutination, or may be present in a lower titre that is detectable with a Coomb's test. Red cell autoantibodies may also fix complement, which will result in intravascular hemolysis. IMHA is the most common cause of hemolysis in dogs living in temperate and northern climates. It may be primary, or secondary to another disorder or treatment. When a cause cannot be found, IMHA is assumed to be primary. This is the most frequent diagnosis.

There are two broad forms of IMHA: the subacute to chronic form, where there is a slowly progressive history of inappetance and exercise intolerance; and initial treatment is on an out-patient basis using prednisone; and the acute to fulminant form which is the focus of this chapter. In the acute to fulminant form, the average mortality rate reported during first hospitalization from referral hospitals has been ≈ 55% for more than two decades. Negative prognostic indicators of variable strength include persistent agglutination during corticosteroid treatment, degree of leukocytosis, degree of thrombocytopenia, decreased albumin, degree of bilirubinemia, degree of elevation in ALT, prolonged clotting times, degree of polypnea, intravenous catheterization, use of cyclophosphamide and number and type of transfusions.

DIAGNOSIS

History/Signalment

- Acute onset of depression, inappetence, weakness, and exercise intolerance.
- Variable vomiting and diarrhea.
- Discoloured urine (bilirubinuria, hemoglobinuria).

Clinical Signs/Physical Examination

- Pale mucous membranes; jaundice is common.
- Tachycardia and prominent pulses; a heart murmur due to anemia may be present.
- Polypnea and, occasionally, dyspnea.
- Variable abdominal pain and fever.
- Petechiae and ecchymoses may be evident if there is concurrent immune-mediated thrombocytopenia (ITP).

Laboratory Evaluation/Diagnostic Imaging

The goals of work-up are to:
- Confirm the diagnosis and rule-out non-immune causes of acute hemolysis, i.e., hypophosphatemia (*see Diabetic Ketoacidosis p. 263, Hypophosphatemia p. 390*), poisoning (zinc, onion, garlic, acetaminophen), red cell infections (*Mycoplasma haemocanis* [haemobartonellosis], *Babesia* spp *p. 307*), hereditary red cell enzyme deficiencies (Springer Spaniels, Basenjis and black Miniature Poodles).
- Identify underlying causes of autoimmunity, i.e., inflammation/infection/parasitism, neoplasia, drugs (including vaccinations).
- Identify concurrent disorders of autoimmunity, i.e., glomerulonephritis, polyarthritis, dermatitis, vasculitis, ITP (*p. 451*).
- Identify consequences of hemolytic anemia, i.e., hypoxic hepatic necrosis *p. 37*, Pancreatitis *p. 45*, gastrointestinal ulceration *p. 67*, Acute Renal Failure *p. 709*, pulmonary thromboembolism (PTE) *p. 198*, Disseminated Intravascular Coagulation (DIC) *p. 417*.

Stat

Handle blood samples gently because of increased red cell fragility.
- **CBC.** As *Mycoplasma haemocanis* (previously *Haemobartonella canis*) may be a cause for anemia look for the organisms, which appear as individual or chains of small cocci, bacilli or rings, on the red cell surface. The diagnosis of IMHA is most commonly made on the basis of a CBC demonstrating a regenerative anemia and spherocytosis and/or agglutination.

- **Agglutination.** Gently mix equal volumes of EDTA blood and saline in a tube (this minimizes rouleaux formation) and observe for gross agglutination (blood is flocculent). If agglutination is not seen, place several drops of the mixture on a glass slide and gently rock the slide back and forth to observe for agglutination within 1 minute. (After several minutes rouleaux formation will increase on a glass slide as the sample dessicates.) It is **impossible** to distinguish rouleaux and agglutination macroscopically. In all cases place a coverslip on the slide and examine the wet-mount microscopically, especially if the diagnosis is based on the presence of agglutination. Preparing a wet-mount will also facilitate detection of microscopic agglutination. The common practice of simply observing a drop of whole blood on a glass slide for flocculence and dispersion of potential rouleaux by adding saline is discouraged. Rouleaux microscopically appear as **"stacks of coins"** and agglutination appears as **"clusters of grapes".** If it is not clear whether rouleaux or agglutination is present repeat using a 4% red cell suspension (*see Transfusion Therapy p. 672*).
  - Verify anemia as the cause of pale mucous membranes and characterize severity. Gross agglutination may interfere with automated red cell counts, so examine a microhematocrit tube to assess anemia. Severe gross agglutination may interfere with microhematocrit tube readings (frequently reading higher than the true value), so spin tubes for 10 minutes if serial microhematocrit tube values are inconsistent.
  - Regeneration (polychromasia, reticulocytes) should be present in most cases after 3 days. Occasionally the anemia is non-regenerative because of destruction of immature red cells in the bone marrow.
  - Evidence of red cell antibody on the stained blood film includes microscopic agglutination (rafting of red cells), spherocytes (resulting from extravascular hemolysis), and ghost red cells (resulting from intravascular hemolysis).
  - A neutrophilia with or without a left shift is common, due to stress, bone marrow stimulation and tissue necrosis. The higher the neutrophil count the more likely microthrombi are present. Other variable findings include thrombocytopenia (ITP, DIC), schistocytes (DIC), and rarely leukemia (underlying disorder).
- **Biochemical profile** is required to fully assess multiple organ effects. Urea and creatinine may be increased due to renal damage; ALT, ALP, lipase and amylase are frequently increased due to hypoxic/ischemic necrosis of liver or pancreas, respectively. Bilirubin is increased due to increased red cell destruction and hepatic dysfunction. Hypophosphatemia is a differential diagnosis for intravascular hemolysis. Phosphorous may be increased with cellular injury due to necrosis. Observe sample for hemoglobinemia. Check for interference by bilirubin and hemoglobin for methods used to measure serum chemistry parameters.
- **Venous blood gases** to assess severity of poor oxygen delivery to tissues, which results in a metabolic acidosis.
- **Serum electrolytes** may be altered and should be known to guide fluid therapy.
- **Coagulation.** The ACT and/or PT/PTT is required for baseline information prior to potential heparin therapy. May be prolonged if DIC is present.
- **Urinalysis.** The specific gravity, presence of casts (renal damage), bilirubinuria, hemoglobinuria (intravascular hemolysis), and proteinuria will reveal severity of disease and guide fluid therapy. The presence of white cells may suggests infection requiring culture and sensitivity.
- **Radiology**
  - **Abdomen.** Obtain if intravascular hemolysis is present; check for radiopaque material indicative of a penny or carrying kennel lug nut (zinc) (*see Toxicity, p. 641*).
  - **Thorax:** Obtain if dog is dyspneic; normal findings are supportive of PTE.

Extended Laboratory Data Base

The extent of work-up varies with the risk of the patient for underlying or complicating disorders.
- **Coomb's test** to identify red cell antibody if agglutination is absent. A negative Coomb's test does not rule-out IMHA. Flow cytometry is more sensitive but not as available.
- **Thoracic radiographs** to rule-out underlying infection or neoplasia.
- **Abdominal radiographs and ultrasonographic examination** to rule-out underlying infection or neoplasia. Note than hepatomegaly and splenomegaly are common with primary IMHA,
- **Serology** to rule-out heartworm, *Ehrlichia canis* and *Babesia* spp, infection
- **PCR to rule out** *M. haemocanis* infection.
- **Urine culture,** as therapeutic immunosuppression in the presence of a urinary tract infection may lead to sepsis.
- **Blood culture** if fever is present that is not attributable to hemolysis.
- **Serum zinc assay** if zinc toxicosis suspected.
- **Coagulation profile.** PT, PTT, fibrinogen level, fibrin degradation products, and D-dimer will help identify and characterize DIC. D-dimer is also elevated by PTE.
- **Bone marrow biopsy** if anemia is non-regenerative after 3 – 4 days, if other cell lines are depressed, or to rule-out hematopoietic neoplasia.
- **ECG** if arrhythmia detected (myocardial hypoxia, pancreatitis).
- **Arterial blood gases, D-dimer, non-selective angiocardiogram** and **pulmonary scintography** if PTE suspected on basis of dyspnea inappropriate for degree of anemia and/or changes on thoracic radiographs.

MANAGEMENT

A. Immunosuppression.

1. dexamethasone sodium phosphate 0.3 – 0.5 mg/kg IV q24h OR
2. prednisolone sodium succinate 2 – 4 mg/kg IV q24h (administered over 10 mins).
3. Do not initially use oral preparations in severe cases because of the risk for vomiting and impaired absorption due to gastrointestinal ischemia.
4. When **clinically stable** change therapy to **prednisone 2 mg/kg PO q24h** for a minimum of 2 weeks. An attempt may be made to taper corticosteroids after 2 – 6 weeks if the Hct is >0.35 L/L (35%). Typically the dose is reduced by 25% every 2 – 4 weeks, verifying that the Hct is stable. If chronic corticosteroid therapy is needed a target dose is 1 mg/kg PO q48h.
5. Where *Mycoplasma haemocanis* is identified, corticosteroids are only used in severely anemic animals and are tapered as soon as the PCV recovers (*see Antibiotics G below*).
6. NOTE: The high mortality rate has prompted the use of numerous other **drugs for additional immunosuppression,** few of which have proven benefit. Drugs include azathioprine, cyclophosphamide, chlorambucil, cyclosporine, danazole, human intravenous immunoglobulin, mycophenolate, or leflunomide. Various treatment practices include 1) use of one of these drugs in addition to corticosteroids as initial therapy in severe cases; 2) use in cases not responding sufficiently to treatment with corticosteroids; and 3) use in cases where corticosteroids cannot be tapered. The authors prefer **concurrent initial use** of

    a. **azathioprine 2 mg/kg PO q24h** in severe cases, followed by
    b. **cyclosporine 5 mg/kg PO q12h** for refractory cases.
    c. **aspirin 0.5 mg/kg PO q24h and azathioprine 1.4 – 2.2 mg/kg PO q24h,** resulted in a markedly improved survival rate of >80%, according to a recent preliminary report.
    d. **If concurrent ITP requires treatment, consider vincristine 0.5 mg/m² IV** (*see Thrombocytopenia p. 451*).

7. **Plasmapheresis** may be used to remove circulating autoantibodies, complement and products of hemolysis. It should be considered for cases with severe intravascular hemolysis, but is expensive and labour intensive and is restricted to hospitals with a large-capacity centrifuge or plasmapheresis machine.
8. **Splenectomy** is usually reserved for cases not well-controlled with immunosuppressive drugs, but may be considered in acute management if there is a poor response to corticosteroids.

B. **Intravenous fluids.** If the dog is drinking well and is well-hydrated, then intravenous fluids are not necessary. Initial fluid choice is Plasma-Lyte® A, Plasma-Lyte® 148, Normosol® R, lactated Ringer's solution, or equivalent. Replace estimated deficits over 12 hours followed by maintenance fluid rate. Caution is required when administering fluids (*see Pharmacology 2. below and Fluid Therapy p. 347*). A **jugular catheter** may be considered in more severe cases to facilitate fluid therapy and blood sampling. It is controversial whether intravenous (and especially jugular) catheters increase the risk of PTE. If a jugular catheter is used, heparin or aspirin should definitely be given.

C. **Thromboprophylaxis.** Historically **heparin** has been used most although benefit is unproven. The recommended dose is **150 units/kg SC q8h OR** a CRI of **12 – 15 U/kg/h.** The CRI is recommended when jugular catheters are in use. Monitor PTT or ACT before each SC heparin dose, or twice daily with the CRI. The goal of heparin therapy is to achieve an PTT or ACT of 1.5 – 2 times normal prior to the next dose. At OVC normal ACT (human axillary incubation) is 75 – 120 sec and the target value with heparin therapy is 150 – 180 sec. Taper slowly; do not stop abruptly. More recently **aspirin 0.5 mg/kg PO q24h** has been advocated (*see Ac above*). Heparin and aspirin at the above doses may be given concurrently.

D. **Oxygen therapy.** Indications are dyspnea, concurrent respiratory disease, pulse oxymeter value <95%, PaO$_2$ <90 mmHg, PCV <20.

E. **Monitor PCV/TS q8–12h.** Give **blood transfusion** with DEA 1.1/1.2 negative packed red cells (less than 12 days old) if PCV ≤ 12, or if PCV ≤ 18 with signs of tissue hypoxia (arrhythmia, elevated ALT/ALP, seizures), or moderate to severe depression. Transfuse to achieve PCV of 20 – 22 (*see Blood/Plasma Transfusion p. 667*). Give corticosteroids ideally at least 1h prior to transfusion in an effort to reduce destruction of transfused cells. If red cells are not available or in case of intravascular hemolysis, use **Oxyglobin** (if available) **10 mL/kg q24h in 3 mL/kg/h aliquots.** If the situation is emergent, higher rates may be used. Caution is required as hypervolemia (and resulting dyspnea) may occur.

F. **Gastrointestinal protectants: Famotidine 0.5 mg/kg IV q12h** (*see Gastrointestinal Hemorrhage p. 67 for additional drugs*).

G. **Antibiotics** are not routinely used. IMHA patients often are febrile with moderate to marked leukocytosis, therefore, these parameters alone should not be used to institute antibiotic therapy. Where *Mycoplasma haemocanis* is identified commence doxycycline 5 – 10 mg/kg PO, IV q12h. *See Pharmacology section (12) for specific indications.* Obtain blood cultures if sepsis suspected.

H. **Feed** only **low-fat foods** because of the risk for pancreatitis. Withhold food if vomiting.

I. **Monitor respiration** for dyspnea, a sign of PTE (*p. 198*) or pleural effusion (*p. 558*). Monitor central venous pressure if these are suspected.

J. Establish continuous **ECG monitoring** or frequently **auscultate the heart** in order to detect arrhythmias resulting from myocardial hypoxia. Treat arrhythmias as required (*see Ventricular p. 179 or Supraventicular Tachycardia p. 170*).

K. **Monitor urine** output for quantity, specific gravity, casts and hemoglobinuria, in order to detect renal failure and intravascular hemolysis, and to adjust fluid therapy.

L. **Monitor other clinical and laboratory abnormalities** as indicated by clinical status and initial abnormalities.

M. *See Chapters 9 Acute Moderate to Severe Pancreatitis and 101 Acute Renal Failure* which may complicate IMHA.

N. **Exercise restriction** upon discharge to reduce risks for PTE.

PHARMACOLOGY

1) The most important acute action of **corticosteroid** therapy in IMHA is impairment of extravascular hemolysis by macrophages. Corticosteroids also reduce antibody production, decrease antibody affinity for red cells, decrease the complement cascade, and increase reticulocytosis. It is not known if one corticosteroid is superior to another. Generally dexamethasone is used for injectable therapy, prednisone is used for oral therapy, and prednisolone may be used for both.

2) **Intravenous fluids** are used to support the microcirculation to reduce tissue hypoxia and as prophylaxis for DIC. Dilution of existing red cell mass will not aggravate hypoxia, however fluid rates should be conservative because dogs are at risk for pleural effusion, ascites, and subcutaneous edema because anemia activates mechanisms for water retention thus increasing the risk for volume overload, and there may be cytokine or vasculitis-associated capillary leakage (vasculopathy).

3) **Heparin** is given for its anticoagulant activity as treatment for DIC and PTE. Most of its anticoagulant effect is due to its effect on antithrombin. Heparin therapy should be tapered over several days to a week, which may involve owners injecting heparin SC at home, in order to prevent rebound hypercoagulability.

4) **Aspirin** impairs platelet function and at the low-dose advocated here (0.5 mg/kg PO q24h) does not increase the risk of gastrointestinal ulceration with concurrent use of corticosteroids. Improved survival associated with its use in IMHA may be due to other effects in addition to effects on platelet function.

5) **Transfusion** is given to improve oxygen carrying-capacity of the blood. There is theoretical concern that transfusion may "add fuel to the fire"; this must be balanced against the detrimental effects of tissue hypoxia. Red cell transfusion should be withheld for as long as possible in cases of intravascular hemolysis because of the devastating consequences of such hemolysis. Crossmatching in IMHA may be unrewarding because autoantibody may be directed against antigens present on most dogs' red cells, but should be attempted in an effort to identify the most compatible donor. Red cell transfusion will increase cardiac pre-load. **Oxyglobin®** (**Biopure**) is a solution of purified polymerized bovine hemoglobin. Its main benefits over blood is long shelf life, more-rapid oxygen delivery to needy tissues, and lack of substrate (red cell membrane) for immune destruction. Hemoglobin binds nitric oxide, a molecule responsible for vasodilation, therefore Oxyglobin treatment may promote vasoconstriction and increase cardiac afterload, but minimally so. Oxyglobin also contributes to plasma oncotic pressure with subsequent increase in intravascular volume. Slow administration is advised as many patients with IMHA are already hypervolemic and fluid overload must be prevented.

6) **Gastroprotectants:** *See Gastrointestinal Hemorrhage p. 67 for additional drugs.*

7) **Azathioprine, cyclophosphamide, and chlorambucil** are cytotoxic drugs that have various immunosuppressive effects. Azathioprine is an antimetabolite. The initial dose is 2 mg/kg q24h. The drug may be tapered in the same fashion as prednisone. Several retrospective studies support its use. Cyclophosphamide is an alkylating agent given IV/PO as 50 mg/m^2 every other day or 4 days on/3 days off, or as 200 mg/m^2 q2 weeks. It is not recommended because of studies demonstrating either no benefit or increased risk of mortality. Chlorambucil is another alkylating agent typically given at a doses ranging from 20 mg/m^2 to 1.4 mg/kg PO q2 weeks. Side-effects are minimal, especially at the lower dose, but it is likely to be as effective as cyclophosphamide. All cytotoxic drugs may cause myelosuppression, necessitating initial weekly to bi-weekly monitoring of CBCs, and may reduce reticulocytosis.

8) **Cyclosporine** impairs release of interleukin-2 and other cytokines from T-helper cells, ultimately suppressing cell-mediated immunity and antibody production. The initial dose is 5.0 mg/kg PO q12h. It has an unpleasant taste and dogs should be given some food after dosing. Obtain a trough (end of 12-hours and prior to next dose) blood level at six days of treatment (1 mL, purple top tube). Adjust the dose to aim for a trough level of 300 – 500 ng/mL using a whole blood monoclonal assay.

9) **Human intravenous immunoglobulin G** blocks macrophage Fc receptors and has other immunosuppressive effects, and is thus similar in action to corticosteroids. The dose is 0.5 – 1.5 g/kg IV over 12 hours. Anaphylaxis may occur, so if possible do not give it at the same time as a transfusion. If possible give prior to transfusion to help reduce destruction of transfused red cells. This drug may be cost-prohibitive and is not available in some areas. The drug was first introduced into veterinary medicine in chronic IMHA, and its use in fulminant IMHA has not shown a benefit in outcome.

10) **Danazole** is a modified androgen with several immunosuppressive effects, including modification of macrophage Fc receptors. It does not appear to have an immediate effect, it may be hepatotoxic, and results of retrospective studies do not support its use, therefore it is not recommended for acute management.

11) **Mycophenalate** and **leflunomide** are other antimetabolite-like drugs. There are reports of treatment successes, but experience with the drugs is limited and they are expensive. They may be considered in dogs failing other treatments.

12) **Antibiotics.** Give doxycycline 5 – 10 mg/kg PO, IV q12h if ehrlichiosis or *Mycoplasma haemocanis* (haemobartonellosis) are suspected (note that ehrlichiosis does not typically cause fulminant hemolytic anemia). If the dog is febrile and there is a high index of suspicion of sepsis, give enrofloxacin 5 mg/kg IV (15 min slow bolus) q12h + cefazolin 30 mg/kg IV q8h, or cefoxitin 30 mg/kg IV q8h. Response to empirical antibiotic therapy may be used to rule-in/rule-out sepsis. Patients with IMHA have an increased temperature and an increased white blood cell count that can be very high. If infection is not identified, antibiotics should not be used.

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3. Weinkle TK, Center SA, Randolph JF, Warner KL, Barr SC, Erb HN. Evaluation of prognostic factors, survival rates, and treatment protocols for immune-mediated hemolytic anemia in dogs: 151 cases (1993-2002). J Am Vet Med Assoc 2005; 226(11):1869-1880.

NOTES

INTRODUCTION

Refer to acute immune-mediated hemolytic anemia (IMHA) in dogs (*p. 411*) for a detailed overview. Acute IMHA is much less common in cats than in dogs. Prognosis is better than with dogs, with survival of approximately 70%. The causes, clinical signs, diagnostic evaluation and management are similar to the dog (*p. 411*). Some key features/differences in cats are:

Laboratory Evaluation

- Chronic non-regenerative forms of IMHA (pure red cell aplasia, pancytopenia) are more common and fulminant disease is rare.
- Spherocytosis is more difficult to detect. Neutrophilia and a left shift are uncommon, but lymphocytosis is present in about 50% of cases, whereas lymphopenia occurs in dogs.
- *Mycoplasma haemofelis* (previously *Haemobartonella felis*) organisms appear as individual or chains of small cocci, bacilli or rings, on the red cell surface. *Mycoplasma haemominutium* cannot be distinguished from *M. haemofelis* on cytology alone, but it is much less likely to cause acute anemia.
- *Cytauxzoon felis* organisms in red cells may have a bipolar ('safety-pin') appearance. Other forms include rings, tetrads and small dots. Cytauxzoonosis is often a fulminant disease.
- Heinz body (granule-appearance within the red cell) anemia is more common in cats than dogs.
- Cats positive for FeLV and FIV may present with hemolytic anemia, therefore, all cats with IMHA should be tested for these viruses.

Etiology/Treatment

1. The main cause of acute hemolysis is *Mycoplasma haemofelis* infection (haemobartonellosis), and consequently **doxycycline 10 mg/kg PO q24h** for 2 – 3 weeks is routinely incorporated into the treatment even if organisms are not seen on a blood smear. A blood sample for PCR testing should be submitted prior to treatment. If **corticosteroids** (*see Dogs p. 413*) are ineffective alone, **cyclophosphamide 10 mg/kg PO q2weeks** is preferred over azathioprine, as the former appears to be effective and well-tolerated in cats while the latter is more likely to cause severe myelosuppression. **Cyclosporine 5 mg/kg PO q12h** is recommended for refractory cases.
2. Treatment of Heinz body anemia requires removal of the underlying etiology (e.g., onion powder in baby foods, propofol, propylene glycol in semi-moist foods, Vitamin K, benzocaine, acetaminophen).
3. Cats do not commonly require thromboprophylaxis during therapy for IMHA.
4. Gastroprotectants are not routinely used.

SUGGESTED READING

See Immune-mediated Hemolytic Anemia in Dogs.

PHARMACOLOGY

See Immune-medicated Hemolytic Anemia in Dogs.

NOTES

INTRODUCTION

Disseminated Intravascular Coagulation (**DIC**) is an acquired syndrome representing a hypercoagulable state potentially progressing to multiple organ failure and hemorrhagic symptoms. Despite criteria for diagnosing DIC, DIC remains difficult to definitively diagnose. Distinguishing between clinical features attributable to the underlying disease and those of DIC is also difficult in some instances. Disseminated intravascular coagulation results from overwhelming systemic activation of the coagulation, fibrinolytic and anti-thrombotic (CFA-T) systems. The mechanism of DIC is very complex and is triggered by an underlying disease process (Table 1). Recognizing these triggers is important in daily practice as early intervention in treating the primary problem can reduce or eliminate the secondary effects on the hemostatic system resulting in DIC. There are two forms of DIC, acute (acute and fulminant) and chronic (compensated). The **chronic form** is not overwhelming or life-threatening as there is an increased production of all components of the CFA-T systems to compensate for their utilization. The primary clinical features of this are petechiae, ecchymoses, and mild bleeding in areas constantly abraded such as the gingiva. The coagulopathy associated with the chronic and acute form of DIC is caused by the enzymatic action of plasmin on fibrinogen and fibrin with production of peptides known as fibrin degradation products [FDP's] or fibrin split products [FSP] and their effect on platelets and fibrin polymerization. One peptide fragment known as D-dimer is used in diagnosing DIC in humans and veterinary medicine to a lesser degree. The chronic form of DIC, unlike the acute form, may not require emergency treatment, however the underlying disease process must be identified and removed.

TABLE 1. Predisposing Factors of DIC

Endothelial Damage	Abnormal Blood Flow	Hypercoaguable State
IMHA	Endocarditis	Liver failure
Other immune-mediated disease	Polycythemia	Cushing's
Pancreatitis	Dehydration	Pancreatitis
Arteriosclerosis	Shock (*p. 603, Table 1*)	All infections
Atherosclerosis	Cardiac Disease	PLE and PLN
Heartworm	Neoplasia	Neoplasia
Vasculitis	Hyperviscosity	Thrombocytosis
Endotoxin	Gastric dilation-volvulus	Snake envenomation
All infections	Hypovolemia	Platelet hyperreactivity
Pneumonia	Hyperthermia	IMHA (red cell stroma)
Neoplasia		Brain injury
Trauma		Acidosis
		Hypoxia
		Trauma

This chapter will focus on the **identification and therapy of acute DIC,** which will be present in many of the pathological situations presented in this manual. The clinical spectrum of DIC is one of coagulation and thrombosis followed by fibrinolysis and hemorrhage. A very brief pathophysiological discussion of the mechanism of DIC is presented in order to familiarize the reader with the rationale for suggested laboratory tests and therapy.

Three 'trigger' mechanisms are involved (1) **activation of the extrinsic coagulation pathway** by tissue factor released during cell injury; (2) **contact activation of the intrinsic coagulation pathway** secondary to vascular endothelial injury and exposure of the sub-endothelium; and (3) **direct activation of coagulation factors** by various components, for example, enzymes such as trypsin and elastase in pancreatitis. Also, many of the underlying diseases or 'triggers' for DIC listed in **Table 1** are inflammatory with production of a variety of cytokines. **Cytokines** stimulate cells of the immune system which further up-regulate cytokine production and procoagulation. Injury to endothelium also occurs during inflammation. Experimental studies, based on models of gram-negative sepsis, show that DIC is characterized by strongly enhanced inflammatory activity, where activated neutrophils play a pivotal role in the pathophysiology of

DIC, particularly by contributing to inflammation and vascular injury. All procoagulant stimuli ultimately result in **thrombin generation** mediated by the extrinsic (tissue factor/factor VIIa dependent pathway) system. Thrombin converts fibrinogen to fibrin monomers; factor XIIIa activated by thrombin, 'firms' the fibrin monomers into a stable clot. Widespread microvascular thrombosis occurs when the fibrin clots gain access to the systemic circulation. As there is reduced perfusion in these areas, ischemia (causing multiple organ dysfunction [MOD]), cell death and ultimately organ failure (multiple organ failure [MOF]) can occur. Thrombin can also act as a potent agonist for platelet activation. Platelet activation also occurs as a direct effect of endotoxins or cytokines. **Thrombocytopenia** due to consumption, and thrombopathia due to coating of the platelets by FRA contributes to hemorrhage. Antithrombin is a major inhibitor of thrombin and factors XIIa, XIa, Xa, IXa, plasmin kallikrien and plasmin, thereby inhibiting the intrinsic and common pathways. **Consumption of antithrombin** during DIC promotes potential thrombosis. Thrombomodulin-Protein C-Protein S is an endothelial-based inhibitor system, which binds thrombin, preventing amplification of procoagulant activity. During DIC, this system is consumed resulting in unopposed coagulation. Activated Protein-C is used to treat selective critically ill human patients with DIC due to overwhelming inflammation. Inhibitors of fibrinolysis are α2-antiplasmin, plasminogen activator inhibitor, α2-macroglobulin, a1 antitrypsin and C1-inhibitor, which may also contribute to DIC by inactivating plasmin. Activation of complement also occurs as plasmin activates C1 resulting in red cell and platelet lysis. Peptides produced through complement activation increase vascular permeability resulting in decreased perfusion and edema, with subsequent reduction in oxygen delivery to tissues. The contact system is also activated by complement with production of kinins. These vasoactive peptides result in hypotension, ischemia and shock. If perfusion status is not improved, the reduced blood flow results in acidosis and hypoxia, both triggers for DIC.

As you can see, DIC is a spectrum from initiation of coagulation through to multiple organ failure and hemorrhage. The key to managing this disease is (1) **know it exists** based on the presenting illness or injury, even though there may be no visible, or on occasion, laboratory evidence, (2) **treat and prevent further microthrombi** and progression of the disease through improving perfusion and oxygen delivery to the tissues; (3) **treat and prevent further hemorrhage** if this is present; and (3) **treat the underlying disease or remove the inciting focus as soon as possible.**

DIAGNOSIS

History/Signalment

- The diagnosis of DIC is commonly made on physical examination and in association with an underlying disease predisposing to DIC. Laboratory tests support the diagnosis.
- As DIC is not a primary disease, the history will vary according to the presenting illness. Questions to the owner will depend on presenting signs and the generated list of differential diagnoses.
- DIC is more common in dogs and rare in cats.

Clinical Signs/Physical Examination

- Patients with chronic DIC may have no, or minimal (petechia, ecchymoses or minimal gingival hemorrhage) clinical signs which may be noted on routine physical examination. However, an underlying problem may be identified.
- As inflammation is a 'trigger' for acute DIC and DIC involves a spectrum of events, clinical signs may initially only be referrable to an underlying problem and the initial stages of DIC are only detected on laboratory evaluation (e.g., thrombocytopenia, prolonged ACT, neutrophilia).
- With more serious illness, **acute DIC** may be suspected if petechia and ecchymoses are present in a patient that has an underlying illness predisposing to DIC (Table 1).
- As DIC progresses, signs referrable to multi-organ dysfunction due to microvascular thrombosis/injury may be recognized:
  - Hematoma at venipuncture sites
  - Dyspnea with lung involvement
  - Oliguria/anuria or hematuria as renal failure approaches
  - Hemoptysis, hematochezia and melena with gastrointestinal involvement
- As **fulminant DIC** approaches, the patient is depressed/moribund due to shock with massive bruising and hemorrhage.
- Clinical signs associated with **DIC may be due to DIC itself in addition to those of the underlying disease,** or may be similar to the underlying disease itself. For example, hematuria in dogs with leptospirosis may be due to DIC or injury to the kidney by the spirochette. However, these dogs have DIC based on the pathophysiology of the disease.

- Abnormalities in **heart rate** (increased or profoundly decreased) and **rhythm** (frequently tachycardia or ventricular arrhythmias), **respiratory rate** and **effort** (increased and may be dyspneic if pulmonary thromboemboli, or ARDS are present), **systemic blood pressure** (frequently hypotensive), **pulse pressure** (weak), **mucous membrane colour** (variable), **mentation** (usually depressed) are all dependent on the underlying disease, advanced nature of the problem and severity of DIC.
- **Abdominal palpation** may reveal a mass (i.e., hemangiosarcoma of liver or spleen); free fluid may be due to hemorrhage or peritonitis.
- **Auscultation of the thorax** may reveal reduced lung and heart sounds due to pleural fluid (blood, pus, or effusion secondary to a neoplastic process).
- **If in hospital** bleeding from catheter sites or previous venipuncture sites, surgical incisions etc.

Laboratory Evaluation/Diagnostic Imaging

Stat. All must be performed to obtain basic information on an emergent basis. This information and the physical findings are used to formulate an immediate treatment and further diagnostic plan.
- **PCV, TS** (both are usually below normal values).
- **Blood smear** (mature and immature neutrophil count and platelet count).
- **Stick BUN, urea or creatinine** may be increased.
- **Blood glucose** is usually low.
- **ACT** is always performed in our institution. We suggest incubation of the blood sample tight into the axilla, beneath the white coat, if no heating block at 37°C is available. Hand held is not advised. Consistency in testing is important when trending. **Commonly the ACT is increased (>120 secs in dogs and >90 secs in cats) and platelet count decreased below normal range (<100 x 10^9/L).** These two point-of-care tests are very useful when DIC is suspected (*see Suggested Reading 1*). Usually animals are presented beyond a very early stage of illness where the procoagulant phase of DIC may have been missed. However, should the animal be presented early in the spectrum of illness, the ACT may be shortened to <70 secs in the dog and <60 secs in the cat. The platelet count may be in the low normal range at this time.
- The **PT/PTT** may be increased, however these tests are unreliable as a diagnostic test for DIC, unless severe, in this author's experience as they may remain within normal range.
- **Serum electrolytes** are required to identify abnormalities and aid in fluid selection.
- **Venous blood gases** will determine acid-base status (*p. 407*). Acidosis worsens DIC.
- **ECG** as ventricular (*p. 179*) or supraventricular (*p. 170*) arrhythmias may be noted .
- **Systemic blood pressure** must be measured as it is frequently low.
- Where physical examination indicates, perform **radiographic or ultrasonographic examination** of the thorax and/or abdomen.
- **Aspirates** of abdominal (*p. 28*) or pleural fluid (*p. 574*) should be evaluated. Caution: Use as small a needle as possible to avoid hemorrhage.
- **Buccal mucosal bleeding times are not recommended** as bleeding may be difficult to stop.

Extended Data Base

- **CBC** must be performed to identify leukocytosis, leukopenia, left shift (*p. 588 for criteria of sepsis*), anemia and thrombocypopenia. The presence of **schizocytes** (red cell fragmentation) may support a diagnosis of DIC, however, these are not consistently present in DIC and may occur with other conditions such as hemolytic uremic syndrome.
- **Complete biochemical profile** to assess organ function. Pancreatic enzymes may be increased and be a cause of DIC. Liver disease/failure (*p. 37*) may also be a cause of DIC.
- **Diagnostic imaging** to focus on identifying underlying pathology.

As many of the following tests are not performed in-house, and some only performed weekly in laboratories, do not wait for results prior to diagnosing the patient with DIC.
- **PT/PTT** may suggest DIC if prolonged due to reduced clotting factors as described above. However, due to the various actions of thrombin, normal or shortened times may be reported. Values will be reported together with controls by the laboratory.
- **FDP's/FSP's** may be significantly increased (**>40**) in DIC, but are not consistently so as adequate levels detectable by the test may not be present resulting in a false negative test. (*see Suggested Reading 3*). Also, FDP's are not specific for DIC and may be increased following surgery, in patients with hematomas, and patients with liver or renal failure.

- **Fibrinogen** concentrations are frequently low but, depending on the stage of illness, may be high as fibrinogen is an acute phase protein and increased in inflammation. It is also increased in dehydration. Concurrent inflammation and dehydration makes interpretation difficult. Values will be reported together with controls by the laboratory.
- **D-Dimer** evaluation is commonly used in human medicine as part of the evaluation for DIC. D-dimer is a protein formed as a result of plasmin degradation of cross-linked fibrin, therefore an elevated D-dimer concentration is a specific marker for clot lysis distinguishing this from primary fibrinolysis. This test has a very high negative predictive value for DIC indicating that a negative test means that DIC is **not** occurring (confidence level of 99.5%). An ELISA-based assay has recently become available and may be of benefit in the future for veterinary patients. Also, D-Dimers are not specific for DIC and may be increased with other diseases involving thrombosis (i.e., PTE).
- **Antithrombin** values are decreased (relative to normal) and are considered an accurate marker in most animals with an illness predisposing to DIC.

MANAGEMENT

As previously mentioned, the underlying disorder must be treated; when identified, refer to appropriate chapter. Refer to Sepsis and Septic Shock *p. 588* for detailed guidelines on therapy. The following is directed towards general management of DIC.

A. **Oxygen** therapy by flow-by where indicated to improve potential hypoxia.

B. **IV catheter placement into a peripheral vein.** Do not attempt jugular catheterization as the bleeding will be difficult to control.

C. **Fluid therapy** is an essential part of managing or preventing DIC. As hypoxia, blood stasis, and acidosis contribute to DIC, these must be avoided by using appropriate fluid therapy. Fluid therapy also removes activated clotting factors and fibrinolytic factors from the microcirculation improving perfusion of all organs preventing organ dysfunction or failure. Optimizing perfusion of the gastrointestinal tract and the kidney is essential. Assuming all patients will have an underlying inflammatory condition there is a definite 'art and science' to fluid administration, therefore refer to *Sepsis/Septic Shock p. 588 and Fluid Therapy p. 347* for guidelines.

1. Balanced electroyte solution (Plasma-Lyte® A or 148, Normalsol® R, lactated Ringer's, or in the rare alkalemic patient, 0.9% sodium chloride). The rate to be administered will depend on severity of condition.
2. Some of these patients have capillary leak, therefore the volume of crystalloids must be carefully administered noting respiratory rate and effort and subtle signs of edema. (*see **Monitoring** in Sepsis/Septic Shock p. 591, Fluid Therapy p. 347*).
3. If a reduced volume of crystalloid solution is required due to capillary leak, fresh frozen plasma, synthetic colloids or 25% Human Serum Albumin is required.

D. **Fresh frozen plasma (FFP).** This author administers FFP to patients with acute DIC, but does not incubate with heparin. Antithrombin in the FFP will be available to combine with heparan sulfate on the endothelium. Anti-proteases, α-macroglobulins, coagulation factors and other potential factors (e.g., protein C) present in FFP may confer a benefit.

E. **Synthetic colloids** (pentastarch, hetastarch or Dextran-70) may be required to increase colloidal osmotic pressure and retain fluid within the intravascular space. This author cautiously administers these products for resuscitation in patients with capillary leak associated with pancreatitis, as the smaller molecules appear to leak into the pulmonary interstitial space (personal observation). Capillary leak associated with sepsis *may* not be as great an issue in this regard; the author considers the individual patient prior to administration of these products.

F. **25% Human Serum Albumin (HSA)** is considered by the author in hypoalbuminemia (≤15 g/L [1.5 g/dL]) and capillary leak situations. (*see Hypoalbuminemia p. 431, Sepsis/Septic Shock p. 588 , Acute Pancreatitis p. 45*).

G. **Whole fresh blood** is recommended for active hemorrhage as this will supply clotting factors and platelets. *See Transfusion Therapy p. 667* for further component therapy.

H. Heparin. It is not known whether heparin administration is of benefit as no veterinary clinical trials have evaluated this. This author administers heparin to patients where hemorrhage is not apparent, the ACT or PT/PTT are not higher than 1.5 – 2x high normal value, the platelet count is low normal or higher, and there is an associated illness predisposing to thrombosis (e.g., pancreatitis, IMHA, hyperadrenocorticism, and others listed in Table 1). This author does not routinely administer heparin during sepsis. FFP should be transfused prior to heparin therapy. If ACT is >1.5 – 2x normal prior to FFP, repeat ACT after FFP transfusion; if reduced heparin may be instituted. Absolute guidelines for heparin dosages are not available, however suggested therapeutic dosages are:

1. **Heparin 75 – 100 U/kg IV** followed by 10 – 15 U/kg/h, OR
2. **75 – 100 U/kg SC q8h** for both dogs and cats
3. **Alternative dosages recommended are:**
   a. 200 – 250 U/kg (dog), 75 U/kg (cat) SC q8h
   b. Dosages **up to 500 U/kg SC q8h**
   c. **300 U/kg IV initially followed by 12 – 15 U/kg/h** as a CRI
4. All dosages are suggested to achieve an ACT or PT/PTT 1.5 – 2x upper end of normal.
5. ACT or PT/PTT should be monitored prior to each SC dose, or twice daily where the CRI is employed. This author does not routinely administer heparin during sepsis.

I. Vitamin K 1 mg/kg SC q24h therapy may be beneficial as this may be deficient in critically ill patients, and may be a source of coagulopathy and hemorrhage. Also, patients with DIC can also become vitamin K depleted due to increased consumption.

J. REMOVAL OF THE UNDERLYING PROBLEM

1. Where a surgically correctable problem exists this should be performed as soon as possible. Waiting until the patient is 'stable' may be too late as it is the underlying disease that is causing the problem. Stability in this instance is administering the above fluids to improve perfusion and adequate systemic blood pressure, administering blood products to prevent hemorrhage and ongoing microvascular thrombosis, administering anti-arrhythmic therapy to reduce the rate (not necessarily to eliminate the rhythm) of a malignant arrhythmia.
2. Where a surgical problem exists that predisposes to DIC in a stable patient (i.e., splenic hemangiosarcoma, diaphragmatic hernia with organ entrapment), surgery should still be performed as soon as possible before DIC becomes fulminant. This often occurs even with appropriate medical support because the underlying problem is fueling the process.
3. Where a medical problem exists, early definitive therapy is also essential

K. Analagesia is essential. Opioids are the analgesics of choice.

1. **Butorphanol 0.2 – 0.4 mg/kg q2h** can be tried initially for mild to moderate pain and continued as a CRI of 0.1 mg/kg/h or to effect. Stop the CRI for 30 – 60 minutes if the patient appears overdosed and reinstitute at one-half the previous dose. If butorphanol is not adequate, then
2. **Hydromorphone 0.025 – 0.1 mg/kg** q3–4h, or to effect. This dose may be given as a CRI over a 3 – 4h period. You may have to increase the dose of hydromorphone if butorphanol has already been administered due to its antagonistic effect.
3. **Morphine or methadone 0.2 – 0.4 mg/kg very slowly IV,** followed by CRI (*see Morphine Infusion Chart p. 251*) is also effective.
4. **Fentanyl 4 – 6 µg/kg bolus IV, followed by 4 – 6 µg/kg/h CRI** (*see Fentanyl Infusion Chart p. 237*).

Remember, pain activates the sympathetic nervous system, which causes vasoconstriction and therefore poor splanchnic perfusion (especially pancreas and this, in itself, can cause pancreatitis).

SUGGESTED READINGS

1. Bateman SW, Mathews KA, Abrams-Ogg ACG, Lumsden JH, Johnstone IB, Hillows TK. Diagnosis of Disseminated Intravascular Coagulation in Dogs admitted to an intensive care unit. J Am Vet Assoc 1999;215:805-810.
2. Bateman SW, Mathews KA, Abrams-Ogg ACG. Disseminated Intravascular Coagulation in Dogs: Review of the literature. J Vet Emerg Crit Care. 1998;8(1):29-44.
3. Levi M. Sepsis and the Coagulation System. Advances in Sepsis. 2000;1(1):16-21.

INTRODUCTION

By definition a temperature >39.2°C for more than 2 – 3 weeks without an apparent cause, despite initial testing and diagnostic investigation, is a fever of unknown origin (FUO). Hyperthermia, or a non-pyrogenic fever, develops due to an animal's inability to dissipate heat; there is an imbalance between heat production and heat loss. For further information on non -pyrogenic fever (i.e., fever secondary to severe environmental conditions, seizures, enclosure in a vehicle) (*see section Heat Stroke p. 297*). The main difference between hyperthermia/non-pryogenic fever and a true fever is that the thermoregulation set point is not altered in the hyperthermic patient. In general, temperatures greater than 41°C are more often associated with hyperthermia. Most FUO are usually between 39.5°C and 41°C. It is uncommon for a FUO to rise above 40.6°C. Within the definition of FUO, the most straightforward and common causes of fever should have been ruled out. In veterinary medicine this would include viral infections, uncomplicated abscesses, post surgical fevers along with other antibiotic responsive infections and other self-limiting illness. Many cases will present with a history much shorter than three weeks but based on the lack of obvious cause they are still classified as a FUO.

The four main categories of pyrogen production are infectious, inflammatory, neoplastic and miscellaneous. From a recent evaluation of three separate studies, the combined diagnoses from 170 FUO cases show that immune-mediated polyarthritis is the single most common cause of FUO in dogs (44 cases), followed by lymphoid neoplasia (15 cases), discospondylitis (8 cases), myelodysplasia (8 cases), hypertropic osteodystrophy (HOD) (6 cases), and blastomycosis (6 cases)[5].

TEMPERATURE CONVERSION: °F = 1.8 x °C + 32; °C = (°F – 32) / °C.

DIAGNOSIS

History/Signalment

When presented with a patient with a fever of unknown origin the primary complaint may be vague and nonspecific where a thorough history (Fig. 1) and physical examination (Fig. 2) is imperative. Breed related diseases and congenital abnormalities should always be considered (Fig. 3).

Laboratory Evaluation/Diagnostic Imaging

Basic laboratory tests should be performed followed by specific tests indicated by findings obtained from the history, signalment and physical examination (Fig. 1 – 3).

It is suggested that you quickly review the following prior to commencing MANAGEMENT (at the end of the chapter) as collection of blood and other fluids may be required prior to establishing fluid and other therapy.

DEVELOPING YOUR DIAGNOSTIC PLAN

I. LOCALIZING SIGNS

- Approach each case in a logical stepwise matter focusing on initial tests related to the organ systems affected.
- Diagnostic testing will take time to perform and results may take several days to weeks, therefore client communication is essential. In the majority of cases a diagnosis will be made; a small percentage will remain unresolved.
- Collect enough plasma and serum to save serum for future testing, and EDTA whole blood (purple top tube) for future PCR testing.
- Consider **IV or urinary catheter sepsis** as a cause of FUO in hospitalized patients if the catheter has been present for more than 48 – 72 hours. Culture blood drawn from the catheter prior to removal, remove the catheter aseptically and culture the tip. Obtain urine aseptically prior to catheter removal, do not submit the urinary catheter tip as you will obtain erroneous results.
- **Aspirate joints** (cytology, culture) as the MOST COMMON CAUSE for FUO (dogs) is immune mediated disease with polyarthritis predominating. Note: this may be geographically dependent.
- **Bone marrow aspirate/biopsy,** to rule out primary bone marrow abnormalities (e.g., myelodysplasia, myeloma, leukemia).
- **Culture** appropriate fluids for anaerobic and aerobic organisms.

- Consider mycoplasma cultures for chronic pneumonias or single joint effusion in an immunosuppressed dog or cat.
- Consider L-form bacterial infections in cats with joint disease or suspect bacterial infections that are negative on culture.
- Note anaerobic organisms are difficult to grow and may result in a negative culture.
- Always ask for a gram stain as means of tailoring therapy in advance of culture results, especially where bacteria may not grow well or quickly (i.e., current or previous antibiotic use)

- **Biopsies**
  - Consider talking to the pathologist prior to collecting biopsies to determine if frozen biopsies are indicated for possible immunohistochemical analysis.
  - Consider aseptically collected surgical biopsies for culture and acid fast staining especially if suspect Mycobacterium, Actinomyces or Nocardia spp. Submit the ENTIRE sample for histopathology – don't throw anything away.
  - Muscle and nerve biopsies – ensure proper handling/storage of such samples by talking to Dr. Diane Shelton's Neuromuscular Laboratory in CA, website http://medicine.ucsd.edu/vet-neuromuscular/index.html CA.
- Repeat testing may be indicated, however, **the most important aspect in diagnosis is the physical examination.**

II. INITIAL DIAGNOSTIC PLAN

Choose the most appropriate tests relating to patient history and PE. Consider all tests as part of the intial work-up if history and physical examination were non-localizing with respect to a source of fever (Fig. 1 – 3).

- **CBC** and peripheral blood smear (slide agglutination, Coombs test and reticulocytes count if anemic, move to bone marrow aspirate and biopsy if multiple cytopenias noted).
- **Serum biochemistry** panel.
- **Urinalysis** and **culture** via cystocentesis if no concurrent thrombocytopenia. Check for hyphal elements and/or yeast e.g., *Candida.* Consider fungal culture especially if bacterial culture negative discospondylitis is diagnosed.
- **FeLV/FIV** screen.
- **Heartworm screen** for both cats and dogs.
- **Neurological** Examination.
- **Orthopedic** Examination.
- **Fundic** Examination.
- Three view **thoracic radiographs.**
- **Abdominal Radiographs.**
- A **coagulation** panel to facilitate potential invasive procedures or if concerned about the possibility of DIC.
- **Blood Cultures.** The volume of blood collected is the most important. One should focus on maximizing a sterile blood collection over obtaining multiple samples. For large dogs 20 mLs can be collected and 10 mLs aseptically injected into an aerobic and anaerobic culture vial. The area must be aseptically prepared and sterile gloves must be worn if palpation of the vessel is required. If the patient has been on antibiotics then the appropriate blood culture vials with resin beads should be used to facilitate bacterial growth in the face of antibiotic therapy. If possible, blood should be collected from separate sites to ensure that a positive culture is not due to contamination. Five mL can be used in conjunction with the small vials in small dogs and cats. The ratio of blood to broth should not exceed 1:5.

III. ADVANCED DIAGNOSTICS

Choose the appropriate tests below based on localizing signs or consider these test as the next step when diagnostic tests performed so far have not elucidated a diagnosis.

- **Abdominal Ultrasound** (FNA or biopsies if abnormalities detected).
- **Arthrocentesis** for cytology and culture. Small blood culture vials with or without the antibiotic resin beads should be used to improve the likelihood of a true positive result. If suppurative inflammation detected consider Erhlichia titres +/- PCR and Borrelia IFA or Western Blot.
- **Lymph node** aspirates.
- **Cerebrospinal fluid** for cytology, culture, titres (even if a pleocytosis is not present – e.g., FIP cats), flow cytometry, or PCR and/or immunohistochemistry.
- **Echocardiogram** and **EKG** to rule out endocarditis. Consider *Bartonella vinsonii* and *berkoffi* titres +/- PCR if standard blood cultures are negative but endocarditis is still suspected based on the echocardiogram.
- **Infectious titres** such as Tick Titre Panel for *Erhlichia*, Rocky Mountain Spotted Fever, *Borrelia*; Fungal titres along with *Toxoplasma* and *Neospora* titers especially in association with inflammatory CNS disease or mysositis; or Pythiosis ELISA (Pythium Laboratory, Louisiana State University) for suspect cutaneous or GI pythiosis.

FIGURE 1. History.

Travel	Vaccine Hx	"Trauma" Hx	Flea & Tick Control	Medication
Many **tick-borne** diseases are limited to a geographic region i.e., • Borrelia • Ehrlichia • Rickettsial • Babesia • Leishmania and Bartonella (vector not confirmed)	**Unvaccinated** • Canine **Distemper** and • Canine **Adeno Virus** are primarily diseases of dogs less than one year of age and unvaccinated	Previous **trauma** Consider • bile duct rupture → bile peritonitis • diaphragmatic hernia with incarcerated bowel → peritonitis, • ruptured ureter → uroabdomen	Consider Infectious causes i.e. • *Mycoplasma Hemofelis* along with • **Bartonella** in cats with Fleas	Previous **Chemotherapy** • check nadir for specific drug • consider **neutropenia** and **secondary infection**
Other infectious diseases also limited to geographical location • **Fungal** (i.e., blastomycosis, cryptococcus, coccidio-mycosis, and histoplasmosis) • **Protozoal** (i.e., toxoplasmosis, neosporosis)	Consider • **inflammatory** and **possibly** • **immune mediated** i.e., HOD (especially Wiemeraners), IMHA, ITP, or meningitis (no definitive proof as of yet)	Previous **Dog Fight** Consider • abscess • abdominal hernia • incarcerated bowel **Note:** If it was a **Pit Bull** – *Babesia gibsoni* has been transmitted after bite wounds inflicted by Pit Bulls in Southern States	• Tick-Borne or other vector See Travel	Cats • tetracycline
Refer to **Suggested Reading 3** for more information	NOTE: **Important for testing** i.e., • **FIV** vaccine prevents accurate testing • Prior **Lyme** vaccine – test via Western Blot • **Leptospira** vaccine – can produce a positive titre if within the previous 2 – 3 months	Previous **Porcupine quills** Consider • **migrating quill** • **abscess** or • **secondary immune-mediated disease** secondary to infection		Dogs • **trimethoprim sulfa** • **procainamide**
		Previous **wound** – Consider • deep **mycotic infection** • **mycobacterium** • **Nocardia** • **Actinomyces,** or • **Sporothrix** (especially if rosebush thorn)		**Check side effects on any previous medication**

Littermates Affected

Consider
- **congenital anatomical abnormality** or
- **immuno-deficiency** or
- **vertical transmission** from bitch/queen

Prior Medical History

Previous **Blood Transfusion**
Consider
- Mycoplasma in cats
- Leishmania along with Bartonella and other Tick Borne Disease in dogs (increased risk from donors that are not well screened)

Ongoing **Chronic infections** since puppy or kitten
Consider
- **immunodeficiency**

Prior neoplasm diagnosed
Consider
- paraneoplastic/immune mediated related fever
- or secondary bone marrow involvement if hemopoetic neoplasm leading to myelophthisis and neutropenia

Previous **Surgery**
Consider
- **implant infection**

Indoor/Outdoor??

Unsupervised increases likelihood of unknown trauma, toxin, foreign body or exposure to infectious agent

Cats – hunter of birds or rodents
Consider
- **Tularemia**
- **Salmonella**
- **Yersinia Pestis** and
- **Toxoplasmosis**

Outdoor lifestyle increases likelihood for retroviral diseases i.e., **FeLV** and **FIV**

Dogs – farm dog or off leash
Increased exposure to groundhogs, racoons, possums, rabbits and ticks and other potential infectious reservoirs. Therefore consider leptospirosis, tick-borne illness etc.

Clinical Symptoms
See PE algorithm for more detail

Waxing and **waning**
- **Immune mediated** i.e., waxing and waning shifting leg lameness or stiffness in IMPA

PUPD
Consider
- occult **pyelonephritis**
- **hypercalcemia** secondary to malignancy
- **Hyperadreno-corticism** or **Diabetes** predisposing to secondary infection

Lethargy/Exercise intolerance – musculoskeletal, cardiovascular or respiratory –
Consider
- **endocarditis**
- **IMPA**
- **fungal pneumonia**
- **Diskospondylitis**
- **Pyelonephritis**

GI – Localize source to GI tract but consider vestibular causes, along with other extra GI source liver, kidney, pancreas, etc.

FIGURE 2. Physical Exam – Examine carefully for specific abnormalities.

Nervous System	Ocular	Skin	Lymph Nodes	Musculoskeletal
Mentation: aside from lethargy are there changes in how the animal interacts within its environment or with the owners to suggest possible CNS disease? **Questions:** Lost in corners, staring into space, decreased interaction with family members, behavioural change such as aggression. Perform full neurological examination Bacterial/fungal/ protozoal/viral and other causes of infectious Meningitis or Encephalitis Immune Mediated Meningitis Portosystemic Shunt – fever secondary to bacteremia (*see Chapter ★★*)	Check for intraocular hemorrhage, petechiae, and icterus Make sure eyes retropulse equally A **fundic examination** is essential Common findings with infectious or neoplastic causes are uveitis, chorioretinitis, granulomatous changes, retinal detachment or optic neuritis	Perform a thorough examination looking for **small lumps & bumps;** red raised, oozing, **draining** and **crusting lesions** that could **represent fungal infectious conditions or neoplasia** **Note:** An impression smear off an oozing skin lesion is much more rewarding than a bronchio- alveolar lavage where blasto- mycoses is suspected. **Ectoparasites?** Areas of edema or swelling that could be potential abscesses **Firm painful SC mass** or swellings? – consider steatitis or panniculitis **Petechia, ecchymoses** and **icterus** may indicate immune mediated disease	Examine all lymph nodes (LN) If **single LN enlargement** carefully inspect region of drainage for that node. **Generalized lymphadenopathy** associated with lymphoma, metastatic neoplasia, numerous infectious organisms i.e., fungal, Leishmania, oomycetes, Nocardia, Toxo- plasmosis and Mycobateria Evidence of enlargement requires LN aspiration and potential biopsy. Lymph-adenitis is a primary inflammatory condition.	**Immune Mediated Polyarthritis** is one of the most common causes of FUO. **Note:** not all cases will have joint swelling; varying degrees of lameness include, the classic "walking on eggshells", inability to rise, mild shifting lameness, or nonspecific pain. **Examine all joints for effusion.** Septic arthritis usually involves the more proximal joints; immune mediated conditions tend to involve distal joints. Distinguish from metaphyseal pain/swelling. **Examine long bones** for pain. **Neck /back pain** could be related to meningitis, diskospondylitis or osteomyelitis; or bony neoplasm **Note:** lumbar pain may be related to pyelonephritis. Careful examination is warranted but may be difficult to distinguish from a spinal lesion. **Generalized muscle pain** is noted with Leptospirosis and Hepatozoonosis

Oral Cavity

Stomatitis is commonly seen with Calici virus, FIV, Systemic Lupus Erythematous (SLE) and renal failure

Pain on opening the mouth could be associated with Temporal Mandibular Joint (TMJ) pain, retrobulbar disease or myositis

Halitosis is commonly associated with renal failure, tooth root abscess, and stomatitis

Note: petechiae, mucus membrane color **(palor/icterus)**

Gastrointestinal

Regurgitation: consider congenital or acquired megaesophagus leading to aspiration pneumonia

Palpate abdomen for **organomegaly, masses, abdominal pain, peritoneal effusion.**

Consider pancreatitis/ pancreatic abscess, cholangiohepatitis, partial GI obstruction i.e., chronic intus- suception, localized peritonitis, splenic torsion or thrombus, necrotic tumor, Histoplasmosis, Pythiosis, FIP, or Prototheca

Note: Thoracic cavity disease (i.e., lung lobe torsion, severe pneumonia) can cause referred abdominal pain.

Note: Vomiting can be a sign of Heartworm disease in Cats

Rectal exam for: frank blood, melena, painful or assymetric prostatic enlargement, anal gland or sublumbar lymph node enlargement, pain on palpation of the L-S junction or pelvic rim; perianal swelling that could be a mass, perineal hernia, or abscess **Rectal scraping** for Histoplasmosis if indicated

Cardiovascular

New Murmur: endocarditis especially if diastolic.
Note: not all cases of endocarditis will have a murmur

Arrhythmia: Primary cardiac disease (i.e., mycocarditis, endocarditis or pericarditis). Extracardiac causes (i.e., splenic disease)

Muffled Heart Sounds: Pericardial effusion secondary to infectious causes (i.e., FIP or fungal), or neoplastic causes (i.e., lymphoma)

Bounding pulses: Secondary to anemia, sepsis or aortic insufficiency.

Asymmetric Pulses: Thrombus, especially if associated with lameness or swelling in that limb

Respiratory

Epistaxis? thrombocytopenia (rickettsial), or thrombopathia (paraproteinemia); infection (aspergillus), or neoplasia

Mucopurulent Nasal Discharge? fungal rhinitis, tooth root abscess; opportunistic bacterial infection secondary to foreign body or immuno- suppression, or neoplasia. Some patients with pneumonia will develop a nasal discharge.

Decreased lung sounds: diffuse due to pleural effusion (i.e., pyothorax, FIP or neoplastic effusions); focal secondary to consolidation (i.e. fungal granuloma, neoplastic mass, foreign body induced focal pneumonia)

Increased lung sounds: pneumonia (bacterial or fungal), or neoplasia

Acute onset dyspnea: pulmonary thrombo-emboli or Dirofilaria emboli

Cough elicited: tracheitis with several etiologies

Urogenital

Vaginal discharge? pyometra, or Brucella infection if prior abortion and discharge is persisting

Note: stump pyometra may not cause a vaginal discharge

Enlarged/ painful prostate: prostatitis or abscess

Swollen painful testicles: orchitis

Kidney size and irregularities can be palpated in cats, but difficult to assess in dogs.

Kidney pain on on palpation – pyelonephritis

Note: absence of pain does not rule out pyelonephritis

FIGURE 3. Signalment algorithm for major pyrogen categories (list is not inclusive).

Inflammatory/Immune Mediated

Panosteitis:
– Young large breed dogs especially German Shepherds

Hypertrophic Osteodystrophy:
– Young large breed dogs
– Weimeraners (often post vaccination)

Shar Pei Fever/Swollen Hock Syndrome

↓

Meningitis-Arteritis:
– Beagles, Bernese Mtn. Dog, Nova Scotia Duck Toller, Boxer and German Short Haired Pointer (GSP)

Meningitis/Polyarthritis:
– Akita, Boxer, Weimeraners, GSP, Beagle, and Rottweilers

Panniculitis – any (Dachshund sterile nodular panniculitis)
Steatitis – any
Hypereosinophillic Syndrome:
– cats
– dogs rare (Rottweilers)

↓

IMHA
– Cocker Spaniels
– Miniature Schnauzers

Immune Mediated Polyarthritis Nonerosive:
– Large breed dogs – Retrievers, Spaniels, Pointers, Doberman Pinschers
– Small breed – Toy Poodles, Lhasa Apsos, Yorkshire Terrier, and Chihuahuas over represented

ITP: fever less common than IMHA
– Old English Sheep Dog
– Cocker Spaniel and Poodles

Systemic Lupus Erythematous
– Collies, German Shepherds, Poodles

Infectious

Species: Cats – Purebreds in catteries have increased incidence of FIP and other viral infections. Hunters? See History Algorithm
Age: Neonates – sepsis
Sex: Intact Female – pyometra

↓

Fox Hounds
– Leishmania
Grey Hounds
– multiple tick borne organisms especially *Babesia canis*
American Pit Bull
– *Babesia gibsoni*
Miniature Schnauzers
– Mycobacterium
Basset Hounds
– Mycobacterium
Siamese Cats
– Mycobacterium
German Shepherds
– *Aspergillus terreus* and other opportunistic fungal infections causing disseminated infection and or diskospondylitis
Jack Russell/Miniature Schnauzer
– congenital megaesophagus causing secondary aspiration pneumonia
Irish Wolfhounds
– pneumonia
Boxers (due to subaortic stenosis) and other large Breeds
– endocarditis
Many Breeds – bronchoesophageal fistula → pneumonia (rare)

↓

Immunodeficiencies (rare) → secondary infection

Pembroke Welsh, Cardigan Welsh Corgi and Basset Hound (X-linked)
– Severe Combined Immunodeciency (SCID)
Jack Russell Terrier - SCID
German Shepherd
– IgA deficiency
Irish Red & White Setter and Irish Setter
– Canine Leukocyte Adhesion Deficiency
Doberman Pincscher – IgM deficiency and Bactericidal defect
Shar Pei – IgA deficiency
Brittany Spaniels – Complement deficiency

Neoplastic

Boxer :
- Mast cells
- Lymphoma

Golden Retriever:
- lymphoma

Flat Coated Retriever, Bernese Mountain Dog, and Rottweiler :
- Malignant Histiocytosis

German Shepherd, Labrador and Golden Retriever:
- Hemangiosarcoma

In General :

Multiple Myeloma :
- German Shepherds and other purebred dogs

Leukemia – any breed (age range 1 – 12 years)

Pheochromocytoma

Any necrotic tumor

Osteosarcoma

- Large → Giant Breed Dogs:

Mammary Adenocarcinoma and Uterine/Ovary Neoplasia
- Intact Female

Other tumors – gastric, hepatic, lung tumors, bone or metastatic disease

Misc

Cats:
- Tetracyclines
- Hydromorphone
- Hyperthyroidism (rare)

Dogs:
- Trimethoprim Sulfa
- Porto Systemic Shunt – small breed dogs

Both Dogs & Cats:
- Procainamide plus other drugs
- always check for possible side effects
- toxins
- intracranial hypothalamic disease

- **ANA** titre. (significance may be questionable)
- **PCR** analysis from reputable laboratory for Mycoplasma hemofelis.
- Survey **spinal radiographs** +/- **long bone radiographs.** Consider fluoroscopic FNA/Biopsy for cytology, gram stain, bacterial and fungal culture and histopathology if a lesion is noted.
- **Nuclear Scintigraphy Scan,** i.e., bone scan looking for a source of inflammation otherwise known as "hotspots" especially in a lame animal. Labeled neutrophils can also help locate an inflammatory focus but availability of this test is limited.
- **Bone marrow** immunohistochemistry +/- PCR for Felv/FIV on an unstained slide, if cytopenias or other unexplained CBC abnormalities are noted, or consider even if CBC is normal and all other diagnostic procedures have failed to identify a cause of fever.
- Diagnostic **peritoneal lavage** if abdominal pain noted.
- **Skin Biopsy** if lesions present and not performed earlier.
- **Fecal Float, Giardia ELISA, Baermann, culture,** *Clostridium difficile* and *perfringens* toxin testing and **rectal scrape** (Histoplasmosis).
- **Medistinal ultrasonographic examination** looking for enlarged lymphnodes, masses or fluid.
- **Endoscopy;** gastrointestinal with biopsies; respiratory with bronchoalveolar lavage (BAL), or transtracheal wash, with cytology and culture.
- Abdominal **Laparoscopy**/Exploratory Laparoscopy to obtain biopsies and culture of various organs.
- **Thoracoscopy** and biopsies of pleura, masses, lung, or pericardium.
- **Immunoelectrophoresis** if globulins elevated along with urine immunoelectrophoresis.
- **Urine protein creatinine ratio** if urine protein elevated with a concurrent inactive sediment.
- **CT** scan/**MRI** of any area in question depending on history and physical findings.
- Positron Emission Tomography (**PET)** scan.
- **Neutrophil** function tests.

As a last resort or if the owners have exhausted all finances consider trial antibiotic therapy, followed by, or in conjuction with, antifungals, and with much consideration, corticosteroid therapy.

MANAGEMENT

A. Rectal Temperature. Obtaining immediate baseline temperature is a priority.
1. Below 41.5°C is rarely harmful, therefore it is essential that thorough consideration as to cause, and appropriate diagnostic testing should be performed prior to empirical therapy.
2. Empirical therapy will confound the course and potentially alter diagnostic tests.
3. If the fever is above 41.5°C *see Heat Stroke/Hyperthermia p. 297* for nonspecific management of hyperthermia.
4. Patient temperature may decline when IV crystalloid fluids are administered.
5. Other forms of active cooling are not recommended with pyrexia unless >41.5°C and rising. Specific therapy with antipyretics and cooling is discussed in *Heat Stroke/Hyperthermia p. 297*.
6. The severity of the fever does not necessarily correlate to the severity of the underlying disease process.
7. Monitor the temperature at least twice daily (or continuously if high and rising) accompanied by complete physical examination.

B. IV access commence fluid therapy.
1. Type of fluids and rate of administration depends on physical and laboratory findings (*see Fluid Therapy p. 347*).

C. **Specific therapy** will be dependent on the diagnosis obtained through physical and laboratory findings. *Refer to readings 4 – 6 for management.*

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INTRODUCTION

Albumin provides 75 – 80% of plasma oncotic pressure. Of the total body albumin, 40% is within the intravascular space and 60% within the interstitium. Albumin normally moves out of the intravascular space into the interstitium and circulates within the lymphatic system. The serum half-life of albumin in normal dogs is 8.2 days with hepatic synthesis normally occurring at 33% of maximum capacity. The albumin molecule functions to reduce microvascular permeability, inhibit endothelial cell apoptosis, and contribute to the overall maintenance of endothelial integrity. As the plasma albumin drops, fewer molecules are available to maintain the integrity of the endothelium, and at a critical point, the endothelium may become more permeable potentially resulting in even greater albumin loss ('hypoalbuminemia begats hypoalbuminemia'). With capillary leak, such as that seen with inflammation, albumin loss is even greater.

A reduction in plasma albumin occurs in critical illness as there is reduced albumin production (a negative acute phase protein), increased utilization associated with the catabolic state, and increased loss (e.g., peritonitis, inflammatory bowel disease). As plasma albumin levels decrease, so does the oncotic pressure. With administration of intravenous (IV) crystalloid fluid therapy, the hydrostatic pressure is raised and the potential for capillary leak is enhanced, especially in patients predisposed to capillary leak. Many critical illnesses are associated with the systemic inflammatory response syndrome (*see Sepsis/SepticShock p. 588*) and endothelial or alveolar epithelial cell injury or dysfunction. Plasma may leak from capillaries into the interstitium, and in the lungs the alveolar space. The consequences are edema of multiple organs, which results in organ dysfunction, respiratory distress and potentially, death. In these situations, a reduction in hydrostatic pressure, using smaller volumes of a crystalloid solution, combined with a colloidal solution, to raise the oncotic pressure, may facilitate adequate organ perfusion while maintaining fluid within the intravascular space. The synthetic colloids are recommended for treatment in low oncotic states in veterinary medicine. However, where capillary leak is associated with the underlying illness, such as in inflammatory states, the potential for leakage of their smaller sized molecules (<60,000 Daltons) is a concern as extravasation of these small molecules may actually draw water into the interstitium (rebound effect).

Albumin has many other important roles in homeostasis. It is a carrier protein for many drugs and endogenous substances, is a direct scavenger of reactive oxygen species and, therefore, may confer protection against ischemia and reperfusion injury. Albumin participates in metabolic and acid-base functions (*p. 406*), reduces platelet aggregation, and augments the function of antithrombin. 25% Human serum albumin (HSA), but not 5% HSA, was shown to inhibit macrophage activation resulting in anti-inflammatory and protective effects against lung injury in a hemorrhagic shock rat model. Most of these specific properties do not exist with the synthetic colloids, therefore, albumin may have additional benefits in managing animals with SIRS and capillary leak disorders. Concentrated (25%), or 5% albumin products are available as human products, unfortunately a similar canine or feline product is not available and plasma is often used in attempt to increase albumin levels in these species. One of the major negative aspects frequently cited in the various human reports is the cost of albumin. While 25% HSA is expensive when compared to crystalloid it is not so when compared to plasma. If the increase in albumin levels in critically ill patients does improve outcome or reduce morbidity, the cost of 25 g (100 mL) albumin (Plasbumin®) is much cheaper than 25 g of albumin obtained from species-specific plasma, which usually contains 25 – 30 g/L (the albumin content of plasma is lower than the normal range for plasma albumin due to dilution with anticoagulant). When comparing the cost of species-specific plasma to that of 25% HSA, one must consider that canine plasma is usually packaged in 250 mL bags, thus requiring 4 bags for an equal amount of albumin in 100 mL 25% HSA. As a large volume of 'fluid' is contained in plasma, repeated plasma transfusions administered to increase albumin content may contribute to an unwanted increase hydrostatic pressure. Frequently, however, fresh frozen plasma (FFP) is recommended as part of the treatment regimen due to the components (i.e., anticytokines, antiproteases, clotting factors) not present in albumin alone.

Recommendations for administration are based on the findings reported in Suggested Reading 2. The use of 25% HSA presented in the published study and discussed here is restricted to 25% Plasbumin®, Bayer Corp. Extrapolation to other similar products cannot be made as variations in preparation amongst products may exist. Indications, administration and potential adverse effects are presented below based on the use of this product at the Ontario Veterinary College, Veterinary Teaching Hospital (OVC-VTH). 25% HSA has been administered to 200 dogs and 2 cats at the OVC-VTH since 1997. Of those previously reported between 1997 and 2001, the age range was 4 months to 12 years, and weight range, 1.4 – 65 kg. Serum albumin and total solids in these patients increased significantly ($p < 0.0001$) above pre-transfusion levels. Similar findings were reported in an abstract (*see Suggested Reading 2. below*). At discharge the increase in serum albumin in most patients was up to 45% above pre-infusion levels with a continuous

increase following transfusion; however dogs with protein-losing enteropathy had an initial increase after transfusion, which started to decline at discharge. This demonstrates that albumin is only of short-term value where ongoing losses are not halted. Systolic blood pressure was also noted to improve significantly (p<0.01).

I. INDICATIONS FOR ADMINISTRATION OF ALBUMIN-CONTAINING FLUIDS

A point to emphasize with respect to hypoalbuminemia is not to assume that broad utilization of albumin-containing fluids is warranted in all critically ill patients, but the use of albumin in specific niche populations may prove to have important clinical benefits. This author believes that the patient's condition and the clinician's careful judgment will dictate the appropriate use of concentrated albumin.

A. Species-specific plasma. Plasma transfusions are frequently administered to critically ill animals with recommendations for maintaining serum albumin >20 g/L (2.0 g/dL) being frequently cited. At the OVC-VTH recommendations for transfusion are in patients with clinical manifestations of hypoalbuminemia (e.g., pleural or abdominal effusion, edema), and to maintain their albumin concentration between 15 – 20 g/L (1.5 – 2.0 g/dL), or higher if specifically warranted. The range for normal canine and feline serum albumin for our laboratory is (29 – 43 g/L [2.9 – 4.3 g/dL]).

1. **Stored plasma** (refrigerated as whole blood for 28 days prior to separation from red blood cells and frozen). *See Transfusion Therapy p. 667.*
   a. Puppies with severe protein loss due to parvovirus diarrhea.
   b. In severe hypoalbuminemic patients (albumin <15 g/L [1.5 g/dL]), requiring volume expansion prior to surgical intervention.
   c. For maintenance of intravascular volume and systemic blood pressure requiring moderate to large volumes of fluids where TS <40 g/L.
   d. In capillary leak situations.
   e. As component therapy (with packed red blood cells) for whole blood loss.
   f. For treatment of warfarin toxicity where FFP not available. Vit K dependent coagulation factors are still effective to a variable degree.

2. **Fresh frozen plasma** (*see Transfusion Therapy p. 667*)
   a. Any inflammatory process or situation with significant cytokine release (i.e., sepsis, pancreatitis, major trauma, neoplasia, major surgery) where antithrombin, alpha-macroglobulins, various anti-cytokines, anti-proteases, and fibronectin are required. Although many of these substances are stable in plasma and whole blood, they do decrease over time. Using fresh (or fresh frozen) plasma ensures their concentration at the maximum possible.
   b. For coagulation factors, specifically Factor VIII and von Willebrand's Factor (vWf), and to a lesser extent Factor V.
   c. Where any of the situations exist in 1 above that also require the components of FFP.

B. 25% Human serum albumin
25% HSA is bottled and stored at room temperature with a long shelf life. The recommended use for albumin is not as a volume replacement fluid, or to increase albumin levels to >20 g/L [>2.0 g/dL], but as an adjunct to current standard therapy where 25% HSA may improve a condition that exists in a critically ill animal (based on individual need).

1. As in 1b – d above.
2. For refractory hypotension where synthetic colloids have failed.
3. In severe hypoalbuminemic patients (albumin <15 g/L [1.5 g/dL]) or <18 g/L [1.8 g/dL] during dehydration and hypovolemia) with ongoing losses (e.g., peritonitis, pleural effusion).
4. Combined with FFP in hypoalbuminemic septic patients.
5. For protein-losing enteropathy prior to surgical biopsy. While low albumin levels are not considered to influence surgical wound healing, one potential protective affect of increased albumin levels prior to biopsy may be a reduction in edema of the bowel with improved perfusion and oxygen delivery influencing healing, rather than a direct relationship to albumin and healing.
6. Markedly hypoalbuminemic patients that continue to vomit (likely due to bowel edema).
7. Reversible liver failure/insufficiency (e.g., porto-systemic shunt, acute hepatitis) where increased albumin levels would reduce morbidity.

II. ADMINISTRATION OF 25% HSA (Plasbumin®, Bayer Inc)

A. 25% HSA is administered peripherally or centrally either alone or in combination with an established crystalloid IV infusion. A vented delivery set is required as the HSA is contained in a bottle. A blood filter set is not used for administration.

B. Aseptic technique is used similar to that required for administration of species-specific transfusions.

C. Where time permits (non-emergent situation), a test dose of 0.25 mL/kg/h given for 15 min while monitoring heart rate, respiratory rate and temperature (baseline prior to transfusion and at end of test dose). If adverse signs such as facial swelling or other signs of anaphylaxis/anaphylactoid reaction are noted discontinue infusion. Vital parameters are again measured upon completion of the transfusion

D. The maximum volume administered to any dog by the author was 25 mL/kg (6.25 g/kg) which was administered continuously over 72h. The mean volume administered to any dog overall, was 5 mL/kg (1.25 g/kg). Higher doses may be administered.

E. The maximum volume given as a slow push or bolus to treat hypotension was 4 mL/kg (1.0 g/kg) with a mean volume of 2 mL/kg (0.5 g/kg).

F. The range for a CRI following a bolus administration was 0.1 – 1.7 mL/kg/h (0.025 – 0.425 g/kg) over a range of 4 – 72h. Infusions were empirically selected so as not to exceed normal albumin levels.

G. Once the bottle is opened, the contents must be used or discarded.

III. POTENTIAL ADVERSE EFFECTS of 25% HSA

A. **Immediate** severe reactions were not noted in any animal at the OVC-VTH following administration of 25% HSA. Facial swelling occurred in two dogs after 2 – 4h of tranfusion. Potential adverse effects reported in Suggested Reading 1 were prolonged clotting time, increased breathing effort, vomiting and fever in a few cases. These complications did not impact on length of hospitalization. For facial edema in cats or dogs:

   1. **Diphenhydramine 1 – 2 mg/kg IM,** may be repeated q8h if required.
   2. *See Anaphylactic Shock p. 615* for more severe reactions.

B. **Delayed** reactions (several days to weeks after administration) are difficult to confirm based on the many medications and synthetic colloids these seriously ill animals also receive. In addition, the effect of their illness may also impact on future presenting signs. Anecdotal verbal reports of potential delayed reactions have been observed, however, the albumin product used is not known by the author. Potential delayed immune-mediated signs following administration of 25% HSA in patients undergoing abdominal, especially intestinal, surgery may be attributed to an enteropathic etiology and not the albumin. For example, enteropathic polyarthritis is linked to lesions of the intestinal tract. However, immunologic reactions may potentially occur.

For potential delayed immune-mediated reactions

   1. **Doxycycline 5 mg/kg q12h x 3 days, reduced to q24h for a further week. If no response in 48 hours add**
   2. **Prednisone 2 mg/kg q12h** on day 1, **1 mg/kg q12h** for two weeks, weaning off during the third week.
   3. **If severe reaction and discomfort,** combine 1 and 2 at the outset.
   4. **Confirmation of non-septic polyarthritis** should be made especially in areas where diseases such as Ehrlichiosis or Lyme disease etc., are prevalent, prior to therapy with corticosteroids.

C. **CLINICAL IMPRESSION** of the use of 25% HSA, Plasbumin● specifically, is a positive one in this author's opinion as many critically ill animals requiring this product may have succumbed to their illness without it. However, it is a foreign protein and potential immune-mediated reactions may occur. It is for this reason that the author only recommends its use after risk analysis is considered and the benefit outweighs the potential risk of a significant adverse event, which we have not noted. This author wishes to highlight that other albumin products *may* have a higher degree of antigenicity *if* preparation differs from that recommended here.

D. Bovine Serum Albumin has been researched for the use of dogs and was shown to be highly immunogenic with severe polyarthritis and glomerulonephritis being observed in some dogs while a milder form appeared in all others (*see Suggested Reading 3.*). Its use is therefore not recommened in dogs.

PHARMACOLOGY

1) **Doxycycline** is suggested here as it has been used in some human patients developing polyarthritis and dermatologic lesions following intestinal surgery. It is felt that bacterial translocation at the time of bowel surgery incited the immune response. Corticosteroids are more commonly administered.

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NOTES

INTRODUCTION

Neutropenia may result from impaired granulopoiesis and/or from overwhelming sepsis where tissue demands exceed marrow granulocyte reserve. Causes of impaired granulopoiesis are presented in Table 1. With cytotoxic chemotherapy, neutropenia most commonly occurs within 5 – 10 days after administration, although some drugs may cause later nadir neutrophil counts (e.g., carboplatin in cats). Examples of overwhelming sepsis are septic peritonitis and pyelonephritis. In parvoviral infections both impaired granulopoiesis and sepsis of gastrointestinal origin contribute to neutropenia. In all cases, neutropenia may be accompanied by thrombocytopenia because of concurrent megakaryocytic hypoplasia and/or disseminated intravascular coagulation.

TABLE 1. Causes of impaired granulopoiesis in the dog and cat

Inherited   Cyclic hematopoiesis in gray collies

Neoplasia
         Lymphocytic leukemia/leukemic lymphoma
         Multiple myeloma
         Myeloid leukemia, myelodysplastic syndrome
         Metastatic cancer to bone marrow (myelophthisis)
         Sertoli cell tumor (dog, paraneoplastic syndrome-estrogen toxicosis)

Infections
         Ehrlichia canis
         Canine and feline parvovirus
         Feline leukemia virus
         Feline immunodeficiency virus

Cytotoxic anticancer therapy causing predictable myelosuppression

Drugs with known risk for causing unpredictable myelosuppression
         Dog: estrogen, phenylbutazone
         Cat: chloramphenicol, griseofulvin, propylthiouracil, methimazole

Drugs with reported idiosyncratic reactions causing neutropenia
         Dog: cephalosporins, sulfonamides, angiotensin-converting enzyme inhibitors, phenobarbital,
                   fenbendazole, albendazole
         Cat: cephalosporins

Toxins   Autumn crocus

Idiopathic
         Immune-mediated neutropenia
         Other (e.g., granulocyte colony-stimulating factor deficiency)

Neutropenic animals are at *increased risk for bacterial and fungal infections*, both from opportunistic organisms and common pathogens. The risk increases exponentially with severity of neutropenia.

TABLE 2. Risk of opportunistic infection during neutropenia

Neutrophil Count	Definition	Risk of Infection
$2.0 \times 10^9/L$ to < lower limit of normal	Grade 0 Neutropenia	minimal
$1.5 \times 10^9/L$ to < $2.0 \times 10^9/L$	Grade 1 Neutropenia	marginal
$1.0 \times 10^9/L$ to < $1.5 \times 10^9/L$	Grade 2 Neutropenia	mild
$0.5 \times 10^9/L$ to < $1.0 \times 10^9/L$	Grade 3 Neutropenia	moderate
$0.0 \times 10^9/L$ to < $0.5 \times 10^9/L$	Grade 4 Neutropenia	high

Other factors increasing the risk of infection during myelosuppression include: 1) increased risk with falling, rather than stable, neutrophil count; 2) gastrointestinal damage (e.g., parvoviral infections, cytotoxic chemotherapy), skin damage (e.g., intravenous catheterization, biopsies) and damage to other mucosal surfaces; 3) concurrent immunosuppression (e.g., myeloma), lymphopenia and monocytopenia; and 4) species – dogs are at higher risk than cats.

The *outcome of infection* is related to duration of neutropenia. If neutropenia lasts <7 days (short duration), infections can usually be controlled with antibiotics. If neutropenia lasts 7–14 days (moderate duration), infections are more difficult to manage. If neutropenia lasts > 14 days (prolonged neutropenia) infections are even more difficult to manage, especially if the neutrophil count is < 0.2 x 10^9/L.

Infections may occur with exogenous organisms from the environment, hospital, or another animal, or with endogenous organisms from the patient's own flora (especially of the intestinal tract) that translocate to other sites. *Escherichia coli* and other gram-negative enteric bacilli are most commonly involved, followed by *Staphylococcus* and *Streptococcus* spp, *Pseudomonas* spp, and, least frequently, anaerobes (potentially more risk with parvoviral infections). Fungal infections with *Candida* and *Aspergillus* spp are not common; the risk increases with a) the duration of antibacterial therapy beyond 1 week (especially those antibiotics disturbing intestinal anaerobic bacteria such as ampicillin, cefoxitin, imipenem-cilastatin, meropenem), and b) concurrent immunosuppressive therapy (e.g., with cyclosporine).

DIAGNOSIS

History/Signalment
- Neutropenia in-itself does not cause signs. Clinical signs are due to the underlying disease and infection – depression and inappetence are the most common signs. Occasionally neutropenia is an incidental finding.
- Vomiting, diarrhea and abdominal pain may be present (parvovirus, cytotoxic therapy, sepsis).
- Review drug history, exposure to toxins, and exposure to infectious agents.
- Review neutering history (Sertoli cell tumour). Note: Sertoli cell tumours have occasionally been seen in non-cryptorchid neutered dogs.

Clinical Signs/Physical Examination
- Most animals with infection will develop a fever. Fever, depression or inappetence in a neutropenic animal should be considered to be due to bacterial infection until proven otherwise. Fever may not be present and in some cases the only signs of infection are lethargy, inappetence, and tachycardia. This is most likely in older animals and animals treated with corticosteroids, which may have blunted febrile responses. A normal temperature may also represent progression from fever to hypothermia in septic shock.
- Local signs of inflammation are subtle if granulopoiesis is impaired. In many cases it is not possible to document a suspected infection.
- Septic animals may be in shock.
- Palpate testicles and abdomen, and examine for signs of feminization in a male dog (Sertoli cell tumour).

Laboratory Evaluation/Diagnostic Imaging
Work-up to diagnose the cause of neutropenia and characterize the illness.
- ELISA test for parvovirus in feces, fluorescent antibody test for *Ehrlichia canis*, FeLV and FIV tests.
- Bone marrow biopsy – most useful to diagnose neoplasia in bone marrow.
- Complete blood count, serum biochemistry profile, urinalysis, thoracic radiographs, abdominal radiographs and ultrasound examination, abdominocentesis and diagnostic peritoneal lavage, in an effort to determine an underlying cause and site of sepsis.
- Cultures of blood, urine, trans-tracheal wash or bronchoalveolar lavage fluids, pleural fluid, peritoneal fluid or other tissues or fluids, in an effort to determine and characterize a site of sepsis.
- Neutropenic animals receiving antibacterial therapy for longer than 10 days: monitor feces by cytology for fungi. Fecal culture for fungi should be performed if a new fever or diarrhea occurs.

Work-up for a febrile episode in a patient receiving cytotoxic anticancer therapy.
- Monitor temperature in the asymptomatic neutropenic animal and in the animal at risk for neutropenia. Axillary temperature measurements facilitate home monitoring and measure 0.5 – 1°C (1 – 2°F) lower than rectal temperatures. A rectal temperature above 39.0°C (102.2°F) in dogs and 39.2°C (102.6°F) in cats should be regarded with suspicion and the animal either treated for sepsis or the temperature rechecked in several hours. A temperature above 39.5°C (103.1°F) usually represents a true fever.
- The duration of neutropenia is typically short, and an extensive diagnostic evaluation is usually not necessary.
- Obtain CBC to confirm neutropenia.
- Consider obtaining baseline serum glucose, urea and electrolyte levels, and urine specific gravity.

- Consider blood cultures. Note that results are often negative and are reported after neutropenia and fever have resolved. Definitely obtain if the patient is severely ill or if the fever is unresponsive after 48 – 72 hours of antibiotic treatment.
- Consider complete serum chemistry profile, abdominal radiographs and abdominal ultrasound examination if any of the following are present: vomiting, diarrhea, abdominal distention, abdominal pain, the patient is severely ill, or the fever is unresponsive after 48 – 72 hours of antibiotic treatment.
- Consider thoracic radiographs. Definitely obtain if the animal is dyspneic, coughing, or has nasal discharge, is severely ill, or the fever is unresponsive after 48 – 72 hours of antibiotic treatment. Note that radiographic signs of pneumonia will be subtle if granulopoiesis is impaired.
- Trans-tracheal wash or bronchoalveolar lavage: obtain if radiographic signs of pneumonia or animal is dyspneic, coughing, or has nasal discharge.
- If animal is not neutropenic, the tests described above should be performed in an effort to determine the cause of fever.

MANAGEMENT

A. **Isolation:** protect animal from exogenous pathogens, reduce contamination of hospital.
- Neutropenic animals at home should be confined to the house and yard.
- Hospitalized animals should have their own thermometer. Personnel should wash their hands thoroughly and change laboratory coats before handling the patient. Gloves, isolation gowns and isolation boots should be considered for severe cases ("reverse isolation").
- Animals with parvoviral infections should be isolated in the hospital's isolation area. Other neutropenic animals should not be placed in this area.
- Animals with severe neutropenia should be fed only dry, canned or well-cooked foods.

B. **Antibiotic therapy:** protect animal from endogenous pathogens, treat existing infections. Antibiotic therapy includes 1) prophylaxis, 2) empirical therapy, 3) therapy of documented infections.
  1. **Prophylactic antibiotics** for the asymptomatic animal should be considered whenever a neutrophil count $< 1.0 \times 10^9$/L is present or anticipated (Table 3).
     a. Prophylactic therapy is directed at the intestinal gram-negative organisms most often responsible for infections. The anaerobic population is left relatively undisturbed as it provides resistance to fungal overgrowth and colonisation by exogenous organisms.
     b. A second objective of prophylactic therapy is to provide sufficient blood and tissue antibiotic concentrations to control an incipient bacterial infection.

TABLE 3. Prophylactic oral antimicrobial therapy for the neutropenic dog and cat (see over for comments)

Antimicrobial Drug	Doses
Sulfonamides **Trimethoprim-sulfamethoxazole/sulfadiazine**	**15 mg/kg (combined dose) q12h** 30 mg/kg (combined dose) q12–24h
Ormetoprim-sulfadimethoxine	55 mg/kg on first day, then 27.5 mg/kg q24h
Fluoroquinolones **Enrofloxacin (dogs)** **Ciprofloxacin (dogs)** Orbifloxacin **Marbofloxacin (cats)** Difloxacin	**5 – 20 mg/kg q24h** **10 – 30 mg/kg q24h** 2.5 – 7.5 mg/kg q24h **2.5 – 5 mg/kg q24h** 5 – 10 mg/kg q24h
β-lactam antibiotics **Cephalexin** Amoxicillin Amoxicillin-clavulanate	**30 mg/kg q12h** 10 – 20 mg/kg q12h 12.5 – 25 mg/kg q12h
Combinations Fluroquinolone + ß-lactam antibiotic	As above

COMMENTS TO TABLE 3

Drugs and dosages presented in bolded text are those most commonly used at OVC. Sulfonamides may cause keratoconjunctivitis sicca with prolonged use and may retard marrow recovery following severe myelosuppression. Sulfonamides, fluoroquinolones at lower doses, and ß-lactam antibiotics do not provide prophylaxis against *Pseudomonas* spp. Prolonged therapy and high doses of fluoroquinolones should be avoided in cats because of the risk for visual disturbances. Amoxicillin and amoxicillin-clavulanate, which suppress intestinal anaerobes, are reserved for cats not tolerating other choices. The combination of fluoroquinolone and ß-lactam antibiotics is reserved for animals with severe, prolonged neutropenia. Anti-fungal prophylaxis is not recommended.

2. **Empirical antibiotic therapy** should be started promptly in the sick neutropenic animal (before culture results are reported).

 a. Properties of the ideal antibiotics are: 1) bactericidal, 2) limited bone marrow toxicity, and 3) active against Enterobacteriaceae, Pseudomonas and gram-positive cocci. Both combination therapy and monotherapy may be used (Table 4). Intravenous therapy is preferred, and in most cases the animals will require intravenous fluids, but there must be strict attention to aseptic catheter placement and catheter care (*see p. 360*).

 b. In the animal with impaired granulopoiesis and opportunistic infection, a reduction in fever and improvement in attitude are expected within 48 – 72 hours and often occur after the first dose. Therapy should be continued for 1 to 7 days beyond achievement of a neutrophil count of 1.0 x 10⁹/L and resolution of fever. During this period a change from intravenous therapy to oral therapy (Table 3) may be attempted.

 c. Oral therapy may also be considered as initial therapy if the animal is clinically stable and not vomiting, as long as provisions are made to institute parenteral therapy if the animal deteriorates. In addition to the antibiotics in Table 3, moxifloxacin 10 mg/kg PO q24h (dogs) should be considered as it has more activity against gram-positive organisms and anaerobes than do the other fluoroquinolones.

TABLE 4. Parenteral empirical antibiotic therapy for the febrile neutropenic dog or cat*

Disease	First choice(s) in the OVC – ICU	Alternative choices
Parvoviral infection	Ampicillin 20 – 40 mg/kg, IV, SC q6–8h Cefoxitin** 20 – 30 mg/kg, IV, SC q6–8h	Ampicillin-sulbactam 50 mg/kg, IV, IM q6–8h, *OR* Ampicillin 20 – 40 mg/kg, IV, SC q6-8h, **AND** Amikacin*** 15 – 20 mg/kg, IV, SC q24h, *OR* Gentamicin*** 5 – 6 mg/kg, IV, SC q24h, *OR* Netilmycin*** 6 mg/kg, IV q24h, *OR* Tobramycin*** 6 mg/kg, IV, IM, SC q24h
Myelosuppression from cytotoxic therapy, toxicoses, FIV/FeLV, neoplasia	**Dogs:** Enrofloxacin**** 5 – 10 mg/kg, IV, IM q12–24h, **AND** Cefazolin** 20 – 30 mg/kg, IV, SC q6–8h, *OR* Cephalothin** 25 – 40 mg/kg, IV, SC q6–8h	Alternative choices for Enrofloxacin: Ciprofloxacin 5 – 10 mg/kg, IV q12–24h, (1-hour infusion) Amikacin*** 15 – 20 mg/kg, IV, IM, SC q24h, *OR* Gentamicin*** 5 – 6 mg/kg, IV, IM, SC q24h, *OR* Netilmycin*** 6 mg/kg, IV q24h, *OR* Tobramycin*** 6 mg/kg, IV, IM, SC q24h
		Alternative choices for Cefazolin and Cephalothin: Ampicillin 20 – 40 mg/kg, IV, SC q6–8h, *OR* Ampicillin-sulbactam 50 mg/kg, IV q6–8h, *OR* Piperacillin 25 – 50 mg/kg, IV, IM q6–8h, *OR* Piperacillin-tazobactam 25 – 50 mg/kg, IV, IM q6–8h *OR* Ticarcillin 40 – 75 mg/kg, IV, IM q6–8h, *OR* Ticarcillin-clavulanate 30 – 50 mg/kg, IV, IM q6–8h
		Alternative single-agent choices: Cefoxitin** 20 – 30 mg/kg, IV, SC q6-8h, *OR* Imipenem-cilastatin***** 2 – 10 mg/kg IV q6–8h, (1-hour infusion), *OR* Meropenem **Dogs:** 13 mg/kg IV q8h; 30 mg/kg SC q12h **Cats:** 15 mg/kg, IV q8h; 30 mg/kg SC q12h , *OR* Ceftazidime** 25 – 30 mg/kg, IV, SC q8h

Disease	First choice(s) in the OVC – ICU	Alternative choices
	Cats: Ampicillin 20 – 40 mg/kg, IV, SC q6–8h Cefoxitin★★ 20 – 30 mg/kg, IV, SC q6–8h	Ampicillin-sulbactam 50 mg/kg, IV, IM, q6–8h, *OR* Cefazolin★★ 20 – 30 mg/kg, IV, SC q6–8h, *OR* Cephalothin★★ 25 – 40 mg/kg, IV, SC q6–8h Ampicillin 20 – 40 mg/kg, IV, SC, q6–8h, *OR* Cefazolin★★ 20 – 30 mg/kg, IV, SC q6–8h, *OR* Cephalothin★★ 25 – 40 mg/kg, IV, SC q6–8h, **AND** Amikacin★★★ 15 – 20 mg/kg, IV, IM, SC q24h, *OR* Gentamicin★★★ 5 – 6 mg/kg, IV, IM, SC q24h, *OR* Netilmycin★★★ 6 mg/kg, IVq24h, *OR* Tobramycin★★★ 6 mg/kg, IV, IM, SC q24h, Alternative choices for cefoxitin and combinations above: Imipenem-cilastatin★★★★★ 2 – 10 mg/kg, IV q6–8h, (1-hour infusion), *OR* Meropenem 15 mg/kg, IV q8h; 30 mg/kg, SC q12h, *OR* Ceftazidime★★ 25 – 30 mg/kg, IV, SC q8h
Ehrlichiosis Mild-moderately ill: Severely ill:	Doxycycline 5 mg/kg, IV q12h (1-hour infusion) Doxycycline 5 mg/kg, IV q12h (1-hour infusion), **AND** Enrofloxacin★★★★ 5 – 10 mg/kg, IV, IM q12–24h, *OR* Ciprofloxacin 5 – 10 mg/kg, IV q12–24h (1-hour infusion)	Tetracycline 5 – 10 mg/kg, IV, IM q8h Doxycycline 5 mg/kg, IV q12h (1-hour infusion), *OR* Tetracycline 5 – 10 mg/kg, IV, IM q8h, **AND** Cefoxitin★★ 20 – 30 mg/kg, IV, SC q6-8h, *OR* Amikacin★★★ 15 – 20 mg/kg, IV, IM, SC q24h, *OR* Gentamicin★★★ 5– 6 mg/kg, IV, IM, SC q24h, *OR* Netilmycin★★★ 6 mg/kg, IV q24h, *OR* Tobramycin★★★ 6 mg/kg, IV, IM, SC q24h
Neutropenia of unknown cause Mild-moderately ill: Severely ill:	As per myelosuppression Imipenem/Cilastatin 2 – 10 mg/kg, IV q6–8h (1-hour infusion), *OR* Meropenem **Dogs:** 13 mg/kg, IV q8h; 30 mg/kg, SC q12h **Cats:** 15 mg/kg, IV q8h; 30 mg/kg, SC q12h	As per myelosuppression As per myelosuppression Alternative β-lactam combination therapy choices: Ampicillin 20 – 40 mg/kg, IV, SC q6–8h, *OR* Ampicillin-sulbactam 50 mg/kg, IV, IM q6–8h, *OR* Cefazolin★★ 20 – 30 mg/kg, IV, SC q6–8h, *OR* Cephalothin★★ 25 – 40 mg/kg, IV, SC q6–8h, **AND** Piperacillin 25 – 50 mg/kg, IV, IM q6–8h, *OR* Piperacillin-tazobactam 25 – 50 mg/kg, IV, IM q6–8h *OR* Ticarcillin 40 – 75 mg/kg, IV, IM q6–8h, *OR* Ticarcillin-clavulanate 30 – 50 mg/kg, IV, IM q6–8h, *OR* Ceftazidime★★ 25 – 30 mg/kg, IV, SC q8h, ± Cefoxitin★★ 20 – 30 mg/kg, IV, SC q6–8h, *OR* Metronidazole 10 – 15 mg/kg, IV q8h (1-hour infusion), *OR* Clindamycin 10 mg/kg, IV, SC q12h

Disease	First choice(s) in the OVC – ICU	Alternative choices
Overwhelming sepsis	Imipenem/Cilastatin 2–10 mg/kg, IV q6-8h, (1-hour infusion), **OR** Meropenem **Dogs:** 13 mg/kg, IV q8h; 30 mg/kg, SC q12h **Cats:** 15 mg/kg, IV q8h; 30 mg/kg, SC q12h	Enrofloxacin (dogs) ******** 5 – 10 mg/kg, IV, IM q12-24h, **OR** Ciprofloxacin (dogs) 5 – 10 mg/kg, IV q12h (1-hour infusion), **OR** Amikacin******* 15 – 20 mg/kg, IV, IM, SC q24h, **OR** Gentamicin******* 5 – 6 mg/kg, IV, IM, SC q24h, **OR** Netilmycin******* 6 mg/kg, IV q24h, **OR** Tobramycin******* 6 mg/kg, IV, IM, SC q24h, **AND** Ampicillin 20 – 40 mg/kg, IV, IM, SC q6-8h, **OR** Cefazolin****** 20 – 30 mg/kg, IV, SC q6-8h, **OR** Cephalothin****** 25 – 40 mg/kg, IV, SC q6-8h, ± Metronidazole 10 – 15 mg/kg, IV q8h (1-hour infusion), **OR** Clindamycin 10 mg/kg, IV, SC q12h Alternative β-lactam based combination therapy choices: As per neutropenia of unknown cause

*   IV administration is preferred. All IV injections are given as a slow push over 15 – 20 minutes unless indicated otherwise.
**   Cephalosporins (Cefazolin, Cephalothin, Cefoxitin, Ceftazidime) are usually given at 30 mg/kg, IV q8h.
***   To reduce the risks of nephrotoxicity with aminoglycoside antibiotics, we prefer the lower doses and once daily administration, and avoid their use in animals that are dehydrated or receiving furosemide.
****   The initial dose in dogs is usually 5 mg/kg, IV q12h. Higher doses are reserved for those cases where *Pseudomonas* spp. is suspected or isolated because of the risk of causing seizures and other neurologic signs, especially with repetitive administration, geriatric patients, hypoalbuminemia, and a history of seizures. Enrofloxacin is approved for IM use only, but the solution is a tissue irritant and IV administration is preferred. For IV injection, the solution should be injected over 20 – 60 minutes; dilution of 1 part parenteral solution with 9 parts sterile water for injection may be used. The parenteral solution should not be injected SC.
***** We usually use 5 mg/kg, IV q8h (1-hour infusion).

d. The fever may not resolve if
  1. it is not solely bacterial in origin
  2. the organism is not sensitive to the antibiotic(s)
  3. drug doses are too low (uncommon)
  4. the drug is not sufficiently penetrating the septic focus
  5. there is such a severe compromise of host defences that the infection and associated fever will not respond to any antibiotic. The latter may occur with severe prolonged neutropenia. Previous culture results may guide therapy, but another empirical choice may be necessary.

e. If the animal is clinically stable, the current antibiotics should be continued.

f. If the animal is deteriorating, additional antibiotics with a different spectrum of activity should be given. The choice depends on which antibiotics were used for initial therapy and on the resistant organism suspected:
  1. **resistant gram-negative organism** (e.g., signs of intestinal damage or respiratory signs) – choices where the spectrum covers *Pseudomonas* include an **aminoglycoside, anti-pseudomonal penicillin (piperacillin, ticarcillin), fluoroquinolone, ceftazidime, imipenem-cilastatin, or meropenem.**
  2. **resistant gram-positive organism** (e.g., signs of phlebitis, injury to the skin or oral cavity, or respiratory signs) – **clindamycin, imipenem-cilastatin (activity against *Streptococcus* spp incomplete) or meropenem.**
  3. **anaerobe – metronidazole, clindamycin, cefoxitin, imipenem-cilastatin or meropenem.** (Imipenem-cilastatin are suitable as a means of increasing broad-spectrum antibacterial activity and in some cases are substituted for existing therapy.)
  4. **fungus – itraconazole 5 mg/kg, PO q12h or fluconazole 10 mg/kg, PO q24h (and IV in dogs).** Empirical amphotericin B is used in humans with non-responding fever, but this is not recommended in animals.

g. If multiple antibiotics are being used, then selective withdrawal should begin once the animal is improving.

3. **Therapy of Documented Infections.** An infection is documented in strict terms when both the site of infection and infecting organism are known. In broader terms an infection is documented if only the site of infection is known (e.g., radiographic evidence of pneumonia).
   a. Bactericidal antibiotics should be used for treatment, with the choice based upon susceptibility testing.
   b. Treatment should be continued to a minimum of seven days beyond recovery of the neutrophil count to 1.0 x 10⁹/L and resolution of clinical and radiographic signs.
   c. Pneumonia is usually treated for a minimum of 6 weeks.
   d. The infection may transiently appear to become worse as the neutrophil count improves.
   e. For fungal infections, clinical (diarrhea) or subclinical intestinal candidiasis are most likely, but intestinal aspergillosis, fungemia, fungal pneumonia and fungal urinary tract infections may also rarely occur.
      1. Recommended treatment for candidiasis (all sites except urinary tract) is **itraconazole 5 mg/kg, PO q12h** until recovery of the neutrophil count to 1.0 x 10⁹/L, at which time treatment is changed to **5 mg/kg** q24h and continued to a minimum of 14 days beyond resolution of clinical and radiographic signs. Intestinal candidiasis can be treated with **nystatin 100,000 U PO q6h,** but treatment with itraconazole is preferred to protect against translocation.
      2. Urinary tract candidiasis is best treated with **fluconazole 5 mg/kg PO q12h** (expensive).
      3. Veterinary experience with aspergillosis in the neutropenic animal is limited. **Itraconazole 5 mg/kg, PO q12h** may be tried as initial therapy in the stable animal. If there is no response, and for fulminant aspergillosis, a suggested protocol is **amphotericin B deoxycholate, 0.25 mg/kg day 1, followed by 0.1 – 0.25 mg/kg q24h** until the neutrophil count has recovered beyond 1 x 10⁹/L. At this time treatment is changed to standard protocols of **0.25 – 0.5 mg/kg 3 times a week.** The **lower doses should be used in cats.** The drug is diluted in 50 – 1000 mL 5% dextrose and infused over 3 – 6 hours (protect from light with aluminum foil). The animal should be well-hydrated and renal function monitored daily. Treatment should be continued to a minimum of 14 days beyond resolution of clinical and radiographic signs or to a maximum **cumulative dose of 4 – 8 mg (cats) and 8 – 10 mg (dogs).** A typical course of treatment is 6 weeks. Lipid-complex formulations of amphotericin B (more expensive) should be used if there is renal impairment or poor response. Chronic follow-up therapy with itraconazole may be required if the animal remains myelosuppressed or immunosuppressed (*see reference 4*).

C. **Removal of septic foci.** Excision or debridement of the site of infection should be performed in animals with neutropenia due to overwhelming sepsis.

D. **Stimulation of neutrophil production.** Recombinant human granulocyte colony-stimulating factor (rhG-CSF) is useful when given to ameliorate neutropenia due to cytotoxic therapy.
   1. Consider for dogs and cats with febrile neutropenia with neutrophil counts <0.5 x 10⁹/L and afebrile animals with neutrophil counts <0.5 x 10⁹/L for >72 hours. The dose is **5 μg/kg, SC q24h** given 1–2 days beyond achieving a neutrophil count of 1.0 – 3.0 x 10⁹/L. Typically 3 – 6 doses are needed.
   2. Prophylactic use of rhG-CSF may also be considered for animals with a previous episode of febrile neutropenia, especially in an attempt to avoid reduction of the chemotherapy dose. The drug should be given at **5 μg/kg SC q24h,** beginning 1 – 5 days post-chemotherapy, and continued until 10 days post-chemotherapy.
   3. If 5 μg/kg once a day does not result in sufficient granulopoiesis, the dose may be increased to **5 μg/kg, SC q12h.**
   4. rhG-CSF is less useful in the management of neutropenia due to overwhelming sepsis, pancytopenia due to idiosyncratic drug reactions, idiopathic causes, or infectious diseases.
   5. Treatment of parvoviral infections has yielded variable results and routine treatment with rhG-CSF is not recommended.
   6. If rhG-CSF is used for the treatment of neutropenia due to a cause other than cytotoxic therapy, **5 μg/kg, SC q12–24h** is recommended, continuing for 2 days beyond achieving a neutrophil count of 3.0 x 10⁹/L, for a maximum of 10 – 14 days.
   7. Lithium carbonate has been advocated for bone marrow stimulation but its use is not recommended.

E. **Neutrophil replacement. Granulocyte transfusions** are impractical in most practices and rarely used. The primary indication is neonatal sepsis (*see Fading Neonatal Puppy and Kitten p. 540*). For further discussion the reader is referred to reference 2.

PHARMACOLOGY

1) **Recombinant human granulocyte colony-stimulating factor** (rhG-CSF, Neupogen, Amgen) and **recombinant human granulocyte macrophage colony-stimulating factor** (rhGM-CSF, Prokine, Immunex) are cytokines that stimulate bone marrow granulocyte precursors. Canine and feline products are not available. Their use in dogs in cats is limited to short-term use (10 – 14 days) by antibody production, which abrogates neutrophil stimulation after 2 – 3 weeks and may lead to neutropenia that can last several weeks to months. In an effort to extend duration of therapy, it is likely that immunosuppression with corticosteroids will not block antibody production. Treatment with cytotoxic drugs or cyclosporine may have such an effect, although it is not well documented. The drugs are expensive and the cost of therapy must be weighed against the potential cost-savings in reducing hospitalization and supportive care. The use of rhG-CSF is recommended over rhGM-CSF, as there is more veterinary experience with the former and it appears to be a more potent stimulator of neutrophil production in dogs and cats. Neupogen is supplied as a single-dose $300\,\mu g/mL$ preservative-free solution. Cost and small doses necessitate multiple dosing from a single bottle when used in animals; care must be taken to penetrate the bottle aseptically.

2) **Lithium carbonate** is a psychomodulating drug that has mild bone marrow stimulating properties in dogs, but not in cats. Results with its use in dogs are variable, and while the drug is inexpensive and readily available, blood levels must be monitored which increases expense. There are a number of undesirable side-effects associated with high blood levels.

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Also see references for Oncologic Emergencies.

NOTES

INTRODUCTION

Patients with cancer are at increased risk for developing critical disorders. These disorders may be due to **treatment** or the **cancer** itself.

Emergencies due to systemic chemotherapy include:

- Severe **neutropenia** and attendant risk for **sepsis** (*see Neutropenia p. 435*).
- Severe **thrombocytopenia** and attendant risk for bleeding (uncommon except with lomustine, (*see Thrombocytopenia p. 451*).
- Severe **gastrointestinal tract injury** or **pancreatitis** (*see Vomiting p. 74, Acute Diarrhea p. 32, Gastrointestinal Hemorrhage p. 67 and Acute Pancreatitis p. 45*).
- Specific toxicoses associated with certain drugs. Specific toxicoses for the most commonly used drugs include:
    1) Anaphylaxis with asparaginase, and anaphylactoid reactions with doxorubicin and epirubicin, and paclitaxel.
    2) **Local tissue necrosis** due to extravasation of **vesicant drugs,** including doxorubicin, epirubicin, actinomysin D, vincristine, vinblastine, paclitaxel, and mechlorethamine. Less severe reactions may occur with **irritant drugs,** including mitoxantrone (occasionally severe), melphalan (occasionally severe), cisplatin, and dacarbazine. Extravasation may occur because of perivascular injection or leakage from fragile blood vessels.
    3) Sterile hemorrhagic **cystitis** with cyclophosphamide (and ifosfamide) in dogs (and uncommonly in cats). This is probably caused by acrolein, a metabolite of these drugs, in the urine. Signs may begin within 2 – 5 days following a high dose of cyclophosphamide (100 – 200 mg/m^2), and usually occur after the first to third dose of typical sequential chemotherapy protocols. If a low-dose cyclophosphamide protocol is being used (e.g., 50 mg/m^2 4 days/week), cystitis usually begins after 4 – 5 months of therapy.
    4) **Acute renal failure** with cisplatin in dogs. (Carboplatin, doxorubicin and methotrexate may also rarely be associated with acute renal failure in dogs or cats).
    5) Severe **pulmonary edema** with cisplatin in cats (drug contraindicated).
    6) **Heart failure** and arrhythmias with doxorubicin and epirubicin in dogs.
    7) **Neurologic signs** (primarily excitation) with use or accidental ingestion of 5-fluorouracil in dogs, and especially in cats (drug contraindicated). Vincristine may rarely cause a polyneuropathy in dogs, and it is not usually an emergency.
- **Tumor lysis syndrome.** This is an uncommon syndrome of metabolic disturbances, most often complicating rapid response to initial treatment of an animal with a heavy lymphoma burden. Additional risk factors include volume contraction, decreased renal function, and decreased hepatic function. Rapid destruction of malignant cells releases intracellular purines (which are metabolized to uric acid), phosphorus and potassium. Renal failure may result (mechanisms include hyperuricemia and nephrocalcinosis), and life-threatening hyperkalemia may occur.

Emergencies due to surgery include:

- **Intraoperative hemorrhage** (increased risk with excision of some tumors – e.g. thyroid carcinoma, adrenal tumors, hemangiosarcoma).
- Post-operative **dehiscence.**
- **Hypocalcemia** following excision of a parathyroid tumor.
- **Hypoadrenocorticism** following excision of an adrenocortical tumour.

Radiation therapy may cause **severe local reactions,** but these do not usually present as true emergencies. (An exception is rectal perforation). Total and half-body radiation therapy may result in side-effects similar to systemic chemotherapy. Swelling of central nervous system tumors during initial therapy may cause worsening of neurologic signs.

Emergencies due to the cancer itself result from invasion, compression, or obstruction of normal tissues, or from paraneoplasic syndromes. In many cases the emergency disorder is the presenting complaint for an animal with an undiagnosed neoplasm. The more common emergencies include (categories are not mutually exclusive):

- Systemic bacterial and fungal **infections.** These may be secondary to neutropenia (leukemia, myelophthisis) and reduced functional immunoglobulins (plasma cell neoplasia). Peritonitis may result from a perforated gastrointestinal ulcer (mast cell tumor, gastrinoma, or primary gastrointestinal neoplasia [lymphoma, adenocarcinoma and others]).

- **Hemorrhage.** This may be due to thrombocytopenia (leukemia, myelophthisis), thrombocytopathia (plasma cell neoplasia), disseminated intravascular coagulation (thyroid carcinoma, hemangiosarcoma, and others), gastrointestinal ulceration (causes listed in above), and rupture of a solid tumour. The latter is most common with hemangiosarcomas, where bleeding may be intraabdominal, pericardial, pleural, pulmonary (bleeding metastases) or subcutaneous. Retroperitoneal bleeding has occurred with renal and adrenal tumors. Bleeding secondary to splenic and hepatic rupture has occurred with lymphoma and other infiltrative hematopoietic cancers.
- **Dyspnea.** This may be due to: a) luminal or extra-luminal laryngeal, tracheal or bronchial obstruction; b) pleural space disorders, including effusion (mediastinal lymphoma, thymoma, metastatic lymphadenopathy, pleural metastases, bleeding hemangiosarcoma or thoracic wall mass, mesothelioma), pneumothorax (ruptured lung mass), and space-occupying mass; c) advanced pulmonary metastases and bleeding metastases (hemangiosarcoma); d) pulmonary thromboembolism (which may be associated with anesthesia and surgery).
- **Seizures and other neurologic signs.** Seizures may be due to intracranial neoplasia, hypoglycemia, and hyperviscosity syndrome. Hypoglycemia is most often due to an insulinoma, but also occurs with intestinal leiomyoma/leiomyosarcoma, hepatoma/hepatocellular carcinoma and rarely other tumors (which are usually large and have a protracted course of development). Hyperviscosity syndrome may be due to hyperglobulinemia (plasma cell neoplasia), polycythemia vera, or leukemia with peripheral blood counts >100 x 10^9/L. Spinal cord compression may cause back pain, apparent lameness (root signature), and paresis/paralysis. Signs may result from primary or metastatic neoplasia to the spinal cord or vertebral bodies, and the latter may result in pathologic fractures.
- **Hypercalcemia.** In the dog, lymphoid neoplasia and anal sac apocrine gland adenocarcinoma are the most common causes. Primary hyperparathyroidism also causes hypercalcemia, but it rarely occurs as an emergency. Hypercalcemia has also been reported infrequently with other neoplasms. Hypercalcemia is uncommon in the cat, but has been reported with primary hyperparathyroidism, squamous cell carcinoma and lymphoma.

Less common emergencies include:

- **Severe weakness** due to polyneuropathy or myasthenia gravis. Polyneuropathy is a common paraneoplastic syndrome. It is typically subclinical or mild, but may be severe with insulinoma. Myasthenia gravis may occur secondary to a thymoma.
- **Hypertension** (pheochromocytoma, hyperviscosity syndrome).
- **Urinary tract outflow obstruction** (transitional cell carcinoma of the bladder or urethra, prostatic carcinoma) causing discomfort ± uremia.
- **Hypoadrenocorticism** (adrenal gland invasion by lymphoma).
- **Thromboembolism** other than pulmonary thromboembolism.
- Numerous other disorders may occur relating to organ dysfunction and lymphatic obstruction (ascites, subcutaneous edema), but, while urgent, do not typically present as true emergencies.

DIAGNOSIS

History/Signalment

- Varies with disorder and organ system involved. Cancer and its treatment may cause virtually any sign.
- Acute depression may be the chief complaint with infection, hemorrhage, disorders predisposing to seizures (including brain herniation and hypoglycemia), hypercalcemia, urinary tract outflow obstruction, hypoadrenocorticism, and tumor lysis syndrome. Other signs of tumor lysis syndrome include vomiting and diarrhea.
- Anaphylactic and urticarial reactions to asparaginase may occur as long as 6 hours after injection.
- Hemorrhagic cystitis is characterized by dysuria, pollakiuria, and hematuria.

Clinical Signs/Physical Examination

- Acute fever, depression or inappetence in the patient receiving chemotherapy should be considered to be due to sepsis until proven otherwise.
- Drug extravasation may not be painful during injection. If not, pain and other signs of inflammation may develop as early as immediately after injection to up to 1 week with **vincristine and vinblastine** and up to 2 weeks with **doxorubicin and epirubicin.** Progressive tissue damage may occur up to one month. The most mild reactions are characterized by erythema and licking of the injection site. The most severe reactions are characterized by deep ulceration and secondary infection.

- Bradycardia due to hyperkalemia may be present in tumor lysis syndrome and acute hypoadrenocorticism.
- Severe local reactions to radiation therapy are usually characterized on the skin by hair loss, erythema, and moist desquamation; in the oral cavity by painful mucositis resulting in hypersalivation, halitosis, and inappetence; and in the pelvic region by signs of proctitis resulting in tenesmus, dyschezia, and hematochezia, and acute fever and depression if rectal perforation occurs.

Laboratory Evaluation/Diagnostic Imaging

- If neoplasia has yet to be ruled-out as the cause of the emergency, perform appropriate imaging and collect appropriate diagnostic specimens for hematology, serum biochemistry analysis, urinalysis, cytology, histology, and microbiology prior to therapy. It is particularly important to collect appropriate specimens for the diagnosis of lymphoma prior to administering corticosteroids (e.g., to treat hypercalcemia).
- If there are signs of hemorrhagic cystitis, the urine should be cultured to rule-out primary or secondary bacterial cystitis.
- If tumor lysis syndrome is suspected, obtain venous blood gas analysis, serum biochemistry profile and uric acid levels. Urea, creatinine, phosporus, potassium, and uric acid levels are normal to increased; calcium and bicarbonate levels and pH are normal to decreased. The most common abnormality in dogs is hyperphosphatemia.
- Further diagnostic evaluation for other disorders, based on clinical and laboratory findings, are discussed in the appropriate chapters in this manual.

MANAGEMENT

A. **Symptomatic and specific treatments** for most disorders based on clinical and laboratory findings (e.g. hypercalcemia) are discussed in the appropriate chapters in this manual.

B. **Chemotherapy-associated gastrointestinal reactions.**
1. Chemotherapy-associated nausea and vomiting is easier to prevent than to treat.
   a. Routine initial prophylatic antiemetic therapy is recommended (used at the OVC) for **dogs** receiving doxorubicin or epirubicin, dacarbazine, and mechlorethamine. A combination of:
      i **metoclopramide 0.2 – 0.5 mg/kg SC, PO q8h and ranitidine 0.5 mg/kg SC, 1 – 2 mg/kg, PO q12h** for 5 – 7 days is practical and inexpensive.
   b. **Butorphanol 0.4 mg/kg IM** should be given 30 min prior to cisplatin treatment.
   c. Dogs receiving other chemotherapy drugs should be given initial prophylactic antiemetic therapy with **metoclopramide and/or ranitidine** if they demonstrate signs of nausea or vomiting on a previous treatment. If these drugs are not effective, other antiemetic agents include
      i **prochlorperazine 0.1 – 0.5 mg/kg, IM, SC, q12h, 1 mg/kg, PO q6–8h**
      ii **chlorpromazine 0.5 mg/kg, IM, SC, q12h, 3 mg/kg, PO q6–8h**
      iii **ondansetron 0.5 – 1.0 mg/kg IV, PO q8–12h**
      iv **dolasetron 0.5 mg/kg IV, SC, PO q24h**
      v **cisapride 0.1 – 1.0 mg/kg PO q8h**
   d. **Cats.** Of the commonly used chemotherapy drugs in cats, cyclophosphamide is the most likely to cause vomiting and inappetance. The drugs recommended for dogs above, may also be used for antiemetic therapy in cats, although metoclopramide is not as effective in this species. Another option for cats is
      i **cyproheptadine 1 – 2 mg/cat, PO q8–12h**
      ii Cats may require **sedation for intravenous chemotherapy,** in which case the use of acepromazine +/- butorphanol will also provide short-term antiemetic therapy.
2. **Gastrointestinal injury** mimics parvoviral infection (concurrent intestinal crypt cell death and neutropenia) and thus familiar treatment strategies may be used (*see Acute Diarrhea p. 32 and Neutropenia p. 435*).

C. **Anaphylactic/anaphylactoid reactions** (*seeAnaphylactic and Anaphylactoid Reactions p. 615 and Angiodema p. 212*). Following anaphylactoid reactions associated with doxorubicin and epirubicin injection, the drugs may be injected again when the reaction has subsided, but at 25 – 50% of the previous rate of injection. Following hypersensitivity reactions to asparaginase given SC, IM, or IP, the drug may be given again by IV constant-rate infusion over 48 hours with administration of **diphenhydramine 1 – 2 mg/kg IM q8h.**

D. Drug extravasation. Prevention is paramount. Ensure the catheter (preferred) or butterfly needle is well-placed by flushing with saline. (Never use direct injection through a regular hypodermic needle). The ability to withdraw blood does not guarantee that the catheter or needle has not punctured the opposite side of the blood vessel, but inability to withdraw blood increases the likelihood that the catheter or needle is not well-placed. If there is ANY concern with venous access, including unusual resistance to flushing, do not proceed with injection. Do not use a vein for treatment that has been used for venipuncture within the last 48 hours or that has signs of a hematoma. Flush the catheter/butterfly with 10 mL saline after injection is complete; **do not draw back on the syringe after flushing.**

E. Drug extravasation general treatment recommendations. The following recommendations are largely based on human treatment recommendations. Treatment of extravasation is controversial and there are few veterinary reports.

1. If extravasation is noted during injection, stop the injection immediately, but leave the butterfly needle or catheter in place. Aspirate any remaining drug in the needle, catheter, and tubing. This may also remove some drug from the tissue.
2. Instill an **intralesional "antidote"** as indicated (see below), ideally through the needle or catheter if no visible drug is remaining. If the needle/catheter has been removed, then administer the antidote through multiple injections in a circular fashion using a 25 g needle.
3. Begin cold or warm **compresses** as indicated (see below).
4. Begin **topical therapy** as indicated (see below). Do not apply a pressure bandage.
5. Use an Elizabethan collar to prevent self-mutilation. Avoid sunburn.
6. Give **analgesics** (opioid and/or NSAID).
7. Consider **topical 1% hydrocortisone cream** if cutaneous erythema is present.
8. Severe lesions may require **surgical debridement,** open wound management, and reconstructive surgery.

F. Drug extravastion specific recommendations:

1. Doxorubicin, epirubicin (anthracyclines)
   a. If extravasation is noted during **administration of concentrated solution (2 mg/mL),** consider
      i **immediate en bloc resection of the area containing the bleb** followed by open wound management.
      ii Another surgical option is the creation of **multiple small incisions** into the affected area for suction and copious saline lavage.
   b. If resection is not performed, or in cases of extravasation of **dilute solutions (e.g., 0.5 mg/mL), dexrazoxane (Zinecard, Pfizer Canada Inc.)** is the treatment of choice in some human hospitals. Based on experimental studies in mice and clinical reports in humans:
      i Immediately **give IV,** where the dose of dexrazoxane = 10 x intended treatment dose of doxorubicin or epirubicin. Repeat in 24 hours, and at half the dose in 48 hours.
      ii Alternatively, **infiltrate affected area** with 1/5 the systemic dose. This should be repeated in 3 and 6 hours.
      iii This treatment is probably not necessary if a small amount of dilute solution is extravasated.
   c. Apply **90% dimethyl sulfoxide (DMSO)** solution (Domoso Solution, Wyeth Animal Health) to an area twice that affected by extravasation q6–12h for 7 – 14 days; allow to air dry, and do not cover with a bandage. Synotic (Wyeth Animal Health) otic solution, containing 60% DMSO and 0.01% fluocinolone acetonide, may also be used.
   d. Apply a **cold compress** continuously for 24 – 72 hours, or an ice pack for 20 – 60 minutes q6h for 24 – 72 hours to localize the drug and reduce cytotoxicosis.
   e. Consider **vitamin C** 100 – 500 mg/day and vitamin E 200 – 800 U/day PO.
   f. **Do NOT infiltrate** affected area with saline, corticosteroids, or sodium bicarbonate, especially if en bloc resection is being considered.
2. Actinomycin D
   a. Consider en bloc resection as for doxorubicin (**F1a above**).
   b. Apply cold compresses as for doxorubicin (**F1d above**).
3. Vincristine, vinblastine, paclitaxel (plant alkaloids)
   a. If available, infiltrate affected area with **150 U hyaluronidase per mg of vincristine or vinblastine extravasated.** Alternatively, use **300 U as a standard dose.** This is probably not necessary if only a small amount of the drug was extravasated.
   b. If hyaluronidase is not available, **infiltrate area with warm saline.**
   c. **Apply a warm compress** for 60 minutes, then for 15 minutes q6h for 1 day to enhance drug absorption. (Experimental studies show improved results with warm compresses with this class of drugs).

4. **Mechlorethamine (nitrogen mustard)**
   a. Infiltrate affected area with **isoosmolar sodium thiosulfate USP.** Mix 1.6 mL 25% sodium thiosulfate (Faulding Pharmaceuticals) with 8.4 mL sterile water for injection, to make 10 mL of a 1/6 molar solution (0.16 mmol/L). (Alternatively, mix 4 mL 10% sodium thiosulfate with 6 mL water). Inject 2 mL per mg extravasated drug. **Injection may be painful.** To be beneficial, injection must be performed immediately after extravasation.
   b. **Apply cold compresses** as for doxorubicin (**F 1d above**).
5. **Dacarbazine**
   a. Infiltrate affected area with **hyperosmolar sodium thiosulfate USP.** Mix 3.3 mL 25% sodium thiosulfate with 6.7 mL sterile water for injection, to make 10 mL of a 1/3 molar solution (0.33 mmol/L). Alternatively, mix 8.25 mL 10% sodium thiosulfate with 1.75 mL water). This has been used with some success experimentally. A suggested dose is 2 mL/100 mg extravasated drug.
   b. **Apply cold compresses** as for doxorubicin. (**F 1d above**)
   c. Avoid exposure to intense light.
6. **Cisplatin**
   a. Usually no treatment is required.
   b. Isoosmolar sodium thisosulfate (F4a above) is recommended **only if** more than 20 mL of concentrated solution of cisplatin, >0.5 mg/mL, is extravasated. Inject 2 mL per 100 mg extravasated drug.
   c. Apply **cold/ice compresses** as for doxorubicin. (**F 1d above**)
7. **Mitoxantrone, melphalan**
   a. Apply **cold/ice compresses** as for doxorubicin. (**F 1d above**)
8. **Extravasation is generally not a concern** with the following drugs: carboplatin, cyclophosphamide, thiotepa, bleomycin, 5-fluorouracil, gemcitabine, methotrexate (may be given IM), cytosine arabinoside (may be given SC).
   a. Apply **cold/ice compresses** as for doxorubicin if there is evidence of phlebitis (**F 1d above**).

G. **Hemorrhagic cystitis**
   1. Prophylaxis is discussed in references 1 & 3.
      a. The most practical and economic approach consists of morning administration of cyclophosphamide, administration of **furosemide (2 mg/kg, SC, PO, 30 min prior to cyclophosphamide), free access to water, and multiple walks** during the day to encourage urination.
      b. **Corticosteroids** are also useful prophylactically (but not against established cystitis) by causing PU/PD.
      c. Other prophylactic treatments include fluid diuresis and mesna.
   2. If cystitis occurs, **cyclophosphamide must be discontinued.** Historically the drug was never given again, but there is recent evidence that it may be re-administerd once cystitis resolves. Suitable alternative alkalating agents include chlorambucil and melphalan (doses will vary with the protocol). Mild to moderate cystitis will resolve over several weeks to months.
      a. The risk of secondary infection is low, but the urine should be cultured and/or empirical antibiotic treatment with **amoxicillin 10 – 20 mg/kg PO q12h** OR **trimethoprim-sulfamethoxazole 15 mg/kg PO q12h** given if the dog is not already receiving antibiotics.
      b. Treatment with **pentosan polysulfate** should be considered (Cartrophen Vet, Arthropharm Pharmaceuticals Inc, **3 mg/kg, SC, q5–7days for 4 treatments; OR** Elmiron, Ortho-McNeil, **suggested dose 8 mg/kg PO q12h to a maximum dose 100 mg/kg q12h).**
      c. Anecdotally, various NSAIDs have been used for **analgesia.**
      d. For dogs with moderate to severe cystitis, characterized by persistent dysuria and hematuria, **bladder irrigation with DMSO** should be considered. The treatment does not appear to be painful and may be performed in the awake animal. The bladder is catheterized (ideally with a Foley catheter) and irrigated with saline to remove blood clots, followed by instillation of either 20 mL or 1 mL/kg 25% DMSO (1 part 90% DMSO:2.6 parts sterile water), and removal after 20 min. The procedure may be repeated in one week.
      e. For dogs with **severe cystitis** characterized by hematuria necessitating transfusion or relentless dysuria, **bladder irrigation with formalin** should be considered. The dog is anesthetized and positioned in sternal recumbency with the cranial part of the body elevated above the caudal part (e.g. by using an inclined table). A rolled pad may be placed under the abdomen in the region of the kidneys. These measures are taken to ensure that the kidneys are higher than the bladder. **Intravenous fluids are delivered at 10 mL/kg/h (surgical rate) and furosemide 2 mg/kg IV** is given to promote diuresis and increase intraureteral

pressure. Positioning and diuresis are intended to minimize the risk of vesicoureteral reflux. The bladder is catheterized with a Foley catheter (catheters of sufficient length for male dogs are available from Global [Cook] Veterinary Products, Inc.), the balloon inflated, and the bladder is then irrigated with saline to remove blood clots. The **vagina is packed with gauze sponges soaked with petrolatum** to minimize formalin contact with the vaginal mucosa. While maintaining mild tension on the catheter to lodge the balloon against the urethral sphincter to minimize formalin contact with the urethral mucosa, 1% v/v formalin (1 part 10% buffered formalin:9 parts water or saline, or 1 part of 37% formaldehyde:99 parts water or saline) is instilled by gravity, raising the formalin container no more than 15 cm above the level of the bladder. The bladder is allowed to fill to capacity. The formalin is drained after 10 minutes, and fresh formalin may be instilled for a total of 3 cycles, after which the bladder is thoroughly lavaged with saline. Similarly, a protocol was recently reported for the treatment of emphysematous cystitis in a Yorkshire terrier where 25 mL of 1% formalin was slowly infused and removed after 10 min. The bladder was lavaged with saline and the cycle repeated once more. With either protocol, it is recommended to leave the catheter in place (attached to a closed urine collection system) for 24 – 48 hours. Post-treatment analgesia should be given.

    f. Other treatment options for intractable hematuria are partial cystectomy, and cystoscopic or surgical direct application of cotton pledgets soaked in 10% formalin to areas of bleeding for 15 minutes. These treatments are feasible because cyclophosphamide-induced injury may be focal.

H. Tumor lysis syndrome
1. **Prophylactic treatments** include **fluid therapy and allopurinol**
   a. Animals with lymphoma/lymphoid leukemia with either very large tumor burdens, dehydration, reduced renal function or reduced liver function should have **fluid deficits corrected prior to starting chemotherapy** and should be mildly volume expanded (using twice the maintenance fluid rate as a starting point) for 1 – 7 days after the first treatment. In most cases these animals will be clinically ill and will already be receiving fluid therapy. **Allopurinol 10 mg/kg PO q8h** has not been well-evaluated for this purpose in dogs, but its use should be considered in dogs with several risk factors, in dalmatians and English bulldogs, and in dogs with evidence of pre-treatment tumor lysis (e.g. hyperphosphatemia).
   b. After fluid therapy has achieved good hydration, prophylactic treatment with **furosemide 1 – 2 mg/kg IV q6h or 0.1 – 0.5 mg/kg/h CRI** should also be considered if there is moderate-marked hypercalcemia (repeatable fasting serum calcium greater than 3.0 mmol/L [12 mg/dl] for dogs and cats) and/or pre-existing renal failure. Renal function must be closely observed and treated should there be an indication of deterioration (*see Acute Renal Failure p. 709*).
   c. Prophylactic urine alkalinization to promote excretion of uric acid is used in humans and hyperlipidemic but is **not recommended** in animals, where hyperuricemia tends to be mild.
2. For **established tumor lysis syndrome**
   a. Begin intravenous fluid therapy with normal saline, lactated Ringer's, or Plasma-Lyte® A at two to three times maintenance fluid rate unless the presence of shock indicates a higher rate (*see Fluid Therapy p. 347*). The fluid rate and composition should then be adjusted based on correction of biochemical abnormalities and renal function (*see Management of Acute Renal Failure p. 709 and Fluid Therapy p. 347*).
   b. **Furosemide** at the above (H1b) and mannitol should be considered (*see Acute Renal Failure p. 709*).
   c. **Sodium bicarbonate** therapy should be considered if there is severe metabolic acidosis (a base deficit > 15 mmol/L is suggested) and/or severe hyperuricemia (a serum uric acid level > 600 μmol/L is suggested), a normal phosphorus level, and urine pH <7.0. Target urine pH is 7.0 – 7.5. An empirical dose of bicarbonate is 0.5 – 1.0 mEq/kg IV over 6 hours.

I. Radiation injury to skin and mucosa
1. **Irrigation of the oral cavity** using a solution of 1 tsp. baking soda in 8 oz water or cool tea will provide some relief for mucositis. In addition, "Pink Lady" may be prepared by mixing 50 mL lidocaine viscous 2% (20 mg/mL) and 50 mL aluminum hydroxide gel 64 mg/mL, and applied at a maximum dose of 0.4 mL/kg q8h to affected oral mucosa of dogs.
2. A feeding tube should be placed if the animal refuses to eat (*see Nutritional Support p. 499*).
3. The **skin may be cleansed** gently if necessary with warm saline or bicarbonate solution (1 tsp baking soda in 1 cup [240 mL] warm water) using irrigation (60 mL syringe and an 18 ga needle) or moistened gauze sponges. Gentian violet topical solution USP 1% dabbed on the skin with a gauze sponge daily is soothing, but may stain fabrics.
4. If **secondary infection** occurs, give **cephalexin 30 mg/kg PO b.i.d.**

5. NSAIDs and opioids appear to provide some **analgesia** for these conditions. Meloxicam and codeine (*see Analgesics and Sedatives p. 81*) are the drugs usually used at OVC.
6. An Elizabethan collar should be used to prevent self-mutilation.
7. **Exposure** of the skin to cold, wind, or sun should be avoided. Sunscreen should be applied to hairless areas once the dermatitis has resolved if there is exposure to the sun.
8. It is important to inform clients that discomfort will resolve within 2 – 3 weeks.

PHARMACOLOGY

1) **Gastrointestinal reactions.** Vomiting is mediated by several neurophysiologic pathways, including the serotonergic, dopaminergic, histaminergic, adrenergic, and cholinergic pathways. The most important pathway for chemotherapy-induced vomiting is the serotonergic pathway involving visceral, vagal afferent and chemoreceptor trigger zone (CRTZ) 5HT3 receptors. **Ondansetron** and dolasetron are serotonergic (5HT3 receptor) antagonists and are the most effective anti-emetic agents, but are expensive. **Metoclopramide** is a dopaminergic and weak serotoninergic antagonist, as well as a prokinetic agent, which probably also contributes to its anti-emetic effect. **Prochlorperazine** and **chlorpromazine** are histaminergic and adrenergic antagonists; cyproheptadine is a histaminergic and mild serotonergic antagonist. **Cisapride** is a mild serotonergic antagonist and prokinetic agent. The apparent anti-emetic effect of ranitidine is likely due to its prokinetic effect. **Butorphanol** is an opioid that probably exerts its antiemetic effect on the CRTZ. **Yohimbine** and **atipamezole**, adrenergic antagonists, have not been well-evaluated as anti-emetic agents for chemotherapy-induced vomiting. **Corticosteroids** help control chemotherapy-induced nausea in humans.

2) **Drug extravasation.** Infiltration of the affected area with saline has been recommended to dilute the offending agent, but this may increase dispersion of the drug in tissue. With the exception of **plant alkaloids**, limiting the drug to a smaller tissue space appears to minimize damage. (Similarly cold compresses are recommended for all extravasations except for plant alkaloids). Infiltration with sodium bicarbonate has been recommended to inactivate **anthracyclines**, but this may further damage tissue. Infiltration with corticosteroids has also been recommended for **anthracyclines**, but inflammation is not a feature of the tissue reaction and corticosteroids may delay healing and result in worse ulceration. Bis 3,5-dimethyl-5-hydroxymethyl-2-oxomorpholin is a radical dimer that inactivates **doxorubicin**, but it is not readily available. Free radical formation is the putative mechanism by which anthracyclines are believed to damage tissue, leading to the use of the free-radical scavenging drugs dexrazoxane (also used to prevent anthracycline-induced cardiomyopathy) and DMSO, and antioxidant vitamins. Dexrazoxane is very expensive. Infiltration with **DMSO** may be used, but topical application is preferred as the drug penetrates all tissue planes. Infiltration with vitamin C and vitamin E solutions show some benefit but is impractical. It is not known if systemic vitamin therapy is beneficial but it will not be detrimental. **Pentoxifylline** has also been used for free radical scavenging. Sodium thiosulfate chemically inactivates alkylating agents. **Hyaluronidase** is an enzyme that degrades hyaluronic acid, thus promoting absorption of injected substances. It is beneficial with vincristine and vinblastine extravasation; results with other drugs are variable. Unfortunately Wydase (Wyeth-Lederle) is no longer available. **Hyalase** (CP Pharmaceuticals) is available for human use in Canada through the Health Canada Special Access program. Hyaluronidase may also be obtained at some compounding pharmacies, but it is impractical to stock solutions in the hospital because of short shelf-life.

3) **Hemorrhagic cystitis.** Pentosan polysulphate is a semisynthetic glycosaminoglycan of plant origin. The injectable formulation (Cartrophen Vet) (Arthropharm Pharmaceuticals Inc) is approved for osteoarthritis in dogs in Canada; the oral formulation (Elmiron) is approved for the treatment of interstitial cystitis in humans in Canada and the USA, and it has been used in the management of hemorrhagic cystitis. The drug is poorly absorbed from the intestinal tract (3% in humans), so the injectable and oral doses cannot be extrapolated from each other. The dose of **Elmiron** in humans is 100 mg q8h. The drug has been used at a dose of **8 mg/kg q12h** for the treatment of idiopathic cystitis in cats. It acts as a local urinary analgesic and anti-inflammatory agent; its mechanism of action is not known, but it may act by helping to restore the glycosaminoglycan layer of the urinary epithelium and bind to inflammatory molecules in the urine. Formalin hydrolyzes proteins and coagulates tissues. The uroepithelium regenerates in about 3 weeks. Complications include acute renal failure, ureteral fibrosis, and urethritis. The risk of complications is proportional to the concentration of formalin; **1% formalin** minimizes risk while maintaining therapeutic effect. Methenamine, a urinary antiseptic drug that is hydrolyzed to formaldehyde in the bladder, is unlikely to be of benefit. Benefits of DMSO are presumed due to antiinflammatory effects and reduction of fibroplasia. Intravesical therapy with hydrostatic pressure, alum, silver nitrate and prostaglandins has been used in humans but not reported in dogs. Hyperbaric oxygen therapy is beneficial but not readily available. Use of phenazopyridine, a urinary tract analgesic, has not been reported in humans for this purpose, and the drug is not recommended for use in dogs and contraindicated in cats.

4) **Tumor lysis syndrome.** Allopurinol blocks the conversion of purines to uric acid by blocking the enzyme xanthine oxidase in the liver. Its use may increase the risk of xanthine crystal nephropathy. Recombinant urate oxidase has also been used in humans to convert uric acid to allantoin, but its use in the dog has not been reported. Sodium bicarbonate may be added to fluids to alkalinize the urine in order to promote excretion of uric acid, but this increases the risks of urinary phosphate deposition, hypocalcemia and nephrocalcinosis. Because this syndrome in animals is characterized by mild hyperuricemia but prominent hyperphosphatemia, urinary alkalinization with bicarbonate therapy is not usually recommended.

SUGGESTED READING

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NOTES

INTRODUCTION

Thrombocytopenia may be congenital or acquired. Most thrombocytopenic hemorrhage is due to acquired disorders. Thrombocytopenia varies from mild to severe, and from an isolated hematologic abnormality to a feature of pancytopenia.

Congenital thrombocytopenia is seen in cavalier King Charles spaniels, greyhounds, and gray collies with cyclic neutropenia. Cavaliers may have platelet counts as low as 35 x 10⁹/L, but do not appear to have abnormal bleeding. Greyhounds typically have platelet counts of approximately 120 x 10⁹/L. In gray collies episodic fever due to neutropenia rather than hemorrhage is the main clinical sign.

Acquired thrombocytopenia may be present in a number of diseases, and a specific disease may cause thrombocytopenia by more than one mechanism. The mechanisms most often causing thrombocytopenia are reduced platelet production (megakaryocytic hypoplasia), increased consumption (disseminated intravascular coagulation [DIC]), and increased destruction (immune-mediated thrombocytopenia [ITP]). Platelet sequestration due to splenomegaly, and platelet loss during marked hemorrhage, do not commonly cause clinically important thrombocytopenia.

The most common cause of marked thrombocytopenia and resultant bleeding in the dog is ITP. The most common cause in the cat is megakaryocytic hypoplasia.

TABLE 1. Causes of Thrombocytopenia

Mechanism	Diseases
Reduced production by bone marrow	Diseases causing marrow failure – See Neutropenia
	Lomustine causes a cumulative thrombocytopenia
	Immune-mediated megakaryocytic hypoplasia (±ITP)
Increased destruction	Immune-mediated thrombocytopenia
	Anaplasma (Ehrlichia) platys infection (usually subclinical)
Increased consumption	Disseminated intravascular coagulation

	Vasculitis
	    Rocky mountain spotted fever
	    Ehrlichiosis

	Local thrombosis
	Hemolytic uremic syndrome (rare)

Sequestration	Splenomegaly
	    Neoplasia
	    Splenic torsion
	    Idiopathic hypersplenism

	Hypothermia
Loss	Marked hemorrhage★

★Hemorrhage alone will not usually cause thrombocytopenia, although it may lower platelet count somewhat within normal range. Mild-moderate thrombocytopenia has been noted with marked hemorrhage secondary to trauma and vitamin K antagonist rodenticide poisoning. DIC is probably a contributing factor with trauma. Volume resuscitation with crystalloids, colloids or platelet-poor blood products following massive hemorrhage will cause mild-to-severe thrombocytopenia.

Risk and severity of bleeding are inversely proportional to platelet count:

TABLE 2. Severity of Bleeding with Thrombocytopenia*

Platelet Count	Risk of Hemorrhage
< 80 x 10⁹/L	increased surgical hemorrhage
< 50 x 10⁹/L	microscopic spontaneous hemorrhage
< 20 x 10⁹/L	spontaneous clinical hemorrhage – mild risk
< 10 x 10⁹/L	spontaneous clinical hemorrhage – moderate risk
< 5 x 10⁹/L	**spontaneous clinical hemorrhage – severe risk**

*These figures are guidelines only and are based on megakaryocytic hypoplasia. Platelet counts vary with the method used, and enumeration is more imprecise at low values. Bleeding is worse if there is concurrent sepsis, coagulopathy, von Willebrand's disease, vasculitis, or a platelet function defect. Platelet function defects may be congenital (i.e., basset hound) or acquired (uremia, liver failure, neoplasia, ehrlichiosis, and drugs). Dogs with ITP typically bleed less than expected, probably because platelets are young and hyperfunctional. Cats do not bleed as severely as dogs at a given platelet count.

DIAGNOSIS

History/Signalment

- Melena, hematochezia, hematemesis, epistaxis, hematuria, excessive bleeding from wounds or during estrus, and occasionally coughing, hemoptysis or dyspnea from pulmonary hemorrhage, may be reported.
- Lethargy, weakness and inappetence if the animal is anemic.
- Vomiting and/or diarrhea may be present. This may be due to the underlying disease, acute anemia and associated pancreatitis or gastrointestinal ischemia, and effect of a large volume of blood in the intestinal tract.
- Other historical findings are those of the disease causing thrombocytopenia.
- Vaccination within one month may be a risk factor for ITP.
- Middle-aged female dogs, spaniels (especially American cocker spaniel), old English sheepdog, and poodles are at increased risk for primary ITP. The disorder is rare in cats.

Clinical Signs/Physical Examination

- Petechiae and ecchymoses, especially on mucosal surfaces and skin of ventral abdomen. Ocular hemorrhages may be present.
- Persistent bleeding from venipuncture sites.
- Neurologic signs are occasionally present due to central nervous system bleeding or underlying disease.
- Fever may be present from concurrent neutropenia, hemolysis or underlying disease.
- Splenomegaly ± hepatomegaly may be present with ITP, ehrlichiosis, and primary splenic disorders.
- Other signs due to underlying or concurrent disorders.

Laboratory Evaluation/Diagnostic Imaging

The goals of work-up are to:

- Confirm thrombocytopenia.
- Identify other bleeding disorders, mechanism of thrombocytopenia, underlying disorder, and concurrent disorders.
- ITP is ultimately a diagnosis of exclusion. The diagnosis is typically made in a dog with thrombocytopenic bleeding that does not have evidence of bone marrow failure or of a disorder that may be causing DIC.

Stat

- **CBC. Confirm thrombocytopenia.** Examine blood smear for platelets: examine monolayer where red cells are close together and about 50% are touching. Normally there are 7 – 30 platelets/oil immersion field (each platelet = 15 – 20 x 10^9/L). If >2 platelets per oil field, spontaneous bleeding is unlikely. If >4 platelets per oil field, then there is minimal risk of excessive bleeding. Rule-out clerical error, and clumping at feather edge as cause of artifactual thrombocytopenia. Look for shift platelets (evidence of platelet production). Characterize changes in other cell lines. Concurrent non-regenerative anemia and neutropenia are consistent with bone marrow failure. An inflammatory leukogram may be indicative of a disorder causing platelet consumption. Characterize severity of hemorrhage – PCV and TS.
- **Identify coagulopathy.** Activated clotting time (Dogs: 70 – 125 secs, Cats: 60 – 90 secs at OVC using the grey top tube [silica earth]).

Extended Laboratory/Imaging Data Base

- **Serum chemistry profile** to identify organ dysfunction.
- **Radiographs** and **ultrasound** of abdomen and thorax to identify tumors or foci of inflammation. Serum chemistry profile and imaging will help identify underlying causes of DIC, autoimmunity and bone marrow failure. Imaging will also help identify local bleeding.
- **Coagulation profile.** Prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen level, fibrin degradation products, and D-dimer will help identify and characterize DIC and local thrombosis.
- **Von Willebrand's factor, platelet function testing** by a research laboratory, if bleeding is considered to be excessive for the platelet count.
- **Tests for infectious diseases.** Specific antigen/antibody tests for FeLV, FIV, Ehrlichiosis, Rocky Mountain spotted fever, leptospirosis, histoplasmosis, heartworm; cytology for histoplasmosis, cytauxzoonosis and bacterial or fungal culture (sepsis causing DIC).
- **Bone marrow biopsy.** Reduced platelet production is characterized by reduced megakaryocytes seen on bone marrow biopsy. The other mechanisms are characterized by normal to increased megakaryocytes. Classically ITP is associated with megakaryocytic hyperplasia, but there may be concurrent immunologic attack against megakaryocytes resulting in normal to reduced numbers. Dogs with immune-mediated megakaryocytic hypoplasia do not appear to have a worse prognosis for recovery of normal platelet counts than do dogs with megakaryocytic hyperplasia, but may take longer to do so. Biopsy will identify neoplasia, aplasia, myelofibrosis, bone marrow necrosis, and histoplasmosis.
- For ITP, identify underlying causes and concurrent disorders of autoimmunity (*see Immune-Mediated Hemolytic Anemia* [IMHA] *p. 411*).
- Antiplatelet antibody tests are not routinely available and have variable sensitivity. The most useful result is a negative test that helps rule-out ITP.

MANAGEMENT

A   **Handle patient gently.** Offer soft food to reduce gingival bleeding.

B.   **Intravenous fluids.** Treat hemorrhage with fluids or whole blood (*see Hemorrhage p. 619*). **Avoid over exuberant fluid therapy**, which may aggravate bleeding, and promote edema formation in anemic animals. Intravenous catheters may be placed in thrombocytopenic patients. Prophylactic platelet transfusion should be considered prior to placement of a jugular catheter. If the animal is drinking well and is well-hydrated, then intravenous fluids are not necessary. If dehydrated, initial fluid choice is Plasma-Lyte® A, or Plasma-Lyte® 148, Normosol® R, lactated Ringer's solution, or equivalent. Replace estimated deficits over 12 hours followed by maintenance fluid rate.

C.   **Avoid IM and SC injections.** Use 23 – 25 g needles for venipuncture. Avoid jugular venipuncture if possible when platelet count <10 x 10^9/L. Apply moderate pressure to venipuncture sites for at least 5 minutes. Apply moderate manual pressure or pressure bandages to major sites of active bleeding.

D. **Avoid drugs that decrease platelet function**, especially NSAIDS with COX-1 inhibition. (Opioids should be used for analgesia.) Many other drugs have mild effects on platelet function. The clinical relevance of these is often not known, but "polypharmacy" is best avoided in animals with moderate to marked bleeding due to thrombocytopenia. Many antibiotics, especially penicillins, interfere with platelet function in humans but any such effects appear to be minimal in dogs and cats.

E. Gastroprotectants are frequently administered as it is difficult to rule-out gastrointestinal ulceration in animals with melena due to thrombocytopenia. Such animals are frequently treated with:

1. **Famotidine 0.5 mg/kg IV PO q12h,** which is the superior H2 blocker and has the least effect on platelets; OR
2. **Omeprazole 1 mg/kg PO q12–24h,** which does not appear to affect platelet function. Omeprazole is superior to famotidine.
3. **Sulcralfate 0.5 – 1.0 g PO q8h,** which does not appear to affect platelet function.

F. **Sedation/Anesthesia** may be required to perform diagnostic procedures. Acepromazine, barbiturates and isoflurane do not appear to affect platelet function in dogs and cats.

G. **Avoid anticoagulants**, except that heparin may be considered in DIC where mild to moderate thrombocytopenia is present and in dogs with concurrent IMHA at risk for pulmonary thromboembolism (*see IMHA p. 411*). Heparin should not be given to dogs bleeding from thrombocytopenia.

H. **Treat underlying cause.** Chronic transfusion support of the thrombocytopenic patient is not feasible in most veterinary hospitals, so the cause should be promptly treated. Treat underlying infections and withdraw offending drugs.

  1. **ITP and immune-mediated megakaryocytic hypoplasia.**
     a. Corticosteroids –
        i. **Dexamethasone sodium phosphate 0.3 – 0.5 mg/kg IV q24h OR**
        ii. **Solu-Delta-Cortef®** (Upjohn) **2 – 4 mg/kg IV q24h (administered over 10 min).** Do not initially use oral preparations in severe cases because of the risk for vomiting and impaired absorption due to gastrointestinal ischemia.
        iii. When **clinically stable** change therapy to **prednisone 2 mg/kg PO q24h** for a minimum of 2 weeks. An attempt may be made to taper corticosteroids after 2 – 6 weeks, but corticosteroid therapy is typically not withdrawn altogether for at least 3 – 6 months.
     b. **Vincristine 0.02 mg/kg (<15 kg) or 0.5 mg/m² IV (>15 kg) IV** bolus. This may be repeated weekly.
     c. Additional immunosuppression/macrophage inhibition (*see IMHA p. 411*).
  2. **Platelet consumption, sequestration**
     Where the underlying cause is a disorder requiring surgery (e.g., splenectomy, excision of a septic focus causing DIC), it is usually best to proceed with surgery and use intensive peri-operative transfusion, rather than to delay surgery and treat the patient medically in an effort to raise the platelet count pre-operatively.

I. **Prothrombotic drugs.** Veterinary experience with such drugs is limited, and they are contraindicated in DIC. The best prothrombic therapy available to veterinarians is red blood cell transfusion.

J. **Thrombopoietic agents.** Drugs that stimulate thrombopoiesis may be beneficial in the treatment of megakaryocytic hypoplasia that is not immune-mediated, but veterinary experience is limited.

  1. **Interleukin-11** (Neumega, Wyeth [not readily available in Canada]) 50 μg/kg SC q24h for a maximum of 14 days may be considered. This drug is very expensive.
  2. **Lithium carbonate 10 – 15 mg/kg PO q12h** may be considered in dogs although its effects are mild at best (*see Neutropenia, p. 435*).

K. **Blood transfusion with platelet-rich blood products** may be lifesaving but is only a short-term solution (a platelet transfusion usually "lasts" 1 – 3 days). Platelet transfusion is most beneficial with megakaryocytic hypoplasia (with normal platelet lifespan), less beneficial with DIC and splenomegaly, and least beneficial with ITP because of rapid destruction of transfused platelets. Platelet transfusion is usually beneficial in thrombocytopathia.

  1. **Platelet-rich blood products** (*see Blood Component Preparation, p. 678*) include fresh whole blood (<8 hours old), platelet-rich plasma and platelet concentrate. Fresh whole blood is often the only practical means of providing

a platelet transfusion. Platelet-rich blood products should be prepared and stored at room temperature, handled gently, and delivered through standard latex-free transfusion sets.

2. **A platelet transfusion** is usually given to reduce active critical bleeding. Prophylactic transfusion to minimize spontaneous bleeding may be considered at a trigger of $10 - 20 \times 10^9/L$ (dogs) or $5 - 10 \times 10^9/L$ (cats) and should be performed prior to surgery at a trigger of $20 - 50 \times 10^9/L$.

   a. A standard platelet transfusion is one unit of platelets/10 kg, where one unit of platelets refers to the platelets contained in one unit of fresh whole blood (about 450 mL for dog and 60 mL for cat). This will raise the platelet count by a maximum of $40 \times 10^9/L$. If such transfusions are not feasible in large dogs, daily to alternate day transfusions of $10 - 15$ mL/kg fresh-whole blood, which will raise the platelet count by a maximum of $10 \times 10^9/L$ and keep platelet counts $>10 - 15 \times 10^9/L$, will usually prevent critical bleeding. With minimal platelet production but no increased loss, platelet counts will fall by $\approx 33\%$/day post-transfusion.

   b. Success of a transfusion is judged by control of bleeding (most important) and by comparing expected and measured platelet counts 1 hour after transfusion. The expected increase in the platelet count of a dog 1 hour after completing the transfusion is calculated as follows:

      i. 1-hour platelet increment = [blood product platelet count $(\times 10^9/L)$ x blood product volume (L) x 0.51]/[Recipient weight (kg) x 0.08 (L/kg)]

      ii. where 0.08 x weight (kg) = estimated blood volume and 0.51 corrects for splenic sequestration of transfused platelets. If the measured platelet count is much below the expected count, then there is increased platelet loss due to destruction, consumption or sequestration.

   c. Platelet alloimmunization will occur rapidly with repetitive transfusions and can be minimized by changing donors. Alloimmunization can be abrogated by cyclosporine, and its use is recommended if multiple transfusions are anticipated. Prednisone and cyclophosphamide, and presumably other cytotoxic drugs, will not abrogate alloimmunization.

3. **Fresh-frozen plasma (10 mL/kg) or cryoprecipitate (1 unit/10 kg)** contain functional platelet microparticles, and may be transfused if platelet-rich products are not available. In addition, red blood cell transfusion may reduce the severity of bleeding due to thrombocytopenia (including ITP) as red cells are procoagulant and bleeding time is prolonged in anemia.

PHARMACOLOGY

1) See IMHA for description of **corticosteroid therapy**.

2) **Vincristine** is a cytotoxic plant alkaloid that disrupts the mitotic spindle in dividing cells. It causes an increase in the platelet count of normal dogs and hastens the recovery of the platelet count in dogs with ITP, by unknown mechanisms. The drug is usually given as a bolus. Alternative methods of administration include infusion of the dose over 6 hours and preparation of vinca-loaded platelets (referral procedure [reference 2]).

3) **Interleukin-11** is a cytokine with thrombopoietic and gastrointestinal protective effects. The maximum platelet count is achieved by 7 days. Although unproven, antibody formation abrogating benefit and causing megakaryocytic hypoplasia is a theoretical risk. For this reason treatment beyond 14 days is not recommended.

4) **Lithium carbonate** is a psychomodulating drug that has mild bone marrow stimulating properties in dogs, but not in cats. Results with its use in dogs are variable, and while the drug is inexpensive and readily available, blood levels must be monitored which increases expense. There are a number of undesirable side-effects associated with high blood levels.

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INTRODUCTION

Epilepsy indicates recurrence of seizures of primary brain origin. The epilepsy is **idiopathic** when there is no underlying structural brain lesion present. This epilepsy is presumed genetic and age-related. Idiopathic epilepsy is not recognized in cats. In cats, the epilepsy is **symptomatic** or **probably symptomatic.** The epilepsy is said to be symptomatic when the seizures are the result of one or more identifiable structural brain lesions and probably symptomatic when the epilepsy is likely symptomatic but no etiology has been identified after testing. (*International League Against Epilepsy's terminology; see Suggested Reading*).

Status epilepticus is present when three or more seizures are occurring with no recovery time between seizures. Practically, it is diagnosed when the cat has been seizing continuously for more than 30 minutes. Seizures occur as a **cluster** when there is more than one seizure per 24 hours. Cluster seizures are treated similarly to status epilepticus because they often degenerate into status epilepticus. It is of utmost importance that status epilepticus be rapidly controlled. Prolonged seizure activity is associated with increases in the amount of drugs and time required to control the seizures as well as increases in recovery time.

The great majority of seizures in cats are secondary to intracranial disease. Only very occasionally do metabolic causes or exotoxins induce seizures in this species. Contrary to dogs, most episodes of status epilepticus in cats are the result of structural brain disease. The most frequent cause of seizures in cats is viral. Although the causative viruses are unknown due to a lack of laboratory tests (polymerase chain reaction or PCR) for virus identification. A prospective study of cats with seizures found that an acute onset of progressive seizure activity in young to middle aged cats, preceded by vague systemic illness two to three weeks prior to seizure development, had an excellent outcome if treated early and aggressively (*see Suggested Reading*). The same study found that feline ischemic encephalopathy was also an important cause of seizures in cats although much less commonly. The syndrome is thought to be associated with larval (Cuterebra) migration. It is believed that the migratory larva by way of a neurotoxin causes vascular spasms leading to a cerebrovascular event. The neurological disease is acute in onset progressing for up to 48 hours with the neurological deficits relating to the cerebral cortex (*see Suggested Reading*).

DIAGNOSIS

History/Signalment

The signalment of the cat, its age at onset of seizures and the seizure pattern (type and frequency) are the most helpful clues towards establishment of the list of probable causes. Physical, neurological and ophthalmological examinations, laboratory data and advanced neuroimaging are necessary to reach a final diagnosis in most cases of epilepsy in cats (*see Suggested Reading*).

Male cats >10 years of age with progressive neurological signs that relate to the cerebral hemispheres are more likely to suffer from a meningioma. A cat with a meningioma may be presented for seizures only, but with a detailed history, these cats always have neurological deficits (an abnormal mental status being one of the deficits always present; *see Suggested Reading*).

While controlling the gross motor activity (see MANAGEMENT), obtain history with regards to:

- Indoor or outdoor cat? Head injury is more likely if the cat has been found outdoors. Exotoxins although rare are more likely to be observed in an unsupervised outdoor cat.
- Duration of current seizure episode to evaluate the gravity of the situation.
- Type, frequency and duration of previous seizure activity. Acute onset of focal seizures that progress over a few days to convulsive status epilepticus in a cat that was previously normal is a common presentation.
- The cat's mental status prior to seizure development. It is often difficult in this species to substantiate behavioral abnormalities. The cat is naturally independent and the behavioral changes may appear subtle to the owner. Any changes from the daily routine if consistent are significant. It is the role of the veterinarian to orient questioning to determine if the changes observed originate from the brainstem (somnolence, stupor, coma) or the thalamocortex (decreased awareness or interest in surrounding).
- Systemic signs surrounding seizure development. Was, or is, there inappetence, coughing/sneezing, gastro-intestinal signs, lethargy, fever, weight loss? The infectious encephalitides, such as cryptococcosis and feline infectious peritonitis (FIP), are associated with concomitant systemic illness whereas vague or mild systemic signs may precede viral self-limiting non-FIP encephalitides by two to three weeks.

- Is the animal on any medication?
- Concomitant illnesses. Is the cat diabetic? When was it given the last insulin injection and was the dose correct?

Clinical Signs/Physical Examination

- While conducting the physical examination and evaluating the type of seizures proceed to MANAGEMENT below and always:
- Obtain the rectal temperature. Hyperthermia may be a direct consequence of the seizures, or linked to the animal's illness. Focal seizures will also cause hyperthermia.
- Evaluate the type (generalized versus focal) of seizures:
  - **Generalized tonic-clonic motor seizures** are defined as bilateral, symmetric, tonic-clonic contractions of muscles, usually associated with autonomic phenomena such as frothing at the mouth, urination, defecation, pupillary dilation (*see Suggested Reading*). The animal is characteristically unconscious. At time of admission, the gross motor activity may have subsided but there may still be twitching of the eyelids with or without limb/body jerking. In these patients, the seizure activity is on-going and should be treated.
  - In **focal (partial) seizures,** only part of one hemisphere is affected although the structural lesion may be diffuse. Characteristically, the cat is conscious but its mentation altered. A cat's focal seizure may have bizarre presentations. The owner may describe the cat as fearful, running away, colliding with objects. The cat may bite its tongue and pull its claws from the nail beds after being caught in carpet fibers; may slowly circle toward one side, then stop and stand while salivating. The most consistent motor activities are the ones associated with the facial musculature. Twitches of the eyelids, whiskers and ears may or may not be symmetrical but often are primarily on one side. There may also be associated unilateral limb motions but the movements of the facial musculature always predominate. These signs may have been present at the onset of the seizure before generalization occurred. In cats, contrary to dogs, focal status epilepticus is most frequent, however often interspersed with bouts of generalized tonic-clonic seizures.
- Components of the neurological examination that target the cerebral cortex are the mental status, menace responses, nasal septum stimulation responses and the proprioceptive positioning. In the patient presented in status epilepticus, focal or generalized, the menace and nasal septum responses may be absent bilaterally as a result of the seizures. If the deficits are unilateral, it is the hallmark for presence of a structural brain disease.
- In the early stage or compensatory phase of generalized motor status epilepticus, there is increased blood flow, metabolism, glucose and oxygen utilization by the brain but without permanent damage. As the generalized seizures continue, there is decompensation with marked secondary deleterious cerebral and systemic effects. In cats, since focal status is the most frequent presentation, the secondary deleterious systemic effects are not often observed. At the level of the cerebrum, brain damage is assumed with on-going seizures.
- Thiamine insufficiency characteristically leads to bilateral vestibular signs in cats. These can be mistaken for seizure activity. There is abnormal head carriage and a poor to absent physiological nystagmus.

Laboratory/Diagnostic Imaging

Stat
- **PCV/TS.** Both may be increased if the animal was found seizing for a long time resulting in dehydration. Dehydration may be present from the cat's illness as well. In suspected cases of the non-effusive form of FIP, TS is frequently elevated.
- **Blood glucose** is frequently elevated in cats due to stress. In cases of insulin overdose, the blood glucose can be very low.
- **Stick BUN** is required for baseline information and to assess potential pre-renal or renal dysfunction. Of particular importance in the aged cat.

Extended Laboratory/Imaging Database

- **CBC** abnormalities are non-specific. A stress leukogram is often present.
- **Biochemical profile** to identify renal, hepatic and electrolyte abnormalities that may be present. The globulins may be high with the non-effusive FIP. There may be concomitant renal disease in the older cat. The ALT and ALP may be elevated if the cat is also hyperthyroid.
- **Creatine kinase (CK)** measurement is important in cats with seizure activity. Even in focal (partial) status epilepticus, the CK can be extremely elevated. CK levels seem to be more representative of the severity and length of status epilepticus than any other routine biochemistry test.
- Urinalysis as part of the renal assessment. Myoglobinuria may be observed with high CK values.

- Consider FeLV, FIV and toxoplasma titers not as causes of seizures but to evaluate the general health of the animal.
- Serum levels of phenobarbital if the animal is being treated with phenobarbital.
- Bile acids only if the characteristic signs of porto-systemic shunting are present, i.e., recurrent hypersalivation and dementia.
- Complete neurological assessment may include: cerebrospinal fluid (CSF) collection and analysis, CT scan in cases of head trauma especially if a fracture or a space-occupying lesion is suspected. In most cases, MRI is preferable to CT because an evaluation of the cerebral parenchyma with respect to the primary cause, and the secondary effects of the status epilepticus can be determined. In inflammatory diseases, the combination of CSF analysis and MRI are the diagnostic tests of choice to reach a definitive diagnosis.

MANAGEMENT

A. Administer oxygen: important as many of these patients are hypoxic.

B. Cool with wet towels and fan if temperature >39.5°C (103 °F).

C. Place an intravenous catheter and obtain samples outlined above.

D. Stop gross motor activity.

   1. **No seizures at time of presentation:**
     a. **phenobarbital 10 mg/kg to a maximum of 60 mg/cat slowly IV (over 15 minutes).** The administration should be very slow to avoid cardiorespiratory depression. To be given at this dosage if the cat is naïve to the drug. If not, go to c. below until the phenobarbital serum levels are known.
     b. **continue** with **oral phenobarbital 7.5 mg – 15 mg q12h** (maintenance dose) 12 h later.
     c. **if seizure activity returns,** add **diazepam at a constant rate infusion (CRI) of 1 mg/cat/h.**
     d. **combination phenobarbital and diazepam** have a synergistic effect. Whenever one is added to the other, great care should be applied to avoid overdose. In this instance, a **CRI** of diazepam is safer than a bolus.

   2. **Seizures (focal or generalized) on-going at time of presentation:**
     a. **diazepam 0.5 – 1.0 mg/kg IV bolus** and continue with a
     b. **CRI at 0.25 – 0.5 mg/cat/h.**
     c. **bolus diazepam** can be repeated once more **5 minutes after the first bolus** if the generalized seizures continue. **In this instance,**
     d. **add phenobarbital as CRI at 4 mg/cat/h.**
     e. **introduce oral phenobarbital 7.5 mg – 15 mg q12h (maintenance dose)** if a second bolus of diazepam is not required.

   3. **Persistent seizures:**
     a. **Propofol 1 – 4 mg/kg to effect anesthesia followed by 0.1 – 0.5 mg/kg/h CRI for three to four hours should be administered to anesthetize the animal** if the combination of diazepam and phenobarbital fail to control the generalized seizures.

E. In most cases, focal seizures are refractory to diazepam and/or phenobarbital treatment. Propofol anesthesia will stop the visible seizures but without EEG monitoring it is unknown if the cortical seizures are also controlled. It is common to succeed in abating the generalized seizures, however focal status may continue for over three days despite all treatments. It is likely that the focal seizures stop once the primary underlying cause is managed.

F. Antiepileptic treatment in the seizing cat is mostly symptomatic. However, where identified, it is of utmost importance for adequate seizure control to treat the underlying cause of the seizures as soon as possible. If there are no contraindications to its use, **dexamethasone 0.25 mg/kg q24h for 1 – 3 days is administered IV.** Unfortunately, dexamethasone interferes with CSF results.

G. **Thiamine,** although advocated for all, and any seizures in cats, is not necessary.

PHARMACOLOGY

1) **Diazepam** is a GABA-ergic drug. The pharmacokinetics are not entirely known in the cat. The half-life is much longer than in dogs. Repeat doses are cumulative. CRI is a safer approach. Acute hepatic necrosis has been associated with diazepam use in cats. Measurement of the ALT and AlkPhos is advised 24 hours after the treatment with diazepam has been initiated.

2) **Phenobarbital** is a barbiturate with a strong antiepileptic effect and comparatively mild sedative effect. Its antiepileptic effect is post-synaptic, prolonging the opening of the postsynaptic cell membrane chloride channel. Phenobarbital equilibrium is reached in the cerebrum in 15 minutes necessitating a 20-minute pause between boluses. The metabolism is slow with a half-life of 40 – 80 hours. Repeat doses are cumulative. Barbiturates and benzodiazepines are synergistic. Therefore, careful titration must be done with combination use, especially in patients with liver dysfunction. Chloramphenicol and cimetidine are to be **avoided** with phenobarbital due to their inhibition of phenobarbital metabolism leading to toxic phenobarbital serum levels even after one treatment. Although thrombocytopenia, neutropenia, pruritis and swelling of the feet have been reported with the use of the drug, those were rare associations and should not deter from its use.

3) **Propofol** potentiates GABA by increasing the frequency of the chloride channel opening. Muscular necrosis with myoglobinuria following prolonged infusion is reported in humans. Although we have not observed this in cats, caution should be applied until more experience with use of this drug is acquired. Prolonged use of propofol (>24 hours) causes Heinz body anemia in cats, therefore duration of administration should not exceed this if at all possible.

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NOTES

INTRODUCTION

Epilepsy indicates recurrence of seizures of primary brain origin. The epilepsy is **idiopathic** when there is no underlying structural brain lesion present. Idiopathic epilepsy is presumed to be genetic and usually age-dependant. The epilepsy is **symptomatic** when the seizures are the result of one or more identifiable structural brain lesions. The epilepsy is **probably symptomatic** when the epilepsy is likely to be symptomatic but no etiology has been identified. (*International League Against Epilepsy's terminology; see Suggested Reading*).

Status epilepticus is present when a dog experiences repetitive seizures (>3) with no recovery time between seizures, or has been seizing continuously for more than 30 minutes. It is difficult to define the time necessary to declare a patient in status epilepticus, but pathophysiologically most human patients in convulsive status have measurable systemic hypoxia within 30 minutes of onset.

Seizures occur as a **cluster** when there is more than one seizure per 24 hours. Although less severe, cluster seizures are treated similarly to status epilepticus because they often degenerate into status epilepticus.

The frequency of seizure activity in a given period of time correlates with the intensity of management, quantity of drugs needed, and time to achieve control and subsequent recovery. It is crucial that generalized seizures be controlled rapidly.

Most patients with single seizures, cluster seizures and status epilepticus have intracranial disease. Extracranial causes of seizure such as that observed secondary to exotoxins and metabolic disorders are rare.

DIAGNOSIS

History/Signalment

The signalment of the animal, the age at onset of seizures and the seizure pattern (seizure type and frequency) are the most helpful clues in determining the cause of the seizures. Increasing frequency of generalized seizures that may not start with an aura in a young dog (6 months – 5 years) that is mentally normal between seizures is the most common pattern observed in dogs with idiopathic epilepsy.

While controlling the gross motor activity (*see MANAGEMENT*), obtain history with regards to:

- Duration of current seizure episode to evaluate the gravity of the situation.
- Type, frequency and duration of previous seizure activity; the owner should be asked to describe the event from the beginning.
    a. Was the animal resting or playing at the time of the first seizure? Hypoglycemic seizures are more likely to occur during exercise whereas most seizures due to idiopathic epilepsy occur while the animal is resting/sleeping.
    b. Did the animal remain conscious during the seizure? In **focal seizures,** the consciousness is preserved although often altered. They are the result of focal brain disease even if the lesion may be diffuse and at times widespread. In **generalized seizures,** there is unconsciousness. Exotoxins lead to continuous generalized seizures.
    c. Was there asymmetry in the initial or late phase of the seizure and if so, which side was abnormal? Symptomatic epilepsy is more likely to be associated with asymmetry indicating the presence of a contralateral thalamocortical lesion.
    d. What did the animal do immediately following the seizure? The description of the episode may not clearly be indicative of seizure activity; however the presence of disorientation, pacing, acting as if blind and drinking or eating excessively following the event are highly suggestive of seizure activity.
    e. Where there any changes in the animal's behavior on the day(s) preceding the seizure episode? If the animal's mental status has been abnormal for a few days to a few weeks preceding the onset of seizures, the seizures are probably the result of a structural brain disease and not idiopathic epilepsy. The evaluation of the mental status is often difficult, as the clinician must rely on his/her ability to question the owner appropriately and on the owner's perception and recall.

- Are there coexisting medical problems (*renal failure p. 709, liver disease p. 37, whelping* [*hypocalcemia*] *p. 377, episodes of weakness hypoglycemia p. 280*)?
- Has there been access to toxins (metaldehyde, mycotoxin from spoiled dairy products or compost, strychnine, lead, chlorinated hydrocarbons, household products, turpentine, *p. 641* and ethylene glycol *p. 655*)?
- Is the dog receiving any medications including **antiepileptic drugs (AED)?**

Clinical Signs/Physical Examination

The physical and neurological examinations, laboratory data and advanced neuroimaging are necessary to reach a final diagnosis in most cases of symptomatic epilepsy.

- Evaluate the type (generalized versus focal) of seizures present.
- **Generalized tonic-clonic motor seizures** as per the International League Against Epilepsy (*see Suggested Reading*) are defined as bilateral symmetric tonic-clonic contractions of muscles, usually associated with autonomic phenomena such as frothing at the mouth, urination, defecation. The animal is characteristically unconscious. At time of admission, the gross motor activity may have subsided but there may still be twitching of the eyelids with or without limb/body jerks. In these patients, the seizure activity is still on-going and should be treated.
- In **focal (partial) seizures,** only part of one hemisphere is affected although the structural lesion may be diffuse or widespread. Characteristically, the dog is conscious, but its mentation is altered in most cases. The motor activity may or may not be asymmetrical. These signs may have been present only at the onset of the seizure before generalization occurred. The **aura,** which is a focal onset, is a subjective phenomenon that often precedes generalized tonic-clonic seizure in dogs. Alone, it constitutes a focal sensory seizure.
- In the early stage, or compensatory phase of generalized motor status epilepticus, there is increased blood flow, metabolism, glucose and oxygen utilization by the brain but without permanent damage. As the seizures continue, there is decompensation with marked secondary deleterious cerebral and systemic effects. Cerebral hypoxia, edema and increased **intracranial pressure (ICP)** ensue. Systemically, **disseminated intravascular coagulation (DIC),** acidemia, hypoxia and myocardial injury may occur. Physical findings associated with these problems may co-exist.
- The rectal temperature should be measured as soon as possible, as hyperthermia frequently occurs. The higher the temperature, the longer the seizure activity has been present, and the more severe will be the metabolic effects noted above.
- Rarely, seizure activity leads to neurogenic pulmonary edema secondary to an outpouring of catecholamines. This may follow one or more seizures. Dyspnea, cyanotic mucous membranes and 'crackles' on auscultation may be present depending on the severity of edema. Fulminant edema results in sanguinous, frothy fluid from the mouth and nose (*see Respiratory Emergencies p. 556*).
- The importance of the extracranial metabolic effects of seizure activity cannot be over emphasized as they are the cause of death. Hypo- or hyperglycemia, hyponatremia, hypokalemia, hepatic and renal dysfunction, coagulopathy and muscular necrosis are all changes that may be observed on the various blood tests. (see appropriate chapters for management of these problems).

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV/TS** may be increased should the animal be unobserved for a long period of time and dehydration is present.
- **Blood glucose** to identify potential cause of seizures (*insulin-secreting tumour p. 283*). Hypoglycemia may be a primary cause of seizures, but it may also be a result of seizure activity (*see p. 280*).
- **Lactate** levels may be increased (>2.5 mmol/L) due to muscle activity.
- **Platelet count** may be low with DIC, or as an indication of tick-borne diseases.
- **Stick BUN or creatinine** is required for baseline information and to assess potential pre-renal or renal dysfunction
- **ECG monitoring** to identify cardiac arrhythmias as a potential cause of extracranial seizure activity (although more commonly associated with syncope), or may be present as a cause of an intracranial lesion.
- **Thoracic radiographs** if respiratory system abnormalities noted, to rule out pulmonary edema. Assessment of cardiac silhouette is required if cardiac disease suspected.

Extended Laboratory/Imaging Data Base

- **CBC** abnormalities are non-specific except for thrombocytopenia in Ehrlichiosis. A stress leukogram is often present, however if infection is suspected this may be supportive.
- **Biochemical profile** to identify renal, hepatic and electrolyte abnormalities that may be present. The creatine kinase (CK) may be markedly elevated.

- Urinalysis as part of the renal assessment.
- Consider if appropriate, samples for toxicologic analysis (*p. 636*); tick-borne disease titres; serum phenobarbital levels; serum potassium bromide levels.
- Complete neurological assessment may include: CSF collection, skull radiographs, CT scan in cases of head trauma especially if a fracture or a space-occupying lesion is suspected. In most cases, MRI is preferable to CT because an evaluation of the cerebral parenchyma can be done not only to reach a diagnosis but also to evaluate the secondary effects of the status epilepticus on the brain parenchyma. In inflammatory diseases, the combination of CSF analysis and MRI are the diagnostic tests of choice to reach a definitive diagnosis.

MANAGEMENT

A. Administer oxygen: very important as most of these patients are hypoxic. Consider D. below.

B. Place an intravenous catheter , obtain blood for samples outlined above.

C. Control gross motor activity

1. **Diazepam** IV bolus: approximately 0.5 – 1 mg/kg
<10 kg: 1 – 10 mg (0.2 – 2 mL)
11 – 25 kg: 5 – 25 mg (1 – 5 mL)
>25 kg: 15 – 25 mg (3 – 5 mL)

Wait 5 minutes for full effect. In the meantime Go to D, E & F immediately; then, if seizure activity is stopped, go to H below. If the **seizures continue,** go to G below. If the animal has been in status epilepticus for more than 30 minutes, the treatment may not be successful at arresting all activity immediately. The animal may continue to slowly paddle. This may not be seizure activity. If, however, the eyelids are twitching 5 minutes after therapy, the seizure activity is still on-going (*go to G below*). In the meantime:

D. Obtain rectal temperature and begin cooling if temperature is greater than 39.5°C. Cool to 39.5°C with towels soaked in cold water and fans. Pass the IV line through a bowl of cold water or place a cold pack on the line.

E. Administer a balanced electrolyte solution at a rate appropriate for degree of dehydration, or if not present, at a maintenance rate (*see Fluid Therapy p. 347*). **Go to (H)** if the seizures are controlled.

F. **If hypoglycemia** (blood glucose <3.4 mmol/L, 60 mg/dL), supplement with dextrose. It is preferable to moisten the oral mucosa under the tongue with a 50% dextrose solution rather than administer it intravenously as a bolus. The glucose solution is well absorbed by the oral mucosa, and avoids dramatic homeostatic shift. However, do not attempt this in the seizing dog as you may get bitten, or cause aspiration pneumonia. (**Dextrose bolus,** administer 0.5 g/kg [0.5 mL/kg of 50% dextrose]) ALWAYS diluted 1:4 with normal saline; give bolus and re-evaluate accordingly (*see Hypoglycemia p. 280*). Low blood glucose is often a result of status epilepticus in the small breeds of dogs, whereas in the large breeds it is the cause (insulinoma). If a low glucose level is measured in a poodle, treat accordingly, but do not necessarily assume it to be the cause of the seizure(s) unless there has been insulin overdose. Conversely, in the large dog, hypoglycemia is more likely to be the cause of the seizures. Hyperglycemia is frequently observed in the early stage of status epilepticus. Whenever hypoglycemia is documented during or after seizures, it should be treated and the patient's glucose reevaluated 48 hours after stabilization.

G. **If gross motor activity continues** 5 minutes after (C) above, repeat bolus of diazepam. If gross motor activity persists, continue with diazepam CRI (*H below*) and add phenobarbital:

1. Administer **phenobarbital** to run concurrently with diazepam but as a separate infusion.
   a. Dogs naïve to phenobarbital:
   An IV bolus is administered **2 – 5 mg/kg** followed by a phenobarbital **CRI at 2 – 6 mg/dog/h.** **Phenobarbital bolus 2 – 5 mg/kg** can be repeated, if necessary, for a total of 16 mg/kg (4 boluses) 20 minutes apart. This high dose of phenobarbital is rarely required.

   Phenobarbital injectable is only available in 120 mg/mL (1 mL) ampoules. The content of the ampoule is diluted with 19 mL of sterile water to create a solution of 6 mg/mL. Sterile water is used to avoid precipitation.

b. If the dog is already on phenobarbital for maintenance therapy, the phenobarbital serum levels should be taken prior to IV administration. One phenobarbital 2 – 5 mg/kg bolus can be administered followed by a phenobarbital 2 – 6 mg/dog/h CRI. *See H below.* Note that phenobarbital and diazepam although reported as effective at controlling experimentally-induced focal seizures are not as effective clinically when the focal seizure has been of long duration. *See editor's note below.*

2. If the patient is still convulsing after 15 minutes, titrate **propofol 2 – 8 mg/kg** to effect followed by a **constant rate infusion of 0.1 – 0.6 mg/kg/min** (*see Drug Infusion Chart p. 259*). Recovery from propofol anesthesia may result in generalized muscle tremors, very different from seizure activity. If the seizures continue despite this measure, isoflurane anesthesia is introduced.

3. **Isoflurane anesthesia:** is preferable to pentobarbital if barbiturate coma cannot be induced with assisted ventilation due to lack of close monitoring and availability of a mechanical ventilator.

4. **Pentobarbital,** an anesthetic agent, is still frequently used to treat status epilepticus in dogs that have failed diazepam and diazepam combinations. It will abate the motor activity, thereby preventing hyperthermia and secondary metabolic changes. However, without barbiturate coma, it is not likely to stop the cortical seizures, which by itself is detrimental to the brain. If used, **pentobarbital 1 – 5 mg/kg IV** is given initially. This can be repeated 5 minutes later if necessary. Monitor for depth of anesthesia as you would for an anesthetized patient. Respiratory depression and hypercarbia may occur with increasing doses of pentobarbital; this must be prevented as it will increase intracranial pressure and worsen the neurological outcome. The paddling of the limbs that frequently occurs during the recovery of pentobarbital anesthesia should not be confused with seizure activity. Eyelid twitching is more indicative of seizure activity.

5. Dogs in the decompensatory phase of convulsive status may benefit from treatment with dexamethasone 0.25 mg/kg q24h for two to three days.

H. **Diazepam constant rate infusion (CRI).** Diazepam is incompatible with other medications. Diazepam should be added to all protocols to reduce the requirement for other drugs. Initiate diazepam infusion at **0.5 mg/kg/h.** It is added to the maintenance hourly fluid therapy in the in-line burette. Prepare, at the most, 2 hours at a time (as diazepam is light sensitive and binds to the plastic tubing). The dosage of diazepam can be safely increased to 1 mg/kg/h for one or two hours if necessary. Once seizure activity has stopped for a minimum of four hours, the infusion can be gradually discontinued over as many hours as it took to control the seizure activity; i.e., if it took 6h to reach control, allow 6h to discontinue the diazepam. Refractoriness to diazepam may be occurring if the seizures continue despite increasingly higher dosages. If generalized seizures are observed following the first hour of diazepam infusion, Phenobarbital CRI is added to the diazepam infusion.

I. **Guidelines for discontinuing therapy:** Dogs with status epilepticus secondary to idiopathic epilepticus should be controlled with the therapeutic approach described above. Dogs with inflammatory diseases and acute onset convulsive status have the poorest prognosis for survival. If a dog continues seizing despite anesthesia for >6 hours, the prognosis for control is poor to nil (*see Suggested Reading 2*).

Maintenance oral antiepileptic therapy is initiated, or resumed, as soon as the animal can swallow. The optimal therapeutic serum levels for phenobarbital is 100 – 120 μmol/L (23 – 28 mg/mL). Below 100 μmol/L many dogs are uncontrolled and above 120 μmol/L, most, with **chronic use,** develop hepatotoxicity. If the animal cannot swallow, give the phenobarbital oral dose as an IM or SC injection (q12h). If the phenobarbital serum levels are already within the optimal range (100 – 120 μmol/L), potassium bromide is added to the oral daily regimen. If the animal is at optimal therapeutic serum levels for phenobarbital and potassium bromide >20 mmol/L (>1.6 mg/mL), contact a neurologist.

Editor's Note: At the time of publication, phenobarbital for injection is not available in Canada. This may be a short term problem but this is not known. For information on availability from other sources, please contact the Pharmacy at the Veterinary Teaching Hospital, Ontario Veterinary College, University of Guelph. Tel: 519•824•4120 Ext 54196 or contact a compounding pharmacy.

PHARMACOLOGY

1) **Diazepam:** GABA-ergic; reaches equilibrium in the cerebrum within 3 minutes necessitating a 5 minute pause between boluses to avoid overdose. The initial bolus facilitates rapid therapeutic serum levels. Diazepam is metabolized within 15 minutes to nordiazepam, a less potent antiepileptic drug. This rapid metabolism renders diazepam safer to use but requires constant rate infusion to obtain and maintain therapeutic serum levels. The drug is metabolized by the liver, so caution must be applied in the treatment of patients with liver dysfunction.

2) **Phenobarbital:** Barbiturate with a strong antiepileptic effect but mild sedative effect. Its antiepileptic effect is post-synaptic acting ultimately on GABA by prolonging the opening of the postsynaptic cell membrane Cl⁻ channel. Phenobarbital equilibrium is reached in the cerebrum in 17 minutes, necessitating a 20 minute pause between boluses. The metabolism is slow with a half-life of 40 to 80 hours. Repeated dose is cumulative. Barbiturates and benzodiazepines are synergistic. Therefore, careful titration must be used with concomitant use especially in patients with liver dysfunction. Chloramphenicol and cimetidine are to be avoided with phenobarbital. Their inhibition of the phenobarbital metabolism leads to toxic phenobarbital serum levels as early as after one treatment.

3) **Pentobarbital:** Barbiturate with strong sedative effect but mild antiepileptic effect. In this protocol, pentobarbital is used to control gross motor activity. At the doses used, cortical seizure activity may continue. Ideally, barbiturate coma should be induced, the patient mechanically ventilated, and the cortical activity monitored with EEG.

   Pentobarbital acts synergistically with diazepam and phenobarbital; therefore lower doses of pentobarbital are required.

4) **Propofol:** potentiates GABA by increasing the frequency of chloride channel opening. Muscular necrosis with myoglobinuria following prolonged infusion is reported in human. Although we have not observed this in dogs, caution should be applied until more experience with this use of the drug is acquired.

SUGGESTED READING

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NOTES

INTRODUCTION

The main role of the vestibular system is to control body posture and balance. Disorders affecting this system usually manifest with a head tilt. Vestibular dysfunction results in facilitation of the extensor muscles on the normal side and deviation of the body in the direction of the abnormality (rolling, falling and leaning toward the side of the head tilt). There are multiple causes of vestibular disease such as otitis media-interna, nasopharyngeal polyps, toxicosis, geriatric vestibular disease, inflammatory conditions of the rostral medulla (viral, bacterial, rickettsial, protozoal, fungal, immune mediated) and neoplasia. Less common causes of vestibular dysfunction include congenital anomaly, hypothyroidism, metronidazole toxicity, head trauma and thiamine deficiency. This chapter will describe the approach to the neurological patient presented with head tilt and outline the important factors to be considered in differentiating peripheral from central vestibular diseases.

DIAGNOSIS

History/Signalment

- Question the owner about patient's mental status and sleep patterns. **Somnolence is one of the main signs of a central disorder affecting the reticular formation located throughout the brainstem.**
- Look for cranial nerve (CN) deficits other than head tilt (CN VIII) such as facial nerve paresis/paralysis (CN VII), difficulty in swallowing or change in voice (CN IX, X).
- Be aware of those breeds reported with potential congenital malformation or degeneration of the inner ear such as: German shepherd, English Cocker, Doberman Pinscher, Siamese and Burmese kittens.
- Age is a critical factor to be considered especially in dogs (dogs tend to be older than seven when idiopathic vestibular disease is suspected). In dogs the syndrome is also known as "geriatric vestibular disease" and "old dog vestibular syndrome". Cats of any age can suffer from idiopathic vestibular disease.
- Owners should be questioned about potential toxicity (aminoglycoside, metronidazole) and recent use of ear cleaning solutions (e.g., chlorexidine).
- Inquire about any history of ear infections.

Clinical Signs/Neurological Examination

- The primary goal is to determine where the lesion is and to differentiate between central and peripheral vestibular disease.
- Falling, rolling and leaning are common signs of vestibular dysfunction but they are **not specific** when localizing the lesion peripherally or centrally. The deficits are usually ipsilateral to the side of the head tilt. Exception to this rule is the presence of a paradoxical vestibular syndrome where the head tilt is contralateral to the side of the lesion.
- **Decreased alertness, somnolence and increased sleepiness are important features to localize the lesion centrally.** The patient may not exhibit these abnormalities at the time of examination due to stress or anxiety. Therefore it is very important to obtain this information from the history.
- Depending on the stage of disease, pathological nystagmus may or may not be present (chronic cases tend to compensate and head tilt may be the only evidence of a vestibular disorder). **If pathological nystagmus is vertical in direction or changes in position, the lesion is usually central.**
- Evaluate carefully other cranial nerves. Involvement of the facial nerve (CN VII) is common with vestibular disease. Dysfunction of CN VII will be manifested by ipsilateral decreased or absent menace response, assymetry of facial structures (droopy ear, eyelid, nostrils and lips) or a weak palpebral closure. The abnormalities are noted on the same side of the head tilt.
- **The presence of Horner's syndrome** (miosis, ptosis, third eyelid protrusion, enophthalmos) along with **head tilt is usually indicative of a peripheral lesion affecting middle and inner ear.**
- Positional ventrolateral strabismus may occasionally be induced by extending the patient's neck.
- The flocculonodular lobe is a cerebellar structure that plays a role in maintaining equilibrium. Clinical signs typical of cerebellar dysfunction (hypermetria, tremors) along with vestibular signs suggest a **central lesion** affecting this particular cerebellar lobe.

- Proprioceptive positioning deficits occur commonly with **central** vestibular disorders.
- Vomiting and profuse salivation may be present due to direct connection between vestibular nuclei and vomiting center located in the reticular substance of the medulla and occurs in both central and peripheral disease.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **CBC** will identify an infection as a potential cause, or thrombocytopenia as a potential cause for hemorrhage
- **Biochemical profile** and **urinalysis** will evaluate the general condition of the patient. High serum cholesterol may be associated with hypothyroidism *(p. 285)* which is occasionally associated with central or peripheral vestibular dysfunction.
- **Blood lactate** elevation may suggest thiamine deficiency where other causes for elevation are not evident.
- **Thoracic and abdominal ultrasound or radiographs** can be useful to rule out neoplasia that may result in metastatic disease.
- A thorough **otoscopic examination** is necessary when a peripheral vestibular disease is suspected. Usually a good evaluation of the ear canal requires heavy sedation or general anesthesia. The purpose of the evaluation is to assess the integrity of the tympanic membrane, look for evidence of fluid accumulation and presence of space occupying lesions. A normal otoscopic exam does not rule out peripheral vestibular disease.
- Radiographs of the bullae may also be indicated to investigate the middle ear.
- If possible **biopsy** any mass detected on otoscopic examination. Tumors of the ear include fibrosarcoma, adenocarcinoma, chondrosarcoma and squamous cell carcinoma.

Extended Data Base
- **Hypothyroidism** has been recognized as a cause of central and peripheral vestibular dysfunction. In these cases, serum cholesterol level has been found markedly elevated along with low serum total thyroxine (T4), low free T4 (best performed by equilibrium dialysis) and high serum thyroid-stimulating hormone (TSH).
- **Brain auditory evoked response** (BAER) is an electrodiagnostic test available at referral hospitals to assess the auditory pathway of the vestibulocochlear nerve which facilitates lesion localization to either the central or peripheral central nervous system.
- Radiological studies must be selected according to the results of the neurological examination. When a peripheral vestibular disease is suspected, **computed tomography (CT)** should be conducted to assess the integrity of the bullae. Alternatively, when a central vestibular disease is more likely, **magnetic resonance imaging (MRI)** of the brain is recommended. The MRI study will reveal the presence of an inflammatory, degenerative, anomalous or neoplastic disorder.
- When a central vestibular disease is suspected, **cerebrospinal fluid (CSF)** should be collected to evaluate white cell count, proteins and cytology for presence of infectious agents (e.g., bacteria, *Blastomyces dermatidis*, *Cryptococcus neoformans*).
- If a central vestibular disease of infectious nature is considered likely, **immunoassays** of CSF and serum are recommended. Antibody titers for *Distemper virus, feline Coronavirus, Ehrlichia canis, Ricketssia ricketssi, Neospora caninum, Blastomyces dermatidis, Cryptoccocus neoformans and Borrelia burgdorferi* are now available.
- Elevation of blood lactate and pyruvate levels in combination with a decreased transketolase erythrocyte activity supports a diagnosis of **thiamine deficiency.**

MANAGEMENT

A. In patients with severe signs of imbalance, a quiet environment and padded bedding around the cage to protect from injury should be provided.

B. The sedative effect of **diazepam** at 0.1 mg/kg PO q8h will help reduce stress and prevent injury from rolling.

C. **Dimenhydrinate** 4 mg/kg q8h to reduce dizziness within the first 48 hours of clinical signs.

D. **Antibiotic therapy** for the treatment of **ear infections** should be based on culture and sensitivity results. When the culture is negative but a bacterial otitis is still suspected administer:

1. **enrofloxacin 5 – 10 mg/kg PO q24h** is recommended (not to exceed 5 mg/kg/24h in the cat).
2. Alternatively a combination of **trimethoprim-sulfadiazine 20 mg/kg q12h** with **cephalexin 22 mg/kg PO q8h** can be used.
3. Continue treatment for 6 – 8 weeks.

E. **Surgical treatment.** Bulla osteotomy may be required in cases of recurrent ear infections. Nasopharyngeal polyps can be surgically removed. Ablation of the external ear canal is often necessary for the treatment of squamous cell carcinomas and other neoplasias.

F. **Levothyroxine 0.02 mg/kg q12h** If the laboratory findings support a diagnosis of hypothyroidism. The serum levels of T4 should be measured after 4 weeks of therapy (*see Hypothyroidism p. 285*).

G. If a toxicosis is suspected, the incriminated agent (e.g., metronidazole, amikacin, gentamicin) should be discontinued immediately. Despite improvement of vestibular signs, permanent hearing damage is common.

H. Glucocorticoid therapy is recommended when the CSF results and radiological findings support a diagnosis of inflammation and if protozoal and fungal infections are unlikely.

    1. Initiate therapy with **dexamethasone 0.25 mg/kg IV q24h** for 4 days.

    2. Continue treatment with **prednisone 1 mg/kg PO q24h** and slowly tapered down to every other day.

    3. Anti-inflammatory therapy may be required for a long period of time. The goal is to control the clinical signs with the minimal dose of corticosteroids required. Treatment length is determined according to patient's response.

I. Fungal, protozoal or bacterial infections will worsen with prolonged steroid treatment. In rare occasions where an etiological agent is identified on CSF analysis, specific therapy can be initiated after one dose of **dexamethasone 0.25 mg/kg.**

    1. **Clindamycin 10 mg/kg PO q8h** is recommended for *Neospora caninum* and *Toxoplasma*.

    2. **Trimethroprim-sulfonamide 20 mg/kg PO q12h** can also been used for the treatment of *Neospora caninum*.

    3. For *Ehrlichia canis* and *Rickettsia rickettsi* antibiotics of choice include

        a. **doxycycline 5 – 10mg/kg PO q12h** for 7 – 10 days or

        b. **tetracycline 22 mg/kg PO q8h** for 21 days. Tetracycline must be administered on an empty stomach which makes compliance very difficult when administering medication three times daily. When any food is present in the stomach, the efficacy of tetracyline is diminished due to malabsorption. For this reason, doxcyline is preferred.

    4. Although bacterial infections of the central nervous system are rare in small animals, some implicated organisms include *Staphyloccocus, Streptococcus, Escherichia coli, Klebsiella, Actinomyces, Nocardia* and anaerobes agents such as *Bacteroides, Peptostreptococcus, Fusobacterium and Eubacterium*. Appropriate antibiotics should be bactericidal, have a low level of protein binding, and be able to cross the blood brain barrier (BBB). Recommended treatments include:

        a. **third generation cephalosporins** (e.g., **cefotaxime 25 – 50 mg/kg IV q8h**),

        b. **metronidazole 10 mg/kg IV q8h** (delivered over 1 hour), OR

        c. **trimethoprim-sulfonamide15 mg/kg IV q12h**.

        d. In general, therapy should be continued for 10 – 14 days after resolution of clinical signs. Re-evaluate clinical signs 48 hours after antibiotic therapy is instituted.

J. **Fluconazole 5 mg/kg PO q12h** is the treatment of choice for fungal infections. Therapy should be continued for 2 – 3 months. An important limitation is the high cost of the medication.

K. Thiamine deficiency can be treated with **thiamine hydrochloride** 5 – 50 mg/dog IV q24h and 1 – 20 mg/cat, by slow infusion.

L. Nursing care is very important. A padded cage is necessary to avoid self-inflicted injury. The area should be quiet; cotton balls in the ear canal may help to reduce environmental noise. Water and food should be offered and hand-fed. Assistance with urination and defecation is required to avoid soiling.

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INTRODUCTION

In small animals, neck pain is usually associated with the involvement of specific neuroanatomical structures including meninges, nerve roots and vertebral bodies. In patients with extreme cervical pain the neurological examination may be challenging and difficult to perform accurately. The most common neurological conditions resulting in neck pain are listed in TABLE 1. Less common differential diagnoses include: polyarthritis, polymyositis, multiple cartilaginous exostosis (osteochondromatosis), spinal cord hemorrhages and intracranial tumors. A careful physical and neurological examination is always required to prevent worsening and eventual de-stabilization of the neurological status.

TABLE 1. Causes of Neck Pain

cervical disc protrusion or extrusion
steroid responsive arteritis-meningitis
infectious meningomyelitis
vertebral fracture/luxation due to spinal trauma
atlantoaxial luxation
caudal cervical spondylomyelopathy (CCSM)
discospondylitis/osteomyelitis
malignant nerve sheath tumor (MNST)
bony neoplasia

DIAGNOSIS

History/Signalment

- Historical and clinical features typical of neck pain include guarded neck motion, intermittent yelping, muscle spasms, stiffness, low head carriage, reluctance to jump, inability to climb stairs and unilateral front limb lameness (also known as "nerve root signature").
- Question the owner regarding possible trauma, both recently and previously.
- **Intervertebral disc disease (IVDD)** is a common neurological condition in dogs but rare in cats. Chondrodystrophic breeds such as the **Dachshund, Shih-Tzu, Cocker Spaniel, Pekingnese, Lhasa-apso and Beagle** commonly experience IVDD. However, the condition rarely occurs in patients younger than 2 years.
- **Caudal cervical spondylomyelopathy (CCSM)** (also known as wobbler's syndrome, cervical vertebral instability or cervical malformation/malarticulation syndrome) is a common neurological syndrome typical of large breed dogs (e.g., Rottweiler, Weimaraner). **Doberman Pinschers** are usually over-represented especially at 5 – 7 years of age. Giant breeds such as the **Great Dane, St. Bernard and Newfoundland** exhibit clinical signs at 1 – 3 years of age. Caudal cervical spondylomyelopathy has been lately recognized in small breeds such as the Yorkshire Terrier.
- **Steroid responsive meningitis-arteritis** (SRAM) most commonly affects **Beagles, Bernese Mountain dogs, Boxers and German Shorthaired pointers** under the age of 2 years.
- Inquire about previous episodes of pain and treatment. Intervertebral disc disease and SRAM can be episodic and resolve without treatment or after a short course of corticosteroid therapy.
- Look for any signs suggesting a **urinary tract, or systemic infection.** Although rare, hematogenous spread of infectious agents can result in bacterial meningitis. A history of uterine, prostatic, urinary or ear infections may be relevant.
- A history of weight loss may indicate **neoplasia.**
- Lameness or reluctance to bear weight on the front limbs is suggestive of a nerve root lesion.
- **Discospondylitis,** SRAM, polyarthritis and bacterial meningitis (rare), can result in fever.
- **Atlantoaxial luxation** is a condition that affects miniature breeds (usually <1 year of age) such as the **Chihuahua, Yorkshire Terrier and Miniature Pinscher**.
- **Intracranial neoplasia** can cause neck pain. It has been postulated that a space-occupying lesion can cause stretching of meningeal nerve endings and blood vessels resulting in neck pain. Historical information that indicates an abnormal mental status may be relevant.

Clinical Signs/Physical and Neurological Examination

- If a vertebral fracture/luxation or atlantoaxial luxation is suspected, the patient MUST be manipulated carefully. **Flexion of the neck can result in death of the patient.**
- Additional signs that may be present include: irritability, reluctancy to walk, fever, arched back, depression, inappetence and muscle spasms.
- Lameness and pain can be elicited on movement of the limb resulting from irritation of the nerve roots that provide innervation to the limb ("root signature").
- A heart murmur may be present if a bacterial endocarditis is the source of discospondylitis or meningitis.
- Involvement of the spinal cord parenchyma in the patient presented for neck pain (e.g., IVDD, meningomyelitis, neoplasia) can be manifested by decreased proprioceptive positioning and proprioceptive ataxia. The deficits (knuckling) will be evident when postural reactions are tested or when the animal is ambulating.
- An abnormal gait characterized by an inconsistent foot placement (proprioceptive ataxia) will indicate a dysfunction of the spinal sensory pathways. This finding may be observed with compressive (e.g. IVDD, neoplastic disease, CCSM) or inflammatory lesions (e.g., advanced SRAM, meningomyelitis). Polyarthritis and polymyositis may result in a stiff gait without ataxia. In polyarthritis pain with or without swelling is usually detected on manipulation of the joints.
- Although rare, presence of neck pain with cranial nerve deficits and concurrent behavioral abnormalities can indicate intracranial neoplasia.
- Lesions affecting the gray matter of the caudal cervical region (C6-T2) may result in a decreased withdrawal reflex.
- A Horner's syndrome is rarely observed in patients presented for evaluation of neck pain. The abnormality results from involvement of the sympathetic chain and has been reported with acute IVDD, and spinal neoplasia.

Laboratory Evaluation/Diagnostic Imaging

Stat

Unless presenting as an emergent patient requiring immediate attention, stat laboratory evaluation is not necessary. However if this is required, *see Triage p. 4.*

Extended Laboratory Data Base

- **CBC.** A neutrophilic pleocytosis can be detected in cases of discospondylitis, SRAM, bacterial meningitis and polyarthritis.
- **Biochemical profile** is required to evaluate the patient's overall status and any potential relationship to neck pain (i.e., hyperproteinemia in multiple myeloma, elevation in creatinine kinase (CK) may be present in cases of polymyositis, hypercalcemia in several other neoplastic disorders), and prior to general anesthesia.
- **Urinalysis and a urine culture** may be helpful to identify infectious agents (*Streptoccocus canis, Staphyloccocus aureus* and *Escherichia coli*), responsible for discospondylitis. If the culture is positive, antibiotic therapy should be guided by sensitivity results. Occasionally, in cases of discospondylitis, fungal hyphae from *Aspergillus* spp. is detected on urine sediment.
- **Blood cultures.** Isolation of infectious agents responsible for bacterial meningitis or discospondilytis is sometimes possible from blood.
- **Serological testing** for *Brucella canis* is recommended if discospondylitis is highly suspected.
- **Arthrocentesis. Cytological evaluation and culture of synovial fluid** should be performed to confirm a diagnosis of polyarthritis.
- **Thoracic and abdominal imaging (e.g., ultrasonographic examination and/or radiographs)** are recommended to rule out neoplasia that may result in metastatic disease.
- **Vertebral column radiographs:**
  - Spinal radiographs should be performed under general anesthesia.
  - When cervical vertebral instability (e.g., fracture, luxation) is suspected, general anesthesia is not recommended since further neurological damage can result from muscle relaxation.
  - If atlantoaxial luxation is possible AVOID manipulation of the cervical region. Plain radiographs can demonstrate an increased space between the atlas and the axis confirming the diagnosis.
  - In IVDD calcified disc material and narrowing of the intervertebral disc space are common findings.
  - Radiographs may be useful to detect lytic and proliferative lesions or pathological fractures associated with neoplasia (osteosarcoma, metastasic carcinoma, metastasic hemangiosarcoma, chondrosarcoma, fibrosarcoma, lymphoma and multiple myeloma).
  - Sclerosis and lysis of the end plates are the radiographic changes characteristic of discospondylitis.
  - In rare situations abnormal proliferation of cartilage from the methaphyseal growth plates (osteoschrondomatosis) is observed in young patients presented for evaluation of neck pain.

- **Cerebral fluid (CSF) collection:**
  - **Cytological** examination of CSF demonstrating a neutrophilic pleocytosis with good cell preservation supports a diagnosis of SRAM. Rarely, lytic neutrophils can be detected on CSF samples indicating a bacterial meningitis. An increased white cell count supports an inflammatory process and potential causes of infectious meningitis/meningomyelitis (e.g., viral, rickettsial, protozoal, fungal) should be further investigated with specific immunoassays.
  - **Immunoassays** on CSF and serum are recommended. Antibody titer determination for *Distemper virus, feline Coronavirus, Ehrlichia canis, Ricketssia rickettsi, Neospora caninum, Blastomyces dermatidis, Cryptoccocus neoformans* and *Borrelia burgdorferi* are now available.
  - **Culture** of spinal fluid may be attempted but is usually negative. In cases of IVDD and neoplasia, the CSF analysis may only reveal an increase in protein concentration with normal white cell count (albuminocytogenic dissociation). Occasionally neoplastic cells (e.g., lymphoma, histiocytic sarcoma) can be detected.
- **Electromyography** can demonstrate positive sharp waves and fibrillation potentials of paraspinal or limb muscles. The abnormality is non-specific but may be observed in several conditions such as CCSM, MNST and polymyositis.
- A **myelogram** is indicated in cases where IVDD is highly suspected. The procedure is also helpful to differentiate spinal cord compression from neoplastic disorders and to confirm a diagnosis of CCSM.
- **Computed tomography (CT)** and **magnetic resonance imaging (MRI)** are both useful diagnostic procedures in cases of IVDD, CCSM, vertebral fracture, osteochondromatosis, atlantoaxial luxation, discospondylitis and bony neoplasia. MRI is recommended to confirm a diagnosis of intracranial neoplasia.

MANAGEMENT

A. Ideally **IVDD** should be treated surgically (*see Disc Herniation p. 476*). Pain/inflammation can be controlled with:

1. **Dexamethasone 0.1 – 0.25 mg/kg PO q24h** until the surgical procedure is conducted.
2. **Prednisone 0.5 – 1.0 mg/kg PO q24h** and **cage rest** (3 – 4 weeks) may alleviate the pain but recurrence of clinical signs is possible. If other neurological abnormalities (e.g., proprioceptive deficits, ataxia) are present in addition to the neck pain, surgery is STRONGLY recommended to relieve spinal cord compression.

B. **Steroid responsive arteritis meningitis** can be well managed with

1. **Dexamethasone 0.25 mg/kg q24h** for 4 days **OR**
2. **Prednisone 4 mg/kg q24h** for 2 days
3. **Treatment 1 or 2 must** be **followed by** prednisone 2 mg/kg q24h for 14 days.
4. If the **clinical signs have improved,** a further reduction can be considered: prednisone 1 mg/kg q24h for 28 days, then prednisone 0.5 mg/kg q24h for 28 days then prednisone 0.5 mg/kg q48h for 2 months.
5. **Azathioprine 2 mg/kg q24h** reducing to 1.5 mg/kg every other day orally may be used if clinical signs are refractory to the steroid medication.
6. **Long-term treatment (6 – 12 months) is usually required.** Some patients will need lifelong therapy Adjustment to the recommended doses may be necessary. The goal is to control the clinical signs with the minimal dose of corticosteroids required. If a high dose of steroids is necessary, gastrointestinal protectants are recommended to prevent ulceration (*see Gastrointestinal Hemorrhage p. 67*). Do NOT administer glucocorticoids unless you are sure about the diagnosis.

C. When the cause of infectious meningitis or meningomyelitis (viral, rickettsial, protozoal, fungal) is confirmed specific treatment should be provided. Fungal, protozoal or bacterial infections will worsen with prolonged steroid treatment. In rare occasions where an etiological agent is identified on CSF analysis, specific therapy can be initiated after one dose of dexamethasone 0.25 mg/kg.

1. **Clindamycin 10 mg/kg PO q8h** is recommended for Neospora caninum and Toxoplasma.
2. **Trimethoropim-sulfonamide 20 mg/kg PO q12h** can also been used for the treatment of Neospora caninum.
3. For *Ehrlichia canis* and *Rickettsia rickettsi* antibiotics of choice include:
   a. **doxycycline 5 – 10 mg/kg PO q12h** for 7 – 10 days OR

    b. **tetracycline 22 mg/kg PO q8h** for 21 days. Tetracycline must be administered on an empty stomach which makes compliance very difficult when administering medication three times daily. When any food is present in the stomach, the efficacy of tetracyline is diminished due to malabsorption. For this reason, doxycyline is preferred.

4. Although bacterial infections of the central nervous system are rare in small animals, some implicated organisms include Staphyloccocus, Streptococcus, Escherichia coli, Klebsiella, Actinomyces, Nocardia and anaerobes agents such as Bacteroides, Peptostreptococcus, Fusobacterium and Eubacterium. Appropriate antibiotics should be bactericidal, have a low level of protein binding, and be able to cross the blood brain barrier (BBB). Recommended treatments include:

    a. **third generation cephalosporins** (e.g., **cefotaxime 25 – 50 mg/kg IV q8h**),

    b. **metronidazole 10 mg/kg IV q8h** (delivered over 1 hour), OR

    c. **trimetropim-sulfonamide15 mg/kg IV q12h.**

    d. In general, therapy should be continued for 10 – 14 days after resolution of clinical signs. Re-evaluate clinical signs 48 hours after antibiotic therapy is instituted.

5. **Fluconazole 5 mg/kg PO q12h** is the treatment of choice for fungal infections. Therapy should be continued for 2 – 3 months. An important limitation is the high cost of the medication.

D. If the results of the **blood and urine cultures** are negative and a bacterial **bacterial discospondylitis is highly suspected,** initiate treatment with

1. **trimethoprim-sulfonamide 20 mg/kg PO q12h and cephalexin 30 mg/kg PO q8h.**

2. If **bacterial cultures identify** an organism, treat with recommended antibiotics.

3. If **fungal discospondylitis** is confirmed, administer **fluconazole 5 mg/kg PO q12h.** Therapy should be continued for 2 – 3 months.

4. If surgical decompression is required.

E. Treatment of **CCSM** is controversial. **Prednisone 0.5 mg/kg PO q24h or q48h** may help to control neck pain and spinal cord inflammation. Various surgical techniques and success rates have been reported.

F. Chemo- and radiation therapy may be useful in some cases of **vertebral neoplasia.** Since neoplastic disorders of the spinal column are extremely painful, pain management is essential.

1. **Morphine 0.05 – 0.4 mg/kg IV over 3 minutes, OR**

2. **Hydromorphone 0.05 – 0.2 mg/kg IV, SC q3–6h** may alleviate severe pain.

3. **Meloxicam 0.2 mg/kg,** followed by **0.1 mg/kg PO q24h (dogs), 0.1 mg/CAT PO q48–72h** for chronic management.

4. **An opioid and** a non-steroidal anti-inflammatory analgesic (NSAIA) may be combined.

5. **Transdermal fentanyl patches** may control chronic neck pain. Since it takes up to 12 hours in cats and 24 hours in dogs to reach therapeutic plasma levels, other analgesic therapy is required during this time. Combine with a NSAIAs.

G. **Atlantoaxial luxation** can be treated with ventral **surgical fusion of the atlantoaxial joint.** A neck brace should be used for 4 – 6 weeks after surgery. The condition can be controlled with **prednisone 0.5 mg/kg PO q24h,** but without surgical fusion severe spinal cord injury is possible. If surgical intervention is not performed a permanent neck brace is recommended.

H. For **polyarthritis** therapy is instituted according to the etiology. If immune-mediated, **prednisone 2 mg/kg PO q12h for 2 days, then 1 mg/kg PO q12h for 2 weeks, followed by 0.5 mg/kg PO q12h for 1 month. Alternate-day therapy of prednisone 0.5 mg/kg PO may be needed for several months.**

I. **Gabapentin 6 – 15 mg/kg q6–8h (start at 10 mg/kg and increase or decrease based on response) PO** may be used for **neck pain refractory to other treatments.** Wean off gradually even if it doesn't work. Must not stop abruptly. *See Analgesics and Sedatives p. 92.*

PHARMACOLOGY

1) **Gabapentin** is an antiepileptic and analgesic agent. It has been suggested that the antiallodynic actions of gabapentin involve a central mechanism of action by binding with the high affinity a2d subunits of voltage dependent calcium channels, blocking calcium currents in cortical neurons and blocking maintenance of spinal cord central sensitization. Gabapentin is excreted by the kidneys; animals with renal insufficiency may require less frequent dosing due to slower elimination. As dosing to effect is the method by which the appropriate dose is selected, once this effect is reached, twice a day rather than three times daily treatment may suffice. Nephrotoxicity is not an issue. The author has found gabapentin useful in treating animals following cardiopulmonary arrest or seizures that are extremely restless, disoriented, vocalizing and/or manic. Signs of overdose are reduced activity and excessive sleepiness, progressing to depression. Tapering the dose down is important, as stopping the drug abruptly may lead to rebound pain which may be severe.

2) **Prednisone** and **dexamethasone** are used as anti-inflammatory, analgesic agents in this setting.

SUGGESTED READING

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2. Lorenz MD, Kornegay JN. Pain. In: Handbook of Veterinary Neurology. Philadelphia: Elsevier Science; 2004:345.
3. Sanders SG, Bagley RS. Myelopathies: Disorders of the Spinal Cord. In: A practical guide to canine and feline neurology. Iowa: Blackwell; 2003:277-336.

NOTES

INTRODUCTION

Spinal injuries can occur following any trauma, frequently caused by automobiles. The most common injuries are luxations, fracture-luxations, or compression, transverse, or oblique fractures. The common sites of injury are at, or near, junctions between mobile and immobile vertebrae such as the craniocervical, cervicothoracic, thoracolumbar, and lumbosacral junctions. In the cervical region, it is the axis, the second cervical vertebra, which is the most commonly fractured.

Peracute disc herniation can occur spontaneously, or with mild activity such as jumping off furniture or strenuous exercise. The clinical signs are highly variable. There may be neck or back pain alone with or without neurological deficits.

Rarely, spinal injury/fractures occur secondary to neoplasia.

DIAGNOSIS

History/Signalment

- If trauma is expected based on history and physical examination, question the owner as to whether the accident was witnessed and if the animal walked after the injury. External trauma should not be listed as primary cause of spinal pathology in an animal found down in the confines of a home.
- The clinical presentation of a dog with **intervertebral disc disease (IVDD)** varies from the presence of back or neck pain without neurological deficits, to paralysis, to total or complete myelopathy. Although the occurrence of neurological deficits may be peracute with IVDD, most of the dogs have shown some signs of discomfort or pain in the few days preceeding the appearance of the neurological deficits.
- Fibrocartilaginous embolic myelopathy (FCEM) is the second most common spinal cord disease of dogs. In many cases, the clinical signs appear while the animal is exercising, thereby giving the impression of a traumatic event. Occasionally, dogs may yelp or cry at the onset of the embolic shower, but following this onset the owner usually does not report the animal to seemingly be in pain. However, dogs with FCEM may show signs of discomfort on palpation of the back.
- Primary vertebral neoplasia or metastatic tumor involving vertebrae cause neck/back pain, which may be moderate to severe. Acute paralysis may occur following a pathological fracture, but signs of pain or discomfort, +/- mild neurological deficits usually precede it by a few days to weeks. Neoplasia of the spinal cord and other surrounding soft tissue structures may cause acute paralysis due to hemorrhage, but this is very unusual. Question the owner as to the presence of systemic signs such as weight loss, inappetence, etc., which are suggestive of a metastatic disease to the spinal canal.

Clinical Signs/Physical Examination

- In trauma, assess airway, breathing, and circulation. Perform lifesaving procedures (*see Triage p. 4*).
- Palpate the spine, from skull to tail, for incongruity and pain. There may be more than one vertebral injury. Injury resulting in lower motor neuron signs in the hind limbs will mask a lesion producing upper motor neuron signs. Therefore, a complete examination of the vertebral column should be performed and not halted when a lesion is found.
- Gait evaluation and postural reactions are not advised in spinal injuries as this may displace the fracture more. However, the spinal reflexes and pain perception should be assessed. If spinal trauma is noted, confirm by diagnostic imaging.
- A complete physical examination should be performed to assess other injuries. Severe soft tissue injuries and limb fractures will influence the results of the neurological examination.

  The **Schiff-Sherrington posture** is observed with acute and severe spinal cord lesions caudal to T2. In the laterally recumbent animal, one can observe hyperextension of the front limbs and neck associated with a marked hypotonia of the hind limbs even though the hind limb reflexes are of the upper motor neuron type. The syndrome results from destruction of neurons within the thoracolumbar spine that act as tonic inhibitors of the extensor muscles of the cervical intumescence. The front limbs are normal since the lesion is below the cervical intumescence. The Schiff-sherrington posture, although indicative of a severe lesion, should not be used as a prognostic indicator because animals can regain function.

- Animals with hind limb paralysis should be evaluated for presence of pain perception. The prognosis for return to function is poor when pain perception has been absent for more than 24 hours. The presence of pain should be evaluated in the hind limbs, then in the tail. The withdrawal of the limb upon toe pinching must not be mistaken for a nociceptive response; the animal that can feel its toes looks at them or cries out in pain when the toes are pinched. Evaluation for pain perception should be performed in a quiet environment where the animal is not distracted by its surroundings. In the patient with severe spinal cord lesion, toe pinching may not be perceived as a painful stimulus but more so as a tingling sensation. Starting caudally, the anesthesia level is evaluated along the vertebral column. The lesion is situated one to four vertebrae above the level of anesthesia. The dermatome corresponding to the thoracolumbar region is vis-à-vis the fourth lumbar vertebra in the dog.
- Fibro-cartilaginous embolic myelopathy (FCEM) is characterized by an acute onset of neurological deficits affecting the limbs. It is differentiated from intervertebral disc disease by the marked asymmetry of the neurological deficits, the lack of back or neck pain, and the non- progressive nature of the clinical signs after the first 6 – 12 hours. Rarely, the asymmetry may be subtle. Occasionally, dogs with FCEM may show signs of discomfort on back palpation. In some cases, FCEM occurs simultaneously with intervertebral disc extrusion. FCEM rarely occur in cats. It must not be mistaken for the ischemic neuromyopathy secondary to feline cardiomyopathy-related thromboembolism. In the ischemic neuromyopathy syndrome, the vascular event although it may affect the spinal cord, takes place outside of the vertebral canal.
- Acute bilateral cruciate rupture may be mistaken for spinal injury or IVDD. The gait is crouched in the hind limbs, and the patellar reflexes may be absent or diminished due to the lack of tension in the patellar tendons following the ligamentous rupture. The diagnosis is made based on the inability to raise tension in the patellar tendons, and pain experienced by the dog upon manipulation of the stifles.
- Peracute disc extrusion can present with similar neurological deficits as external spinal injury. A complete neurological examination should be performed. Although hind limb paralysis is common with thoracolumbar disc extrusion, back pain alone without neurological deficits is also a common presentation. With cervical disc extrusion, pain alone is the most frequent presentation. It may be associated with front limb lameness if the disc extrusion occurs between C4 and T1. With disc extrusion, tetraparesis/plegia (cervical) or paraplegia (thoracolumbar) may be present with or without pain perception. Occasionally, with cervical lesions, the ventilatory pathways are affected and the animal develops respiratory distress.
- Vertebral neoplasia are painful. Where there is no history of trauma, but sudden onset paralysis in a geriatric animal, neoplasia in addition to disc herniation, should be considered.
- Neurogenic shock, due to spinal cord transection, involves loss of peripheral vasomotor control (loss of venous tone) caudal to the injury, resulting in increased venous capacitance and possible distributive shock. On examination, the hind limbs are warmer (increased blood volume) than the front limbs. The front limbs may be cold due to vasoconstriction secondary to hypovolemia (increased capacitance and pooling of blood in the hind limbs) and distributive shock (hind limbs).

Laboratory Evaluation/Diagnostic Imaging

Stat

- If confirmed road injury or any other trauma where blood loss may have occurred (*see Triage p. 4, Hemorrhage p. 619*) secure IV access and obtain blood for:
    1. **PCV** and **TS** to ascertain whether blood loss has occurred.
    2. **Stick BUN** to ensure normal renal function is present.
    3. **ECG** to rule out abnormal rhythm. Arrhythmias may occur in spinal injuries due to catecholamine release.
    4. **Blood pressure** to assess volume status and monitor fluid therapy. Measure on both front and hind limbs if neurogenic shock may be present. Pressures obtained on front limb would reflect effective pressures.

Radiograph(s) of vertebral column whether internal (intervertebral disc herniation) or external (trauma) injury.

1) Trauma:

Survey radiographs of the spine are taken without anesthesia so the animal protects the luxation/fracture site. If anesthetized, the animal should be moved carefully as to not cause/worsen vertebral displacement. A complete vertebral column study should be performed (cervical, thoracic, lumbar and sacral) with attention to alignment of vertebrae especially at the junctions between mobile and immobile vertebrae, intervertebral spaces, spondyles and articular facets for possible luxation and fracture/compression. Even if alignment appears normal on the lateral views, lateral displacement may still be present on the dorso-ventral (D-V) view. Great care should be maintained while positioning the animal for the D-V views, especially if the animal is showing discomfort or pain. In cases of road injuries, it is preferable to move the radiographic beam instead of moving the patient, if at all possible. Radiographic examination may not

always disclose a severe lesion; even if the fracture or luxation are in alignment, complete transection of the cord could still have occurred. Be aware that if there is collapse (contrary to narrowing) of an intervertebral disc space, vertebral luxation has likely occurred and instability is present.

Radiographic evaluation of other areas (assessed by physical examination) may be necessary in the trauma case.

2) Intervertebral disc herniation:

(As above or under anesthesia) survey radiographs show narrowing of the space between articular facets, intervertebral foramen and narrowing but not collapse of the intervertebral space, as the annulous remains in place.

Extended Laboratory/Imaging Data Base

3) In vertebral fractures, CT is preferable to myelography. Myelographic studies may be beneficial but remain controversial in trauma cases. The contrast agent often is not successfully 'pushed' beyond the lesion with lumbar injection and builds up cranially with cervical injection, while in both cases increasing the spinal canal pressure leading to more damage.

4) Should neoplasia be identified, two lateral and one D-V chest views should be performed to rule out metastatic disease.

- Further tests will depend on concurrent injuries or illness and abnormal findings on stat tests. It is advised to perform the following:

- **CBC** to identify any abnormalities and serve as baseline.
- **Biochemical profile** to assess multi-organ function especially in older animals.
- **Coagulation tests. PT/PTT or ACT** if non-steroidal anti-inflammatory analgesics have been administered or other coagulopathic condition may exist prior to surgical decompression.
- **Urinalysis** to assess renal status.
- **Cytology** of cerebrospinal fluid if a lesion other than IVDD or external trauma is suspected.

MANAGEMENT

A. Airway/breathing/circulation/open wounds (*see Triage p. 4*) prior to focusing on the spinal injury.

B. Obtain IV access and establish balanced electrolyte infusion at a rate appropriate for injuries and potential blood loss if a trauma case (*see Hemorrhage p. 619*). Assess hydration status prior to commencing therapy if a non-trauma case. Administer appropriate fluid volume if dehydrated (*see Fluid Therapy p. 351*).

C. Corticosteroid therapy, **dexamethasone sodium phosphate at 0.25 mg/kg IV** should be administered as soon as possible if **spinal injury** is confirmed on radiographic examination, and is associated with minimal to severe neurological deficits, with or without pain perception, even if euthanasia is considered by the owners. Occasionally, owners cannot decide which therapeutic modality to pursue and in these cases medical management of the animal should be initiated regardless.

1. For the patient that exhibits even minimal **purposeful movements, and is treated surgically,** no further corticosteroids are administered.
2. In patients with **more profound neurological deficits or patients treated medically, continue with dexamathasone 0.25 mg/kg PO q24h for 72 hours and then 0.1 mg/kg PO q24h for up to two weeks if there is no improvement in neurological function.**

Previous recommendations for high dose methylprednisolone sodium succinate have since proven to be associated with increased morbidity without improvement in the neurological outcome. Therefore, we do not recommend this therapy.

D. Gastroprotectants.

1. Famotidine 0.5 mg/kg, PO or SC q12h dogs /cats OR
2. Omeprazole: approximately 1 mg/kg PO q24h in dogs (20 mg/dog if >20 kg, 10 mg if 5 – 20 kg and 5 mg if <5 mg). Cats: 0.7 mg/kg PO q24h (*see Pharmacology*).
3. **Omeprazole or famotidine** should be given as ulcer prevention because spinal injury ±corticosteroid administration may result in gastrointestinal ulcers.
4. **Sucralfate Suspension 1 g/10 mL** – suspension preferred over tablets. Administer on an empty stomach 2 hours apart from other medication to avoid interference with absorption (*see Pharmacology*).

   a) **Dogs: 0.5 – 1 g q8h. Loading dose of 3 – 6 g suspension** if severe concurrent gastrointestinal ulcer noted (i.e., vomiting or melena present).
   b) **Cats: 0.25 – 0.5 g q8h.**

E. Indications for surgery in external spinal trauma:

Two factors come into play:

1. Stability of the fracture/luxation site
2. Neurological status

   a) If there is instability, stabilization should be performed regardless of the neurological status if the owners wish to pursue surgical treatment. However, total reduction is rarely achieved adding an uncertainty to the prognosis especially with lesions above L4 where the ratio of vertebral canal/spinal cord becomes increasingly smaller.
   b) Fractures/luxations at L5 – 6, L6 – 7 or L – S carry a better prognosis because the ratio is larger allowing more room for hemorrhage and edema to take place. Roots are also physiologically more resilient than the spinal cord itself.
   c) The lumbar intumescence is situated within the vertebrae L4 – 5 in the dog, and L5 – 6 in the cat. Trauma at this level results in lower motor neuron signs from damage to the gray matter of the intumescence. Lower motor neuron lesions carry a more guarded prognosis because return to function is more problematic due to damage to cell bodies. Also, areflexia and atonia of the limbs and sphincters are more difficult to cope with.
   d) Anesthesia of the hind limbs always carries a guarded-to-poor prognosis in trauma cases, as it is likely that vertebral displacement was worse at the time of impact than what is observed on radiographs. If the vertebral canal is aligned, the outcome is not as poor but it is guarded, similar to that of an animal experiencing disc extrusion with the additional uncertainty of instability where total reduction is not possible.
   e) If there is vertebral displacement but good neurological status, stabilization of the spinal column and/or decompression of the cord, or exploratory laminectomy and durotomy, is recommended.
   f) The presence of pain perception offers a better prognosis than those with absence of pain perception (*see Suggested Reading*).

F. Indications for surgery in internal (disc extrusion) trauma: (IVDD)

1. **Surgical correction** should be performed as soon as possible with disc herniation with paralysis. Even with absence of pain perception, if the owner's decision is to pursue treatment, surgical management is the ideal approach. No pain perception carries a poor prognosis for recovery, but is not a reason to not perform surgery. The extruded disc material often plays the role of a space-occupying lesion. Decompressive surgery, in the hands of an experienced surgeon, is an insurance of a better outcome.
2. Since it has been demonstrated that spinal cord compression was present in most patients presenting with IVDD and back pain alone, and without neurological deficits, it is our opinion that these animals have a better neurological outcome with early decompressive surgery. However, there are divergences of opinions as to when surgery should be performed in this setting.
3. **Dexamethasone 0.25 mg/kg once followed by 0.1 mg/kg daily for up to two weeks** is recommended for patients where surgery is not performed because of presence of other illness, first episode of back pain, or at the owner's request.

G. **General nursing care** is important in recumbent patients. A urinary catheter should be placed to ensure bladder decompression, and avoid soiling and urine scalding of the skin. Bladder expression in patients with spastic urinary retention is not recommended so as to avoid detrusor stretch. The urinary catheter is left in place until purposeful movements have returned or for two weeks until hyperreflexia is fully established. In lower motor neuron sphincter dysfunction, urinary bladder catheterization is also advocated as urinary retention also results in detrusor stretch. This leads to permanent damage of the detrusor muscle tight junctions causing repetitive or chronic urinary tract infections.

H. **Frequent neurological assessments** should be performed to monitor progress especially if there are no purposeful movement, indicating that there is likely **urinary incontinence.** Fecal incontinence is usually not a problem. Constipation does not result. Down dogs or cats defecate less frequently due to lack of exercise. Frequency may be reduced to every other day. Soiling of the animal's tail, hair or skin must be prevented. Physiotherapy, turning the patient over and providing a well-padded bed are essential.

PHARMACOLOGY

1) **Dexamethasone** is a glucocorticoid used in spinal injury to reduce cord swelling and inflammation.

2) **Famotidine (Pepcid®):** H2 receptor antagonist, will help decrease the acidity within the stomach thus preventing acid reflux from further damaging the esophagus. Recent work at the Ontario Veterinary College indicates that ranitidine may not be effective in raising gastric pH, therefore, famotidine is recommended.

2) **Omeprazole (Losec®)** is proton pump inhibitor, which acts to decrease gastric acid secretion. Omeprazole is superior to the H2-receptor antagonists in the blockade of acid production.

3) **Sucralfate (Sulcrate®)** is an aluminum complex of sucrose sulfate that in an acidic environment binds to the injured mucosal surface acting as a barrier against ongoing acidic injury. Sucralfate is also considered a cytoprotective agent. Note: If interferes with dosing of more important medications such as antibiotics or glucocorticoids, rely on proton pump inhibitors or H2 blocking agents.

SUGGESTED READING

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NOTES

INTRODUCTION

Stupor or semi-coma is a state of partial or nearly complete unconsciousness from which the patient can be aroused but only by vigorous stimulation. **Coma** is a state of unconsciousness from which the patient cannot be aroused. **Consciousness** is an ill-defined term that implies the integration of two functions, *arousal* and *cognition*. Arousal is primarily a brain stem function. Cognition is a cerebral cortex function. The **ascending reticular activation system** (ARAS) is the neuroanatomic structure which awakens the brain to consciousness and prepares the cortex to receive ascending impulses from any sensory modality. It is responsible for maintaining wakefulness. The **ARAS** is part of the reticular formation which consists of a network of neurons in the central portion or core of the brain stem which includes the medulla, the pons, midbrain, and the diencephalon terminating at the lamina terminalis. Externally the optic chiasm is directly ventral to the lamina terminalis. When the brain stem is functional, coma may still be caused by a loss of the cognitive component of consciousness when the function of the cerebral cortex becomes totally or near-totally impaired. The degree of alteration in consciousness depends on the extent of injury and speed with which it progresses. Global cortical dysfunction can also cause other disturbances such as confusion, delirium, dullness (obtunded), excess sleepiness (in association with brainstem dysfunction), abnormal behavior (e.g., compulsive activity, abnormal vocalization), which are usually accompanied by spontaneous motor activity. These states may occur prior to stupor or coma where increasing intra-cranial pressure may be present (e.g., hydrocephalus and any rapidly expanding space-occupying lesions).

Conditions that lead to stupor or coma can be generally classified as follows:
- widespread damage in both hemispheres from ischemia, trauma, or other less common brain diseases.
- suppression of cerebral function by extrinsic drugs, hypoxia or by internal metabolic derangements such as hypoglycemia, azotemia, hepatic failure, hypercalcemia or other electrolyte imbalances.
- brainstem lesions that cause damage to the ARAS .

To differentiate intracranial coma/stupor from extracranial causes, a neurologic examination is essential to localize the lesion to specific neuroanatomical structures of the central nervous system (i.e., thalamo-cortex, brainstem). When there are no localizing signs, both intracranial and extracranial problems must be considered.

Specific Causes of Coma/Stupor

INTRACRANIAL
- Space-occupying lesions
  - neoplasm
  - hemorrhage
  - abscess
- Trauma
  - concussion
  - hematoma
  - contusion
  - cerebral edema,
  - iatrogenic pithing during cerebrospinal fluid collection (CSF tap).
- Hydrocephalus
- Primary hemorrhagic or ischemic infarction
  - feline cerebral infarction syndrome or feline ischemic encephalopathy
  - atherosclerosis
  - hypertension (*see p. 205*)
  - coagulation disorders (*see p. 40/451*)
- Hypertensive encephalopathy (*see p. 205*)
- Infections (e.g., severe meningoencephalitis of bacterial, mycotic, protozoan, viral, parasitic, rickettsial)
- Generalized non-infectious meningoencephalities (GME)
  - fulminating reticulosis or steroid-responsive GME, Pug encephalitis, Maltese Terrier necrotizing encephalitis, Cairn Terrier neuronal chromatolysis, Duck Tolling Retriever meningoencephalitis.
- Thiamine deficiency.
- Post-convulsive (post-ictal) state (*see Seizures in dogs p. 460 and Seizures in cats p. 456*).
- Storage diseases (terminal stage of storage disease).

EXTRACRANIAL
- Hypoxia from decreased cerebral blood flow (CBF)
    - postcardiac arrest (*see p. 139*)
    - cardiogenic shock (*see p. 149*)
    - hypovolemic shock (*see hemorrhage p. 619, non-hemorrhage p. 351*)
    - septic shock (*see p. 588/631*)
- Hypoxia with intact CBF
    - severe pulmonary disease (*see p. 567*)
    - anemia
- Carbon dioxide narcosis
- Hypoglycemia (*see p. 280*)
    - insulinoma
    - hepatic disease
    - puppy hypoglycemia
- Diabetic ketoacidosis (*see p. 263*)
- Hepatic encephalopathy (hyperammonemia) (*see p. 40*).
- Severe renal failure (uremic encephalopathy) (*see p. 709*)
- Body temperature abnormalities
    - hypothermia (*see p. 291*)
    - hyperthermia (heat stroke, malignant hyperthermia) (*see p. 297*).
- Exogenous toxins (*see p. 641*)
    - Methanol, salicylates, heavy metals, carbon monoxide, monesin
    - ethylene glycol (*see p. 655*)
    - ivermectin, ethyl alcohol, halucinogenics
    - barbiturates, opioids, anticonvulsants, sedatives (*see p. 81*)
- Hypercalcemia/hypocalcemia (*see p. 373/377*)
- Hyperosmolar states (hyperglycemia (*see p. 279*), hypernatremia (*see p. 381*), diabetes insipidus, severe water loss).
- Water intoxication (*Hyponatremia p. 381*)
- Endocrine disorders
    - hypoadrenocorticism (*see p. 274*)
    - hyperadrenocorticism (*see p. 270*)
    - pheochromocytoma (*see p. 205*
- Electrolyte disorders (*Hypo/Hypernatremia p. 381*)

DIAGNOSIS

History & Signalment
- If the animal is not constantly supervised and is allowed to run free, trauma and poisoning are potential causes. How long has the animal been missing?
- A traumatic incident, such as falling down the stairs, may be assumed to be the cause but on questioning the owner regarding behaviour prior to the event may suggest the animal was already neurologically impaired and this may have precipitated the fall. Brain tumours for example, can be extremely insidious in their progression when suddenly the animal decompensates into a stupor or coma. Only on close questioning may an owner admit that the animal has had a subtle change in behaviour that was just interpreted as 'getting old'.
- Animals with a history of seizures may be found comatose because they have structural disease that has progressed; uncontrolled status epilepticus can result in anoxic brain damage.
- A previous history of systemic illness or wounds, could be indicators of a source of infection that has progressed to the CNS.
- Animals presenting in an Addisonian crisis or with hepatic encephalopathy may have a history of episodic depression, weakness and GI upset and hemorrhage. Constipation may precipitate hepatic encephalopathic coma in a patient with liver failure.
- Question the owner regarding **medication,** especially methionine where hepatic function may be questionable. Non-steroidal anti-inflammatory analgesics may precipitate gastric hemorrhage which may induce encephalopathy should liver function be marginal. Ivermectin, in any animal if overdosed, Old English sheepdogs may be susceptible and any collie breed with recommended single dosing will cause a neurotoxicosis.

Clinical Signs/Physical Examination

General Considerations

- Any patient presented in a comatose or stuporous condition should be quickly examined for important systemic signs that may be primary, or contributing to its diminished state of consciousness (e.g., shock, anemia, dehydration, cardiovascular/pulmonary dysfunction, extreme body temperature, icterus, evidence of trauma).
- With head trauma, there usually is evidence of injury such as unilateral episcleral hemorrhage, epistaxis or blood in the ear canal; however, occasionally there may be no evidence to suggest concussive brain injury. For confirmed cases of head trauma, *see Head Trauma p. 700*, for emergency measures and neurologic evaluation.
- Life-threatening situations must be addressed before progressing to the detailed examination for the level of consciousness. Fluids and oxygen, if indicated, may dramatically improve the neurologic status.
- Petechia may indicate a hemorrhagic disorder that may also involve the brain.
- Although fever associated with coma may indicate infectious etiologies, it can also be caused by drug toxicities or lesions of the hypothalamus itself (*see Fever of Unknown Origin p. 422*).
- Previous medical history and accurate description of the duration and speed of onset of the coma/stupor may provide an obvious clue to diagnosis (e.g., diabetes mellitus – ketoacidosis versus hypoglycemia).
- Animals missing for a period of time and found in a coma or stuporous state are a diagnostic challenge; trauma, poisoning or sudden neurologic deterioration from a space-occupying intracranial lesion are important differential diagnoses.
- In cats feline cerebral infarction syndrome, hypertensive encephalopathy from undiagnosed hyperthyroidism (*p. 288*), and trauma should be considered in addition to previously mentioned causes.
- Conduct an ophthalmic examination to assess the retina. Hypertension and inflammatory conditions also affect the retina.

Neurologic Examination

If external trauma is unlikely, the neurologic examination may aid in more accurately defining the problem.

- **The depth of stupor/coma** in an animal should be progressively assessed by trying to arouse the patient by calling it's name, light touch (especially around the head and inside the nostrils), and then finally with forceps applied to the digits with increasing pressure. If the animal is in a true coma, it cannot be aroused in any way; however, most comatose animals will have flexor and patellar reflexes preserved. Deep barbiturate overdose could eliminate spinal reflexes. Coma caused by intracranial lesions rarely cause loss of spinal reflexes. Severe meningoencephalomyelitis could suppress spinal reflexes but usually only partially and asymmetrically. Rarely, reflexes may be suppressed due to a pre-existing paraneoplastic peripheral neuropathy in conjunction with the neoplastic process also being present in the brain which is causing stupor or coma. An increase in intracranial pressure caused by any of the discussed etiologies may progress to tentorial herniation with brainstem signs.
- **Cranial nerve examination, postural changes and respiratory patterns** can help distinguish structural lesions from that of global encephalopathy of metabolic or toxic origin. **Rarely,** metabolic problems may cause asymmetry (the author has seen severe hyponatremia cause an asymmetric lesion). Structural lesions tend to cause asymmetrical deficits and often, focal cranial nerve deficits. The neurologic assessment described under Head Trauma (*p. 700*) is applicable for other types of structural lesion affecting the brain.
- **Asymmetric pupils,** abnormal pupillary light reflexes, abnormal nystagmus, lack of nystagmus, asymmetric strabismus are important signs of focal midbrain and/or medullary lesions and may be contributing to the stupor/coma.
- **Decerebrate rigidity** often occurs with severe midbrain lesions (the head and neck are extended in a posture of opisthotonos, and all four limbs are rigidly extended). Acute lesions of the cerebellum without damage to the brainstem, cause a posture termed "decerebellate rigidity" with presence of opisthotonus with extension of the forelimbs and flexion posture of the pelvic limbs.
- **If the animal is aroused in response to noxious stimuli,** lift and hold it in a standing position; this may reveal a body turn resulting from an asymmetric vestibular lesion or thalamocortical lesion (adversive syndrome).
- **Respiratory pattern**
  - **Ataxic breathing** (irregular in rhythm and depth) is associated with medullary lesions just prior to death.
  - **Cheyne-Stokes respirations,** a periodic hyperpnea that regularly alternates with apnea, can occur with structural, or global lesions of the cerebral hemispheres, e.g., hypoxia and metabolic disease.

- **Apneustic respiration** (gasp breathing) usually indicates a pontine lesion but can be seen with hypoglycemia, anoxia, or meningitis.
- **Bradypnea** is usual with overdoses of CNS depressant drugs; it is also seen with uremia, diabetic coma and increased intracranial pressure.
- **Hyperventilation** is common with midbrain lesions, hypoxia, metabolic acidosis and fever.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **Blood glucose** must be checked immediately to rule out hyper-, hypoglycemia (*p. 280*).
- **Urine** assessed for glucosuria and ketonuria to rule out diabetic ketoacidosis. Urine specific gravity to assess concentration ability (e.g., hyposthenuria, isosthenuria, ability to concentrate).
- **Blood gases.** Venous to assess perfusion and metabolic status (i.e., alkalosis will worsen hepatic encephalopathy). If hypoxia suspected, perform arterial or pulse oximetry to asses oxygenation.
- **PCV, TS** to rule out anemia or polycythemia (hyperviscosity syndrome).
- **BUN, urea or creatinine.** Evaluate renal function (uremic encephalopathy).
- **Serum electrolytes,** especially sodium to rule out hyper-, hyponatremia (*see p. 386*) as a cause. Potassium, chloride and calcium should also be measured as these may be abnormal secondary to the patient's general condition or as a primary problem.
- **Platelet count** to identify thrombocytopenia as cause of potential cerebral hemorrhage monitoring.
- **ACT** for rapid assessment of coagulation status (normal cat 60 – 90 secs, dog 75 – 125 secs).
- **ECG.** Cardiac arrhythmias may cause stupor/coma, or may occur secondary to brain disease (see section on specific rhythm obtained).
- **Systemic blood pressure** to assess if hypotensive or hypertensive crisis (*see Hypertension p. 205*).
- **Blood NH_3** where hepatic encephalopathy is considered (*see Hepatic Failure p. 37*).
- Save blood, urine and stomach contents for **toxicological investigation** if indicated (*see Toxicological Emergencies p. 636*).
- Consider an immediate CSF **tap** if an inflammatory, neoplastic, or infectious condition is likely, except if increased cranial pressure, coagulopathy, or trauma is suspected, or the patient is systemically unfit for anesthesia. A spinal tap maybe performed in a fully comatose patient with minimum anesthesia and analgesia (*see Chemical Restraint p. 107*). **Analysis:** cytological examination, culture if indicated, immunoglobulin levels and titres for specific infections

Extended Data Base

- **CBC** to confirm stat blood work and identify leukocytosis associated with an inflammatory process, or nucleated red cells and basophilic stipling associated with lead poisoning.
- **Serum biochemical profile** to assess organ function and potential metabolic causes.
- **Urinalysis.** WBCs, casts, crystalluria (ammonium biurate – hepatic failure, calcium oxalate or hippurate – ethylene glycol toxicosis).
- **Thyroid panel** where myxedema (hypothyroid coma) is suspected (*see p. 285*).
- **Plasma osmolarity** may be useful should hyperviscosity (e.g., myeloma) be considered.
- **MRI** where space-occupying lesion or hemorrhage is suspected. Must be stable for anesthesia, or comatose.
- **CT** to determine the presence and severity of skull fractures or presence of foreign objects. Must be stable for anesthesia, or comatose.
- **Bile acids** to confirm hepatic disease (*see Hepatic Failure p. 37*).

A. Regardless of the cause, for sudden onset of stupor/coma, it is imperative that further damage to the brain be prevented. Hypovolemia, hypotension, hypertension, hypoglycemia, hypoxia, hypercapnia, hyperthermia, electrolyte disorders and hyperosmolar states must be recognized and corrected (refer to the appropriate chapter).

B. If a primary brain lesion is suspected and there is evidence of increased intra-cranial pressure as described above, follow the treatment protocol as described in *Head Trauma* (*p. 691*) to maintain adequate cerebral perfusion pressure (CPP).

C. **Antibiotics** if bacterial meningoencephalitis is suspected or confirmed (cats & dogs)
1. **trimethoprim sulfonamide 15 – 20 mg/kg IV, PO q8–12h AND**
2. **metronidazole 10 mg/kg IV as a CRI over one hour q8h OR 10 – 15 mg/kg PO q8h OR**
3. **clindamycin 10 mg/kg IV, PO q12h.**

D. **Glucocorticosteroids** if idiopathic inflammatory
1. **dexamethasone 0.25 mg/kg IV q24h for 3 – 4 days** followed by
2. **prednisone 1 mg/kg IV, PO q24h.**

E. Cats should be given thiamine routinely as supportive treatment and on the slight chance that the condition is thiamine responsive.

F. Cats with feline cerebral infarction syndrome often need sedation or anti-convulsant therapy (*see Seizures Cats p. 456*) and supportive treatment only as they arouse; steroids are contraindicated with ischemic stroke. However, corticosteroids (0.25 mg/kg dexamethasone) might be helpful in the acute presentation of neurological signs but are not necessarily beneficial after 48 hours from the onset of clinical signs. If a hemorrhagic vascular accident is suspected, treatment for increased cranial pressure may be needed (*see Head Trauma p. 691*).

G. For specific toxicities, hepatic and renal disease, please see specific chapters.

SUGGESTED READING

1. Kline KL. Altered States of Consciousness: Stupor and Coma. In Textbook of Veterinary Internal Medicine. Ettinger, EJ, Feldman EC (eds), St. Louis, MO. Elsevier Saunders. 2005:161-163.
2. Rosen P (ed). Emergency Medicine. Concepts and clinical Practice, 4th edition. St. Louis, Mosby. 1998.

NOTES

INTRODUCTION

Syncope is a sudden, transient loss of consciousness, caused by a decrease in cerebral blood flow and hypoxemia or hypoglycemia. The metabolism of the brain is dependent upon the perfusion of oxygen. The storage of high-energy phosphates in the brain is limited, and energy supply depends on the oxidation of glucose extracted from blood. Loss of consciousness may result if cessation of blood flow occurs for as little as 10 seconds. A syncopal event is transient, and complete recovery tends to occur within seconds to minutes. However, sudden death is possible if the cause of syncope is not addressed and treated appropriately. Syncope should be considered a clinical sign rather than a primary disease. The causes of syncope are summarized in Fig. 1.

It is of utmost importance that the clinician differentiates syncope from seizure activity, narcolepsy and catalepsy. Episodic weakness, myasthenia gravis, acute hemorrhage, including cerebral arterial thromboembolism and diseases associated with decreased alertness, must also be distinguished from syncope.

Syncope often develops with generalized muscle weakness, progressing rapidly to ataxia, which may be followed by collapse and loss of consciousness. Initially, the patient is motionless with relaxed skeletal muscles, but rapid progression to uncoordinated muscular activity or jerking motions may occur, thereby giving the impression of seizure activity. Involuntary urination and/or defecation may occur due to loss of control of muscle sphincters. Some animals may cry out during the episode, and this may be misinterpreted as pain or fear. Recovery is usually rapid, although the owner often notes that the episode is followed by a brief period of confusion.

Many of the conditions that lead to hypoxia, hypoglycemia and generalized muscle weakness also cause syncope if cerebral function is impaired, therefore a thorough history and complete physical examination will help differentiate weakness from syncope. While weakness is characterized by chronic or episodic muscle fatigue, recovery between episodes is often slow and incomplete. In addition, weakness is not accompanied by a loss of consciousness.

Laboratory Evaluation/Diagnostic Imaging

A minimum database, includes the tests below. History and physical examination findings, together with these test results, will often help categorize the underlying cause of the syncope listed in Fig. 1. Refer to the appropriate chapters in this manual or those in Suggested Reading for further laboratory tests to confirm the diagnosis and definitive treatment. However, stat tests should be performed to rule out an emergent illness.

Stat
- PCV and TS to rule out anemia/hemorrhage (*p. 639*).
- Blood glucose, as hypoglycemia (*p. 280*) may be a cause and may be life-threatning.
- Systemic blood pressure, as hypotension or severe hypertension (*p. 205*) may be present.
- Complete blood count
- Serum biochemical profile
- Serum electrolytes
- Urinalysis
- Electrocardiogram
- Blood gas analysis

Further diagnostic evaluation includes thoracic radiographs, an echocardiogram, and Holter monitor, or cardiac event recorder. *Videotaping the event may also help differentiate a syncopal episode from seizure activity.*

The clinician may attempt to unmask arrhythmias by physical and/or chemical stimulation of the autonomic nervous system. Direct digital carotid sinus massage or digital pressure on the eye for one to two minutes may increase vagal tone and induce bradyarrhythmias or heart block. However, these latter techniques have not been found to be very reliable in animals. **Atropine 0.04 mg/kg IV** may be used to confirm heart block. The only contraindication to its use is that of a pre-existent tachycardia.

MANAGEMENT

The management and monitoring of patients with syncope are directed at the primary cause, and the reader is referred to the specific chapters in this text.

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                      ┌──────────────────────────────┐
                      │  Decreased Cerebral Perfusion │────────────────
                      └──────────────────────────────┘
                                    │
                ┌───────────────────┴────────────────────┐
    ┌───────────────────────┐              ┌───────────────────────┐
    │ Peripheral or neurogenic│            │   Cardiac Dysfunction  │
    │    dysfunction (heart   │            │    (heart usually      │
    │    structurally normal) │            │       abnormal)        │
    └───────────────────────┘              └───────────────────────┘
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Peripheral or neurogenic dysfunction (heart structurally normal)

1. **Vasovagal** appears to be associated with a sudden incident of either fright or extreme excitement. The animal often becomes immobile for a period of time leading up to the incident. Their respiration usually increases, both in rate and depth, and the pet may appear weak, dazed and confused. Mydriasis occurs just prior to the loss of consciousness. Hemodynamically, there is peripheral arterial vasodilation and venoconstriction. The cardiac output fails to rise despite a decrease in peripheral resistance and venoconstriction. Vagal overactivity results in bradycardia.

2. **Postural hypotension.** Normal animals develop a slight fall in systolic blood pressure and a rise in diastolic pressure with only a slight increase in the heart rate upon rising. In contrast, those with postural hypotension develop a fall in both systolic and diastolic pressure with variable changes in the heart rate. Postural hypotension can be a complication of a number of disease entities, including
   – Diabetes mellitus
   – Hypoadrenocorticism
   – Severe intravascular volume depletion due to disease or intensive diuresis.

3. **Hyperventilation** is usually associated with anxious or hyperexcitable pets. Hyperventilation causes an overaeration of the alveoli and a subsequent decrease in alveolar and arterial PCO_2 concentrations. Low PCO_2 concentrations produce progressive cerebral arterial vasoconstriction along with peripheral vasodilation. With stable or decreased perfusion pressure, a progressive decrease in oxygen delivery to the brain occurs.

4. **Carotid sinus sensitivity.** The underlying reflex occurs as afferent impulses from the carotid sinuses are transmitted via the glossopharyngeal nerve to the vasomotor and cardioinhibitory centers in the medulla. Vagal stimulation in turn causes bradycardia, which in turn causes decreased cardiac output and cerebral blood flow. Cerebral anoxia may result. Examples include:
   – Tight collars
   – Neoplasia of/affecting any component involved in the reflex
   – Inflammatory processes

5. **Glossopharyngeal neuralgia.** Pain in the ear, soft palate or pharynx is transmitted centrally via the glossopharyngeal and vagal nerves and may also give rise to reflex hypotension and syncope.

6. **Micturition or defecation syncope.** Reflex-mediated syncope that occurs at the time of, or immediately following, micturition or defecation.

7. **Cerebrovascular accident.**

8. **Brain tumour.**

9. **Encephalitis.**

Cardiac Dysfunction (heart usually abnormal)

1. **Obstruction to bloodflow**
   – Aortic and pulmonary stenosis
   – Atrial tumours
   – Cardiac tamponade (secondary to pericardial effusion)
   – Dirofilariasis (severe)

2. **Rhythm disturbances**
   – Heart block
   – Bradyarrhythmias
   – Tachyarrhythmias
   – Sick sinus syndrome

3. **Cardiopulmonary dysfunction**
   – Low stroke volume
     • Systolic dysfunction (dilated cardiomyopathy)
     • Diastolic dysfunction (hypertrophic cardiomyopathy)
   – Pulmonary hypertension
   – Pulmonary emboli
   – Congenital heart disease
     • Right to left shunts (patent ductus arteriosus)

4. **Myocardial infarction**

Metabolic Disturbances	Iatrogenic	Miscellaneous
1. anemia 2. polycythemia 3. hypoglycemia 4. hyperkalemia 5. hypokalemia 6. hypovolemia 7. pheochromocytoma 8. hepatic encephalopathy	1. alpha-adrenergic blocking agents 2. angiotensin-converting enzyme inhibitors 3. beta-blocking agents 4. calcium channel blocking agents 5. digoxin 6. diuretics 7. phenothiazine-related medications 8. vasodilators – nitroglycerine 9. anti-depressants	1. **Tussive syncope** (cough-drop syndrome). Coughing raises the intrathoracic pressure, as well as the cerebrospinal pressure. There is a decrease in cerebral blood flow when the cerebrospinal fluid pressure is greater than the intracranial capillary perfusion pressures. The brain becomes rapidly depleted of blood and oxygen, thereby resulting in syncope. 2. **Pulseless disease** occurs when there are major obstructions to one or more major blood vessels supplying the head. The syncopal attack is usually precipitated by activity. 3. **Swallowing.** Syncope associated with swallowing occurs with esophageal diverticula and other obstructive esophageal diseases. Various degrees of heart block develop upon initiation of the swallow reflex. The laryngeal nerves are sensitive to pressure, and these nerves are anatomically related to the carotid sinus. This disease is considered a form of carotid sinus syncope.

FIGURE 1. Syncope.

PHARMACOLOGY

1) **Atropine** is an anticholinergic drug, i.e. it has a parasympatholytic effect. It is used primarily to demonstrate that a bradycardia is of sinus origin or to identify concealed conduction. The response to atropine may also help to identify conduction irregularities.

SUGGESTED READING

1. Davidow EB, Proulx J, Woodfield JA. Syncope: Pathophysiology and Differential Diagnosis. Compendium 2001; 23(7):608-618.
2. Ettinger SJ. Weakness and Syncope. In Ettinger SJ, Feldman EC, (eds). Textbook of Veterinary Internal Medicine Volume I (5th ed). Philadelphia: WB Saunders, 2000:10-16.
3. Rush JE. Syncope and Episodic Weakness. In Fox PR, Sisson D, Moïse NS, (eds). Textbook of Canine and Feline Cardiology. Principles and Clinical Practice (2nd ed). Philadelphia: WB Saunders, 1999:446-454.

INTRODUCTION

"Tetanus" occurs following bacterial infection of wounds (puncture, surgery, lacerations, burns, frostbite, open fractures, abrasions) contaminated by Clostridium Tetani, an obligate, anaerobic, spore-forming, gram-positive rod. Tetanus is a condition that occurs sporadically in dogs but is very rare in cats. Cats are more resistant to infection than dogs.

The incubation period is the time from spore inoculation to the initial signs of tetanus. This period reflects the time needed for germination of the spores, proliferation of the bacteria, and the production of tetanospasmin. Tetanospasmin is a potent exotoxin produced by the germinating spores. The onset period – the time from the first symptom or sign to the first muscular spasm – reflects the progression of the neurological manifestations caused by the tetanospasmin. Released tetanospasmin spreads to underlying tissue and binds to the membranes of local nerve terminals. If the toxin load is high, some may enter the bloodstream from where it diffuses to bind nerve terminals throughout the body. The toxin is then internalized and transported intra-axonally and retrograde to the cell body. When spinal inhibitory interneurons are affected symptoms occur. The spastic effects on the muscles are due to prevention of the release of neurotransmitters, especially inhibitory neurotransmitters like glycine and gamma-aminobutyric acid (GABA). Uncontrolled disinhibited efferent discharge from motor neurons leads to intense muscular rigidity and spasm, which may mimic convulsions. Muscle spasms are intensely painful. Muscles of the jaw, face and head are often involved first because of their shorter axonal pathways. The trunk and limbs follow. The binding of tetanospasmin to presynaptic sites of inhibitory neurons is irreversible; recovery depends on sprouting of new axon terminals.

DIAGNOSIS

History/Signalment

- Tetanus has been reported in both dogs and cats.
- Historically, affected animals are reported by the owners to have relatively acute onset of generalized stiffness, lethargy, photosensitivity and difficulty opening the mouth. However, with careful questioning regarding predisposing incidents, the owner may recollect a 2 – 3 day history of change in normal behaviour. Shorter incubation and onset periods may indicate a poorer prognosis.
- Question the owner regarding contact with other animals and bite wounds.
- Question the owner regarding foreign body injuries (i.e., is the dog a stick chewer).
- Tetanus has been reported following ovariohysterectomy and parturition.

Clinical Signs/Physical Examination

- Tetanus is diagnosed by the 'classical' clinical signs.
- Careful handling of the patient is advised as they may become apprehensive during handling. The whole body is very reactive with abnormal twitching noted with tactile or auditory stimulation. Pain doesn't commonly elicit vocalization.
- Clinical signs occur at variable time (4 – 5 days up to 6 – 8 weeks) after exposure to a wound infected by *Clostridium tetani.*
- Based on the severity of the condition, affected dogs are presented with a multitude of clinical signs ranging from mild lameness and lethargy to an acute onset of extensor rigidity, opisthotonus, and lock jaw.
- Fractures of the limbs or spine may be present in animals experiencing violent tetanic muscle spasms.
- With severe, generalized forms of tetanus, the animal presents in lateral recumbency with head and neck retracted and increased extensor tone on all limbs (opisthotonus). The tail is often rigid. The respiratory rate is usually elevated and increased salivation is observed. The jaws are stiff and the mouth is difficult to open. Affected dogs have trouble eating and drinking; dysphagia is often present. Occasionally, the tongue is swollen with decreased mobility.
- Pupils can be miotic but still responsive.
- The neurological examination often reveals a quiet demeanor, with abnormal facial expression characterized by ears elevated and flattened against the skull, eyelid conformation slit-like, and "smiling" jaw appearance ("risus sardonicus").

- Third eyelids can be prolapsed and retract spasmodically.
- A localized form of tetanus is more common in cats than dogs and is characterized by increased stiffness of a muscle or entire limb in close proximity to the wound. This may progress to the generalized presentation described above.
- Bradycardia may be present with tetanus probably associated with vagal-parasympathetic hyperactivity and/or stimulation/activation of the cardiac inhibitory centre of the nucleus ambiguous. Conversely, tachycardia and hypertension may be present due to increased catecholamine release.
- Tachypnea or dyspnea may be noted if aspiration secondary to salivation or regurgitation occurs. Megaesophagus and hiatal hernia may be identified in these animals.
- Rectal temperature may range from normal to severe hyperthermia (> 42°C) depending on infection, muscle contraction/ spasm and convulsive seizure activity.
- Urine retention/inability to void can also be noted
- The clinical signs may progress to death as a result of rigidity of the respiratory muscles, reflex spasm of the larynx, increased airway secretions and central respiratory arrest.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV/TS** are normal unless dehydration is present resulting in increased values. If blood loss secondary to a wound or surgery occurred, anemia may be present.
- **Serum electrolytes** especially magnesium and calcium, as magnesium supplementation may be beneficial. Calcium concentrations must be normal prior to magnesium administration.
- **Arterial blood gases** in patients with respiratory compromise are necessary to determine if mechanical ventilation is required.
- **CBC** is often unremarkable, or a mild to moderate leukocytosis with neutrophilia and increased band cells can be noted. However, a marked leukocytosis may be present in response to an infected wound or aspiration pneumonia.
- **Biochemical profile** often reveals increased creatine phosphokinase as a result of muscle damage during later stages of the disease. Otherwise, no specific abnormalities are noted.
- **Urinalysis** is usually normal.

Extended Data Base
- **Serum antibody titres to tetanospasmin** for confirmation in equivocal situations.
- **Culture** of the wound for *C. tetani* is often unrewarding and strict anaerobic conditions must be employed. Culture usually takes 2 weeks.
- **Gram stain** of the wound may demonstrate gram-positive rods and dark-staining endospores, however, this finding is similar to many anaerobic bacteria and is not specific for *C. tetani*.

Treatment

Due to the varying degree of severity of illness, the clinician must determine the therapeutic options required for the individual patient. Severely compromised patients with extensive wounds carry a poor prognosis. Treatment for these animals is very expensive.

A. **Airway access** via endotracheal intubation may be required if laryngospasm is present. **Oxygen** by flow-by for respiratory compromised patients is necessary.

B. **IV** access and administration of a balanced electrolyte solution at a rate dependent on the condition of the animal (*see Fluid Therapy p. 347*).

C. **Wound management** (*p. 702*) with wide debridement is necessary to reduce the bacterial and spore load. Frequently wounds are on the extremities. Where a grossly infected, large wound is present, amputation may be the best option to save the animal's life. Mildly affected animals recover from neurological dysfunction following wound debridement and antibiotic therapy.

D. **Antibiotic** therapy is essential to remove any existing organisms and those developing from spores.
  1. **Metronidazole**
     a. **Dogs: 10 mg/kg PO or IV** (administered over 1 hour) **q8h** is the antibiotic of choice and superior to penicillin G (*see Pharmacology below p. 490*) for 10 days.
     b. **Cats: 10 mg/kg as above q12h.**

    c. Rarely seizures may occur therefore, administer acepromazine (if needed) at a different time.

    2. Penicillin G 20,000 – 50,000 IU/kg IV q6h (a portion can be administered IM close to the wound). Penicillin is the second choice (s*ee Pharmacology below p. 490*). **Ampicillin is ineffective.**

E. **Antitoxin** (equine antitoxin) (*see i below first*)

    a. 2.5 – 25 IU/kg dogs (lower dosages for larger dogs), IV slow infusion over 30 min.

    b. 100 IU/CAT IV slow infusion over 30 min.

    c. Some recommend only one dose administration, others recommend **q8h** for 2 – 3 days for severe infections. As therapeutic blood level of antitoxin exists for ~ 14 days after injection, repeated administration is usually considered unnecessary by some.

    d. The IV route is more effective than the SC or IM routes, however, anaphylaxis may occur more frequently than the IM, SC routes.

    e. Test dose 0.1 – 0.2 mL intradermally or SC at least 15 min prior to commencing the therapeutic dose to identify those patients likely to develop an anphylactoid reaction. Erythema usually signals a strong potential for anaphylactoid reaction.

    f. Prepare for an anaphylactoid/anaphylaxis reaction (*p. 615*) prior to administration of the antitoxin.

    g. Administration of an **antihistamine** is recommended prior to delivery of antitoxin.

    h. Local IM administration of 1000 IU around the proximal wound has proven to be effective in laboratory models.

    i. NOTE: In humans an approximate dose of 7 IU/kg (500 IU/patient) proved to be as effective as 42 – 70 IU/kg (3,000 – 5,000 IU/patient).

F. **Muscle relaxation** may be obtained by administration of

    a. Acepromazine 0.01 – 0.1 mg/kg titrated to desired level. Lower dosages when combined with an opioid OR

    b. Diazepam 0.1 – 0.5 mg/kg/h titrated to effect OR

    c. Combination acepromazine and diazepam at dosages to effect.

    d. Methocarbamol 44 – 130 mg/kg PO q8h on day 1, reduced to **22 – 44 mg/kg PO q8h. 44 mg/kg IV** with frequency depending on severity of condition.

G. **Analgesics are necessary** as these animals are painful initially after wound debridement and muscle stiffness, and to lower the dose of a muscle relaxant. **Opioids** have raised concern due to potential for respiratory depression and CNS stimulation. As long as the animal is observed, these potential complications can be avoided with appropriate dosing, and reversal with naloxone (*see Analgesia & Sedatives p. 81*) should this occur. It is **inhumane not to add analgesia.** Titrate to effect

    a. Oxymorphone or Hydromorphone 0.01 – 0.1 mg/kg IV, IM, SC followed by CRI (*p. 241*), OR

    b. Morphine 0.1 – 0.5 mg/kg slow IV, IM, SC followed by CRI (*p. 251*) OR

    c. Fentanyl 0.2 – 4 mg/kg bolus and /h (*p. 237*)

H. **Magnesium sulphate** is recommended in humans for control of spasms in severe tetanus without the need for deep sedation, mechanical ventilation or neuromuscular blockade. **See pharmacology below prior to instituting this treatment.** Caution in patients with renal failure; a lower dose should be administered as magnesium is renally excreted. Hypocalcemia is a contrainidication for magnesium administration. The following is based on human reports, no reports on magnesium administration in animals with tetanus are published but its information is included here as a potential benefit may be observed. Adverse affects are a tendency towards paralysis, hypotension and bradycardia. It is recommended that this therapy should only be attempted where mechanical ventilation is available, or very careful titration be used. The reduction of muscular spasticity and attenuation of the patellar reflex is a guide to dosing, while **significant** attenuation of patellar reflexes is used as a clinical measure of magnesium toxicity. ECG and systemic blood pressure monitoring is also advised **while establishing the dose of magnesium.** Bradycardia, hypotension and paralysis is noted with serum magnesium concentrations at 4 – 5 mmol/L. Due to the potential stressful experience and pain associated with tetanus, it is important that magnesium be instituted after F and G above.

1. **Magnesium dosing.** A **pediatric** report noted successful control of muscular rigidity when used in combination with lorazepam (lorazepam alone failed) using magnesium at **magnesium sulphate 4 mg/kg/h CRI (if 200 mg/mL (20%) solution = 0.02 mL/kg = 0.016 mmol/kg= 0.032 mEq/kg)** with **serum** magnesium levels maintained between 1.05 – 1.35 mmol/L (2.1 – 2.7 mEq/L, 2.55 – 3.28 mg/dL). In **human** adults, with no sedation, **magnesium sulphate 15 – 30 mg/kg/h (0.065 – 0.13 mmol/kg/h ~ 0.13 – 0.3 mEq/kg/h, CRI (= 0.075 – 0.15 mL/kg/h of 200 mg/mL solution)** has been shown to control spasticity; serum magnesium concentrations were maintained between 2 – 4 mmol/L (4 – 8mEq/L, 4.9 – 9.7 mg/dL). However, these levels are at least six times higher than those currently recommended for treatment of depletion in dogs and therefore, may potentially be toxic to dogs and cats. Where these high dosages were used, the magnesium dosage was decreased by 3.5 mg/kg/h (0.014 mmol/kg = 0.028 mEq/kg) once control of spasms was established to ensure that the minimum effective dose was being given. As there are no veterinary reports on magnesium dosing for tetanus, these human dosages are given as a potential guide to administration in cats and dogs. Dosages of 0.12 mEq/kg/min (0.06 mmol/kg/min) with a cumulative dosage exceeding 5.9 mEq/kg (3 mmol/kg) resulted in death.

2. Managing **potential adverse events**
   i. If respiratory rate or tidal volume decreases, reduce magnesium dose and prepare to ventilate.
   ii. If a reduction in blood pressure or bradycardia occurs decrease magnesium and administer **glycopyrrolate 0.005 – 0.015 mg/kg or atropine 0.01 – 0.04 mg/kg IV.**
   iii. If blood pressure or heart rate increase above normal for >1 hour increase the dose of analgesic (opioid).
   iv. **10% Calcium gluconate at 0.5 – 1.0 mL/kg** titrated to effect if marked bradycardia or hypotension occurs. Calcium supplementation is not advised in asymptomatic, normocalcemia as calcium supplementation in the presence of high magnesium levels may lead to soft tissue calcification and renal failure.
   v. Where magnesium is **not administered,** or the low dose magnesium is used, or inadequate relaxation has been achieved go to I below.

3. **Monitor** as frequently as possible, urine output, tidal volume, ability to swallow and cough, ECG, pulse oximetry and signs of hypocalcemia; serum magnesium and calcium levels daily, and chest radiographs where needed.

I. Neuromuscular Junction Blockade (NMJ) may be necessary when GABAergic agents are unable to control **serious** tetanic spasms, However, its use in animals has not been reported and should be avoided if at all possible. If NMJ is deemed necessary, **vecuronium** is the current agent of choice in people because it induces minimal autonomic instability. Pancuronium bromide is **not** recommended as it is associated with tachycardia, hypertension, and elevated cardiac output, which may be confused with the autonomic effects of tetanus. Although atracurium has also been recommended for humans it is also recommended that it should be **avoided** in tetanus patients because of its potentially epileptogenic metabolite laudaunosine, which is also a potential problem in cats and dogs. In addition to clinical observation, neurophysiologic monitoring is recommended to insure optimal dosing of the NMJ blocking agent (e.g., train-of-four stimulation). During the period of NMJ blockade, the patient must be adequately sedated to prevent the conscious perception of this frightening situation. Because autonomic signs cannot be relied upon to signal inadequate sedation in this setting, electroencephalographic monitoring is indicated.

J. **Sustained bradycardia or tachycardia** may require treatment with glycopyrrolate or labetalol respectively.

K. **Gastric** protection is advised as tetanus is extremely stressful and these patients are at risk for gastric ulceration. **Famotidine 0.5 mg/kg IV q12h** is recommended.

L. **Oropharyngeal suctioning** may be required due to accumulation of mucous secondary to inability to swallow. In severe cases, intubation may be required to prevent aspiration.

M. **Nutrition.** As some of these animals may have difficulty eating, parenteral nutrition or enteral feeding via esophagostomy or gastrostmy tube is necessary. (*see Nutrional Support p. 499*). Small, frequent feedings are advised to avoid esophageal reflux, regurgitation and aspiration.

N. **Nursing care** is essential. A quiet, temperature-controlled room with reduced lighting; cotton balls in the ear canals and lots of TLC is required. Handle the patient carefully. Ensure bedding is clean, well padded and dry. Be cognizant of requirements to urinate and defecate. Be sure constipation does not become a problem. It may take 1+ weeks until improvement is seen and up to 4 weeks before normal function is resumed.

O. **General monitoring** should include vital signs, blood gases (especially CO_2 levels), pulse oximetry and especially respiratory rate and effort is essential on a continuous basis. See recommendations for mechanical ventilation (*p. 577*) should the work of breathing become excessive or ineffective.

P. **Supplemental oxygen and mechanical ventilation** may be required.

Q. **Complications** include fractures of long bones, spine and skull resulting from violent tetanic or convulsive episodes. Constipation secondary to recumbency and hypertonic anal sphincter may require warm water enemas. Urinary retention occurs due to hypertonic urethral sphincter requiring continual or intermittent urinary catheterization.

PHARMACOLOGY

1) **Metronidazole** is an antibiotic directed toward anaerobic bacteria. The recommendation for metronidazole over penicillin is based on a trial showing that patients given enteral metronidazole did better than those given intramuscular penicillin. Another potential advantage is that non-anaerobic commensal organisms are not targeted.

2) **Penicillin G** is an antibiotic directed toward anaerobic and aerobic bacteria. Penicillin, as a GABA antagonist, may carry the risk of worsening tetanic spasms and for this reason is not recommended. Penicillin may act synergistically with tetanospasm worsening the spasms and may diminish the efficacy of the benzodiazepine.

3) **Benzodiazepines** are the best agents currently available for the relief of spasms and rigidity. They are GABAA agonists, thereby indirectly antagonizing the effects of the toxin on inhibitory systems. High dosages may be required. Tapering the benzodiazepine over a 2 week period is recommended to avoid withdrawal symptoms. Dosages from 0.6-4.6 mg/kg/24 h in people have been required to control the spasms.

4) **Magnesium.** In humans, a prospective study of magnesium as an antispasticity agent suggests that this ion may have substantial efficacy both for control of spasms and for prevention of autonomic dysfunction. Spasms were controlled in most patients at a serum magnesium concentration between 4-8 mEq/L (2-4 mmol/L). Raising concentrations beyond this resulted in hypotension and bradycardia.

5) **Morphine,** in addition to conferring analgesia, may also counteract an effect of tetanospasmin because tetanospasmin inhibits the release of enkephalins, which may play a modulatory role in the autonomic system. A loading dose followed by a CRI, is often effective in human patients.

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NOTES

INTRODUCTION

Weakness is a reduction in the strength of one or more muscles. While in human medicine weakness may be classified as subjective (the person feels weak, but has no measurable loss of strength), or objective (measurable loss of strength as noted in a physical exam), in veterinary medicine, weakness is a non-specific objective clinical sign determined by history, and supported by physical and neurological examination, and laboratory data. Weakness may be generalized (total body weakness), or localized to a specific area, side of the body, limb, or muscle (localized or focal weakness). Localized weakness may follow to a systemic disorder (ventroflexion of the neck in hypokalemic cats), a central nervous system lesion (cranial nerve deficit following brain infarct; asymmetric motor deficits related to fibrocartilagineous embolic myelopathy), or a peripheral nervous system disease involving motor nerve roots (flaccid paresis/paralysis in polyradiculoneuritis), peripheral nerve (plantigrade stance in feline diabetic neuropathy), neuromuscular junction (megaesophagus in myasthenia gravis), or muscle (fibrotic myopathy of the German shepherd dog). Weakness may be clinically classified as continuous or episodic. The continuous form is a persistent loss of muscle strength (tetraparesis in polyradiculoneuritis) whereas episodic weakness has a period of normalcy alternating with generalized muscle weakness (exercise intolerance in myasthenia gravis). This chapter will focus on the neurological manifestation of weakness, and the reader is directed to refer to chapters for other identifiable causes of weakness.

FIGURE 1. Lesion Localization for Origin of Weakness.
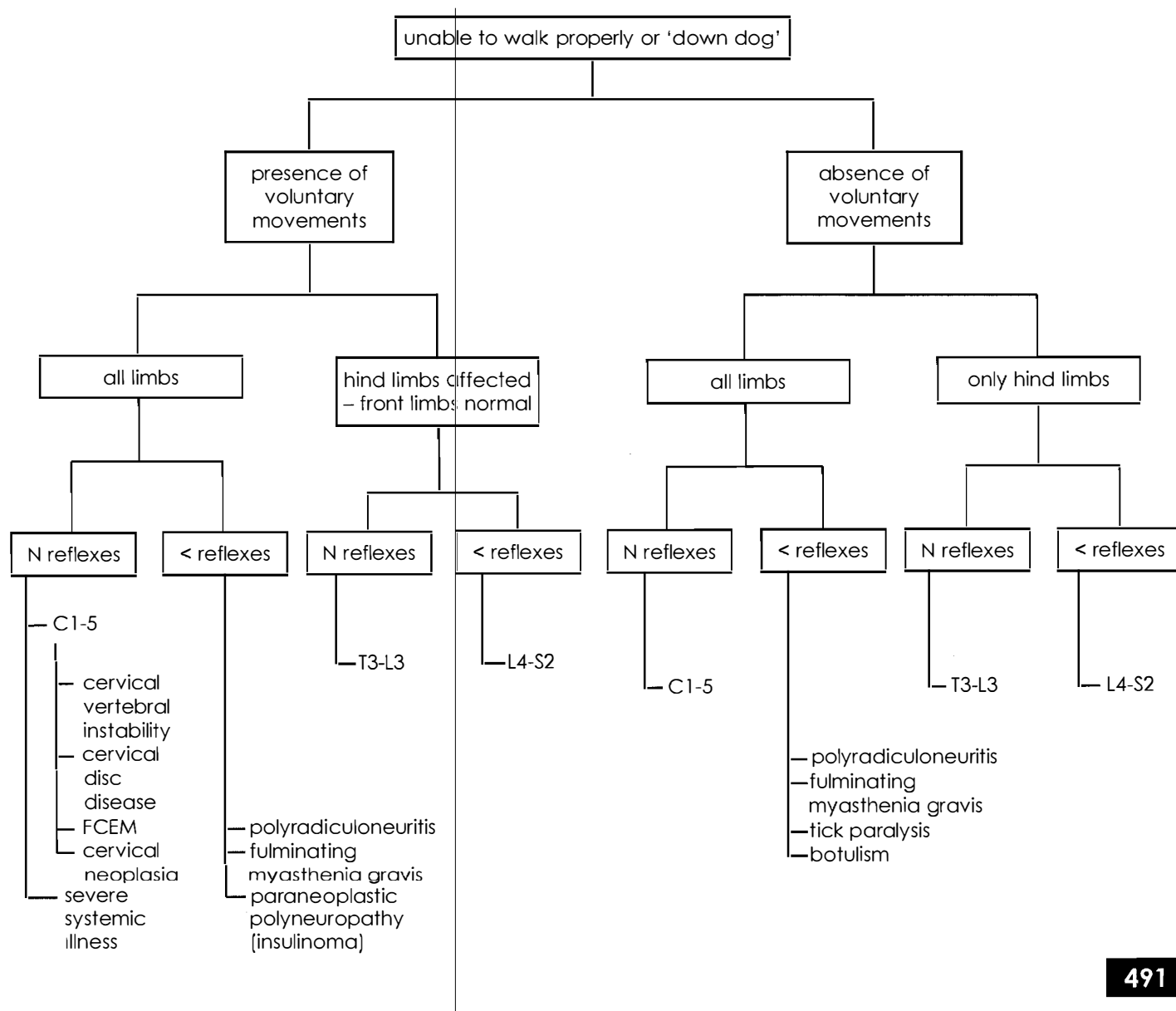
History

A detailed history must be obtained in order to localize the problem to metabolic, toxic or neurologic

TABLE 1. Medical history questions documenting the weakness in detail may include:

Time Pattern	• When did the weakness begin? • Did it begin with an illness or injury? • Did it occur suddenly or gradually? • Is the weakness noticed after strenuous activity or exercise? • Did it start following a systemic disease or after a vaccination?
Quality	• Is the weakness constant or does it come and go? • Does the weakness affect breathing? • Does it affect barking, chewing or swallowing? • Does it affect walking, climbing stairs, sitting, getting up? • Is there pain associated with the weakness?
Location	• Is the weakness generalized or limited to a specific area?

Aggravating Factors	• What makes the weakness worse?
	  – Physical activity
	  – Rest
	  – Pain
	  – Stress

Relieving Factors	• Does anything help relieve the weakness?
	  – Rest
	  – Pain relief

Other Symptoms	• What other symptoms are also present?
	  – Fever – Diarrhea
	  – Injury – Change in mental status, alertness or responses
	  – Pain – Weight loss
	  – Vomiting – Change in skin appearance

Important Information	• What medications are being taken? • Are they any know allergies? • Unsupervised access to potential toxins? (e.g., organophosphate)

Clinical Signs/Physical Examination

Measurable weakness may result from a variety of conditions including metabolic, neurologic, primary muscular diseases, and toxic disorders. See algorithm for neurologic assessment. During the neurological assessment metabolic and toxic disorders must be ruled out.

METABOLIC
- Endocrine disorders
  - Diabetes mellitus
  - Hyperadrenocorticism
  - Steroid myopathy
  - Hypoadrenocorticism
  - Hypothyroidism
  - Hyperthyroidism
  - Hypoglycemia (Insulinoma)
- Hypokalemia, Hyperkalemia
- Hypocalcemia, Hypercalcemia
- Metabolic defects:
  - Hyperchylomicronemia in cats
  - Hyperoxaluria in cats
  - Dysautonomia

- Neoplastic
  - Paraneoplastic neuropathy
- Toxic (including drugs)
  - Organophosphate toxicity
  - Vincristine-associated peripheral neuropathy

The MAJORITY of these disorders cause a GENERALIZED, CONTINUOUS WEAKNESS (total body weakness). Only on a few occasions (insulinoma, electrolyte disorders), the weakness may be FOCAL and EPISODIC in nature.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **CBC** is required to identify potential infectious, systemic disease responsible for weakness.
- **Serum/Blood electrolytes,** especially potassium, to rule out hypokalemia in cats.
- **Venous blood gases** to assess acid-base status (perfusion and ventilation).
- **Arterial blood gases** to assess oxygenation and ventilation.
- **Blood urea and creatinine** to assess renal function. Pre-renal may indicate dehydration.
- **Creatine kinase** is consistently elevated in myopathies.
- **Blood glucose.** Hypoglycemia may suggest a diagnosis of insulinoma; hyperglycemia may indicate diabetes mellitus.
- **Serum calcium** levels to rule out hypercalcemia or hypocalcemia.
- **Thyroid function** to rule out hypothyroidism and hyperthyroid.
- **Resting and ACTH stimulated cortisol** tests to rule out hypoadrenocorticism or hyperadrenocorticism.
- **Serum acethylcholine** receptors antibody titer (AchR) to confirm a diagnosis of myasthenia gravis. An AchR antibody titer greater than 0.6 nmol/L in dogs and greater than 0.3 nmol/L in cats is diagnostic of canine and feline myasthenia gravis.
- **Urinalysis** to screen for a potential source of infection, assess hydration, renal disease.

Extended Data Base

- **Electromyography** to assess muscle function (i.e., abnormal in myopathic disorders), and nerve conduction velocity to assess function of the peripheral nerves (i.e., abnormal in polyneuropathy – polyradiculoneuritis).
- **Cerebrospinal fluid** analysis: abnormal in polyradiculoneuritis or infectious dz.
- **MRI** of the head and spine to rule out or define central nervous system diseases (i.e., cerebrovascular infarct, neoplasia, inflammation, spinal cord injury).
- **Muscle and nerve biopsy** to reach a final diagnosis when a peripheral nervous system disease is suspected (i.e., abnormal biopsies in polyneuropathies and/or myopathies).

TABLE 2. Clinical Signs/Patient Evaluation for Specific METABOLIC Causes of Weakness

Metabolic Disease	Clinical Signs	Patient Evaluation	Treatment
Diabetes Mellitus (DM)	Exercise intolerance Plantigrade stance Paraparesis Distal muscle atrophy Hyporeflexia	CBC Biochemistry profile Urinalysis Serum glucose Serum electrolytes Acid-base status EMG/NCV	Treat DM *See Diabetic Ketoacidosis p. 263*
Hyperadrenocorticism	Generalized muscle atrophy Tetraparesis Generalized stiffness Percussion myotonia	CBC Biochemistry profile Urinalysis Serum CK Serum electrolytes Acid-Base status EMG	Treat Hyperadrenocorticism *See Hyperadrenocorticism p. 270*

Steroid myopathy	Generalized muscle atrophy Tetraparesis	CBC Biochemistry profile Urinalysis History	Steroid reduction *See Hyperadrenocorticism p. 270*
Hypoadrenocorticism	Tetraparesis Regurgitation Dysphagia	CBC Biochemistry profile Urinalysis Serum electrolytes Acid-base status Chest radiograph: Megaesophagus	Electrolyte disorders – Correct imbalance *See Hypoadrenocorticism p. 274*
Hypothyroidism	Tetraparesis Hyporeflexia Unilateral cranial nerve deficit (V, VII, VIII CN) Regurgitation Laryngeal paralysis Stiffness, myalgia Muscle wasting	CBC Biochemistry profile Urinalysis Thyroid profile Chest radiographs: Megaesophagus	Thyroid supplementation *See Hypothyroidism p. 285*
Hyperthyroidism	Tetraparesis Exercise intolerance Muscle wasting Ventroflexion of the neck Muscle tremors	CBC Biochemistry profile Blood pressure Total T4	Methimazole *See Hyperthyroidism p. 288*

NEUROLOGIC

See algorithm for details on neurological examination findings.

Central Disorders

- Weakness is one of the multiple neurological signs observed with disorders of the central nervous system. Weakness can be generalized if related to diffuse CNS disease (i.e., encephalitis, CNS toxicity–organophosphates, brain tumour), or localized to specific cranial nerves (i.e., brain tumor localized to the brainstem) or appendicular muscles (i.e., fibrocartilagineous embolic myelopathy, nerve root compression from intervertebral disc disease).

Peripheral Disorders – see Table 3 for details

- Polyradiculoneuritis (Coonhound paralysis)
- Tick paralysis
- Botulism
- Polyneuropathy
- Myasthenia gravis
- Myopathy

Polyradiculoneuritis: Also known as "Coonhound paralysis."

The **etiology** is still unknown. An immune-mediated process following contact with the saliva of raccoons potentially triggers the neurological signs.

Historically, a change in quality of bark precedes the onset of the neurological signs by a few hours to several days.

Clinical signs begin in the hind limbs with presence of paraparesis and exercise intolerance in approximately 75% of affected dogs. Based on the degree of severity of the immune-mediated reaction, the clinical condition may progress to the front limbs leading to tetraparesis and inability to walk. There is NO ATAXIA. Voluntary movements are usually preserved, although occasionally complete paralysis is present. In 25% of affected dogs a descending paresis has been reported beginning in the front limbs, progressing to the rear end. Once the clinical signs appear, progression continues for 4 to 5 days. Respiratory paralysis may occur leading to death. The ventral motor roots are primarily affected leading to classical lower motor signs including tetraparesis, decreased reflexes, hypotonus and muscle atrophy. The perineal reflex is usually preserved. Prognosis is variable pending the progression of the neurological status. The majority of

affected dogs tend to improve spontaneously after approximately 10 days from the onset of the clinical signs. Recovery is very slow, and it may take several months for a complete axonal regeneration and remyelination to occur. However, the dog is usually able to stand and walk in approximately 2 weeks post-onset. Hypotonus and muscle atrophy associated with decreased spinal reflexes are present for a long time. Occasionally, in severe cases, the clinical signs may progress to severe respiratory paralysis and death. Initially, these dogs are presented with severe abdominal breathing, increased rectal temperature, cyanotic mucous membranes, and abnormal acid-base status (increased pCO_2 and decreased SpO_2). Most of these cases require assistance with mechanical ventilation making the prognosis very guarded. Phrenic nerve paralysis and denervation of the intercostal muscles are principally responsible for the onset and progression of the respiratory signs. Fever in excess of 42°C may occur and may not be associated with work of breathing.

Treatment is supportive (*see Management below*). Corticosteroids have not proved to be beneficial; we DO NOT advise the use of corticosteroids.

Tick Paralysis

Tick paralysis is a pre-synaptic disorder of the neuromuscular junction responsible for the inhibition of the release of acetylcholine from the terminal axon. The clinical signs vary from rapidly progressive paraparesis to flaccid tetraplegia, cranial nerve deficits (facial nerve paresis), or respiratory difficulties due to involvement of the phrenic nerve and intercostal muscles. There is an abnormal gait with presence of tetraparesis or tetraplegia. NO ATAXIA. Voluntary movements may or may not be present based on the severity of the clinical signs. The spinal reflexes are decreased or absent with hypotonus and progressive neurogenic atrophy.

The **etiologic agents** are ticks, *Dermacentor variabilis* and *Dermacentor andersoni* in North America and Ixodes holocyclus in Australia. Theories regarding the initiation of the neurological disorder put forth the claim that the action of a neurotoxin present in the tick's saliva interferes, in a temperature-dependant way, with the acetylcholine release, resulting in neuromuscular blockage.

The severity of the clinical signs is likely dependent on the interaction between the host's immunity and neurotoxin released by the tick. A single tick can trigger severe neurological signs.

Diagnosis and treatment are based on the identification and prompt removal of the tick. The clinical signs improve immediately after the tick is removed (marked improvement within 24 hours and complete recovery within 72 hours). For this reason, it is very important to perform a thorough physical examination. Neurological signs tend to progress to respiratory paralysis and death, if no immediate action is taken to identify and remove the tick.

Treatment with supportive care (*see management below*), tick removal, and dips in appropriate insecticide solutions are necessary to eliminate the primary source of infection.

Botulism

Botulism is a rare condition affecting the peripheral nervous system of dogs following ingestion of carrion and spoiled food.

The **etiology** is ingestion and absorption of the type C neurotoxin released by *Clostridium botulinum* contained in the carrion and spoiled food. The primary target of the neurotoxin is the pre-synaptic terminal (inhibition of calcium entry and acetylcholine [Ach] release).

Clinical signs vary from mild paresis to flaccid tetraplegia, cranial nerve deficits, hyporeflexia, and occasionally megaesophagus and aspiration pneumonia. Respiratory paralysis may occur requiring assisted ventilation.

Diagnostic laboratory tests are often unremarkable and the ultimate diagnosis is usually made after isolation of the neurotoxin from the gastric contents, serum, vomitus, and feces.

Treatment is supportive (see management below) and prognosis varies based on the amount of ingested neurotoxin. Oral antibiotics and *C. botulinum* antitoxin are of no benefit. Complete recovery should occur within 1 – 3 weeks.

Polyneuropathy

Different **etiologies** have been implicated in the development of polyneuropathy ranging from metabolic diseases (hypothyroidism, diabetes mellitus, paraneoplastic disease, drug-related polyneuropathy) to primary neurologic disorders (breed-related, inherited polyneuropathy, polyradiculoneuritis, tick paralysis, botulism, or post-rabies vaccination).

The **clinical presentation** is variable, depending on the primary etiology, severity of the disease, and the host-immune response.

Diagnosis is usually made based on the neurological examination (see algorithm) suggestive of hyporeflexia, histological examination of nerve biopsies, electrodiagnostic studies, and correlation with a systemic metabolic disorder (hypothyroidism, diabetes mellitus, neoplasia) or chemotherapeutic drugs (i.e., vincristine).

Treatment is primarily aimed at the causative disorder. Prognosis for neurological recovery is usually favorable if adequate treatment is promptly established.

Myasthenia Gravis

Myasthenia Gravis (MG) is a disorder of neuromuscular transmission resulting from either a deficiency (congenital MG), or acquired disorder (immune-mediated depletion of AchRs), of the nicotinic acetylcholine receptors (AchR).

Clinically, three forms of MG have been described: localized, generalized and fulminating.

The **localized form** is clinically characterized by the presence of regurgitation, dysphagia, voice change and occasional decreased palpebral reflexes. Megaesophagus is often noticed on thoracic radiographs. Historically there is no report of generalized weakness or exercise intolerance.

The **generalized form** is characterized by clinical signs varying from mild exercise intolerance or inability to stand (often hind limbs only) to severe tetraparesis, regurgitation, and other clinical signs typical of the localized form. If an early diagnosis is made, megaesophagus might be identified on thoracic radiographs without concurrent clinical signs of regurgitation. NO ATAXIA OCCURS. Aspiration pneumonia is the greatest complication secondary to megaesophagus and is the primary cause of death in myasthenic patients. The neurological examination is characterized by normal mentation, occasional decreased palpebral reflex, exercise intolerance and tetraparesis. The spinal reflexes are usually intact, although withdrawals are occasionally difficult to elicit due to profound generalized weakness. Back pain is not a feature.

The **fulminating form** is rarely reported in dogs and must be differentiated from polyradiculoneuritis (coonhound paralysis). Affected patients are usually found acutely recumbent and unable to rise with minimal voluntary movements. NO ATAXIA OCCURS. The cranial nerve examination reveals decreased palpebral reflexes. Because of the acute nature of the disease, there is no previous history of regurgitation despite the presence of megaesophagus. Clinical signs of regurgitation and aspiration pneumonia may occur within 24 – 48 hours or later from the onset of the neurological signs. The spinal reflexes are decreased to absent on all limbs, simulating the features of polyneuropathy or polyradiculoneuropathy. The degree of abnormal reflexes is determined by the amount of non-functional AchR.

Diagnostic and laboratory tests (Table 3): Serologic test for AchR antibodies is considered the "gold standard" for the diagnosis of immune-mediated MG. The test consists in the demonstration of serum autoantibodies against muscle AchRs by immunoprecipitation radioimmunoassay. Intravenous administration of the short-acting anticholinesterase drug **edrophonium chloride (Tensilon®), dogs 0.1 – 0.2 mg/kg IV and cats 0.25 – 0.5 mg total dose,** may be used to provide a presumptive diagnosis of acquired MG while waiting for results of confirmatory testing. A lack of improvement in muscle strength does not eliminate a diagnosis of MG. Overdose or use in a non-myasthenic animal may cause salivation, retching, vomiting and diarrhea.

Treatment is based on the administration of long-acting anticholinesterase drugs, **pyridostygmine bromide (Mestinon®), 1 – 3 mg/kg PO q8–12h;** or **neostigmine bromide (Prostigmin®) 2 mg/kg PO q24h** in divided doses to effect. For critical animals, **CRI of pyridostigmine bromide 0.01 – 0.03 mg/kg/h** may be used until oral feedings are resumed or a feeding tube is placed. To prevent gastrointestinal signs (i.e, nausea, cramps, diarrhea), excessive salivation, and lacrimation often induced by administration of anticholinesterase drugs, small doses of atropine are recommended along with the administration of the medication after meals when feasible. Corticosteroids may be added to the current treatment. Low-dose prednisone 0.5 mg/kg every other day has been recommended for dogs.

Myopathy

Myopathies are uncommon diseases of dogs and cats. They are often unrecognized due to their sub-clinical, chronic, and non-painful appearance.

The **etiology** may be: **primary neurological** in nature (i.e., muscular dystrophies, congenital myotonia); secondary to metabolic (hypothyroidism, hyperadrenocorticism, hypoadrenocorticism); infectious (toxoplasmosis, neosporosis, leptospirosis, ehrlichiosis); or idiopathic (masticatory muscle myositis, polymyositis) causes.

Clinical signs include generalized stiffness, exercise intolerance, muscle pain, dysphagia, voice change, regurgitation, bilateral exophthalmus, and muscle atrophy. No ATAXIA is noted. Occasionally, the clinical signs are localized to specific muscles (i.e., temporal and masticatory muscles in canine masticatory muscle myositis, cervical muscles in hypokalemic cats, or thiamine deficiency).

Diagnostic laboratory data may indicate abnormalities related to a primary systemic disease, elevated creatine kinase (CK) and other muscle enzymes (ALT), electromyographic abnormalities, and muscle biopsies confirmatory of the suspected findings.

Treatment is usually aimed toward the primary source of myopathy. Clinical signs are reversible if the original disorder is successfully corrected. Corticosteroids i.e., prednisone 2 – 4 mg/kg/day, are required if the primary cause responsible for the onset of polymyopathy is suspected to be immune-mediated.

TABLE 3. Clinical Signs/Patient Evaluation for Specific NEUROLOGICAL Causes of Weakness

Metabolic Disease	Clinical Signs	Laboratory Data	Treatment

Polyradiculoneuritis	Exercise intolerance
	Flaccid paraparesis
	Flaccid tetraparesis
	Hypotonus
	Hyporeflexia
	Muscle atrophy
	Change in voice
		CBC
		Biochemistry profile
		Urinalysis
		Acid-base status
		Rectal temperature
		Chest radiographs:
		– NO megaesophagus
		Cerebrospinal fluid:
		– Increase in proteins
			Acid-base status
			Nasal oxygen
			Supportive care
			  – Changing of side
			  – Urinary catheter

Tick Paralysis	Exercise intolerance Flaccid paraparesis Flaccid tetraparesis Hypotonus Hyporeflexia Muscle atrophy	CBC Biochemistry profile Urinalysis Acid-base status Rectal temperature Chest radiographs: – NO megaesophagus	Remove the whole tick
Botulism	Exercise intolerance Flaccid paraparesis Flaccid tetraparesis Hypotonus Hyporeflexia Muscle atrophy	CBC Biochemistry profile Urinalysis Acid-base status Rectal temperature Chest radiographs: – Megaesophagus	Supportive care Intensive care
Polyneuropathy	Exercise intolerance Flaccid paraparesis Flaccid tetraparesis Hypotonus Hyporeflexia Muscle atrophy	CBC Biochemistry profile Urinalysis Acid-base status EMG/NCV Nerve biopsy	Treat metabolic dz. Supportive care

Myasthenia gravis	**Localized form:**
	  – Regurgitation
	  – Dysphagia
	  – Voice change
	  – Decreased palpebral reflex
	Generalized form:
	  – Exercise intolerance
	  – Paraparesis/Tetraparesis
	  – Regurgitation
	  – Dysphagia
	  – Decreased palpebral reflex
	Fulminating form:
	  – Acute tetraparesis
	  – Hyporeflexia
	  – Regurgitation
	  – Decreased palpebral reflex
		CBC
		Biochemistry profile
		Urinalysis
		Chest radiographs:
		– Megaesophagus
		Serum AchRs Ab titer:
		  – > 0.6 nmol/L (dog)
		  – > 0.3 nmol/L (cat)
		  – "Tensilon test":
		Edrophonium chloride
		  – 0.1 – 0.2 mg/kg IV (dog)
		  – 0.25 – 0.5 mg total (cat)
			Pyridostigmine:
			  – 1 – 3 mg/kg orally
			Pyridostigmine CRI:
			  – 0.01 – 0.03 mg/kg/h
			Neostigmine:
			  – 2 mg/kg/d orally/IM
			Prednisone:
			  – 0.5 mg/kg EOD

Myopathy	Stiffness Tetraparesis Muscle atrophy Pain on muscle palpation Regurgitation	CBC Biochemistry profile Urinalysis Electromyography Muscle biopsy Chest radiographs: Megaesophagus	Treat systemic dz. Prednisone: 2 – 4 mg/kg/day

The management is supportive. Refer to Tables 2 and 3 for treatment options for specific etiologies. The key points are:

A. **Supplemental oxygen** where required in animals with respiratory muscle weakness (polyradiculoneuritis, tick paralysis, botulism or fulminating myasthenia gravis). Mechanical ventilation may be required should there be progression of the neurological signs (*see Respiratory Emergencies p. 577*).

B. **Respiratory rate and effort** should be assessed hourly. If the rate and effort increase, body temperature may rise.

C. **Rectal temperature** should be monitored when respiratory rate and effort are noted. If possible, constant temperature monitoring is advised in the severe acute polyneuropathies, because the temperature can rise very quickly.

D. A **circulating air fan** should be placed in close proximity to keep the ambient air cool to reduce the work of breathing (panting) expended in cooling.

E. Place the animal on **soft bedding** on a 'grate' to allow urine to pass through if a urinary catheter is not in place. It is wise to measure urine volume and specific gravity to guide fluid therapy.

F. The patient should have a position change q6h.

G. Care should be taken to prevent decubitus ulcers.

H. Put **stool softners** (i.e., mucilose) in food to prevent constipation.

I. **Maintenance IV fluids** if the patient cannot drink (i.e., myasthenia gravis, botulism).

PHARMACOLOGY

1) **Pyridostigmine bromide:** Anticholinesterase agent used in the treatment of acquired myasthenia gravis in dogs and rarely in cats. It inhibits the hydrolysis of acetylcholine by directly competing with acetylcholine for attachment to acetylcholinesterase resulting in accumulation of acetylcholine at cholinergic synapses and resultant cholinergic activity. The onset of action after oral dosing is generally within one hour. Adverse effects are generally dose related and cholinergic in nature. Overdosage may induce a cholinergic crisis and symptoms of cholinergic toxicity include gastrointestinal signs (nausea, vomiting, diarrhea), salivation, sweating, respiratory effects (increased bronchial secretions, bronchospasm, pulmonary edema, respiratory paralysis), ophthalmic effects (miosis, blurred vision, lacrimation), cardiovascular effects (bradycardia or tachycardia, cardiospasm, hypotension, cardiac arrest), muscle cramps and weakness.

Treatment of pyridostigmine overdosage consists of both respiratory and cardiac supportive therapy and atropine if necessary. Overdoses in myasthenic animals can be very difficult to distinguish from the effects associated with myasthenic crisis. The time of onset of symptoms or an edrophonium chloride test may help to distinguish between the two. Doses: 1 – 3 mg/kg PO q8–12h.

2) **Neostigmine bromide:** Neostigmine competes with acetylcholine for acetylcholinesterase (see Pyridostigmine bromide for mechanism of action, adverse effects and overdosage). Poorly absorbed after oral administration. Onset of action after parenteral administration begins within 10 – 30 minutes and can persist for up to 4 hours. Doses: 0.04 mg/kg IM q6h.

3) **Edrophonium chloride** (see Pyridostigmine bromide for mechanism of action, adverse effects and overdosage): Anticholinesterase agent that is very short acting and is used in the diagnosis of myasthenia gravis. After IV injection, a short-term increase in muscle strength is seen in a positive test. However, this increase is not necessarily specific for myasthenia gravis, which causes both false positives and negatives. Edrophonium chloride is only effective when given parenterally. The onset of action after intravenous administration is within one minute and effects may persist for up to 10 minutes. Doses: 0.1 – 0.2 mg/kg IV

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INTRODUCTION

Anorexia, and contraindications to oral alimentation are problems frequently encountered by veterinarians. Primary anorexia may be associated with psychological factors and intracranial disorders. More commonly however, anorexia is secondary to pain or systemic diseased states. Pseudoanorexia refers to animals with a normal appetite but an inability to consume adequate calories i.e. associated with abnormalities of prehension, mastication or swallowing, including injuries of the head, neck and esophagus. Contraindications to oral feeding may include selected injuries and surgical procedures of the oral cavity, oropharynx, pharynx, esophagus and stomach, pancreatitis and gastroenteritis. The period of food deprivation associated with many of these problems can be extensive. Early nutritional support or encouragement of voluntary food intake, while treating the primary problem can decrease both morbidity and mortality at minimal additional cost.

The metabolic rate associated with injury and systemic illness is increased proportionately with the degree of illness. The catabolic process cannot be prevented, even with appropriate nutrition, however, the degree of catabolism is influenced by nutritional support. If adequate caloric intake is not achieved the increased energy demands are met utilizing body fat and protein sources of the body. This in turn results in an accelerated catabolic state following which secondary problems can arise such as hepatic lipidosis or immunologic incompetence. *However, the amount to feed differs with degree of illness and reparative needs of the patient. The caloric requirements to be administered to critically ill animals are less than those required to maintain body condition under normal, active, physiological condition. Caloric requirements of animals recovering from illness or injury vary with the individual condition and may be more or less than that required in health; this is discussed below.* By assessing the nutritional requirements, selecting the appropriate diet, and administering via the appropriate route, reduced catabolism of body fat and protein occurs and morbidity will be reduced. Unlike the 'stress' response associated with illness or injury, healthy animals deprived of food (i.e., inadvertently locked in the garage!) for variable periods of time go into 'hibernation' where a state of metabolic adaptation occurs by limiting the extent of endogenous catabolism.

The route of nutritional support (enteral vs parenteral) is important to consider. The presence of nutrients in the bowel lumen has several beneficial effects in addition to nutrient absorption. The trophic effects of enteral feeding on the mucosal barrier that isolates luminal organisms from the blood stream, has shown to reduce translocation of bacteria from the gut into the blood stream. Enteral feedings also may stimulate the release of trophic substances (e.g., biliary IgA) and indirectly promote mucosal growth. The mucosal disruption that develops when luminal nutrients are removed (just a few days) will result in malabsorption when feeding resumes. This is one of the causes of "refeeding diarrhea" seen after prolonged periods of bowel rest, and emphasizes the need to continue enteral feedings in any volume possible to limit this problem. An enterally delivered 5% dextrose solution has been shown to increase splanchnic perfusion and possibly increase glomerular filtration rate, therefore even this 'microenteral' nutritional support is beneficial. Enteral feedings therefore, can maintain the absorptive function of the intestinal mucosa and may help to maintain the mucosal barrier that isolates enteric pathogens from the systemic circulation. These non-nutritive effects may be as important as the nutritional benefits of enteral feedings. Therefore, whenever possible, the enteral route should be used. However, there are situations where the parenteral route is advised *(see Parenteral Nutrition p. 511)*.

When formulating a nutritonal regimen, this author considers two categories of patients: **(1) the non-critical** patient recovering from moderate illness or injury (i.e., post-surgery, post-injury, pseudoanorexia, and **(2) the severely ill patient** experiencing the 'peak steady state' of critical illness (i.e., septic peritonitis, acute severe pancreatitis, multi-trauma, and those whose condition is declining from these illnesses). The approach to nourishing these two groups differs. With few exceptions, **in the critically ill patient** immediate caloric requirements to be administered are less, and the parenteral route of administration is used more frequently, than the non-crical patient. In general, when calculating the illness energy requirements (IER) for the individual animal, both the resting energy expended (REE – the number of calories expended by an awake, resting, normal animal in a post-absorptive state and thermoneutral environment), and additional energy expended by the stress factor, are considered. An estimate of the IER is based on the resting energy requirement (RER), which must equal REE, and the stress factor associated with the illness. Indirect calorimetry is required to determine more precisely the individual's caloric requirements, however, this is not practical in most instances. Until more specific guidelines for caloric requirements in various ill states are elucidated, the product of RER and the illness energy factor can be used to **estimate** the IER. This formula, in the author's ICU patients, met the requirements in ~50% of dogs, overestimated requirements in ~25% and underestimated in ~25%, when compared to indirect calorimetric measurements. However, this formula is still used at the Ontario Veterinary

College (OVC-VTH) as an acceptable estimate of nutritional requirements together with appropriate monitoring and adjustments based on clinical findings. Permissive underfeeding for a short duration in human patients is preferred to over-feeding as overfeeding has been shown to be detrimental in critically ill patients. As PPN is used most often in critically ill animals in the OVC-VTH ICU, based on IER calculations and volume of PPN administered, over-feeding does not occur (*see Parenteral Nutrition p. 511*).

The author's category (1) non-critical patient

Several formulas for estimating REE have been published. However, when the various formulas and exponentiation functions are used for calculations in the veterinary literature, approximately the same value is obtained. The author uses the following RER equation **70 x Body weight in kg$^{0.75}$**. If your calculator does not have the exponentiation function (**kg$^{0.75}$**), this can be calculated by BW kg cubed, then square root twice. For example in a 10 kg dog 10 x 10 x 10 = √1,000 = √31.6 = 5.6; complete by multiplying by 70. For practical purposes, but not quite as accurate, some use the formula (30 x body weight in kg) + 70 for animals >2 kg and <35 kg.

The 'stress factors' given below are extrapolated from humans and may not be appropriate for all veterinary patients. However, the author finds that the non-critical patient requires more than RER and the IER derived from these stress factors are representative of the estimate of caloric requirements in ~ 60% of patients.

TABLE 1. Estimation of IER. Based on the minimum estimated REE for all animals = 70 x (Body weight in kg$^{0.75}$), and the illness (stress) experienced by the animal.

The IER (kcal/day) =	stress	factor (x)	X	RER
	cage rest	1.20	X	RER
	post surgery	1.25 – 1.35	X	RER
	trauma or cancer	1.35 – 1.50	X	RER
	sepsis	1.50 – 1.70	X	RER
	major burn	1.70 – 2.0	X	RER
	*cats IER up to	~1.40 (= MER)	X	RER
	normal dog maintenance	~2.00	X	RER

For ill animals the energy requirement is less than that required for **normal** animals where the 'stress' factor is ~2 in dogs and *1.4 in cats. This is referred to as the normal **maintenance energy requirement (MER).** As with humans, a reduction or increase in MER is indicated based on the individual activity of the animal, even cats! When calculating IER, this author starts at the lower end of the factor scale and increases or decreases based on the individual's response. For example the estimated IER for a 10 kg dog recovering from a fracture repair is

$$[70 \text{ X } 10^{0.75}] \text{ x } 1.25 = 394 \text{ x } 1.25 = 492 \text{ kcal/day}$$

As a check of your mathematics, run through the method again but selecting 1.2 as the IER and compare your value with the fluid chart (*see Fluid Therapy p. 366*) for daily water requirements. These should be the same.

Once the caloric requirements are calculated, the amount to feed is determined by the diet selected, which, in turn, is dependent upon the underlying illness, i.e., low protein diet for renal and hepatic disease. The nutritional characteristics of formulated diets are available from manufacturers. One should keep in mind that this is an estimate only and the amount fed should be adjusted to the individual patient's requirements based on physical examination, weight gain or loss, history and tolerance of a specific volume, all easily monitored in any practice. Vigilance is important when feeding through 'tubes' as the animal is not permitted to meet its own requirements by voluntary feeding (especially in **pseudoanorexia** where appetite is normal). As an example, the author managed a dog with gastrostomy feeding where the energy demands of healing (for severe orofacial trauma), plus re-establishing normal body weight was 4 x MER. Bi-weekly weight monitoring was required in this case. This case demonstrates that without continuous indirect calorimetry, it is impossible to determine the exact caloric requirement on a daily basis, and frequent monitoring facilitated adjustment to food intake.

Parenteral nutrition (*see p. 511 below*) may be indicated in the non-critically ill patient where the presence of food or fluid within the gastrointestinal tract will exacerbate the underlying disease process i.e., moderate to severe pancreatitis, gastric outflow or intestinal obstruction, intractable vomiting, as a supplement to enteral feeding or rare cases of

FIGURE 1. Selection of method of nutritional support.

Can the patient be managed via the enteral route?

Yes / No

Is feeding via the oral cavity or esophagus possible? — Is patient well nourished?

Yes:
1. Feed IER of a palatable diet.
2. Gentle force feeding.
3. Pharmacological appetite stimulants.

No: Is duration of nutritional support >3 – 4 days?

Give fluid and electrolyte needs parenterally. Assess daily.

Total or partial parenteral nutrition.

After 24 hours, is maintenance caloric intake obtained without undue patient stress?

No: Feed via nasoesophageal tube. After 4 days.

Yes: Feed via gastrostomy or esophagostomy tube.

Has adequate voluntary food intake resumed?

Commence oral feeding when possible. The gastrostomy feeding tube must remain in place for at least two weeks.

Feed IER of a palatable balanced diet.

Feed via gastrostomy or esophagostomy tube.

*IER = Illness Energy Requirement (basal energy x illness "stress" factor)

intestinal surgery, chylothorax, maldigestion/malabsorption. If malnutrition is evident and/or if enteral nutrition will not be possible for several days, total or partial parenteral nutrition is recommended. Based on the author's experience, partial parenteral nutrition is adequate for up to 2 weeks in selected patients.

If body condition is good, and anorexia of ≤3 days is expected, intravenous fluid therapy alone with special attention to electrolyte and vitamin requirements can be given. However, these animals will be in a negative nitrogen and caloric balance during this period of fasting. Daily assessment, including body weight is required. Average weight loss through not eating is ~ 0.1 – 0.3 kg/1,000 kcals of caloric requirement. This should be kept in mind when assessing fluid requirements as weight lost in an animal not eating should not be considered as 'dehydration' with a subsequent increase in IV fluid administration. Nutritional supplementation should be instituted if the period of fasting is prolonged.

Management of Anorexic Animals

Where appropriate, anorexic animals may be tempted to eat with warm, palatable food, hand feeding and petting. Ensure that the nose is clean. As the sense of smell is involved in regulation of food intake any obstruction of the nares due to dry blood or mucous will suppress appetite, especially in cats. If the animals still won't eat, pharmacological appetite stimulants may be used where there are no contraindications.

A. **Encourage eating.** Warm food to between 26 – 39.5°C (no hotter) to volatise the odour. Feed odiferous food e.g., canned fish, lightly cover canned food with spaghetti sauce or a *very* small sprinkling of garlic powder. If hypokalemia exists (*p. 394*), supplement the animal with potassium gluconate or potassium chloride at 2 – 4 mEq/CAT/day PO, divided q8h (*see p. 395*). Anorexia may be associated with water-soluble vitamin deficiency, especially B_{12} (50 – 100 m/day/cat and 100 – 200 m/day/dog PO) and low serum zinc levels (supplement at 1 mg/kg/day).

B. **Force feeding.** Only use when voluntary eating attempts fail, there is a normal swallowing reflex, and the animal is co-operative. Some animals will swallow food voluntarily when small quantities are placed gently into the back of the mouth while being petted. Do not continually 'force' the food into the mouth. A palatable and caloric-dense diet such as A/D® (Hill's) 1.2 kcals/mL or Nutritional Recovery Formula® (Iams) 2.1 kcal/mL is recommended for cats and dogs. Liquid diets such as Clinicare® (Pet Ag Inc) at 0.98 kcal/mL may be slowly syringed into the mouth or administered through an orogastric tube. Human baby foods (avoid those containing onions) may also be used to encourage voluntary food intake. As these foods are not nutritionally balanced they should be used for no longer than 2 – 3 days. Force-feeding can be tedious and stressful. If force-feeding is necessary for more than one day, tube feeding should be instituted.

C. **Pharmacological appetite stimulants (primarily for cats).**
   1. **Cyproheptadine (Periactin®) 2 – 4 mg/cat q8–12h, 1 mg/kg (dogs) q8h** is preferred.
   2. **Benzodiazapenes (diazepam 0.05 – 0.4 mg/kg – typical dose 1 mg q12h IV or 2.0 mg PO in cats, or oxazepam 2.5 mg/cat)** have been used with some success, however, due to underlying illness and the potential for liver injury, the author does not prescribe them for anorexia.
   3. Appetite stimulants are typically used for one or two treatments. They may not work well for dogs.
   4. Food should be available at the time of administration if the IV route is used.
   5. Do not pursue if the animal does not respond initially.

D. In most instances, **'tube' feeding** is more expedient and less stressful to the animal than force-feeding. If anorexia persists, or if oral food intake is contraindicated for longer than 72 hours, tube feeding should be instituted. Dogs and cats may be fed via, nasoesophageal, esophagostomy, gastrostomy or enterostomy routes. **Orogastric and pharyngostomy routes are not recommended due to complications associated with these techniques.**
   1. **Nasoesophageal** (NE) intubation is simple and quick to perform, with minimum stress to the patient. A NE tube may be left in place for several days and is usually well tolerated by both cats and dogs. As the tube size is relatively small, the animal can eat and drink with the tube in place should voluntary food intake occur. Several medical feeding tubes are available. *See Techniques p. 508 below.*
      a. **Indications.** Where short-term nutritional support is indicated. May be used in the semi-comatose or comatose animal with caution. The head, neck and shoulders should be elevated above the level of the stomach to prevent aspiration. *See complications and Techniques.*
      b. **Contraindications.** Injuries to the head and neck where the possibility of iatrogenic injury may occur due to mal-direction or mal-placement of the tube. Diseases, injuries, or surgical procedures of the nasal cavity, pharynx and esophagus.
      c. **Complications.** Accidental tracheal intubation in any animal may occur, especially animals with suppressed swallowing reflex (i.e., sedated or comatose). Rhinitis may occur with traumatic or prolonged placement. Reflux esophagitis may result if the tube is placed in the stomach, rather than the distal esophagus. Expulsion or malpositioning of the tube may occur following vomiting or regurgitation. Rarely, patients remove the tube. Although no sedation is required for tube placement, the occasional uncooperative patient may have to be sedated.

2. **Esophagostomy** tube feeding is easy to perform in any animal with minimal equipment required, and is recommended for long-term feeding. The tube can remain in place for several months. Dogs and cats tolerate the tube well and can resume normal activity around the house. *See Techniques p. 510 below.*
   a. **Indications:** Any systemic diseased state resulting in prolonged anorexia i.e., hepatic lipidosis, anorectic diabetics, cancer therapy patients. Long-term support for patients with oral, nasal or esophageal injuries or disease. Comatose or semi-comatose animals.
   b. **Contraindications:** Those with disease or injuries of the esophagus. Vomiting patients. A potential complication associated with incisions greater than a few millimeters in cachectic animals is cellulitis. Therefore, incisions should be minimized (~5 mm).
   c. **Complications:** A minor problem which may occur is a temporary discharge around the stoma. This requires that the area around the tube be cleaned with warm water, and wiped dry, every two days (owners can do); usually resolves in 1 – 2 weeks. The tube may be expelled should the patient vomit. Do not feed until the position of the tube is verified to be in the normal position.

3. **Gastrostomy** tube feeding is recommended when nutritional support is required for more than 7 days. Gastrostomy tubes have remained in place for at least one year in cats and dogs while being cared for by the owner. Owner acceptance is high. Both dogs and cats tolerate the tube well and can resume normal activity around the house. The tube may be placed
   - **at laparotomy** (*see Suggested Reading 1 & 2*) OR
   - **through a left flank incision** (*see Suggested Reading 1 & 2*), OR
   - **by incisionless percutaneous placement** utilizing a flexible endoscope (*see Techniques p. 508 below*). The percutaneous placement of a gastrostomy tube is quick (15 minutes) and safe.
   - Bolus feeding should be withheld for 24 hours; however, a CRI of 5% dextrose/electrolyte solution can be infused immediately after placement. Due to the large tube size, a balanced pet food can be prepared into a gruel and passed into the stomach. This is less expensive than the prepared liquid diets. Medications can also be administered through the tube. The patient can be managed safely at home as there is no fear of aspiration due to entrapment of the epiglottis, and voluntary food and water intake can resume as the patient's health improves. (*see Enteral Nutrition Worksheet p. 506 for feeding guidelines*).
   a. **Indications.** As for esophagostomy tube and where esophagostomy tube feeding is contraindicated.
   b. **Contraindications:** Any condition where food or fluid in the stomach or duodenum is contraindicated.
   c. **Complications:** A common, minor problem is a temporary discharge around the stoma (*see esophagostomy for management*). Rarely, the animal pulls the tube out. Peritonitis is a potential problem. It is recommended that percutaneously placed gastrostomy tubes remain in place for at least two weeks to ensure a strong adhesion has formed between the stomach and abdominal wall prior to tube removal. Tubes are removed by traction while counter-pressure is placed on the abdomen, around the stoma. When voluntary food intake occurs, tube feeding should be reduced to encourage eating. In this instance tube feeding is used to supplement voluntary eating to ensure adequate daily caloric intake. Providing the tube has been in place for at least two weeks, it can be removed when the patient has consistently consumed adequate calories voluntarily for one week.

4. **Enterostomy** tube feeding is indicated when the presence of food or fluid in the stomach or duodenum is contraindicated i.e., selective cases of surgery of the stomach, duodenum and pancreas, chronic vomiting of various etiologies. Enterostomy feeding requires the use of specifically formulated liquid diets (e.g., Clinicare® or Renalcare®) because the digestive action of the stomach and duodenum is being by-passed. Technique for placement can be obtained from Suggested Reading 4. Initially commence feeding with a dextrose-containing crystalloid solution (e.g., Plasma-Lyte® 56 with 5% dextrose or Normasol® M) at 0.1 mL/kg/h, increase to 0.3 mL/kg then 0.5 mL/kg/h if well tolerated. Continue for approximately 12 hours to ensure patient tolerance of volume. At this rate, RenalCare® or CliniCare® may be mixed 1:1 with the crystalloid solution and the patient assessed for tolerance at 12 hours. The IER is then calculated and the volume of 100% liquid diet is determined (*see Enteral Worksheet for details*). It should take ~3 days to reach the patient's full caloric requirement. The volume to be administered over a 12-hour period is placed into a sterile bag and delivered as a CRI. The volume and feeding period is adjusted based on patient tolerance and clinic supervision (i.e., 12-hour practice vs a 24-hour practice). All food must be handled in a clean manner to avoid bacterial contamination and potential enteritis. *See E 6 below* if the tube becomes obstructed.

E. **General instructions for nasal, esophagostomy and gastrostomy, tube feeding.**
   1. The patient's head and neck should be elevated above the level of the stomach during feeding and for a few minutes after, to reduce the chances of reflux and aspiration. In the depressed, semi-comatose or comatose

animal place a pillow under the head to the shoulders. In the reasonably bright patient, encourage them to remain sitting, or in sternal recumbency with the head raised.

2. See Enteral Nutrition Worksheet for detailed instructions PRIOR TO FEEDING (*p. 506*).

3. In cases where **gastric emptying is prolonged,**
   a. **metoclopramide 0.2 – 0.4 mg/kg** can be administered SC or via the tube or
   b. **cisapride 2.5 mg/**(2 – 5 kg animal), **5.0 mg** (6 – 20 kg animal), **10 mg** (>20 kg animal) via the feeding tube, three times daily. Cisapride can only be formulated for veterinary use in pharmacies that specifically formulate veterinary medications.

4. No hard and fast rule can be given with ongoing feeding. Volume adjustments, (empirical reductions) may be required until gastric emptying is facilitated.

5. Delivery of food should stop if the patient appears uncomfortable (restless, vocalizes, swallows excessively, retches) as this may indicate gastric distension.

6. **Continuous tube feeding** can be delivered via the NE, esophagostomy, or gastrostomy tube (*see Enteral Worksheet p. 506 for details*). A liquid diet such as Clinicare® can be placed in an empty sterile intravenous fluid bag and delivered through intravenous tubing to the feeding tube. The food should not hang for more than 24 hours as sterility is not guaranteed during removal from the can. In the comatose or semi-comatose animal, or where delayed gastric emptying results in reduced caloric intake because of skipped meals, continuous tube feeding is recommended during clinic hours. Delayed gastric emptying typically resolves within 2 – 3 days. Should the tube block, place Coca Cola® into the tube and leave in place for 4 – 6 hours, then flush. If this fails, place a pancreatic enzyme slurry into the tube and flush after 4 hours. Longer time may be required.

TABLE 2. Preparation of Diets for Gastrostomy and Esophageal Tube Feeding

Blend at high speed for 2 – 5 minutes. Some foods may require straining through 1 mm strainer
Due to possible changes in texture of diets from batch to batch, it is recommended that the gruel made from blending canned food with water be passed through a 'test tube' ex vivo prior to feeding. Start with adding one-quarter can water and increase water content to facilitate passage through feeding tube. Dilution will not eliminate particulate material; where this is present, straining is necessary. CliniCare® or RenalCare® used out of the can will not block any sized tube provided the tube is flushed after each feeding. The following are kcal/can.

DOGS	CATS
Medical Diets Royal Canin Veterinary Diet	
Canine Renal LP 643 kcal/385 g	FelineRenal L P 125 kcal/85 g pouch
Canine Renal Medium Protein 532 kcal/380 g	Sensitivity chicken and rice 162 kcal/165 g
Canine Low Fat LF 377 kcal/385 g	Feline Sensitivity Venison and rice 85 kcal/100 g
Canine hypoallergenic 450 kcal/396 g	Feline Calorie Control 99 kcal/165 g
Canine Development 445 kcal/396 g	Feline reducing 111 kcal/170 g
Canine Gastrointestinal diet 455 kcal/396 g	Feline development 216 kcal/170
Hills	
A/D (1.2 kcal/mL) 180 kcal/170 g	Feline k/d 200 kcal/157 g
AD k/d 512 kcal/420 g	Feline k/d 517 kcal/420 g
Canine i/d 548 kcal/420 g	Feline k/d with chicken 183 kcal/157 g
Feline p/d 213 kcal/158 g	Feline c/d 164 kcal/157 g
	Feline c/d 424 kcal/420 g
	Feline c/d with chicken 166 kcal/157 g
	Feline c/d with seafood 158 kcal/157 g
	Feline p/d 213 kcal/158 g
Iams	
Eukanuba Maximum Calorie 340 kcal/170 g	Eukanuba Maximum Calorie 340 kcal/170 g
Low Residue 447 kcal/396 g	Low Residue 165 kcal/170 g
	Urinary Feline 198 kcal/156 g
	Kidney Feline 205 kcal/156 g

Purina	
Canine Gastrointestinal 543 kcal/354 g pouch Kidney Management 500 kcal/354 g	Feline Gastrointestinal 118 kcal/42.5 g Kidney Management 234 kcal/156 g Urological 217 kcal/156 g Cardiovascular 223 kcal/156 g
Prepared Liquid Diet It is suggested that these diets be diluted 50:50 with water for feeding during the first 12 hours to reduce the potential for 'cramping' and diarrhea.	
CliniCare® Canine, 0.99 kcal/mL	CliniCare® Feline, 0.92 kcal/mL RenalCare® Feline, 0.84 kcal/mL
Volume of diet required = IER (kcal/day)/energy density of diet e.g., If IER of an animal = 100 kcal/day and the blended diet had a caloric density of 0.80 kcal/mL the volume required per day is 100.0/0.8 = 125 mL.	

F. **Enteral feeding schedule for tube feeding**

1. **Bolus feeding schedule** is dependent on digestive function and gastric capacity and will vary from patient to patient (*see Enteral Nutrition Worksheet p. 506*). The **maximum distended** stomach capacity (**this will cause vomiting**) of **puppies** is 90 mL/kg, **adult dogs** 80 mL/kg; **kittens** weighing 0.5 – 1 kg is 100 mL/kg; 1 – 1.5 kg is 70 mL/kg; 1.5 – 4 kg is 60 mL/kg and **cats** 4.0 – 6 kg is 45 mL/kg. As a guide to the volume/feeding **it is recommended that less than one-third of this volume be given at each feeding** initially and increased according to what the individual can tolerate. Do not be in a hurry to achieve full feed in a patient that has been anorectic for more than five days. It should take at least 3 – 5 days to reach caloric requirements otherwise diarrhea and vomiting may occur. The goal is to achieve the IER with feeding intervals such that the owners can manage at home.

2. **Continuous (CRI) tube feeding**
   Patients with a history of vomiting (now controlled), anorexia >3 days, will benefit from a **CRI of electrolyte solution at 0.5 mL/kg/h** via an intravenous delivery set attached to the nasoesophageal, esophagostomy or gastrostomy tube immediately after placement. Hourly boluses of 0.5 mL/kg may be an alternative to the CRI, if tolerated. Intravenous fluids such as Plasma-Lyte® 56 or Normasol®M are preferred because of the dextrose and higher potassium content; however, other balanced electrolyte solutions with added dextrose are suitable. Once feeding is commenced, intravenous fluids can be reduced as enteral volumes are increased. If the electrolyte solution is well tolerated after ~ 12 hours, a **liquid diet** (CliniCare® or RenalCare®) can be diluted with the electrolyte solution (1:1) for the next 12 hours and delivered as a CRI. If this is tolerated, deliver full strength and gradually increase the volume reaching full IER over 3 days. Alternatively, a dilute blended diet can be used and delivered by small bolus feedings hourly (*see Preparation of Diets for Tube Feeding p. 504*). Bolus feeding should commence as soon as the patient can tolerate it. Specific formulations for hepatic and renal disease (i.e., low protein diets) should be used where indicated.

SUGGESTED READING

1. Bartges J. Symposium on placing feeding tubes. Veterinary Medicine 2004;99(7):587-632.
2. Howard B Seim III, Willard MD. Post-operative Care of the Surgical Patient. *In* Small Animal Surgery 2nd ed. Fossum TW, Medlund CS, Hilse DA, Johnson AL (eds). Philadelphia PA. Mosby 2002:69-91.
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ENTERAL NUTRITION WORKSHEET CATS AND DOGS: Non-critically ill

NAME _____ HOSPITAL FILE #_____

Date enteral nutrition initiated _____ Method of enteral nutrition _____

Actual body weight (BW) = _____ kg

If obese, use estimated (midpoint between ideal and actual) BW = _____ kg

A. Resting energy requirement (RER) = 70 x BW kg$^{.75}$ = _____ kcal/day

B. Illness energy requirement (IER) = RER x Factor* = _____ kcal/day
*Factors: cage rest = x 1.25; post surgery = x 1.25 – 1.35; trauma/cancer = x 1.35 – 1.5; sepsis = x 1.5 – 1.7; major burn = x 1.7 – 2.0; When **at home = x 2.0+**
Note: for cats maximum IER = RER x 1.4 unless active at home.

C. Volume of liquid diet required
Diet selected _____ Energy density of diet = _____ k cal/mL or per can. For tube feeding, add volume of water to canned diet to facilitate administration through feeding tube selected. Blend on high speed for 2 minutes. Test using a similar sized feeding tube to that placed. Add small volumes (measure) of water to the can of food (with known caloric density) until consistency of food will pass easily through the tube. Energy density/milliliter of final product = kcal of canned food ÷ final volume (mL). Volume to be administered (IER) = kcal/day ÷ kcal/mL = _____ mL /day

D. Transition to gastrostomy, esophagostomy or nasogastric feeding:

   i. Patient with prolonged anorexia:
      Day 1 = 1/3 of total requirement + remainder (2/3) as water*
      Day 2 = 2/3 of total requirement + remainder (1/3) water*
      Day 3 = total requirement (with 5 – 10 mL water to flush tube).

   ii. Patient taking some food orally:
      Day 1 = 1/2 of total requirement + remainder (1/2) water*
      Day 2 = total requirement (with 5 – 10 mL water to flush the tube).

*If patient is receiving maintenance fluids IV, proceed as above without giving water, however the tube must be flushed with 5 – 10 mL of room-body temp water. The extra water for maintenance is supplied by the IV fluids. The IV fluid volume must be decreased by the mL food + water administered via the tube. **Adjustments in fluid requirements are based on daily assessment of hydration.**

E. Frequency of feeding:
Patient dependent; q8h in acute injury setting, or q4h–q2h, or CRI (*see below*) initially in prolonged anorexia. Frequency is reduced and volume increased as patient tolerance is demonstrated. Feeding regimen outlined on a daily basis (*see instructions below*).

F. This formula is suggested for caged hospitalized animals and is only used as a guideline to calculate POTENTIAL (estimated) energy requirements. Once discharged home, energy requirements may increase to normal animal maintenance requirement ~ 2 x RER (or potentially more). Weigh and assess hydration within a few days, and then weekly to ensure that optimal weight is being achieved as weight loss or excessive weight gain may occur. Feeding and fluid adjustments should be made accordingly. One cannot predict caloric requirements. The author has requirements in excess of 2 x RER to gain lost weight and also to maintain normal weight.

VOLUME OF FOOD TO BE ADMINISTERED

Day 1: Total volume: Divide into   feedings

Day 2: Total volume: Divide into   feedings

Day 3: Total volume: Divide into   feedings

NOTES:

1. **Bolus feeding instructions for gastrostomy tubes:**

   i.   Aspirate tube with an empty syringe prior to feeding.
        If ≥50% of previous feeding, reduce next feeding by 50%. Do not replace gastric contents. **At next feeding,** if residual volume <50%, discard gastric contents and increase to normal volume, continue with feeding schedule. If ≥50% present, discard gastric contents, feed half previous volume and administer a promotility drug (cisapride or metoclopramide). **Following feedings.** Measure residual volumes until little is present, but replace gastric contents to avoid electrolyte abnormalities then discontinue measuring. No hard and fast rule can be given with ongoing feeding. Volume adjustments, (empirical reductions) may be required until gastric emptying is facilitated.

   ii. Administer room-body temperature (NOT hot) meal over 5 – 10 minutes.

   iii. Flush tube with 5 – 10 mL of warm (NOT hot) water and recap.*

2. **Bolus feeding instructions for esophagostomy and nasogastric tubes assuming previous placement confirmed:**

   i.   Aspirate tube with empty syringe prior to feeding. There should be negative pressure. If you get air continuously, retract the nasogastric tube and replace with neck ventroflexed. Test again. Radiograph the neck and thorax to ascertain proper placement of the tube if in doubt. Patients with esophagostomy tubes will require radiographic assessment, and/or anesthesia with examination of the pharynx, to ascertain position.

   ii. Administer room-body temperature (NOT hot) meal over 5 – 10 minutes with patient in sitting or sternal (forequarters raised at least 30°) position to avoid aspiration.

   iii. Flush tube with 5 – 10 mL warm (NOT hot) water and recap.*

3. **Continuous feeding instructions for all feeding tubes:**

   i.   The total volume of food calculated for a 24h period to be divided over 24h or the maximum number of hours with supervision (i.e., 12, 16, etc.) = _____ mL/h.

   ii. Periodically aspirate the tube to ensure large volumes are not pooling in the esophagus (NE tube), or being retained in the stomach (G tube). Stop feedings should this occur. Consider promotility drugs. Ensure forequarters raised if nasogastric tube placed.

   iii. *Note: Should tube obstruct, instil Coca Cola and leave for 1 – 2h (may require several hours) to digest contents.

TECHNIQUES

PLACEMENT OF NASO-ESOPHAGEAL FEEDING TUBE

Indications

Short term nutritional support for the anorectic or injured cat or dog.

Materials

A 5 Fr or 8 Fr Pediatric Feeding tube usually placed in the awake animal. Sedation is usually not required. Anesthesia of the ventral meatus is achieved using lidocaine (0.5 – 1 mL) or 5 – 10 drops of any ophthalmic local anesthetic i.e., Proparacain 2% topical solution. Do not use excessive volumes of local anesthetic to avoid desensitizing the pharynx and possible aspiration of mucus into the airways.

Technique

Pre-measure to the 7th intercostal space.

Cats

Pass the tube ventromedially into ventral meatus. Hold head in normal position but flex the neck down once the catheter has passed into the ventral meatus. This will reduce the risk of tracheal intubation. If the patient coughs pull back and redirect. The 5 Fr (15") Pediatric feeding tube will not reach 7th intercostal space in all cats. The author places so the hub of the tube sits between the cat's ears.

Dogs

Push up on the planum nasale and place as for cats. If not successful, place ventro-medially without elevation of the planum nasale. The alar fold in dogs makes the passage of the tube more difficult than cats. It must pass along the ventral meatus. Flex the neck down to avoid tracheal intubation. If coughs, pull back and re-direct.

To verify esophageal placement, aspirate the tube with a syringe. There should be negative pressure. Excessive air indicates tracheal placement; a small amount of air may normally be present in the esophagus. If tracheal placement has occurred, pull the tube back and re-direct; aspirate again. Following negative pressure on the syringe, remove the tube by approximately 2" and aspirate again, if negative pressure is still present place 5 – 10 mL sterile saline into tube (this is a check as bronchial placement of the tube may result in negative pressure). If patient coughs, replace the feeding tube. If patient licks lips or does not cough, then placement is correct. Secure tube with a very small bleb of tissue glue or Krazy glue at the junction of the lateral aspect of the planum nasale and the hair. Krazy glue causes an exothermic reaction; large blebs are very uncomfortable for the patient and cause difficulty when removing the tube. Always ensure esophageal placement prior to feeding. If the animal is depressed a cough reflex may not occur; verify position with a lateral radiograph to include the pharyngeal region to the caudal cardiac silhouette.

PERCUTANEOUSLY PLACED GASTROSTOMY TUBE

Indications

For nutritional support of long duration (> 14 days).

Methods

Percutaneous placement of a gastrostomy tube utilizing an endoscope and biopsy forcep.

Materials

An endoscope long enough to enter the stomach and a biopsy forcep.
16 gauge over the needle Sherwood catheter (without hub).
1 metre or longer, mersilene suture material.
Bard Pezzer mushroom tipped catheter 14 – 22 Fr (feeding tube).
14 Fr small cats; **16 Fr** large cats and small dogs; **18 Fr** 10 – 25 kg; **20 Fr** 25 – 40 kg; **22 Fr** >40 kg.
A French Pezzar mushroom-tip catheter (Bardex, Bard Urological Division, Mississauga, ON), is the recommended gastrostomy tube to be utilized. Balloon tip catheters should **not** be used as these are reapidly deflated by gastric acid resulting in migration of the tube out of the stomach with the potential for peritonitis.

Technique

Prepare the feeding tube using sterile instruments and gloved hands. Do not discard the package – Cut the round tip ('nipple') off the mushroom of the feeding tube to make a larger area for food to pass through. Next, make two flanges using material from the distal end of the feeding tube. Cut off the wide end. Place a 0.5 cm slit in the centre of the cut off wide end for the **outer** flange. Cut another piece of tubing, just slightly longer than the width of the mushroom at the opposite end of the catheter, to make an **inner** flange. Make a 0.5 cm slit in the middle of this piece of tubing and pass it over the feeding tube to rest next to the mushroom end. Flanges should fit snuggly over the tube but not occlude the lumen. Again, cut the end of the feeding tube to a 30 – 45° angle. Replace into the package until required.

Under general anesthesia, place the patient in right lateral recumbency. Clip and surgically prep an area 6 x 6 cm centred over the distal end of the last rib. Make a 2 mm skin incision 5 mm ventral and 10 mm caudal to the last rib. This will be a landmark for placing the Sherwood catheter. Lubricate the endoscope and pass it into the mouth. Straighten and extend the head and neck as you are passing the tube through the esophagus and into the stomach.

When the endoscope is in the stomach, visualize the light through the abdominal wall (turn the room lights down) as a guide to its location within the stomach. Inflate the stomach until it is tense and firmly against the abdominal wall. *This is important to push abdominal organs away and ensure correct anatomical placement of the catheter into the stomch. Also, if the stomach is not firmly against the abdominal wall it will push away as you attempt to pass the Sherwood catheter into the stomach.* Insert the Sherwood catheter and inner needle through the landmark incision avoiding any large gastric vessels (evaluate with scope). Remove the inner needle; pass the mersilene through the Sherwood catheter into the lumen of the stomach. Visualize the mersilene endoscopically and grab the mersilene with biopsy forceps. *Do not pull the mersilene and forceps through the endoscope.* Pull the endoscope and forceps with the mersilene as a unit into the esophagus and out of the mouth.

Remove the Sherwood catheter from the abdominal wall, over the mersilene. Place a hemostat on the mersilene to avoid inadvertent pulling into the stomach.

Take the Sherwood catheter, previously used to penetrate the skin, and *pass the suture through the lumen of the tip end exiting through the funnel end.* Suture the mersilene to the tapered end of the feeding tube using a horizontal mattress stitch. Slowly pull the suture at the tip of the catheter, pulling the tapered end of the feeding tube into the flared end of the Sherwood catheter. Stretch the feeding tube at the same time while pushing the tapered end of the feeding tube into the funnel end of the Sherwood catheter. Be sure that this coupling is smooth as it has to pass through the stomach and skin. Apply a little sterile water-soluble jelly to the catheter and feeding tube.

Pull the mersilene with steady traction, at the abdominal wall end. As the catheter appears through the skin **DO NOT PULL ON THE Sherwood CATHETER AS IT WILL PULL OFF THE FEEDING TUBE. Continue pulling the mersilene with steady traction.** If you are having difficulty pulling the Sherwood catheter through the skin, make a small (2 – 3 mm) releasing incision in the skin around the catheter. If you find it difficult pulling the wide end of the Sherwood catheter plus tube through the skin, be patient and continue with steady traction, or grasp the Sherwood catheter and the feeding tube within it as a unit as they both exit at the skin level, with a hemostat (only if you can grasp both) and pull gently. Continue to pull the feeding tube gently until you can palpate the mushroom tip against the abdominal wall.

Re-introduce the endoscope and visualize the mushroom tip and inner flange snugly against the gastric mucosa. The feeding tube should not be 'hanging' in the stomach.

Secure the tube in place by passing the outer flange (flared end of the catheter previously prepared) over the feeding tube and placing it next to the abdominal wall (not tightly). Place a small piece of tape on the feeding tube distal to the flange to prevent the flange from slipping back. Cap the tube to prevent aerophagia. A piece of tape placed adjacent to the tube over the flank area can be used to suture the tube to (not the skin) to prevent the tube from protruding through the 'shirt'.

A T-shirt or tube gauze body shirt should be placed over the feeding tube to prevent catching on furniture or chewing and pulling out. Do not place any ointment around the stoma or under the flange. Cleaning under the flange around the stoma with warm water and wiping dry is sufficient care once a week. Loosen the flange if pressure is evident.

Canned food prepared in the blender will pass easily through the tube. The tube should remain in place for at least two weeks to ensure a good adhesion. To remove the feeding tube, (withhold food for 6 hours) place counter pressure onto the abdominal wall, with one hand around the tube, and pull with gentle traction with the other hand. Place a single wrap of bandage over the stoma. The stoma will seal almost immediately. Withhold food for 8 hours. Should the tube be inadvertently removed prior to the two-week period, withhold food for a minimum of 12 hours and then only feed a very small meal for 24 hours to prevent gastric distension.

PLACEMENT OF AN ESOPHAGEAL FEEDING TUBE

Indications

Long-term nutritional support, usually longer than one week.
Where nasoesophageal feeding is contraindicated.

Contraindications

Any disease/injury of the esophagus and those for gastrostomy feedings. In patients where vomiting occurs. A potential contraindication is in a cachectic animal. These animals do not form adhesions well and leakage through the esophageal stoma may occur causing a cellulitis. A gastrostomy tube, where the tube can be stabilized (inner and outer flange – *see Gastrostomy above*) to prevent leakage, is suggested. However, extreme care with placement and maintenance is necessary.

Materials

1. Carmalt forceps of appropriate size for the patient.
2. Red rubber feeding tube of 12 – 16 Fr depending on the size of the patient. **12 Fr** small cats; **14 Fr** cats and very small dogs; **16 Fr** dogs >15 kg.
3. Suture material 2 – 0 prolene on a curved cutting needle.

Technique

Place the anesthetized patient in right lateral recumbency. On the left side, clip and surgically prep an area from the angle of the mandible to the mid-cervical region and the wing of the atlas to the trachea.
Pre-measure the catheter from the 7th intercostal space (tip of the catheter) to the point where the feeding tube will exit the esophagus (slightly distal to the hyoid apparatus) and mark with a felt pen.

Place the carmalt forceps into the mouth and into the proximal esophagus. Avoid the jugular groove.
Make a small incision (5 mm), over the tip of the carmalt forceps. Dissect medially towards the lumen of the esophagus. Make a 'nick' in the esophagus, over the carmalt forceps, and force the tip of the carmalt through the incision. Place the "closed end" of the feeding tube in a parallel fashion into the tips of the carmalt forceps and pull the tube into the esophagus. At this point, the tube can be directed posteriorly down to the distal esophagus or pulled cranially into the mouth. If the tube is pulled cranially into the mouth, the tube is then re-directed back into the oropharynx and down to the distal esophagus. The latter technique can be cumbersome BUT ensures proper placement of the tube in the esophagus and is the author's preferred method. With the former technique, the tube may inadvertently be driven through the subcutaneous tissue.

A purse-string suture is placed around the incision and snugly apposed around the tube. A finger-trap suture is placed around the tube to secure it in place. For additional security of the tube it can be fixed in place by passing the suture through the periosteum of the wing of the atlas, this may decrease tube movement and be more comfortable for the patient. The tube is capped to prevent aerophagia and comfortably bandaged. Once weekly, clean around the stoma with warm water and dry. Feed blended canned food. Flush with warm tap water after feeding to avoid clogging of the tube.

NOTES

INTRODUCTION

Parenteral nutritional support is the provision of nutritional needs via the intravenous route. **Total parenteral nutrition** (TPN) is the provision of total nutritional needs (100%) based on RER and has to be administered via a central (jugular vein) due to its hypertonicity. TPN in animals may be required if parenteral nutrition is required beyond one week. **Partial parenteral nutrition** (PPN) is administration of only a portion of the estimated RER (~40 – 70%), and is designed to allow administration via a central or peripheral vein in some instances. Parenteral solutions should **only be administered** to resuscitated and normally hydrated individuals. There are four basic components of parenteral nutrition solutions; dextrose, amino acids, lipids and electrolytes. Multivitamin preparations are added to the final solution. **Total parenteral nutrition** may be calculated using the RER equation, subtracting the protein calories from this, with the remainder being non-protein calories. Recommendations for non-protein calories: 50% be supplied as carbohydrate (dextrose) and 50% lipid solution (*see TPN p. 515 for details*).

Indications

- Critically ill patients (*category 2 see above p. 499*)
- Where the enteral route is contraindicated:
    - Gastrointestinal obstruction, impaired motility or malabsorption
    - Ischemic bowel
    - Severe diarrhea or vomiting
    - Severe inflammatory bowel diarrhea
    - Selected surgical procedures of the gastrointestinal tract
    - Moderate-severe pancreatitis
    - Imminent endoscopy
- Supplement to the enteral route where caloric requirements cannot be met
- Instances where feeding tube placement is not possible
- Other individual circumstances

Components of OVC In-house Compounded PPN Solution (see *PPN worksheet attached*)

- 330 mL of 10% amino acid solution
- 660 mL of a maintenance electrolyte solution (Plasma-Lyte® 56 or Normasol M® – 5% dextrose)
- Lipid (10% or 20% solution) added based on requirement

Preparation of PPN

Ideally preparation of PPN should be performed under a fume hood but in veterinary practice, a clean area such as the surgery room will suffice. Mask, cap and sterile gloves must be worn. **Standard final product of 1 litre** = 330 mL **amino acid** (**3.3%** or **33.3 g/L protein**) and 660 mL of **5% dextrose/electrolyte solution** (**3.3%** dextrose or **33.3 g/L**) this equates to **protein 4 kcal/g (133 kcal/L [0.133 kcal/mL])** and **dextrose (112 kcal/L) [0.112 kcal/mL])** for a **total of 245 kcals/L**. When administered through a central line, the dextrose content may be increased (*see Hypoglycemia p. 280 for calculations*). However, caution is advised (*see Potential Complications p. 512 below*). Lipids 10 – 50% are administered to make up all, or a portion of, the 50% non-protein calories. Animals receiving propofol as a CRI, may not require lipid supplementation as the lipid requirement may be exceeded in the propofol formulation. The recommendations in critically ill human patients is to deliver 30 – 60% of their total estimated caloric requirement. This standard PPN solution, with adjustments made in lipids administered, will provide this. The **osmolarity** of the PPN solution is ~650 mOsm/L which is hyperosmolar to plasma (290 – 310 mOsm/L). The addition of lipids (350 mOsm/L) will reduce this somewhat depending on the volume administered. Even though PPN can be administered peripherally in larger dogs, in small patients (<15 kg) phlebitis will occur at 24 hours; therefore, it is recommended that the solution be delivered through a central line. However there are always rare exceptions. With utmost care, PPN may be introduced through the highest (most proximal) port in the maintenance fluid line where fluids are run at maintenance, or higher, rates. In small patients, if PPN cannot be diluted with crystalloid fluids then delivery through the jugular vein is required. An alternative is to reduce the amino acid content to 170 mL/L rather than 330 mL/L, and deliver at twice maintenance rate through a peripheral catheter. Animals in renal failure or hepatic disease should receive a one-third reduction in amino acid content (220 mL vs 330 mL of 10% Travasol). Do not add the lipid to the PPN until it is to be administered. Lipid should hang no longer than 48 hours. If a thin oil layer begins to form the solution should be discarded. The lipid bottle should not be invaded repeatedly.

Other recommendations for caloric requirements in veterinary medicine for PPN is 0.7 X RER, with a range of 25% – 60% of the non-protein calories as lipid (large dogs to small dogs and cats respectively), added to the PPN solution.

Commercial products that may be delivered peripherally are 2.75% amino acid + 5% dextrose (Clinimix and Quickmix, Clintec Nutrition, Deerfield, Il., USA) and 3% amino acids + 3% glycerol (ProcalAmine, McGraw Inc., Irvine, CA, USA). Similar to the compounded PPN above, these products only provide 30% – 50% of RER.

Administration

If peripheral administration is desired, a 22 gauge (for animals <15 kg) or 20 gauge (for animals >15 kg) catheter is placed in a peripheral vein. The **smallest gauge catheter** is advised to reduce phlebitis. Catheters made from violon material (Becton-Dickinson Vascular Access, Sandy, Utah) are used by the author for all peripheral IV fluid administration as they are minimally thrombogenic. Thrombophlebitis is a major concern with parenteral nutrition, therefore teflon catheters should not be used. Strict aseptic technique is required for placement and maintenance. When catheters are placed into the jugular vein (contraindicated in patients with a coagulopathy or head injury), catheters made from the least thrombogenic material should be used. Hind limb administration is not recommended due to the potential of urine and fecal soiling. However, if a large gauge catheter is placed into the medial or lateral saphenous in the hope that it is placed into the caudal vena cava, you must ensure that it is placed in that vein prior to PPN administration. A **severe phlebitis/cellulitis** will occur (~24 – 36 hours) if placed into the smaller femoral or iliac vein. A wide area over the catheter insertion site should be shaved and prepared as for a surgical procedure. Material in contact with the catheter insertion site should be sterile. The covering bandage must be changed whenever soiled. The catheter should be dedicated to PPN delivery, if this is not possible, adapters (Multi-flo Adapter, Becton-Dickinson Vascular Access, Sandy, Utah) placed into the hub of the catheter facilitating independent fluid administration of 2 or 3 different infusions may be a viable option where a second catheter cannot be placed. An exception is for smaller animals discussed above, **BUT absolute aseptic technique** when invading the line is essential (wipe the injection port closest to the patient with alcohol, allow to dry ~ 1 minute). **Prior to drug administration,** clamp the administration IV line, flush with 0.9% saline, slowly administer the medication with a slow flush of 0.9% saline, then open the clamp on the IV line. Many commonly used medications are compatible with amino acid solution (*see Suggested Reading 2 below*). All connections should be wrapped in tincture of chlorhexidine or povidone-iodine soaked gauze. The line should not be disconnected for any reason (walks, diagnostics etc.). The line should be clamped off, or the infusion pump taken with the patient (to diagnostic areas) with PPN continually running. The delivery lines should be changed every 48h. Should the line become disconnected at the catheter hub and not contaminated, clean all around the catheter hub with alcohol and attach a new IV extension set. If an extension set is not used, change the IV delivery set. If gross contamination has occurred, the catheter should be replaced into a different vein.

Volume to be Administered

At the OVC-VTH, the PPN is usually given at hourly fluid maintenance rate (cage rest 1.2 x Body weight in kg[♦75] *see Fluid Chart p. 366*) initially. Use the actual body weight unless obese where an estimate between actual and ideal weight can be used. Based on calculations of content given above, 1L of standard PPN would last 24 hours for a 25 kg dog based on a normal maintenance fluid rate (**normal** sensible and insensible losses), ongoing losses are delivered separately with a crystalloid solution. As fluid requirements and caloric requirements are usually the same, normal maintenance is calculated as cage rest (IER = 1.2 x RER). For the 25 kg example, the RER = 782 and IER is (782 kcal x 1.2) = 936 kcal/24h. Therefore, the standard compounded solution without lipids (133 protein and 112 carbohydrate kcal) would provide 245 kcal/L/936 kcal or 0.26 of the IER for our 25 kg dog. However, PPN can be delivered up to 1.5 times maintenance depending on the condition of the patient. Up to 50% of the non-protein calories (936 – 133 = **803 non-protein kcal**) can be administered as lipid (400 kcal). The lipid solution is either added directly to the PPN solution where volume allows (~100 mL can be forced into a full 1L bag), or delivered via a separate infusion pump into the PPN line, or the PPN plus lipid can be compounded in smaller (e.g., 500 mL) bags for small patients. Delivering the lipid within the PPN line is advised as this will reduce the osmolarity of the delivered solution. The basic crystalloid maintenance solution should be reduced accordingly to avoid fluid overload in the patient. Multi-vitamins are added (*see Parenteral Nutrition p. 511*).

Potential Complications

The major problem associated with PPN is phlebitis and perivascular extravasation. Thrombophlebitis of the jugular vein has rarely occurred in dogs receiving 50% of non-protein calories as lipid. Careful monitoring of the venipuncture site and surrounding area should be performed several times daily, especially in small and active animals. Should any swelling occur, the infusion should be stopped and the catheter removed. Hot pack the area several times daily. If there is any clinical indication of sepsis, perform complete blood count and physical examination. Remove the catheter and

culture a 1 cm length from the tip to identify any bacterial growth as a cause of infection. Due to the adequate amino acid concentration and low glucose concentration of these parenteral solutions, increased urea and hyperglycemia are usually not a problem. However, these parameters should be monitored q48h at least. As the glucose concentration of the standard solution is only 3.3%, this can be raised. However, it will be necessary to deliver through the jugular vein as the osmolarity will be too high for any sized peripheral vein. It has been this author's experience that increasing the dextrose concentration to higher than 7%, especially in weak animals, increases respiratory effort. It is assumed that the metabolism of the carbohydrate increases CO_2 production requiring an increase in the work of breathing to ventilate and remove the CO_2. Imposing this extra work utilizes energy and is counterproductive. Depending on the concentration of lipid hyperbilirubinemia may occur, especially in patients with liver disease, sepsis or after several days of administration of >40% lipid calories. This is due to parenteral nutrition-induced hepatic lipidosis and is reversible after discontinuing the lipids. In the author's experience the administration of lipids to patients with severe pancreatitis appears to worsen their condition. Another guideline suggested for patients with pancreatitis is not to administer lipids if serum triglyceride levels are increased. Fluid overload may occur if crystalloid solutions are not reduced during PPN administration. Weigh the patient daily. Should there be any weight loss or gain over time, determine whether this is due to inadequate, or excessive fluids, or inadequate nutritional support. PPN should be discontinued once enteral intake is approximately 50% of IER.

PHARMACOLOGY

1) **Travasol™**, (Baxter) is a 10% (100 g/L) amino acid and electrolyte solution containing non-essential and all essential (except taurine with regards to cats) amino acids and non-essential. The electrolyte composition is Na 70 mEq/L, Phosphate 60 mEq/L, Cl 70 mEq/L, Ca 0 mEq/L, K 60 mEq/L and Mg 10 mEq/L.

2) **Intralipid®**, (Clintec) is a fat emulsion containing fractionated soybean oil, fractionated egg phospholipids and glycerin. The osmolality is 350 mOsm/kg water. This product should be stored in a glass container at room temperature or in the refrigerator once invaded. As this product is a great medium for bacterial growth, frequent invasion is contraindicated. Once the bottle has been invaded it should be used within 48h. It is suggested that an IV delivery set with a filtered vent be inserted into the bottle which is then delivered to the patient. After 48h this should be discarded and replaced if necessary.

3) **Magnesium sulfate** is an important electrolyte in critical illnes as many patients are depleted (*see Magnesium p. 403*). Attention must be paid to the concentration of magnesium in the preparation. Most pharmaceutical preparations label the weight in mg/mL as heptahydrated magnesium sulphate which is much heavier than the atomic weight of elemental magnesium i.e., 200 mg/mL heptahydrated magnesium sulphate = 0.8 mmol/mL = 1.6 mEq/mL. Dosing recommendations in mg usually refers to the heptahydrated magnesium or salt of magnesium (e.g., magnesium sulphate) on the label.

SUGGESTED READING

1. Chan D. Parenteral Nutritional Support. In Textbook of Veterinary Internal Medicine, 6th Edition. Ettinger SJ, Feldman EC eds. St. Louis, MO. Saunders Elsevier;2005:586-591.
2. Trissle LA. Handbook on Injectable Drugs 12th ed. American Society of Health-System Pharmacists, Bethesda, Maryland. 2003.

NOTES

PARTIAL PARENTERAL NUTRITION (PPN) WORKSHEET
for cats and dogs

Actual body weight = _____ kg

If obese, approximate between actual and estimated ideal body weight = _____ kg

A.   Resting energy requirement (RER):
  = 70 x Body weight in kg$^{.75}$ = _____ kcal/day

B.   Illness energy requirement (IER):   = factor   x RER ~ energy expenditure
  – cage rest   = 1.20   x RER
  – post surgery   = 1.25 – 1.35 x RER
  – trauma or cancer   = 1.35 – 1.5   x RER
  – sepsis   = 1.5 – 1.7   x RER
  – major burn   = 1.7 – 2.0   x RER
  – cats as above but to a maximum of   = 1.4   x RER

  IER = factor_____ x RER = _____ kcal/day. Protein calories 4 kcal/g (133 kcal/L [0.133 kcal/mL])=
  _____ administered in this solution. Non-protein calories = RER – protein calories _____. Carbohydrate in
  this solution is dextrose 0.112 kcal/mL (112 kcal/L).

C.   A **3.3%** amino acid solution (maximum concentration for peripheral vein) is required. In patients <15 kg a 1.75%
  solution is to avoid phlebitis; ~2.2% for renal and hepatic failure.

Materials

  i.   10% amino acid with electrolytes (10 g/100 mL). Travasol®, Baxter.

  ii.   Isotonic electrolyte solution containing 5% dextrose (IES 5%), Plasma-Lyte® 56 or Normasol® M.

  To prepare a 1L 3.3% solution, remove 330 mL from the bag of IES 5% (save for oral supplement) and
  add 330 mL of amino acid solution to each bag. For small quantities add 33 mL amino acid per 100 mL
  final solution and place in a burette. (For animals <15 kg add 18 mL amino acid per 100 mL).

  Deliver at hourly, maintenance fluid requirement: Calculate daily fluid requirements (1.2 x BER = 70 x
  BW kg $^{.75}$ = ____ mL) ÷ 24 for hourly rate = ____.

  iii. 20% lipid (2 kcal/mL). To supply up to 50% of non-protein calories (_____ kcal) need _____ mL of lipid.
  Do not use in lipemic patients or in patients with severe fulminant pancreatitis. Use 10% in liver disease;
  20 – 30% in sepsis. Lipids can be added to the amino acid/dextrose 5% solution or delivered separately.
  Lipid adsorbs into plastic therefore add to the bag for no longer than 48h. To prevent contamination,
  avoid multiple invasions of the bottle. Deduct calories received via a propofol infusion.

  iv.   Multivitamins (MVI – 12) should be added at 0.25 mL/kg/day. Should be added to a ≤24 hour volume.
  Vitamin K$_1$ 0.5 mg/kg SC on 1st day and weekly as necessary. When not contraindicated, add 10 mL of
  10% calcium gluconate to each litre of solution to give a Ca concentration of 5 mEq/L.

  v.   Electrolyte content of the final solution must be considered to avoid overdosing on potassium. There is
  60 mEq/L (0.06 mEq/mL) potassium in original amino acid solution (Travasol) with 330 mL (~ 20 mEq
  K$^+$) added to the IES/5% solution which contains 13 mEq/L (~9 mEq K$^+$) with a total of ~30 mEq/L K$^+$
  in the solution. This is the average K$^+$ concentration in our maintenance solutions.

D.   This PPN solution is given at hourly fluid maintenance rate initially (*see Fluid Chart p. 366*), and increased if
  tolerated to meet the patient's needs.

COMPONENTS OF TPN SOLUTION

A. **10% amino acid solution with electrolytes added** (e.g., Travasol®, Baxter Corp.). Provides protein requirements. This is an all-purpose solution which contains all the essential amino acids for dogs and cats, with the exception of taurine. If a low aromatic amino acid solution is required for severe liver disease with encephalopathy, Hepatamin® should be considered. Renal failure patients can be managed with a lower volume of Travasol® (*see TPN Worksheet p. 517*).

B. **20% lipid solution** (e.g., Intralipid®, Clintec Inc.). To provide up to 50% (some recommend up to 70%) of the non-protein calories (*see TPN Worksheet p. 517;* provide <30% in liver disease or sepsis. Contraindicated in hepatic lipidosis. Avoid in patients with severe pancreatitis due to occurrence of jugular vein thrombosis observed by the author even with heparin therapy.

C. **50% dextrose solution.** Can provide up to 50% of the non-protein calories (see TPN Worksheet). It is suggested that only half this amount be used on the first day. In the author's experience, higher levels of dextrose tend to increase CO_2 production and subsequently the work of breathing to eliminate it. In ventilated patients where there is a fixed tidal volume, hypercarbia is noted with excessive dextrose infusions. Occasionally hyperglycemia, hyperosmolality and glycosuria occurs requiring insulin therapy. In the short term (~72 hours), continue with 25% of non-protein calories as dextrose (or half the calculated volume required) to avoid these problems especially when lipids are being administered. The full dextrose requirement can be slowly increased after 72h especially if lipids are not being administered and the patient can tolerate it. Blood and urine glucose should be monitored at least once daily.

D. Final TPN solution should have electrolyte concentrations as follows:

Sodium 35 – 45 mEq/L   Chloride 35 – 45 mEq/L
Potassium 35 – 45 mEq/L   Phosphate 10 – 15 mmol/L
Calcium 4 – 5 mEq/L   Magnesium 4 – 5 mEq/L

Additional electrolytes may be added according to the patient's needs. As an alternative to adding the electrolytes to the TPN solution, they can be added to crystalloid fluids which are administered through a peripheral line. This is advised as changes in rate of administration and concentration can be made easily through the peripheral line, whereas the TPN solution is more difficult to change.

E. Multivitamins (e.g., M.V.I.-12®, Rhone-Poulenc Rorer) to provide all fat- and water soluble vitamins except vitamin K_1 which is administered subcutaneously once weekly. With liver pathology (i.e., hepatic lipidosis) and an increased activated clotting time (>125 sec in the dog and >95 sec in the cat), vitamin K_1 0.5 – 1 mg/kg q12h SC is recommended for 2 – 3 days or longer if indicated.

F. Heparin 1 U/mL (1,000U/L) may be added to the final TPN solution to reduce thrombosis, maintain catheter patency and enhance lipid clearance.

PREPARATION OF TPN SOLUTION

- Preparation of TPN solution ideally is performed under a fume hood. However, in veterinary practice a clean area, such as the surgical suite, will suffice. Sterile gloves, mask and cap should be worn.

- The solutions are mixed in order of dextrose to amino acids, followed by the addition of lipids (optional). The solution (without vitamins) can hang at room temperature for 48h.

- Lipids can be piggy-backed into the TPN line from a separate bottle. Filtered vents are required for the lipid bottles, or the lipid can be removed and added aseptically to a burette. Lipids are stored at room temperature.

- If dextrose, amino acids and lipids are pooled, it is recommended that ethylene vinyl acetate bags with filtered vents be used. This solution can be stored in the refrigerator for a week. Polyvinylchloride bags can only be used if the solution is used immediately after compounding as the leaching of diethylhexylphthalate may occur with storage.

- Extra crystalloid solution can be added to make the volume up to daily maintenance. A second IV line however, is preferred for additional fluids.

- Strict aseptic technique is required at all levels. All ports should be swabbed with 70% alcohol. Bacteria grow rapidly in lipid and amino acid solutions.

ADMINISTRATION

A. A central catheter is placed via the jugular vein. Strict aseptic technique is required for placement and maintenance of catheters and IV lines. Materials in contact with the insertion site must be sterile. All connections should be wrapped in tincture of chlorhexidene or povidone-iodine soaked gauze. The catheter should be dedicated to TPN delivery. Blood sampling or injections of medications should not be performed through this catheter. The delivery lines should be changed q48h.

- The covering bandage must be changed whenever soiled. If the line becomes disconnected at the catheter hub, clean all around the catheter hub with alcohol and replace the IV extension set. If an extension set is not in-line, change the IV delivery set. If gross contamination has occurred, the catheter should be replaced into a different vein if possible.

- The hourly rate of administration is based on the total calculated daily volume divided by 24.

- If the patient cannot be supervised on a 24 h basis, the volume should be divided by as many supervised hours as possible (~15 h). The infusion is then stopped and the line flushed (utmost sterility) with 2 mL sterile heparinized (10 U/mL) saline, dedicated to this patient, to prevent catheter occlusion. Hyperglycemia (due to increased volume) and subsequent hypoglycemia (during off feeding) may occur and should be avoided. Volume overload and sepsis (due to catheter invasion) also are potential problems.

- Blood and urine glucose should be monitored daily. Hyperglycemia may occur in dogs and frequently occurs in cats. Should this persist, reduce the glucose by half. If this continues add 10 Units of Regular insulin/L solution. Hyperglycemia should be prevented to avoid polyuria and dehydration and hyperosmolar syndrome. An increase in lipid calories (if possible) can compensate for the reduced carbohydrate-source calories. Examine the animal carefully for possible sepsis if hypoglycemia persists in the absence of insulin.

- Serum urea should be monitored q24h until TPN administration and the patient are stable. If urea is increased in the presence of normal creatinine and a stable, euvolemic patient, an excess of protein calories may be the cause. Reduce the protein by 1g/kg/day and reassess the urea in 24 h. Patients with renal insufficiency should have a lower protein content of the TPN. If urea is elevated in these patients, reduce the protein by 0.5 g/kg/day.

- Serum electrolytes should be monitored daily. If hypokalemia occurs, supplement with added potassium (*see Hyperkalemia/Hypokalemia p. 394*). Hypokalemia is not unusual if insulin is added to the TPN solution. Magnesium levels should also be monitored as these are frequently below normal and can contribute to hypokalemia. In severe deficiency magnesium sulphate 1 – 1.5mmol/kg (2.0 – 3.0 mEq, 20 – 40 mg/kg) – *see Pharmacology p. 513 for definition*) administered over 3 – 4 hours 2 – 3 times daily for one day, and reduced thereafter depending on the serum levels. This will also increase serum potassium. And improve patient well-being. Must ensure normal serum calcium prior to magnesium therapy.

- Lipemia may occur within 2 to 3 days and the amount of lipid should be reduced. Hyperbilirubinemia may occur in patients with liver disease, sepsis or after several days of administration. This is due to TPN-induced hepatic lipidosis and is reversible after discontinuing the lipids.

- If there is any clinical indication of sepsis, perform complete blood count and physical examination. Remove the bandage and examine catheter site. If there is any evidence of contamination/infection, remove catheter and submit a 2 cm length from the tip for culture and sensitivity. Place another catheter in the opposite side when signs of infection have resolved.

- Weigh the patient daily. Should there be any weight change over time determine whether this is due to inadequate or excessive fluids, or inadequate nutritional support.

- Total parenteral nutrition should be discontinued as soon as enteral intake is 50% of IER. Discontinue TPN by decreasing the volume by one-third each hour. Hypoglycemia is the major concern with discontinuation of TPN.

TOTAL PARENTERAL NUTRITION (TPN) WORKSHEET: DOGS

NAME _____ HOSPITAL FILE # _____

Date TPN initiated

Actual body weight (BW) = _____ kg

If obese, use estimated ideal BW = _____ kg

A. Basal energy requirement (BER) = 70 x BW kg$^{0.75}$ = _____ kcal/day

B. Illness energy requirement (IER) = BER x Factor* = _____ Non-protein kcal/day 1

*Factors: cage rest = x 1.25; post surgery = x 1.25 – 1.35; trauma/cancer = x 1.30 – 1.5; sepsis = x 1.30 – 1.7; major burn = x 1.7 – 2.0; cats = up to x 1.4

C. Protein requirement:

Adult dog = 4 g/100kcal/day 1   = IER x 0.04 = _____ g/day
Dog with extraordinary protein loss = 6 g/100kcal/day1   = IER x 0.06 = _____ g/day
Dog with renal failure = 1.5 g/100kcal/day1   = IER x 0.015 = _____ g/day

D. Volumes of nutrient solutions required:

  a. 10% amino acid solution* = 100 mg protein/mL. Volume = 10 x protein requirement. (C above)
                                       = _____ mL/day

  b. 20% lipid solution (e.g., Intralipid) = 2 kcal/mL. To supply up to 50% of non-protein calories
     = IER (B above) x 0.5 = _____ kcal ÷ 2 = _____ mL of lipid solution/day
     [Do not use lipid in lipemic, hypertriglyceridemic or severe fulminant pancreatitis patients. Deduct caloric volume received via a propofol infusion].

  c. 50% dextrose solution = 1.7 kcal/mL. To supply up to 50% of non-protein calories
     = IER (B above) x 0.5 = _____ kcal ÷ 1.7 = _____ mL 50% dextrose/day
     [Use 1/2 this amount on 1st day and increase to full amount on 3rd day if no glucosuria or increase in respiratory rate].

E. Total volume of TPN solution = Da) + Db) + Dc) = _____ mL/day
+ Extra fluids added: _____ mL of _____ = Total _____ mL/day
Divide total by 24 = _____ mL/h FOR 24 HOURS

F. Extra fluids
  i. Add 10 mL 10% calcium gluconate per litre of solution (calcium concentration of 5 mEq/L) or more if hypocalcemic (*see Hypocalcemia p. 377*)= _____ mL

  ii. Add 2.5 mL/10 kg/day Multivitamins (MVI-12) immediately prior to administration = _____ mL

  iii. Other additives: e.g., Magnesium 1.0 – 1.5mmol/L (2.0 – 3.0 mEq, 20 – 40 mg/kg)

G. Vitamin K. Administer 0.5 mg/kg vitamin K SC on 1st day and weekly thereafter = _____ mg

Repeat dates: _____   _____   _____

Note: Recommended electrolyte concentrations for the final solution:
    Na 35-45 mEq/L   Phosphate 10 – 15 mmole/L
    Cl 35-45 mEq/L   Ca 4 – 5 mEq/L
    K 29-35 mEq/L   Mg 4 – 5 mEq/L

If modification to this electrolyte composition is required, note changes: _____

TOTAL PARENTERAL NUTRITION (TPN) WORKSHEET: CATS

NAME _____ HOSPITAL FILE # _____

Date TPN initiated

Actual body weight (BW) = _____ kg

If obese, use estimated ideal BW = _____ kg

A. Basal energy requirement (BER) = 70 x BW kg$^{.75}$ = _____ kcal/day
For cats >2 kg   BER = [30 x BW kg] + 70 = _____ kcal/day

B. Illness energy requirement (IER) = BER x Factor* = _____ Protein + Non-protein kcal/day _____
*Factors: cage rest = x 1.25; post surgery = x 1.25 – 1.35; trauma/cancer = x 1.30 – 1.4;
sepsis = x1.30- 1.4; major burn = x 1.4

C. Protein requirement:

Adult cat = 5 g/100kcal/day   = IER x 0.05   = _____ g/day
Cat with renal or hepatic failure = 3.5 g/100kcal/day   = IER x 0.035 = _____ g/day
Protein calories = 4 kcal/g, therefore protein contribution to IER = 4 x above   = _____ kcal/day

D. Volumes of nutrient solutions required:
  a. 10% amino acid solution* = 100 mg protein/mL. Volume = 10 x g protein requirement (C above)
     = _____ mL / day
  b. 20% lipid solution (e.g., Intralipid) = 2 kcal/mL. To supply 20% to 50% of non-protein calories
     = [IER (B above) – protein kcal (C above)] x 0.2 – 0.5 = _____ kcal ÷ 2 = _____ mL of lipid solution/day
     [Do not use lipid in lipemic, hypertriglyceridemic or severe fulminant pancreatitis patients].
  c. 50% dextrose solution = 1.7 kcal/mL. To supply 35 to 50% of non-protein calories
     = Non-protein kcal x 0.35 - 0.5 (as per 'b' above) = _____ kcal ÷ 1.7 = _____ mL 50% dextrose/day
     [Use 35% on 1st day and increase to full amount on 3rd day if no glucosuria or increase in respiratory rate or
     effort is noted].

E. Total volume of TPN solution = Da) + Db) + Dc) = _____ mL/day
+ Extra fluids added: ____ mL of _____ = Total _____ mL/day
Divide total by 24 = _____ mL/h FOR 24 HOURS

F. Extra fluids
  i. Add 10 mL 10% calcium gluconate per litre of solution (calcium = 5 mEq/L) = _____ mL

  ii. Add 1.5 mL/5 kg/day multivitamins (MVI-12) immed. prior to administration = _____ mL

  iii. Other additives: i.e., increase calcium and magnesium if indicated

G. Vitamin K$_1$. Administer 0.5 mg/kg SC on 1st day and weekly thereafter = _____ mg
Repeat dates:
Note: Recommended electrolyte concentrations for the final solution:
     Na 35 – 45 mEq/L, Cl 35-45 mEq/L, K 29-35 mEq/L,
     Phosphate 10 – 15 mmole/L, Ca 4-5 mEq/L, Mg 4-5 mEq/L.

     If modification to this electrolyte composition is required, note changes: _____

Further Notes: Dogs & Cats

i. The patient's jugular catheter is now a dedicated line, where possible do not use it for giving medications, or taking blood samples. If the line is used for blood sampling, there is a great risk of infection. The blood must be flushed out of the catheter immediately. Do not measure CVP or break the line for any reason. When moving the animal, clamp the line, remove the unit from the pump, and carry the bag with you, being sure to keep the drip chamber upright. Preferably, take the pump with the patient, keeping the bag above the pump. If medications are to be given, a peripheral catheter should be placed. If this is not possible, call a hospital pharmacist regarding medications compatible with TPN or *refer to Suggested Reading 2.* Only single use ampules for drug administration must be used (no multi-vial meds). The risk of sepsis increases with any invasion of the line (*see Fluid Therapy – Central line maintenance p. 370*).

ii. Monitoring is very important in patients on TPN. Special attention to attitude, hydration status and respiratory rate and effort should be made frequently. The orders should also include:

– weight q24h (same scale, same time of day)
– check urine for glucose at least q12h
– check body temperature at least q12h

iii. If you have any questions or problems, contact a local hospital pharmacist. If you are not experienced in TPN preparation, you are advised to contact a hospital pharmacist or veterinary nutritionist prior to preparation.

iv. ★Travasol® 10% Amino acid solution contains:

Na 70 mEq/L	Phosphate 30 mmole/L
Cl 70 mEq/L	Ca 0 mEq/L
K 60 mEq/L	Mg 10 mEq/L

NOTES

INTRODUCTION

Ocular emergencies are conditions that lead to significant vision reduction, vision loss or loss of the globe if not treated rapidly after recognition of the problem. Ocular proptosis and glaucoma are two typical examples. Few emergencies need immediate surgical treatment but they all have to be treated medically as quickly as possible. The removal of a penetrating corneal foreign body is a typical example of a surgical emergency. Most conditions listed below can wait to see a specialist for 12 – 24 hours if the necessary medical treatment is started right away.

NOTE: Many of the surgical techniques described in this chapter are considered "referral surgeries".

TRAUMATIC PROPTOSIS

INTRODUCTION

Proptosis is an acute extreme forward displacement of the eye beyond bony orbit and eyelids.

DIAGNOSIS

History/Signalment

- Commonly associated with trauma (i.e., hit-by-car, facial trauma and dog fights), occurring most often in brachycephalic breeds.
- Excessive physical restraint may also be a predisposing cause!

Clinical Signs/Physical Examination

- Extreme exophthalmos with the eyelid margins trapped behind the eye at the orbital rim.
- The medial rectus muscle is often damaged resulting in lateral deviation of the globe (strabismus).
- Conjunctival hyperemia, hemorrhage and chemosis because of the trauma.
- Corneal desiccation and ulceration develop quickly because of inability to blink.
- Intraocular hemorrhage, uveitis, pupillary abnormalities, blindness or a combination thereof can be present as a result of the trauma.
- Assess duration, degree of exophthalmos, strabismus, corneal drying, corneal ulceration, pupillary light reflexes, intraocular damage, and intraocular pressure.
- Pupil size is **not** a good prognostic indicator.

Prognosis:
- Prognosis for vision is guarded to poor.
- Prognosis for the globe is good to poor, depending on extent of trauma.
- **Fair prognosis:** if mild damage, and short duration.
- **Poor prognosis if:**

  – severe facial trauma
  – optic nerve rupture
  – severe muscle damage
  – extensive corneal drying and ulceration
  – globe rupture
  – intraocular damage (hyphema)
  – glaucoma
  – proptosed for >3h without treatment
  – most cats and dolichocephalic dogs have a poor prognosis

●wners should be warned that blindness and strabismus may persist.

Goals are to prevent further damage by desiccation and reposition globe as soon as possible.

A. Stabilize patient and keep cornea moist!!! As long as the eye is completely covered with antibiotic ointment (neomycin, polymixin B, bacitracin/gramicidin or fusidic acid) no further desiccation will happen. A saline soaked gauze can be placed on the eye.

B. Surgical

1. **Enucleate** the eye if optic nerve is ruptured, multiple extraocular muscles are severed or the eye is severely traumatized (laceration) (**Fig. 1a**).
2. **Reposition** the eye, as soon as patient is stable enough. The goal is to close and suture eyelids over globe (**Fig. 2**). This temporary tarsorrhaphy is necessary to prevent globe from re-proptosing. In brachycephalics gentle pressure on globe may be enough to reposition globe.
3. A third eyelid flap is not strong enough to keep globe in position and adds pressure to the globe!
4. Leave tarsorrhaphy for 14 – 21 days. An Elizabethan collar will prevent further damage to the area. Remove sutures earlier only if persistent pain, copious mucopurulent discharge, or pyrexia develop.

C. Medical

1. Topical antibiotics: Triple antibiotics (neomycin, polysporin B, bacitracin/gramicidin or fusidic acid) are effective against a large number of bacteria. Drops and ointments are available. Apply 3 – 6 times daily.
2. Topical atropine 1%: Drops and ointments are available. Apply 2 – 4 times daily. Atropine relaxes muscle spasms in iris and ciliary body and moves iris away from lens by dilating it. This will prevent synechia formation and reduce discomfort. Use if there is uveitis or a miotic pupil and the intraocular pressure is normal or low.
3. Topical steroids (prednisolone 1%, dexamethasone 0.1%): Apply 3 – 4 times daily only if cornea is **not** ulcerated to reduce intraocular inflammation.
4. Systemic broadspectrum antibiotics.
5. Systemic anti-inflammatories: prednisone 1 mg/kg, aspirin 10 mg/kg or meloxicam 0.1 mg/kg to reduce orbital and ocular inflammation.

D. Preparation for Referral

1. Stabilize patient, examine eye and cover eye completely with lubricating/antibiotic ointment, then refer.

LID INJURIES

History/Signalment
- Frequently associated with trauma and bite wounds.

Clinical Signs/Physical Examination
- Lid trauma is associated with swelling, edema, hemorrhage, loss of lid margin or a combination thereof. Lacerations can be partial or full thickness.
- Globe and nasolacrimal system could be injured as well.

Prognosis:
- Prognosis is good if laceration is attended to quickly and repair is performed technically correct.

Goals are to prevent further damage by rubbing and repair to regain normal function.

A. Medical

1. Apply cold compresses to contused eyelids.
2. Topical antibiotics (neomycin, polymixin B, bacitracin/gramicidin or fusidic acid): apply 3 times daily to treat or prevent infection.
3. Systemic broadspectrum antibiotics.
4. An Elizabethan collar will prevent further damage.

B. Surgical

1. If the lid margin is involved, repair the eyelid surgically as soon as possible. Assess the eye and patient carefully before general anaesthesia.
2. Repair eyelids quickly for first intention healing.
    a. Wound debridement is minimal to avoid additional loss of tissue.
    b. Lids are very vascular and infection is unlikely.
    c. Do not use soap for preparation because of irritation to the cornea and conjunctiva. Be careful with clipping to avoid further trauma.
    d. Eyelid margins must be apposed perfectly. Always start suturing at the eyelid margin! **ALL LID SUTURING MUST START AT THE EYELID MARGIN.**
    e. Avoid suture contact with globe on conjunctival side.
3. Repair a full thickness eyelid lesion with 2 layer suturing for added strength.
    a. Simple V-shaped laceration: Use 5:0 – 6:0 absorbable suture (polyglactin 910) for tarsoconjunctiva or deep layers in a simple interrupted or continuous pattern, and 4:0 nonabsorbable (silk/nylon) for skin.
    b. First skin suture: figure-8 or simple interrupted at lid margin followed by simple interrupted sutures.
    c. Irregular laceration: reappose lid margin <u>first</u> as above, then place strategic sutures to allow proper apposition, then fill in the gaps with simple interrupted sutures.
4. Repair large eyelid defects with sliding skin and conjunctiva or buccal mucosal grafts. If using sliding grafts with possibility of corneal irritation from skin hairs and sutures, use third eyelid flap or temporary tarsorrhaphy for corneal protection.
5. For extensive laceration requiring debridement, debride the minimal area necessary for accurate closure. Create fresh viable tissue edges. Fill defect with sliding skin/conjunctival grafts.
6. For lacrimal canaliculi involvement; cannulate punctum and canaliculus with nylon suture. Use nylon to thread polyethylene tubing through the punctum and canaliculus and suture tubing in place. Leave tubing for 3 weeks or more. Repair laceration of skin and conjunctiva in usual manner. Sutures remain in place for 7 – 10 days.

C. Preparation for Referral

Perform detailed eye exam to determine extent of trauma. Keep wound moist by applying antibiotic ointment, then refer.

CONJUNCTIVAL INJURIES

INTRODUCTION

Conjunctival lacerations are rare without damage to other tissues.

DIAGNOSIS

History/Signalment
- Cat scratch, foreign body, contusion.

Clinical Signs/Physical Examination
- Examine globe carefully when conjunctival injuries present.
- Subconjunctival hemorrhage is common after trauma.

MANAGEMENT

Goal is to prevent infection.

A. No treatment is necessary if conjunctival surface is intact and eye is normal.

B. Surgical

    a. Conjunctival lacerations do not need suturing if sclera and lids are intact.

C. Medical

    a. Triple antibiotics (neomycin-polymixin-B, bacitracin/gramicidin): apply 3 – 4 times daily or fusidic acid 2 times daily if there is a conjunctival wound.

DIAGNOSIS

CORNEAL INJURIES

History/Signalment
- Blunt or sharp trauma, chemical burns.

Clinical Signs/Physical Examination
- Corneal injuries can result in a variety of lesions from superficial abrasions to full-thickness lacerations.
- Topical anaesthesia or even sedation may be necessary to examine the eye carefully.
- Perform neurological evaluation before sedation.
- Use fluorescein dye to evaluate extent of corneal damage.
- Examine eyelids and 3rd eyelid for foreign bodies or injuries.
- Examine eye carefully to determine how severely affected the intraocular structures are.

Prognosis:
- Prognosis is good to poor depending on severity of trauma.

Laboratory:
- Take swab for culture and sensitivity testing if mucopurulent discharge present.
- Also consider taking sample for cytology if organisms are suspected.

MANAGEMENT

See below under:
- Superficial corneal ulcers.
- Deep corneal ulcers.
- Complicated infected corneal ulcers/melting ulcers.
- Penetrating/perforating corneal wounds.
- Ocular foreign bodies.
- Ocular chemical burns.

UVEAL INJURIES

INTRODUCTION

Uveal trauma causes inflammation of the uveal tissue including iris, ciliary body and choroid.

DIAGNOSIS

History/Signalment
- Blunt or sharp trauma. Blunt trauma may result in uveitis only, while sharp injuries will affect other tissues as well.

Clinical Signs/Physical Examination

Prognosis:
- Prognosis is good to poor depending on severity of trauma.

See below under:
- Anterior uveitis
- Hyphema
- Retinal detachment

SUPERFICIAL CORNEAL ULCERS

DIAGNOSIS

History/Signalment
- Trauma or spontaneous development in older animals, foreign body, Herpes (FHV1) infection in cats.

Clinical Signs/Physical Examination
- All or a combination of the following clinical signs can be present.
- Blepharospasm, epiphora.
- Conjunctival hyperemia, conjunctival swelling.
- Superficial corneal lesion (shallow defect!), corneal edema in ulcerated area.
- Possibly mild secondary uveitis with miosis.
- Fluorescein dye positive.

Prognosis:
- Prognosis is good if there is no infection present.

MANAGEMENT

Goals are to prevent or alleviate infection and support healing.

A. Medical

DO NOT USE STEROIDS ON ANY ULCERATED CORNEAS!
1. Topical antibiotics: triple antibiotics (neomycin, polymixin B, bacitracin/gramicidin) 4 – 6 times or fusidic acid 2 – 4 times daily.
2. Topical atropine 1%: apply 2 – 4 times daily or to effect. Atropine dilates the pupil by relaxing the iris muscles. Use it if the pupil is miotic.

DEEP CORNEAL ULCERS

DIAGNOSIS

History/Signalment
- Trauma, foreign body, progression from superficial ulcer due to infection, underlying KCS (keratoconjunctivitis sicca).

Clinical Signs/Physical Examination
- All or a combination of the following clinical signs can be present.
- Blepharospasm, epiphora or mucopurulent discharge, swollen lids.
- Hyperemic conjunctiva and sclera.
- Corneal edema, **deep crater** in corneal surface, corneal cellular infiltrates, corneal vascularization if chronic.
- Aqueous flare, miotic pupil.
- Fluorescein dye positive in ulcerated area. Descemet's membrane does not stain with fluorescein.

Laboratory:
- Swab of affected area for corneal culture and sensitivity, and scraping for cytology to look for bacteria and condition of cells.

Prognosis:
- Prognosis is guarded. Could lead to rupture of globe!

MANAGEMENT

Goals are to prevent or alleviate infection, restore corneal thickness, and support healing.

A. Medical
1. Topical antibiotics: (tobramycin 0.3%, or ciprofloxacin 0.3%): apply every hour to every 4 hours daily.
2. Topical atropine 1%: apply 2 – 4 times daily to dilate pupil, decrease discomfort and prevent synechiae.
3. If patient is very uncomfortable oral aspirin 10 mg/kg or meloxicam 0.1 mg/kg can be given.

Never prescribe topical anesthetic for ulcer treatment. Proparacaine is very epitheliotoxic if used repeatedly!

B. Surgical
1. If the cornea is so thin that a rupture of the eye is anticipated, surgical intervention to strengthen the cornea is necessary. A conjunctival flap, a corneal-conjunctival transposition or glue is indicated.
2. A third eyelid flap is contraindicated on descemetoceles or large stromal defects because of pressure on the globe. This can lead to rupture underneath the flap.
3. After surgery medical therapy is continued as described above.

C. Preparation for Referral
1. If referring immediately, place E-collar. Otherwise take a swab, start with the medical therapy immediately, place E-collar, then refer.

COMPLICATED INFECTED CORNEAL ULCERS/MELTING ULCERS

INTRODUCTION

Corneal ulcers not responding to medical therapy need to be carefully assessed to determine the cause of the refractory behaviour. Culture and sensitivity testing and cytology from the affected area need to be done.

DIAGNOSIS

History/Signalment
- Trauma, progression from superficial ulcer to complicated ulcer because of infection, and/or rapid breakdown of corneal collagen that leads to melting appearance. The breakdown can be caused by pseudomonas, streptococci, fungi and extensive damage to keratocytes can cause melting.

Clinical Signs/Physical Examination
- All or a combination of the following clinical signs can be present.
- Blepharospasm, mucopurulent discharge, swollen eyelids.
- Hyperemic and chemotic conjunctiva, hyperemic sclera.
- Edematous cornea, **yellow corneal infiltrates** in ulcerated area, **gelatinous**, soft, protruding cornea if melting.
- Aqueous flare, miotic pupil, uveitis, possible blindness.
- Positive fluorescein dye test.

Laboratory:
- Swab for culture and sensitivity and scraping for cytology.

Prognosis:
- Prognosis is guarded to poor. Patients need intensive medical and possibly surgical therapy. Often leads to rupture of globe.

Goals are to prevent rupture, alleviate infection/melting, restore corneal thickness, and support healing.

A. **Medical**
1. If gram+ organisms or cocci are found on cytology, medical therapy should include Cefazolin eyedrops. Dissolve 1 g of Cefazolin powder with 10 mL of sterile water and apply one drop to eye every 1/2 hour to 2 hours.
2. If gram- organisms or rods are found on cytology medical therapy should include tobramycin 0.3% or ciprofloxacin 0.3% or ofloxacin 0.3%. Apply to eye every 1/2 hour to 2 hours.
3. If both types of organisms present treat by alternating both medications.
4. Topical atropine 1%: apply 4 – 6 times daily to dilate pupil, to decrease discomfort and prevent synechiae.
5. Systemic broadspectrum antibiotics (amoxicillin, cephalosporines, clavamox).
6. Low dose systemic anti-inflammatories like aspirin 5 – 10 mg/kg or meloxicam 0.1 mg/kg to decrease inflammation and discomfort.
7. If cornea has melting, "mushy" appearance apply autologous serum topically every 1 hour to 4 hours. Take blood from dog or cat, let stand for 10 minutes, spin, remove serum and keep in red-top tube, fill tuberculin syringe and apply serum to eye. Keep in refrigerater. Renew every 48 hours.

B. **Surgical**

DO NOT PERFORM STRIATE KERATOTOMY ON A COMPLICATED ULCER!

1. If corneal melting cannot be stopped or if rupture is imminent surgical repair is required.

C. **Preparation for Referral**
1. If referring immediately, place E-collar. Otherwise take swab, start medical therapy, place E-collar, then refer.

PENETRATING/PERFORATING CORNEAL WOUNDS

INTRODUCTION

Penetrating and perforating corneal injuries are surgical emergencies which require general anesthesia. They need to be repaired quickly, ideally within 24 hours. If at all possible a careful assessment of the eye and extent of damage is performed.

DIAGNOSIS

History/Signalment

- Sharp trauma, severe blunt trauma, progression from superficial to deep ulcer with perforation due to infection, melting or foreign body. In young dogs often due to cat scratch.

Clinical Signs/Physical Examination

- All or a combination of the following clinical signs can be present.
- Blepharospasm, epiphora, mucopurulent or blood-tinged discharge, swollen eyelids.
- Conjunctival and scleral hyperemia.
- Corneal edema, corneal infiltrates, corneal vascularization if chronic, fibrin and hemorrhage at site of perforation, iris prolapse.
- Aqueous flare, miotic pupil, anterior synechia, intraocular hemorrhage, blindness.

Laboratory:
- Corneal swab for culture and sensitivity.
- Corneal scraping for cytology if progression of infected ulcer.

Prognosis:
- Prognosis is good to guarded if minimal intraocular trauma and quick repair (within 24 hours).
- Prognosis is guarded to poor if severe intraocular trauma or delay in repair (>48 hours).
- Prognosis is poor if globe sustained severe blunt trauma.

Goals are to save globe if possible, restore comfort, and restore vision if possible.

A. Medical Presurgical
Medical treatment always precedes surgical treatment:
1. Topical antibiotics eyedrops (neomycin, polymixin B, bacitracin/gramicidin, or tobramycin 0.3%, or ciprofloxacin 0.3%) every hour. Do **not** use topical **ointment** because of toxic effects when penetrating into eye!
2. Topical atropine 1%: apply every 2 hours to dilate pupil, decrease discomfort and prevent synechiae.
3. Systemic broadspectrum antibiotics.
4. Systemic anti-inflammatories (aspirin 10 mg/kg, meloxicam 0.1 mg/kg).

B. Surgical
1. Most penetrating corneal wounds require a conjunctival flap or a corneo-conjunctival transposition to strengthen the damaged cornea at the wound site.
2. If intraocular content is protruding through a large wound, if eye cannot be examined because of intraocular hemorrhage or if eye is severely deformed enucleation should be considered (**Fig. 1b**).
3. If fibrin plug and/or iris is in the small corneal wound, and if intraocular tissues and pupil can be identified surgical repair can be successful.

C. Medical Postsurgical
1. Topical antibiotics solutions (tobramycin 0.3%, ciprofloxacin 0.3%, ofloxacin 0.3%): apply 4 – 6 times daily.
2. Topical atropine 1%: apply 2 – 4 times daily.
3. Topical steroids or NSAID may be considered if no infection present (prednisolone, dexamethasone, diclofenac) to reduce uveitis: 3 – 4 times daily.
4. Systemic broadspectrum antibiotics.
5. Systemic steroids (prednisone 1 mg/kg) or NSAID (aspirin 10 – 15 mg/kg, meloxicam 0.1 mg/kg).

D. Preparation for Referral
1. Start medical therapy, place E-collar, then refer.

OCULAR FOREIGN BODIES

INTRODUCTION

Ocular foreign bodies are often very painful. Sedation may be necessary to perform examination. Try to determine location of foreign body and assess damage done to ocular tissues.

History/Signalment
- Many foreign bodies are of plant material.

Clinical Signs/Physical Examination
- Clinical signs depend on location, size of foreign body and chronicity.
- Behind 3rd eyelid and under lids: Painful eye with blepharospasm, epiphora or mucopurulent discharge, conjunctival hyperemia, protrusion of 3rd eyelid, and possible concurrent corneal ulceration.
- On cornea: Often painful eye with blepharospasm, serous to mucopurulent discharge, corneal lesion.
- In cornea: Painful eye with blepharospasm, serous to mucopurulent discharge, corneal lesion and possible secondary uveitis with aqueous flare and miotic pupil.
- Through cornea: Painful eye with blepharospasm, serous to mucopurulent discharge, corneal lesion, secondary uveitis with aqueous flare and miotic pupil, possible injury to lens and iris.

Prognosis:
- Prognosis is good to guarded if foreign body behind third eyelid or lids, on cornea or in cornea with minimal corneal damage.
- Prognosis is guarded to poor if foreign body through cornea, into lens or iris or severe damage to cornea.

Goals are to remove foreign body safely, prevent or alleviate infection, restore comfort.

A. Medical

1. Topical antibiotics (tobramycin or fusidic acid): every hour until removal.
2. Topical atropine 1%: apply 2 – 4 times daily if pupil miotic.
3. Systemic broadspectrum antibiotics if foreign body through cornea.
4. Systemic anti-inflammatories: aspirine 10 mg/kg, meloxicam 0.1 mg/kg if foreign body through cornea.

B. Surgical

1. Foreign bodies on surface of cornea may be flushed out or removed under topical anesthesia using a cotton tip applicator.
2. Intracorneal foreign bodies need to be removed surgically under general anesthesia. A corneal incision is often necessary. The cornea is sutured with 8-0 polyglactin 910 (vicryl) or similar absorbable material.
3. Foreign bodies perforating the cornea and entering the anterior chamber should not be removed without being ready to suture the cornea. A corneal incision under general anaesthesia is often required.
4. If the lens is damaged lens extraction is indicated. Lens perforation results in severe medically uncontrollable phacoclastic uveitis in almost all patients.
5. Foreign bodies in the posterior segment may not be accessible without additional severe trauma to the eye.
6. If intraocular infection is suspected or severe intraocular damage enucleation is performed (Fig. 1a, b).

C. Preparation for Referral

1. Start medical therapy immediately, place Elizabethan collar to avoid further damage and mildly sedate especially if foreign body penetrates cornea and could cause more damage to eye during transport, then refer.
2. Do not remove penetrating foreign body.

OCULAR CHEMICAL BURNS

INTRODUCTION

Can cause severe corneal ulceration and damage to the ocular surface. Alkaline substances cause most serious damage to cornea resembling a melting ulcer. Acid ulcers don't tend to progress as deeply as alkaline ulcers.

DIAGNOSIS

History/Signalment
• Caused by alkalis, acids or detergents.

Clinical Signs/Physical Examination
• All or a combination of the following clinical signs can be present.
• Often severe discomfort with blepharospasm and epiphora, later mucopurulent discharge.
• Lid swelling, lid abrasions, conjunctival hyperemia, swelling, ulceration.
• Corneal ulceration, edema, and melting.
• Secondary uveitis with aqueous flare and miotic pupil.

Prognosis:
• Prognosis is guarded to poor depending on extent and substance.

MANAGEMENT

Goals are to remove toxic agent, prevent infection, and prevent rupture of globe.

A. Medical
1. Wash eye with large volumes of saline.
2. Apply autologous serum every hour to every 4 hours if cornea is melting (*see melting ulcer p. 525*).
3. Treat like complicated ulcer with topical broadspectrum antibiotics (tobramycin 0.3%, or ciprofloxacin 0.3%) 4 – 6 times daily.
4. Topical atropine 1%: apply 2 – 4 times daily.

B. Preparation for Referral
1. Lavage with copious amounts of saline, start antibiotic therapy, then refer.

ANTERIOR UVEITIS

INTRODUCTION

Inflammation of the anterior uvea, including iris and ciliary body.

DIAGNOSIS

History/Signalment
- Can be caused by trauma, neoplasia, systemic inflammatory or infectious diseases and occurs concurrently with corneal ulceration.
- Most common infectious causes in the cat include **FIP, FeLV, FIV** and **Toxoplasmosis**.
- **Blastomycosis** and **Leptospirosis** are more often diagnosed in the dog.

Clinical Signs/Physical Examination
- All or a combination of the following clinical signs can be present.
- Blepharospasm, epiphora due to pain and photophobia.
- Swollen lids if severe inflammation and conjunctiva and scleral hyperemia.
- Corneal edema due to endothelial damage.
- Keratic precipitates, aqueous flare, -/+ hyphema, fibrin and/or hypopyon are present in the anterior chamber because of leaky blood vessels. Aqueous flare is seen in eyes with uveitis as a result of an increase in protein and cells.
- Miotic pupil due to iris muscle spasm.
- Thickened, swollen iris, discoloration of iris.
- Thorough eye exam and physical exam to determine presence of underlying systemic disease.

Laboratory:
- CBC and chemistry profile.
- Serology (esp. cats) for common infectious diseases: FIV, FeLV, and Toxoplasmosis in cats, Ehrlichia, Leptospirosis, and appropriate diseases in dogs.
- UA, possibly chest radiographs to determine presence of infection, inflammation, and neoplasia.

Prognosis:
- Prognosis is good to poor depending on the severity and chronicity of uveitis.

Goals are to treat underlying disease, decrease uveal inflammation, prevent posterior synechiae, restore comfort and maintain or regain vision.

A. Medical

If underlying disease is identified, specific therapy is commenced immediately.

1. If there is no corneal ulcer: topical steroids (prednisolone acetate 1%, dexamethasone 0.1%) or NSAID (diclofenac, ketoralac) 4 – 12 times daily.
2. For anti-inflammatory treatment use strong medication like prednisolone acetate and dexamethasone phosphate.
3. If concurrent use of an antibiotic is preferred choose neomycin-polymixin-B-dexamethasone (Maxitrol), or tobramycin-dexamethasone (Tobradex). Do not use a combination medication which contains hydrocortisone, it is not strong enough to treat intraocular disease. Gentocin-betamethasone (Gentocin Durafilm) is more effective than hydrocortison combinations.
4. Topical atropine 1%: apply 2 – 6 times daily or to effect to dilate pupil. Atropine is used to dilate pupil to prevent posterior synechia formation by keeping iris away from lens, and to relieve iris and ciliary body spasms that cause discomfort.
5. Systemic NSAID (aspirin 10 mg/kg, meloxicam 0.1 mg/kg).

B. Preparation for Referral

1. Thorough eye exam, physical exam, and laboratory tests as described above. Start uveitis treatment with anti-inflammatories and atropine, then refer.

HYPHEMA (Blood in the Anterior Chamber)

History/Signalment

- Hyphema can be a result of trauma, severe uveitis, intraocular neoplasia, pre-iridal fibrovascular membrane or, especially if bilateral, bleeding disorders or other systemic diseases. In most cases hyphema is accompanied by moderate to severe uveitis.

Clinical Signs/Physical Examination

- Depend on severity of hemorrhage.
- **Acute hyphema:** anterior chamber is partially or totally filled with fresh bright red blood. Conjunctival and scleral hyperemia, corneal edema, aqueous flare, or a combination thereof.
- **Chronic hyphema:** blood becomes dark red and a blood clot may form.
- Possibly intraocular fibrin, and miotic pupil.
- Often intraocular structures cannot be identified and the patient is blind.
- Low, normal or high intraocular pressure possible.
- Thorough exam of both eyes and physical exam.
- Ultrasound of the eye may be required to check for vitreal hemorrhage, retinal detachment, neoplasia.

Laboratory:
- Coagulopathy work up (platelet count, clotting time, PTT, APT).

Prognosis:
- Prognosis is good if minor trauma and hyphema restricted to anterior chamber.
- Prognosis is guarded to poor if sign of coagulopathy or other systemic diseases.
- Prognosis is poor if severe trauma, neoplasia or hemorrhage also in vitreous.

Goals are to restore vision, prevent further hemorrhage, and find the underlying cause.

A. Medical

1. Topical steroid (prednisolone acetate, dexamethasone): 3 – 4 times daily, if no corneal ulcer present.
2. Topical atropine 1%: apply 2 – 4 times daily, or to effect if pupil can be seen.

   Check intraocular pressures before and during treatment. Atropine is contraindicated if intraocular pressure is high normal to above normal (>23 mmHg), and if pupil is dilated.

   Mild hyphema resolves in 10 – 14 days.

B. Preparation for Referral

1. Thorough eye and physical exam. Start treatment, then refer.

ACUTE GLAUCOMA

INTRODUCTION

Acute glaucoma is a true ophthalmic emergency. If the problem is not recognized quickly the high intraocular pressure (IOP) will result in permanent damage to optic nerve and retina and cause irreversible blindness.

Normal IOP is 15 – 28 mmHg. On the Schiotz Tonometer scale: 3 – 10 is normal with 5.5 gram weight.

DIAGNOSIS

History/Signalment

Primary glaucoma:

- Breed related, hereditary, no concurrent ocular disease, caused by goniodysgenesis (abnormal drainage angle): Pectinate ligaments are not formed properly.
- Bilateral, but not usually at the same time (6 months – 2 years between eyes), average age 5 – 8 years old.
- May develop because of abnormal biochemical metabolism at the trabecular cells.
- Breed predisposition: Bassett, American and English Cocker Spaniels, Siberian Husky, Toy and Miniature Poodle, and many others also reported.

Secondary glaucoma:

- Group of primary diseases in which IOP can become elevated: Severe uveitis with posterior synechiae and iris bombé, intraocular neoplasia, anterior lens luxation, pre-iridal fibrovascular membrane, very large number of iris cysts, or rapidly enlarging intumescent cataract, cellular debris and more.
- Unilateral or bilateral.

Mechanisms that lead to glaucoma:

- Obstruction of drainage angle:
  - Neoplasm (melanoma): direct infiltration of angle
  - Preiridal fibrovascular membrane: occluding pupil and angle (result of chronic inflammatory process)
  - Melanocytes (in melanocytic glaucoma): accumulation in drainage angle
  - Large numbers of iris and ciliary cysts: interfering with drainage
  - Peripheral anterior synechiae: occlusion of drainage angle

- Pupillary block glaucoma: movement of aqueous humor through pupil is blocked
  - Intumescent (swollen) cataract
  - Anterior lens luxation or subluxation
  - Vitreous prolapse, attached to displaced lens or free
  - Posterior synechia with iris bombé

Congenital glaucoma:

- Anterior segment anomaly causes increased IOP soon after birth. Unilateral or seldom bilateral, isolated defect or with other systemic anomalies.

Clinical Signs/Physical Examination

Acute primary glaucoma:
- Painful if pressure is very high, little pain in early glaucoma.
- Conjunctival mild hyperemia to severe congestion, scleral hyperemia to severe congestion due to reduced venous drainage.
- Mild to generalized severe corneal edema because of damage to corneal endothelium.
- Mydriatic (dilated) pupil in primary glaucoma because of pressure on nerves and muscles.
- From normal menace response and pupillary light reflexes to blind with non-responsive pupil depending on IOP and duration and the resulting damage to retina and nerve.
- Intraocular structures may not be visible due to severe corneal edema.

Prognosis:
- Prognosis for primary glaucoma is guarded to poor.

Acute secondary glaucoma:
- If glaucoma is secondary to other diseases additional clinical signs will be seen.
- Anterior chamber may be filled with hyphema, fibrin, hypopyon (white blood cells), tumor mass, or a sub- or luxated lens.
- Pupil size depends on cause of glaucoma.

Prognosis:
- Prognosis for secondary glaucoma depends on cause of glaucoma, severity of primary disease and severity and chronicity of glaucoma. It ranges from good to poor.

Chronic glaucoma:
- Mildly to severely painful eye depending on pressure and size of eye.
- Enlarged globe and blind with absent pupillary light reflex due to optic nerve and retinal damage.
- Corneal edema because of endothelial damage.
- Fibrosis, vascularization, ulceration of cornea and endothelial tears due to stretching.
- Possible secondary lens luxation.
- Retinal atrophy, optic nerve cupping.

MANAGEMENT

Goal is to reduce intraocular pressure as fast as possible!

A. Medical Treatment for Acute Glaucoma
1. The first step in glaucoma therapy is to reduce the pressure to prevent further damage.
2. When the pressure has returned to normal range, think about cause of glaucoma and further management can be contemplated.
3. Start with Mannitol **and** topical anti-glaucoma medications immediately to reduce the pressure as fast as possible. Intravenous Mannitol 20 – 25%: 2 g/kg. Given intravenously as 1 g/kg bolus over 20 min. Easiest when intravenous catheter placed. Followed by 1 g/kg slowly over 30 – 40 min. No water for 2 – 3 hours after Mannitol treatment.
4. Mannitol therapy can be repeated after 12 hours if pressure still high.
5. Topical carbonic anhydrase inhibitors (CAI): Dorzolamide 2% (Trusopt) and Brinzolamide 1% (Azopt). Apply 3 times daily.
6. Oral carbonic anhydrase inhibitors are not recommended because of the new and safer topical CAIs. If still used: Methazolamide (Neptazane). Apply 2.5 – 10 mg/kg twice daily.
7. Topical sympathomimetics: Dipivefrin 0.1% (Propine). Apply 2 – 3 times daily.
8. Topical beta-blockers: Timolol maleate 0.5% (Timoptic), Betaxolol 0.25% (Betoptic), Levobunolol 0.5%. Apply 2 – 3 times daily.

B. For Primary Glaucoma Only
Both these medications cause miosis which is contraindicated in certain secondary glaucomas.
1. Topical prostaglandin analogues: Latanaprost 0.005% (Xalatan) or Travoprost 0.004% (Travatan). Apply 1 – 2 times daily.
2. Topical parasympathomimetics: Pilocarpine 1 – 4%. Apply 1 – 4 times daily (uncomfortable).
3. Topical pilocarpine is often recommended as glaucoma treatment. It is safe to use in primary glaucoma cases, however, dangerous to use in cases with uveitis and anterior lens luxation! It increases permeability of blood vessel and therefore further exacerbates uveitis. It may cause a pupillary block and severely increased IOP in eyes with anterior lens sub- or luxation.

C. Additional Therapy Depends on Cause of Glaucoma
1. If uveitis, see topic above.
2. If anterior lens luxation, see topic below.
3. If intraocular neoplasia, recommended treatment: enucleation.

D. Surgical
1. If medical therapy does not lower IOP "surgical" therapy may be tried: laser cyclophotocoagulation, cyclocryotherapy, valve placement, shunt placement (referrals).

E. Surgical Treatment for Chronic Glaucoma
1. If a patient has an obviously enlarged globe the glaucoma has been present for a prolonged period, and damage has occurred (not a true emergency).
2. Enucleation (Fig. 1a, b), evisceration with prosthesis or chemical ablation of the ciliary epithelium.

F. Preparation for Referral
1. Start glaucoma treatment, then refer.

ANTERIOR LENS LUXATION

INTRODUCTION

Anterior lens luxation can cause glaucoma because of pupillary block and obstruction of the iridocorneal angle.

DIAGNOSIS

History/Signalment

- Inherited condition in the Terrier breeds, Border Collie, Shar pei and others.
- In other breeds and cats anterior lens luxation is usually secondary to chronic uveitis or glaucoma.
- Chronic uveitis weakens the zonules, enlargement of the globe in glaucoma stretches the zonules.

Clinical Signs/Physical Examination

- Primary anterior lens luxation is usually painful because of the secondary glaucoma.
- Blepharospasm, epiphora, conjunctival and scleral hyperemia.
- Corneal edema axially and ventrally due to rubbing of lens on endothelium.
- Lens in anterior chamber with iris trapped behind it, deep anterior chamber, lens acts like magnifying glass. By examining the eye from the side the lens can most easily be identified in the anterior chamber.
- Severity of signs depend on severity of glaucoma.

Prognosis:
- Prognosis is good if IOP normal or elevated mildly for short period of time and lens removed quickly.
- Prognosis is guarded to poor if chronic with high IOP.

MANAGEMENT

Goals are to reduce IOP, remove lens and restore vision if possible.

A. Medical
Glaucoma therapy is started prior to surgery to reduce intraocular pressure.

B. Surgical
An anteriorly luxated lens needs to be removed surgically.

C. Preparation for Referral
Start anti-glaucoma therapy, then refer.

ACUTE BLINDNESS

RETINAL DETACHMENT

INTRODUCTION

Most patients with retinal detachment are presented because of acute vision loss. Blindness occurs with complete bilateral detachments.

DIAGNOSIS

History/Signalment

- Causes of retinal detachment include: systemic inflammatory diseases (uveodermatologic syndrome), systemic infectious diseases (fungal), intraocular neoplasia, hypertension, bleeding disorders, severe trauma and idiopathic.
- Detachments are either rhegmatogenous (with retinal tear) or non-rhegmatogenous. In the cat, the most common cause for retinal detachment is hypertension.

Clinical Signs/Physical Examination

- Abnormal menace responses and abnormal pupillary light reflexes. Pupils often widely dilated.
- Retinal vasculature may be seen with a focal light source when looking at the eye from a distance because the retina has moved anteriorly to be placed just behind the lens.
- The retina is seen as a grey veil containing blood vessels in the vitreous cavity.
- If the retina is torn in periphery, it may fold and fall ventrally covering the optic nerve head and exposing a hyperreflective tapetum (rhegmatogenous detachment).

Prognosis:
- Prognosis is guarded to poor depending on duration and severity of detachment and underlying disease.
- Thorough eye exam and physical exam.

Laboratory:
- Laboratory tests to possibly identify underlying infectious or inflammatory diseases include CBC, chemistry profile, UA.
- Check systemic blood pressure in cats and dogs to rule out hypertension.
- Chest x-rays, abdominal ultrasound.

MANAGEMENT

Goals are to treat underlying cause and reattach retina if possible.

A. Medical

1. If no infection suspected, systemic steroids: Prednisone 2 mg/kg.
2. If anterior uveitis present, see above.

OPTIC NEURITIS

INTRODUCTION

Patients with optic neuritis often have a history of acute vision loss.

DIAGNOSIS

History/Signalment
- Often unknown. Possible causes include granulomatous meningo-encephalitis, distemper, toxoplasmosis, and blastomycosis.

Clinical Signs/Physical Examination
- No mencace responses, no pupillary light reflexes, widely dilated pupils.
- +/- abnormal (swollen, red) optic nerve head (if papilla involved in inflammatory process), or normal optic nerve head (if inflammation in posterior portions of nerve).
- Retina looks normal.
- Thorough eye and neurological exam.

Laboratory:
- CBC, chemistry profile, UA, to possibly find indications of infectious or inflammatory diseases.
- CSF, CT, MRI to better investigate the extent.

Differential Diagnosis:
- Differential Diagnosis: If optic nerve looks normal optic neuritis is difficult to differentiate from sudden acquired retinal degeneration (SARD). An electroretinogram demonstrates normal retinal function with optic neuritis.

Prognosis:
- Prognosis is good to poor depending on cause and duration.
- Pale optic nerve suggests optic atrophy.

MANAGEMENT

Goals are to find underlying disease and restore vision.

A. Medical
1. Look for underlying disease and treat it.
2. Systemic steroids for idiopathic optic neuritis: Prednisone 2 mg/kg.

Untreated optic neuritis results in optic nerve atrophy with irreversible blindness.

SUDDEN ACQUIRED RETINAL DEGENERATION (SARD)

INTRODUCTION

SARD often affects middle age, female, overweight, small dogs. Some dogs also show signs of Cushing's disease.

DIAGNOSIS

History
- The cause is unknown. A toxic effect on the retina is suspected because of the rapid destruction of the retina.

Clinical Signs/Physical Examination
- No menace responses, absent or moderately to severely reduced pupillary light reflexes, mid to fully dilated pupils in room light, no other abnormalities.
- Diagnosis is made by electroretinography. It demonstrates partial to complete loss of retinal function.
- Differential Diagnosis: Without an electroretinogram SARD is difficult to differentiate from optic neuritis.
- Prognosis is poor for vision.

A. Medical

1. There is no therapy for SARD.
2. If uncertain whether patient has SARD or optic neuritis treat for optic neuritis of inflammatory nature treat for optic neuritis if considered safe (no underlying infectious disease). Optic neuritis responds to steroid therapy often within hours; if no response in 24 – 48 hours diagnosis of SARD more probable.

PHARMACOLOGY/FORMULARY

Topical antibiotics:

Bacitracin, neomycin, polymixin B:	Bacitracin zinc 400IU, neomycin sulphate 3.5 mg, polymixin B 5000 IU/g ointment
Ciprofloxacin:	Ciprofloxacin hydrochloride 3.5 mg/mL solution
Fusidic acid:	Fusidic acid 10 mg/mL slow release solution
Neomycin, polymixin B, gramicidin:	Neomycin 75 mg, polymixin B 10 000 IU, gramicidin 0.025 mg/mL solution
Ofloxacin	Ofloxacin 3 mg/mL solution
Tobramycin	Tobramycin 3 mg/g(mL) ointment or solution

Topical steroids and non-steroidals:

Dexamethasone:	Dexamethasone sodium phosphate 0.5 mg/g ointment, 1 mg/g(mL) ointment, suspension or solution
Diclofenac:	Diclofenac sodium 1 mg/mL solution
Ketoralac:	Ketoralac tromethamine 5 mg/mL solution
Prednisolone:	Prednisolone acetate 1 mg/mL, 1.25 mg/mL or 10 mg/mL suspension

Topical antibiotic/steroids:

Gentamicin, betamethasone:	Gentamicin 3 mg, betamethasone 1 mg/mL solution
Neomycin, polymyxin B, dexamethasone:	Neomycin 3.5 mg, polymixin B sulphate 6000 IU, dexamethasone 1 mg/mL suspension
Tobramycin, dexamethasone:	Tobramycin 3 mg, dexamethasone 1 mg/g(mL) ointment, or suspension

Topical anti-glaucoma medications:

Dipivefrin:	Dipivefrin hydrochloride 1 mg/mL solution
Dorzolamide:	Dorzolamide hydrochloride 20 mg/mL solution
Latanaprost:	Latanaprost 50 μg/mL solution
Pilocarpine:	Pilocarpine hydrochloride 10 mg/mL, 20 mg/mL, 30 mg/mL, 40 mg/mL solution
Timolol maleate:	Timolol maleate 2.5 mg/mL or 5 mg/mL solution
Travoprost:	Travoprost 40 μg/mL solution
Brinzolamide:	Brinzolamide suspension 10 mg/mL

Topical mydriatics:

Atropine:	Atropine sulphate 5 mg/mL solution, 10 mg/mL(g) solution or ointment

Topical anesthetics:

Proparacaine:	Proparacaine hydrochloride 5 mg/mL solution
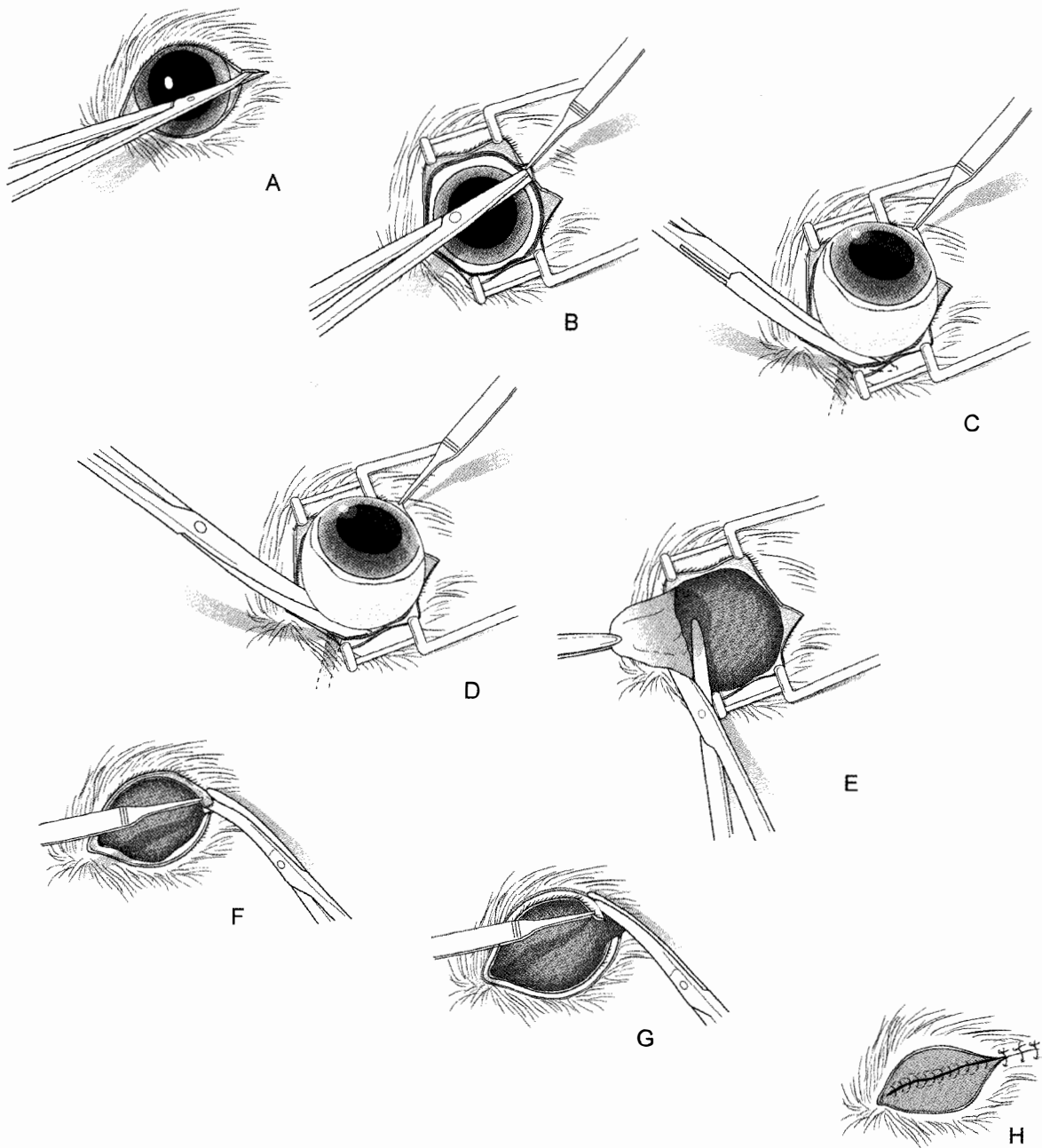
FIGURE 1a. Subconjunctival Enucleation.

A. The lateral canthus is extended to allow for better exposure.

B. The bulbar conjunctiva is incised with scissors 3 mm posterior to the limbus 360 degrees. The globe is dissected free using blunt dissection and by severing the muscle attachments at the insertions.

C. One or two curved hemostats are placed on the optic nerve and vessels for 5 minutes.

D. The clamps are taken out and the globe is removed using scissors.

E. The third eyelid is removed completely.

F. The palpebral conjunctiva is dissected along the lids and removed.

G. The lids are incised 3 mm posterior to the margin and removed using a scalpel and scissors.

H. At least one deep simple continuous layer of absorbable suture is placed before the skin is closed with simple interrupted sutures.
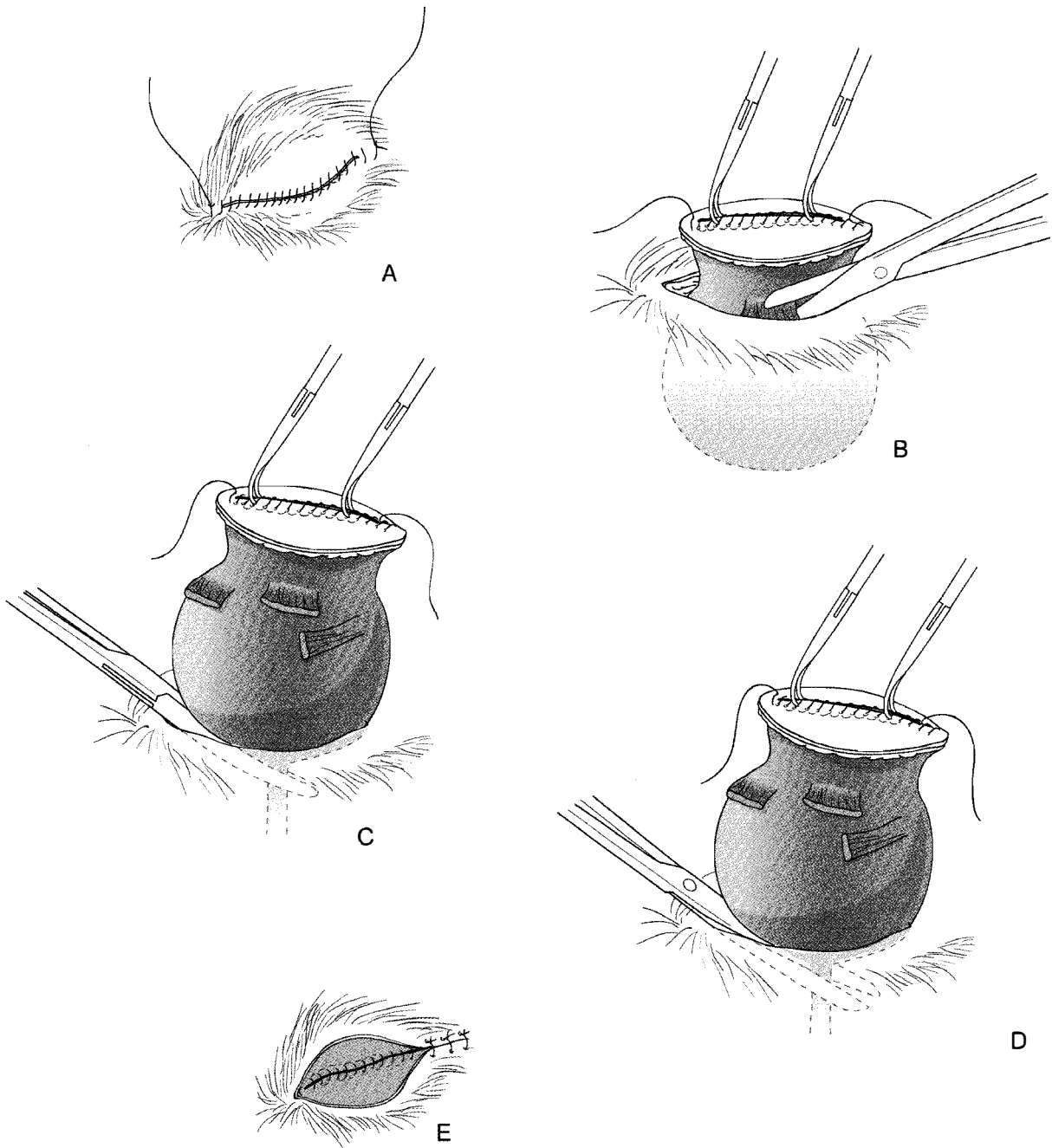
FIGURE 1b. Transpalpebral Enucleation.

- **A.** The lids are sutured closed and sealed with a simple interrupted suture pattern. The ends are left long.
- **B.** The skin is incised 5 mm posterior to the lid margin 360 degrees. Blunt dissection in the direction of the orbital bones is used to free the globe. At the level of the orbital rim the dissection continues in the direction of the globe. The muscle insertions are severed.
- **C.** One or two curved hemostats are placed on the optic nerve and vessels for 5 minutes.
- **D.** The clamps are taken out and the globe is removed using scissors.
- **E.** At least one deep simple continuous layer of absorbable suture is placed before the skin is closed with simple interrupted sutures.

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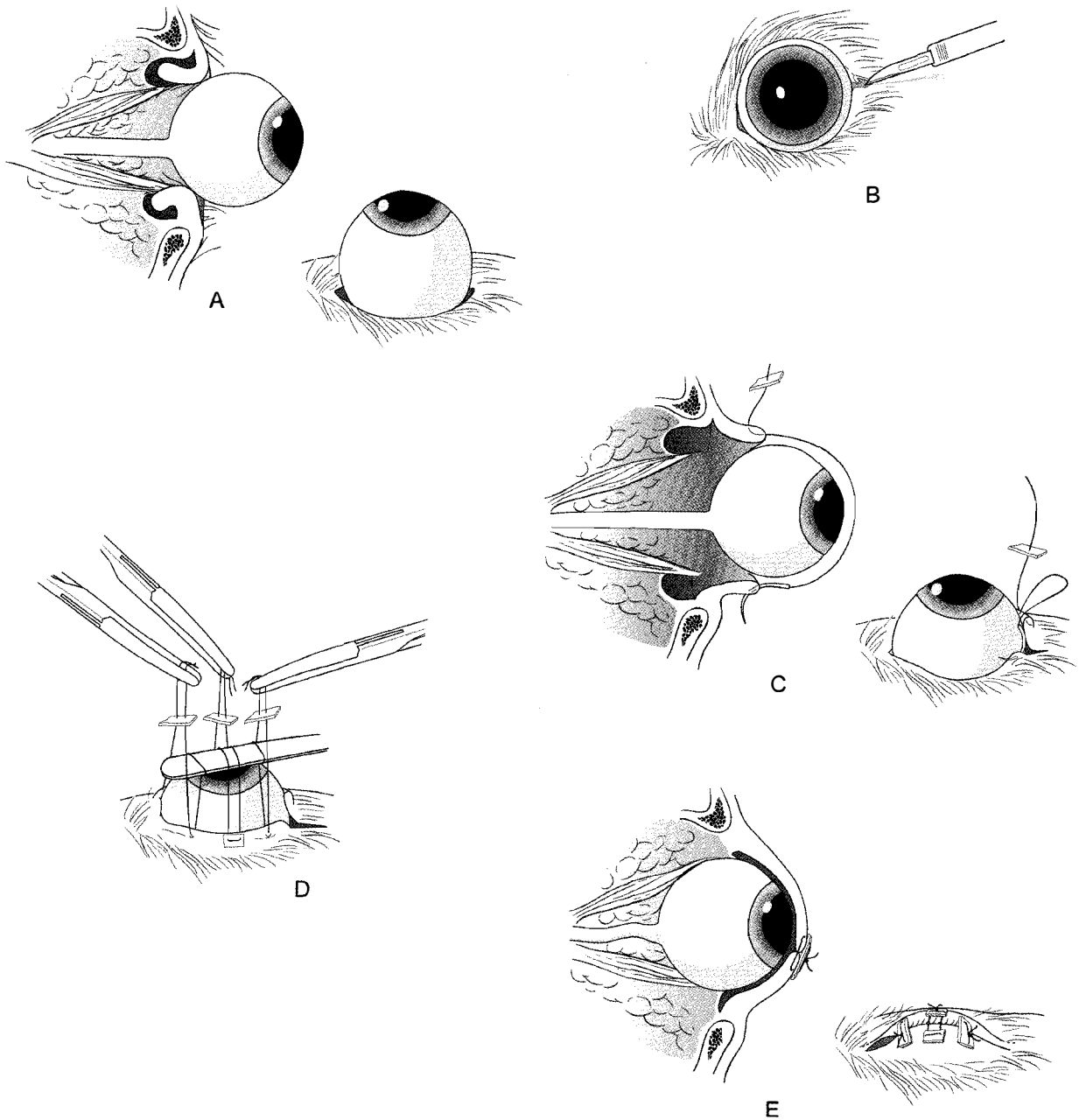
FIGURE 2. Repositioning of the proptosed globe.

A. Proptosed globe.

B. A lateral canthotomy is usually require to allow access to the lid margin. The incision is made with a scalpel very carefully as not to injure the globe.

C. The lids are everted starting at the lateral canthus and 2 – 3 simple interrupted or horizontal mattress sutures [3-0 or 4-0 silk or polypropylene (monofilament)] are placed but not tied. Enter upper lid 3 mm dorsal to lid margin and exit through Meibomian gland opening, enter lower lid through Meibomian gland openings and exit 3 mm ventral to lid margin. The use of stents is highly recommended. A small opening can be left near the canthus to allow for treatment.

D. Take flat instrument, like scalpel handle, and apply gentle pressure to the globe beneath the loose sutures.

E. Tighten sutures over instrument while repositioning globe and very gently remove instrument.

INTRODUCTION

The first two weeks post-partum is the neonatal period; it represents a period of unique physiology and disorders. The most common disorder is the fading syndrome, where puppies and kittens appear to be healthy at birth, but then stop nursing, become weak and thin, and die. In narrow terms, fading refers to this syndrome if there is no immediately apparent cause and more specific signs are absent. In broader terms, fading includes the syndrome when more specific signs (such as diarrhea), or an identified cause (such as pneumonia), are present. Causes for fading include inherited internal anatomical or metabolic defects (purebreds are at higher risk), neonatal isoerythrolysis (kittens with type A or AB blood born to type B queens), thymic deficiency (associated with inbreeding in dogs and FeLV infection in cats), possibly thyroid dysfunction (kittens), hypoxia and trauma incurred during parturition, viral infections (especially herpesvirus in pups, FeLV infection in kittens), bacterial sepsis (bacteremia, pneumonia, gastroenteritis, usually due to *Escherichia coli* and ß-hemolytic *Streptococcus* spp, but also *Klebsiella* spp and other enterobacteriaceae, *Pseudomonas* spp, and *Staphylococcus* spp, and less frequently *Brucella* spp, *Bordetella* spp, *Pasteurella* spp and *Campylobacter* spp), toxoplasmosis (kittens), hookworms (*Ancylostoma caninum*) in pups in tropical and subtropical areas, malnutrition (primary or secondary agalactia, maternal neglect), taurine deficiency (kittens), and trauma incurred after birth. In the past infectious canine hepatitis virus and canine and feline parvoviruses were implicated in fading, but herd immunity is such that these diseases are now uncommon causes of neonatal death. Even with good management practices the pre-weaning mortality rate for dogs and cats is 10 – 15% (including stillbirths which account for about half the losses), of which 50% occurs in the first 3 days, and 65% in the first week, and most of the remainder within the second week.

Risk factors for fading include illness in previous litters, prolonged parturition and dystocia, first and last pups born in a large litter, prematurity, and low birth weight. Neonates at increased risk should be observed very closely for signs of illness, especially in the first 3 days post-partum.

Fading is frequently accompanied by maternal neglect. If the entire litter is being neglected, there may be a maternal illness or behavioral disturbance, and fading is the result of malnutrition and/or maternal aggression. If only one or two animals in a litter are being neglected, this may be an appropriate culling response to an abnormal neonate.

Successful management of the fading neonate is a challenge. **Early identification** of problems and **immediate intervention** is of paramount importance. Cases due to malnutrition (e.g., *from maternal agalactia p. 550*), cases with specific treatable disorders, and cases with trauma are the most rewarding to treat. A number of cases may be euthanised because of cost, or die because of the underlying disease.

DIAGNOSIS

History

The history should review any previous problems with the neonate, littermates, dam, previous litters, and related animals. Investigate a) the gestational environment, b) parturition, c) the post-partum external environment (including behaviour of the dam).

- **Gestational environment:** Gestational problems contributing to mortality are usually associated with a **low birth weight.** Investigate the following parameters in the dam – general health, age, nutrition, evidence of infectious disorders, parasitism, sanitation, and genetic factors. Low birth weight in an individual neonate is likely due to a congenital anatomic or metabolic defect.
- **Parturition:** Problems with parturition contributing to mortality are usually associated with a **normal birth weight.** Most problems involve hypoxic episodes. Review history for evidence of prolonged labor, dystocia and early placental separation.
- **External environment:** Problems with the external environment contributing to mortality are usually associated with a **normal birth weight** if they are the sole cause. However, environmental problems may also affect the gestational environment, maternal behaviour, and parturition. Investigate temperature and humidity (elevations in predispose to bacterial infections), sanitation, parasitism, population density (high density can be disturbing to dam and affect sanitation and parasitism), and noise level (disturbance). Review maternal behaviour, which may be affected by environment as well as intrinsic factors and age (nervous, inexperienced, and older dams may ignore neonates in need or inadvertently traumatize them more readily). Review nutrition of dams and neonates, evidence of colostrum ingestion, evidence of regular suckling, and timing of weaning.

Clinical Signs/Physical Examination

Physical examination of the dam:
- Assess temperament.
- Assess milk production.
- Examine for signs of illness, especially mastitis and metritis, which may be causing agalactia or maternal neglect. Note that the early signs of mastitis may only be lethargy and fever, without localizing signs of mammary gland inflammation.

Physical examination of the neonate:
General
- Examine the **entire litter.**
- Restraint of neonates requires **gentleness and patience.** Exercise caution when approaching the new mother. Some prefer to examine the neonates without the dam's presence.
- The neonate has an **increased susceptibility to infection,** especially if there is failure of passive transfer. The immune system is almost fully mature at birth, but it is naïve, response to antigens is slower and antibody production is lower compared to mature animals. For in-hospital examination, avoid contaminated areas of the hospital, examine the neonate on a clean or sterile, padded, warm surface, and thoroughly wash your hands ± wear gloves.
- Consider a **house call** to avoid transporting the mother and whole litter, and to minimize the risk of infection. However, sick neonates may have to be hospitalized, especially if the mother is rejecting the neonate.
- **Eyes open** between 5 – 14 days (average 8 – 9); the cornea is cloudy at birth; the iris and tapetum are blue-grey; vision, and menace and pupillary light reflexes, are present when the eyes open but are weak (may not be detectable) and mature by 3 – 4 weeks. **Ear canals open** at 6 – 14 days; ceruminous and squamous debris forms when the canals open. Neonates respond to loud noises; hearing is mature by 3 – 4 weeks. Olfaction is well-developed at birth.
- **Urogenital System:** All nephrons are present at birth but maturation continues until 3 weeks of age, therefore, GFR, concentrating ability and homeostatic functions are reduced, achieving normal by 8 weeks. The kidneys and bladder are palpable. Neonates are unable to voluntarily urinate for 2 – 3 weeks (kittens have some ability); urination is stimulated by the mother licking the anogenital region (this reflex is present in kittens up to 40 days).

Kittens may be sexed using anogenital distance		birth	3 weeks
	♂	12.9 ± 1.5 mm	17.8 ± 2.1 mm
	♀	7.6 ± 1.0 mm	10.1 ± 1.1 mm

Testes descend by 4 – 7 weeks of age but may be difficult to feel; diagnose cryptorchidism if not palpable by 16 weeks.

Non-specific clinical signs of illness
- **Isolation, restlessness, persistent vocalization and poor nursing.** A content neonate is sleeping, nursing, or being groomed. The individuals in the litter are usually sleeping fairly closely together for the first few days, but then gradually spread out over the first 3 weeks. Ambient temperature will also affect their proximity, and a litter piled up on each other is a sign of being cold. An isolated animal should be seeking its mother or the rest of the litter. Normally the neonate cries for only a few minutes at a time (and not longer than 20 minutes), and the mother promptly responds. Nursing occurs within a few minutes to hours of birth and every 2–3 hours thereafter (25% of the first week of life is spent nursing).
- **Dull hair coat.** A healthy neonate appears "fat and sleek" and has a shiny hair coat.
- **Weakness is often the first physical sign of illness** and rapid clinical deterioration follows. Unless it is disturbing to the mother, the neonates should be observed daily and activity and strength compared within the litter and from one day to the next. A healthy neonate feels firm, plump and vigorous when handled, and is very responsive to noxious stimuli (e.g. venipuncture). Weak neonates feel limp when handled. Evaluation of neonatal reflexes is very useful in judging vigor.
  - The righting reflex is present at birth and continues to strengthen over the first 4 weeks. Place the neonate on its back on a padded surface – healthy neonates will right themselves promptly.
  - The rooting (nuzzling) reflex is present for the first 2 weeks (strongest in the first week). This is the reflex used by the neonate to locate a nipple for nursing. For pups, make a circle with your thumb and index finger and place over the muzzle – healthy pups will vigorously push forwards. For kittens, hold the palm of your hand against the muzzle tilted at a 45° angle away from the head – healthy kittens will root in the palm and try to climb up.

– The suckling reflex is strongest in the first 3 weeks (especially the first week). Place a little finger or nursing bottle in the mouth – healthy neonates will mouth vigorously. If using a finger, rinse it thoroughly with warm water first.

- **Low birth weight and failure to gain weight.** Inexpensive dietary scales may be used at home. Weigh neonates daily and at least twice daily if there are any signs of illness. The animals should be weighed at the same time each day and at the same time with respect to feeding. As the animals grow older the frequency of weighing may be decreased. Low birth weight is associated with poor performance, mortality, and congenital defects; it is the single most important predictor of survival. Small neonates should be watched especially closely for weakness and other signs of illness. Normally up to 10% body weight may be lost within the first 24 hours; any other weight loss and failure to gain weight is abnormal. **Failure to gain weight is a consistent early sign of illness.**

  - **Kittens** on average weigh 100 ± 10 g at birth, should gain a minimum of 7 – 10 g a day (may gain 15 – 30 g/day), and should double birth weight within the first two weeks. Kittens with birth weights <90 g are at increased risk for fading.
  - **Puppies** weigh 100 – 200 g (toy breeds), 400 – 500 g (large breeds) and ≥ 700 g (giant breeds) at birth, and should have a daily gain of 5 – 10% of birth weight or 1 – 1.25 g/455 g of anticipated adult weight and double their birth weight within 7 – 10 days.

- **Dehydration.** Neonates are prone to dehydration because total body water is approximately 80% at birth, skin is more permeable, surface area-to-volume ratio is greater, water turnover is 2 – 3 times higher than in the adult, and renal homeostatic mechanisms are immature. The latter also predisposes to volume overload and electrolyte and acid-base disturbances. With normal hydration status the oral mucous membranes should be moist, and hyperemic for the first 4 – 7 days, and lighter pink thereafter. (Sepsis may also cause hyperemic mucous membranes, and this sign may be harder to detect in the first week). Dark and dry oral mucous membranes indicate dehydration. With more advanced dehydration the skin will lose turgor and remain tented or spontaneously wrinkle. (The ventral abdomen is a useful region to evaluate for hydration status, as well as for evidence of anemia, cyanosis, hemorrhage, edema and umbilical disorders). Constipation may be another sign of dehydration. In shock mucous membranes become pale.

- **Hypothermia.** Normal digital thermometers may be used to obtain rectal temperature. Neonates are essentially poikilothermic for the first 2 weeks and are prone to hypothermia because of greater surface area- to-volume ratio, immature metabolism, impaired shivering reflex (which develops at 6 days and is not strong until 2 weeks) and vasoconstrictive ability, and because they are normally hypothermic compared to mature animals. **Normal rectal temperature at birth** is 35 – 37°C (average 36°C) [95 – 98.6°F, average 97°F], and gradually increases to adult temperature (38 – 39°C, 100.4 – 102.2°F) over 4 weeks. In one study of outdoor kittens, normal temperature (mean °C ± SE) was 36 ± 0.3 at birth, 36.6 ± 0.5 at 1 week, 37.4 ± 0.3 from 2 – 4 weeks, and 37.8 ± 0.2 from 5 – 7 weeks. (Temperatures above these values are due to excessive external warming or fever.) Hypothermia causes unresponsiveness (which may lead to maternal neglect), bradycardia, respiratory depression, and ileus (bowel sounds absent). Cold neonates may pile on top of one another. Because neonates have difficulty mounting a fever, normothermia and hypothermia do not rule-out infection. **Hypothermia is a common sign of sepsis.**

- **Bradycardia.** Heart rate is usually > 200 bpm, with a minimum rate of about 130 bpm. Bradycardia is usually due to hypothermia. (Innocent murmurs may be present and a continuous murmur of a patent ductus arteriosus may be present for the first 2 – 3 days.)

- **Persistent/reversion to flexor dominance (fetal position) after day 4.** In the **pup,** flexor dominance exists through day 3 – 4; when the pup is held by its head or scruff, it will curl its body inwards. Extensor dominance is present through the 3rd week; when sleeping the legs tend to be more stretched out, and when held by the head or scruff the pup will extend its head and stretch its legs out, appearing to arch backwards. After 3 weeks the pup is normotonic. Flexor and extensor dominance is more variable in kittens, and varies with body position. Crawling begins approximately day 7 – 14, walking approximately day 10 – 12 (cat) and 12 – 16 (dog), and the gait is fairly normal by 21 days.

Specific clinical signs of illness

- **Cleft palate.** This is the most common congenital defect.
- **Vomiting, diarrhea, tenesmus.** Meconium is passed for the first 2 days; it is soft, yellow-brown, and relatively odour-free. Feces of nursing neonates are then of a light to medium brown colour, are pasty, and may be poorly formed. Feces become solid when the pups/kittens are weaned at 4 – 8 weeks. As with urination, neonates normally only defecate when stimulated by the mother licking the anogenital region. Stroking the perianal region with a warm, moist cotton ball will permit evaluation of feces. Liquid diarrhea is abnormal, common in sick neonates (>50%), and potentially serious, especially if it is green and foamy (bacterial gastroenteritis), bright yellow (canine herpes virus) or blood-tinged (sepsis). Blood may also be seen in feces with hookworm infection.

Bowel sounds are normally auscultable. Neonates have a vomiting reflex and vomiting is abnormal.

- **Abdominal distension and abdominal pain.** These typically result from gas accumulation associated with gastroenteritis. Abdominal pain may also be present due to widespread necrosis in canine herpes virus infection.
- **Constipation.** Constipation may occur from dehydration or imperforate anus/atresia ani.
- **Dyspnea.** Respiration is normally regular and unlaboured, with a rate of 15 – 35 breaths/minutes. Dyspnea is usually due to pneumonia or trauma, and may be accompanied by cyanosis (detectable in mucous membranes and ventral abdomen). Dyspnea may also be due to overheating. A pulse oxymeter may be placed on the hairless skin of the ventral abdomen – normal oxygen saturation is >90%.
- **Nasal discharge.** This is usually due to cleft palate or pneumonia. Blood-tinged nasal discharge is probably a sign of sepsis.
- **Soft and erythematous umbilicus.** The umbilical cord normally drops off by 2 – 3 days and the umbilicus is dry. A soft and erythematous umbilicus is a sign of bacterial omphalitis, and discharge may be present. This may be the entry site for bacteremia and pneumonia. Other umbilical abnormalities include herniation, evisceration, and knotting during whelping, especially in large litters.
- **Erythema of the genital area.** This may occur in orphaned animals due to misdirected suckling by a littermate. The littermate responsible may show rooting behavior after a feeding and have urine or feces on its head.
- **Erythema or ulceration of extremities.** Eythema and sloughing of the tip of the tongue, nose, tail and limbs are signs of bacterial sepsis. Erythema of the extremities may also be due to overheating. Tail tip necrosis may occur in neonatal isoerythrolysis in kittens. Misdirected suckling may also cause erythema and skin lesions on feet and ears.
- **Hemorrhage.** Fading neonates should be closely examined for hemorrhage as a sign of trauma. Hematuria, epistaxis, lingual and ventral abdominal ecchymoses in pups may be due to vitamin K deficiency. Internal hemorrhage may occur if the dam chews off the umbilical cord too close to the body; umbilical hemorrhage may be present. Petechiation may occur with canine herpesvirus infection. Intestinal hemorrhage may be severe in pups with hookworms; hematochezia may or may not be present. Hemoglobinuria (mimics hematuria) will occur rapidly with neonatal isoerythrolysis after colostrum intake in kittens.
- **Anemia.** Examine tongue and ventral abdomen. Anemia is due to hemorrhage (trauma, coagulopathy, hookworms in pups, fleas), or isoerythrolysis in kittens.
- **Icterus.** Neonatal jaundice does not occur in pups and kittens, unlike in humans. Jaundice in the kitten is likely due to isoerythrolysis.
- **Incomplete haircoat.** Sparse hair on the dorsal aspect of the feet indicates slight prematurity. Missing skin may be due to epitheliogenesis imperfecta or maternal aggression.
- **External parasites.** Fleas and lice may be present on neonates raised under poor conditions. They are most likely to be encountered in stray, orphaned kittens.
- **Musculo-skeletal defects.** Evaluate skeleton for completeness and deformity. Examine for an open fontanelle, which may be associated with fading or future neurologic signs. Many toy breeds normally have open fontanelles, and small open fontanelles may be normal in kittens. Most fontanelles close by 9 – 12 weeks, but some remain open in apparently normal animals, especially with Chihuahuas. An open fontanelle is most likely to be a significant sign of deformity if it is large, or if the animal is weak or showing neurologic signs.
- **Traumatic injuries.** Fading neonates should be closely examined for external evidence of trauma.
- **Protruding eyelids.** Ophthalmia neonatorum is due to an infection with *Staphylococcus* spp. or other normal flora under the eyelids before they fully open, resulting in protruding eyelids ± purulent drainage.

Laboratory Evaluation/Diagnostic Imaging

- Obtain samples from the jugular vein (easily accessed) using a 22 – 27 g needle and a 1 – 3 mL syringe. Maximum sample size in mL = body weight (g)/125 (pup) or 150 (kitten). A minimum laboratory database can be obtained using several drops of blood. Normal ranges are based on limited studies of laboratory animals.
- **CBC.** Measure hematocrit with a capillary tube. Estimate WBC and perform differential count from a blood smear. Alternatively the Unopette Microcollection System (Becton Dickinson and Company) or QBC VetAutoRead (Idexx) may be used to obtain actual WBC count.
  - Causes and response to **anemia** are similar to adults. A variable mild physiologic anemia is present 2 – 6 weeks reflecting change from fetal to adult MCV and rapid weight gain where circulatory volume exceeds red cell mass. There is relative reticulocytosis compared to adults and some nucleated red cells are normal reflecting normal regeneration.

TABLE 1. Pup PCV by Hematology Analyzer

Beagles		Beagles Golden Retrievers German Shepherd Dogs*		Mixed-Breed	
Time	PCV	Time	PCV	Time	PCV
Birth	45 – 53%	Day 1 – 3	28 – 54%		
1 week	33 – 52 %				
2 weeks	29 – 34 %	Day 8 – 10	23 – 37%	Day 7 – 15	25 – 33%
3 weeks	27 – 37 %				
4 weeks	27 – 35 %	Day 28 – 33	20 – 33%	Day 16 – 35	24 – 32%
6 weeks	27 – 36 %				
8 weeks	31 – 39 %	Day 50 – 58	25 – 41%	Day 36 – 73	26 – 38%

* German shepherd dogs tended to be at lower end of range.

TABLE 2. Kitten PCV by Hematology Analyzer

Time	PCV
1 – 2 weeks	31 – 39 %
2 – 4 weeks	25 – 28 %
4 – 6 weeks	26 – 29 %
6 – 8 weeks	29 – 31 %

- WBC counts are at the upper end of normal adult range and responses to infection and stress are similar to adults except that marrow granulocyte reserve is limited and rapidly exhausted in sepsis. A normal neutrophil count in a sick neonate may herald impending neutropenia.

TABLE 3. WBC Reference Intervals for Healthy 2 week-old Neonates

Parameter	Pup (Beagle)	Kitten
Nucleated cells (x 10^9/L)	8.10 – 15.10	8.53 – 10.81
Segmented neutrophils (x 10^9/L)	3.20 – 10.40	4.60 – 7.32
Band neutrophils (x 10^9/L)	0 – 1.20	0.02 – 0.10
Lymphocytes (x 10^9/L)	1.50 – 7.40	2.69 – 4.77
Monocytes (x 10^9/L)	0.20 – 1.40	0 – 0.03
Eosinophils (x 10^9/L)	0.08 – 1.80	0.10 – 1.82
Basophils (x 10^9/L)	0	0 – 0.04

- Platelet numbers and responses are similar to adults. Thrombocytopenia is most likely a sign of sepsis or canine herpesvirus infection.

Serum Chemistries

- Serum proteins. Estimate using total solids from a capillary tube. Albumin is low to low normal adult value. Globulins are low at birth, rise with colostrum ingestion, reach a nadire value at 3 – 4 weeks, and adult value by 6 months. Total protein will decrease with hemorrhage.

TABLE 4. Pup Total Protein by Chemistry Analyzer

Time	TP (g/L)
1 – 3 days	31 – 58
8 – 10 days	33 – 44
28 – 33 days	37 – 48
50 – 58 days	40 – 53

- Glucose. Use point-of-care instruments, but these tend to read low. Glucose levels are similar to adults. Hypoglycemia is a common finding due to poor glycogen reserves, reduced gluconeogenesis, malnutrition, hypothermia, and sepsis.
- Urea and creatinine. Use chemistry strip to measure urea. Normal to slightly elevated at birth, and then slightly low compared to adult values reflecting anabolic state. Creatinine follows a similar trend, reflecting relatively low muscle mass. Elevations will occur with dehydration, ruptured bladder, and renal failure.

TABLE 5. Pup Urea by Chemistry Analyzer

Time	Urea (mg/dl)
1 – 3 days	30 – 118
8 – 10 days	29 – 67
28 – 33 days	13 – 46
50 – 58 days	17 – 61
Adult	20 – 68

- Liver enzymes. ALT is slightly lower than adult values; it rises with hepatic necrosis due to canine herpesvirus. GGT and ALP rise with colostrum ingestion in pups and give an indirect assessment of occurrence (see Suggested Reading 4). In this study median GGT and ALP before suckling were 24.0 U/L and 350 U/L respectively, and increased to 1,070 U/L and 2110 U/L on day 1 post-partum. In colostrum-deprived pups fed a milk replacer, pre-feeding median GGT and ALP were14.2 U/L and 364 U/L, and increased to 17.0 and 373 U/L on day 1.

TABLE 6. Serum Chemistry Reference Intervals for Healthy 2 Week-old Neonates

Parameter	Pup (Beagle)	Kitten
Urea (mmol/L)	< 84	< 84
Glucose (mmol/L)	6.2 – 8.1	4.2 – 7.2
Total protein (g/L)	36 – 44	40 – 52
Total bilirubin (umol/L)	2 – 9	2 – 17
ALT (U/L)	10 – 21	11 – 14
ALP (U/L)	176 – 541	68 – 269
GGT (U/L)	4 – 77	0 – 3

- Electrolytes. Mild hyponatremia and hypochloremia may be present.
- Coagulation. Point-of-care instruments have not been evaluated in neonates. Neonatal pups are deficient in vitamin-k dependent coagulation factors compared to adults.
- Cortisol. Baseline cortisol is lower than adults but there is a normal response to ACTH stimulation.

Urinalysis. Urine specific gravity in **neonatal kittens and pups** can only be minimally concentrated. Maximum urine concentration is probably ~1.030. After nursing urine specific gravity will be ~1.015 or lower. A value >1.017 indicates dehydration (this may be a normal finding immediately prior to an episode of nursing). Urine can be well-concentrated by **4 weeks** and maximally concentrated by **8 weeks.** Glucosuria can be normal in pups up to 8 weeks. Proteinuria may be present for the first 24 hours when receiving colostrum.

TABLE 7. Pup mean urine sp. gr. (5 dogs)

Time	sp. gr.
Fetal	1.014 (1.025 in one pup)
4 weeks	1.015
8 weeks	1.023
12 weeks	1.038
16 weeks	1.034
20 weeks	1.039
24 weeks	1.040

TABLE 8. Kitten urine sp. gr. range

Time	sp. gr.
2 days	1.015 – 1.030 (3 kittens)
4 weeks	1.020 – 1.038
8 weeks	1.080 achievable

- **Examination of feces** for parasitic ova. Hookworms acquired via the milk may cause a severe hemorrhagic anemia in pups > 1 week of age. A negative fecal examination does not rule-out hookworm infection as ova from trans-mammary infection are not passed in the feces until the third week. (Roundworms may cause unthriftyness in older pups and kittens).
- **Cultures** of blood, urine, diarrheic feces, umbilical discharge, and tracheo-bronchial aspirates (use a tomcat catheter) should be cultured prior to antimicrobial therapy. For blood culture draw 0.5 – 1 mL and innoculate into 20 mL blood culture vials (BBL SEPTI-CHEK TSB, Becton Dickinson and Company). Cultures should also be obtained from the dam's milk and any vaginal discharge.
- **Necropsy.** Prompt necropsy of dead neonates will assist in managing the rest of the litter as well as the kennel and cattery. Necropsy is best performed by a pathologist. An empty gastrointestinal tract and full gall bladder at necropsy of neonates surviving up to 48 hours indicates that suckling did not occur.
- **Radiology.** Reduce kVp and use detailed film-screen combination.
  - **Thorax.** Radiology is very useful to identify bacterial bronchopneumonia, aspiration pneumonia, congenital atalectasis, heart failure due to a congenital defect, and pectus excavatum.
  - **Abdomen.** Radiographic interpretation is difficult because of lack of abdominal fat contrast. It is most useful to document gaseous distension.
  - **Skeleton.** Radiographic interpretation is difficult due to minimal mineralization of bones, incomplete ossification of epiphyses, and breed variations.
- **Ultrasound.** Excellent for human fetal and neonatal imaging, but currently limited experience in dogs and cats. It is probably most useful for diagnosing congenital heart defects, portosystemic shunts, and, in older pups and kittens, hydrocephalus.

MANAGEMENT

A. **Empirical practical treatment of the sick neonate.** Most neonatal illness is characterized or complicated by the 4 H's: **hypothermia, hypoglycemia, hypoxemia and hypovolemia (dehydration)** and each one of these conditions can lead to the other. **Hypocoagulability** and **hypofunction** of organs may also be present. Often a specific diagnosis cannot be made and disorders are rapidly fatal, so empirical treatment must be initiated promptly. Any disorder may prompt maternal neglect and lead to systemic illness. The weaker the animal, the more aggressive should be the therapy.
  1. **Isolate** from mother and rest of litter.
  2. **Re-warm** in 1 – 3 hours at about 29 – 32°C (85 – 90°F) ambient temperature and relative humidity of 55 – 65%. A hypothermic neonate should not be rewarmed above normal since this may result in heat stress (neonates cannot pant) or dehydration. Aim for a rectal temperature of 37°C (98.6°F) in the first 3 days, 37.5 – 38.0°C (99.5 – 100.4°F) the next 4 days, and 38.0 – 38.5°C (100.4 – 101.3°F) during week 2. Heat sources include a warm room, incubator, heat lamp, circulating hot water blankets, warmed oat bags, and, with caution, insulated hot water bottles and electric heating pads.

3. **Fluid therapy.** Fluids may be given by gavage (See Hand-Rearing Newborn Puppies and Kittens), per rectum (unless diarrhea is present), SC, IP, IV, and IO. The latter two are preferred in very sick or comatose neonates (*see Fluid Therapy for IO technique p. 360*). For initial rehydration give 1 mL/30 g BW warm (35 – 37°C [95 – 98.6°F]) lactated Ringer's solution IV/IO (or SC as poor third choice). This may be repeated q15min until mucous membrane colour improves and urine forms. Stimulate the neonate to urinate by wiping the caudal abdomen and anogenital region with a moist cotton ball when first treating and periodically thereafter to monitor urine production. Maintenance fluid therapy requirements are 120 – 220 mL/kg/24h. Hydration status may be judged by clinical signs, weight, and dilution of urine.

4. **Glucose.** If mild hypothermia, hypoglycemia and weakness are present, give 0.25 mL/25 – 30g body weight of 5 – 10% warm glucose (1 mL of 50% dextrose to 10 mL water = 5% solution) by gavage q1h until normothermic, normoglycemic and stronger, then give formula as described in Hand-Rearing Newborn Puppies and Kittens. (Do not give formula to hypothermic animals as digestion is impaired). If vomiting is present, 4 – 8 mL of 0.45% NaCL + 2.5% dextrose may be given SC. If the animal is comatose, give 0.25 mL/25g body weight 20% dextrose IV/IO. Owners at home may rub 50% dextrose, corn syrup or honey (2 – 5 drops) on gums. Fluid therapy should be adjusted according to volume of glucose solution given.

5. **Oxygen.** Use oxygen tent, cage, nasal tube or face mask to deliver 30 – 40% oxygen until stable and pulse oxymetry measures >90%.

6. **Umbilical care.** Clean umbilicus, drain abscesses, and disinfect with 10% povidone-iodine solution.

7. **Antibiotics.** Ampicillin 25 mg/kg IV/IO (preferred) or IM/SC q8h. If a specific organism is cultured (i.e., from feces), then the antibiotic should be chosen based upon antimicrobial susceptibility testing.

8. **Relieve abdominal distension.** If severe gaseous abdominal distention is present (confirm with radiograph), pass a stomach tube or rectal tube, or trocharize the stomach or intestinal tract with a 20g hypodermic needle.

9. **Vitamin K[1]** for pups (kittens?) 1 – 4 days old, 0.5 – 2.5 mg/kg SC once prophylactically or if obvious hemorrhage is occurring.

10. **L-thyroxine** for kittens, 5 μg PO once daily (give 1/5 of a 25 mg tablet).

11. **Examine the rest of the litter** for any signs of impending problems, including culling by the dam. If there is no obvious cause of the affected animal's deterioration (e.g. congenital defect, runt of the litter), consider treating the entire litter with ampicillin, amoxicillin, or amoxicillin-clavulanate. If there is a high degree of suspicion of, or confirmed, sepsis, then the entire litter should definitely be treated with the choice guided by antimicrobial susceptibility testing. The litter should be separated from the mother and hand-raised if she is the likely source of infection (e.g., mastitis, metritis).

B. **Additional treatments for septic neonates**
   1. **Adult dog or cat serum** 20 – 50 mL/kg IP q8h, or 60 – 150 mL/kg IV/IO over 24 hours (higher doses preferred) should be given if there was failure of passive transfer and should be considered if sepsis is likely.
   2. **Recombinant human granulocyte colony-stimulating factor (rHuG-CSF, filgrastim [Neupogen, Amgen])** 5 μg/kg SC q12–24h.
   3. **Granulocyte transfusion** has been used successfully to treat sepsis in experimental pups and in human neonates. The technique is feasible in some veterinary practices but rarely performed because of cost and personnel limitations. Hetastarch (Hespan, DuPont Pharma, Wilmington, DE) or pentastarch [Pentaspan, DuPont Pharma] is added in a 1 to 8 ratio to a unit of fresh whole blood. After a 1-hour sedimentation period, the plasma and buffy coat are expressed into a satellite bag, which is centrifuged at 5000 x g for 5 min at room temperature. The plasma is then expressed, leaving the granulocytes in 20 mL of plasma. The initial dose is 1 x 10^9 granulocytes/kg in a volume of 15 mL/kg q12–24h. Assuming a donor neutrophil count of 4 x 10^9/L and a yield of 75%, approximately 175 mL of whole blood will be needed to prepare a granulocyte transfusion for a 0.5 kg neonatal recipient. The transfusion should be given IV through a standard 170 um filter over 2 hours.

C. **Hemorrhagic anemia** due to trauma, coagulopathy, or hookworm infection in pups. *See Transfusion p. 667.* Red cell transfusions to neonates may be given IV, IO, or IP. The latter will result in slower correction of anemia. IV or IO transfusion is necessary in peracute hookworm infection. Pups with severe ancylostomiasis should be treated with **pyrantel pamoate 5 mg/kg PO weekly,** or **milbemycin 0.5 mg/kg PO q2weeks,** until 12 weeks of age. Pups from subsequent litters of the bitch should be similarly treated, beginning at 2 weeks of age. Trans-mammary transmission in subsequent litters may also be reduced by treating the bitch with fenbendazole 50 mg/kg, PO daily from day 40 of pregnancy to day 14 after whelping, or with ivermectin 0.5 mg/kg PO 4 – 9 days before whelping and 10 days later.

D. To prevent **isoerythrolysis,** type A or AB kittens should **not** be permitted to nurse from a type B queen for the first 24 hours. If a queen is potentially of B blood type and the tom potentially of A blood type, then the blood type of the queen and the kitten (using umbilical cord or venous blood) should be determined (*see Transfusion p. 667*). If isoerythrolysis occurs, the kitten should be immediately removed from the queen and given supportive care as described above. The mortality rate is high. Transfusion with the queen's washed red cells may be considered.

E. **Umbilical cord knotting.** Ligate each cord with absorbable suture, transect, and disinfect with 10% povidone-iodine solution.

F. **Nervous bitches with agalactia** *see Agalactia p. 550.*

G. **Fleas and lice** on neonates are best treated by manual removal using a fine-tooth comb and daily changing of bedding. For heavy flea infestations a dilute pyrethrin-based shampoo may be used. An alternative in kittens is to apply one drop of imidocloprid (Advantage, Bayer) to the base of the skull (extra-label use).

H. **Ophthalmia neonatorum.** Soften the exudate with moist, warm compresses, and try to part eyelids carefully with fingers or a blunt instrument. If the lids do not part easily, a sharp instrument is needed – i.e., iris scissors or a stitch cutter scalpel blade. It may be sufficient just to incise at the medial canthus, then a blunt instrument can be used to part the lids the remainder of the way. Apply an antibiotic ointment (tetracycline or chloramphenicol in cats, neomycin-bacitracin-polymyxin in dogs) q8h for 3 – 4 days or until any corneal ulcers (most likely in kittens) have healed. Tear production does not start until the eyes open fully, but the ointment will usually prevent desiccation. Analgesia/anesthesia is required (*p. 81*).

PHARMACOLOGY

1) **Antibiotics.** Pharmacokinetics in the neonate are different than in the adult because of higher percent total body, reduced liver metabolism and renal excretion, potentially increased intestinal absorption, and increased blood-brain barrier permeability. The volume of distribution for water soluble drugs in pediatric patients is higher than in adult animals, so they need to be dosed at the higher end of the flexible dose range to reach therapeutic plasma concentration compared to the dose in an adult animal. Specific data are lacking for neonatal dogs and cat. The penicillins and cephalosporins are the safest drugs to use, and, as they are water soluble, they are generally dosed q8h at the upper value of the adult dose. Absorption with the IO route has been shown to be equivalent to the IV route for ampicillin, cefazolin and gentamicin in 6 – 9 week old kittens and puppies. The SC route in neonates is effective, but IM injection is **not** recommended.

2) **Adult serum** may provide beneficial immunoglobulins to the septic neonate. Preparation is described in Hand-Rearing Newborn Puppies and Kittens *p. 554*. Concentrated immunoglobulin therapy is beneficial in septic neonatal humans, but concentrated canine and feline immunoglobulins are not available.

3) Recombinant human granulocyte colony-stimulating factor is a cytokine that stimulates bone marrow granulocyte precursors, and thus helps to replenish the marrow granulocyte reserve. It has been advocated in the treatment of human neonatal sepsis. Benefit in neonatal pups and kittens is not known.

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INTRODUCTION

Newborn puppies and kittens need to be reared by hand if the dam is too weak to care for her young, or if she has agalactia, has abandoned or rejected the neonates, or has died. Maternal weakness is usually a complication of dystocia, and may resolve such that the mother can eventually care for her young. Maternal weakness may also be due to illness (e.g., mastitis, metritis, retained placenta). Primary agalactia refers to poor milk production (due to inadequate mammary development, malnutrition, or failure of prolactin secretion) or blockage of milk ducts (e.g., due to scarring). In some cases of primary agalactia the newborns need only be fed, as the mother will otherwise care for them. Also, rarely, some bitches may commence lactation 1 to 3 days after whelping. Failure of milk letdown is more common, and may be due to anesthesia (e.g., for C-section), anxiety of the dam, or mammary gland disorders (galactostasis, mastitis).

Most cases of apparent abandonment involve stray cats. The mother may have been injured or may be out hunting. If a litter has been found and taken to the veterinary hospital, it is probably better to hand-rear the young than to return them to the nest in anticipation of the mother's return. However, when a litter is discovered, it is best not to disturb it for several hours while awaiting the mother's return. If the mother does not appear, then the young should be hand-reared.

A newborn may be rejected because of a primary maternal behavioral disorder (usually the entire litter is rejected) or because the newborn is abnormal (usually a single animal is rejected). Hand-rearing may also be needed for supportive care of a sick neonate although the dam is not rejecting it, because it is too weak to nurse. Prompt implementation of hand-rearing will usually result in normal development, unless an underlying disease causing neonatal fading is untreatable or improperly managed. Hand-rearing is usually accomplished by owners. The care of the neonates is intensive, but only for a short period of time, and it is rewarding.

Fostering is an alternative to hand-rearing a litter if a nursing mother is available. Fostering is often successful if there is less than a 2-week age difference between the fostered young and the mother's own litter. Fostering between dog breeds should only be done if the breeds are of similar size. The animals should be unobtrusively observed to ensure that the young are not rejected or savaged.

Only 5 – 10 % of maternal antibodies are transferred transplacentally in dogs; the amount is even less in cats. Consequently, puppies and kittens will suffer from failure of passive transfer of maternal antibodies if they do not nurse within the first 12 hours post-partum. Puppies deprived of colostrum have a markedly increased susceptibility to experimental infections. However, failure of passive transfer in small animals has not been associated clinically with the same morbidity as in large animals. This may be because well-managed litters are raised in a relatively isolated environment. In any case, neonatal puppies and kittens deprived of colostrum are considered to be at increased risk for sepsis and fading. A colostrum substitute is therefore desirable if there is failure of passive transfer. Failure of passive transfer is generally not a problem in apparently abandoned litters, which are usually found after the first day of life.

DIAGNOSIS

History/Signalment

- Review history for evidence of dystocia or illness that may cause maternal or neonatal weakness.
- Agalactia should be suspected when neonates are attempting to nurse but are restless and vocalizing, and their abdomens are not becoming distended with milk. Investigate disturbance in surroundings and evidence for anxious behaviour that may be causing failure of milk letdown.
- Galactostasis may occur during peak early lactation when milk production exceeds neonatal need, or more commonly at weaning.
- History of maternal abandonment, rejection, or death.

Clinical Signs/Physical Examination

- Examine dam for normal mammary development and engorgement with milk ("milk bar"), and normal teats.
- Signs of galactostasis are warm, diffusely firm and edematous mammary glands. The dam appears uncomfortable and is inappetent, but is not febrile. Well-fed, heavily lactating bitches are most at risk.
- Signs of mastitis are warm, discoloured and painful glands. The dam is febrile, lethargic and anorexic. The milk is thin, yellow to brown in colour, and may contain clots.

- The neonates should be examined for abnormalities (*see Fading Neonatal Puppy and Kitten and Miscellaneous Neonatal Disorders p. 540*). If the litter appears healthy, no evaluation is necessary other than observation and weighing the young (initially daily) to ensure that they are growing.

Laboratory Evaluation/Diagnostic Imaging

- Milk should be cultured if **mastitis** is suspected, as should be abscessed mammary glands. Vaginal discharge should be cultured if metritis is suspected.
- **Colostrum ingestion** may be confirmed by measuring serum gamma-glutamyltransferase (GGT) and alkaline phosphatase (ALP) activities in pups (*Suggested Reading 2*). In this study, median GGT and ALP before suckling were 24.0 U/L and 350 U/L respectively, and increased to 1,070 U/L and 2110 U/L on day 1 post-partum. In colostrum-deprived pups fed a milk replacer, pre-feeding median GGT and ALT were 14.2 U/L and 364 U/L, respectively, and increased to 17.0 and 373 U/L on day 1.

MANAGEMENT

I. AGALACTIA

A. Agalactia may be treatable, in which case this will minimize the need for hand-rearing.

1. **Primary agalactia. Metoclopramide 0.1 – 0.2 mg/kg SC, PO q6–8h** may stimulate lactation. Give until milk production is adequate. Ensure good nutrition.

2. **Anxiety-induced failure of milk letdown.**
   a. **Acepromazine 0.1 – 0.25 mg/kg SC q8h–12h** with adjustments to achieve satisfactory sedation as higher dosages may be required in smaller dogs. **AND/OR**
   b. **Oxytocin 1 – 5 U SC.** (Milk letdown should occur within 5 minutes). **OR**
   c. **Oxytocin nasal spray (40 U/mL), 1 light spray into one nostril, q6–8h** or more frequently as needed to promote milk letdown.

3. **Galactostasis.** Applying either warm or cold compresses to the mammary glands should be considered and judged to see if these are providing comfort.
   a. The neonates should be allowed to nurse if the dam will let them, but should be closely observed for success. Nursing will stimulate prolactin release, and in severe cases of galactostasis it may be necessary to hand-rear the neonates for several days.
   b. Consider massage of the mammary glands and attempting to strip milk from grossly distended glands q4–6h to help reduce congestion, promote milk flow and prevent mastitis. However, massage of the glands may also stimulate prolactin release, and benefit of massage must be balanced against possible increase in milk production.
   c. When galactostasis occurs at weaning, withhold food for 24 hours and limit water intake to 40 mL/kg for 24 hours to reduce milk production. If necessary, also restrict ration up to 75%, 50% and then 25% over the next 3 days. Consider **furosemide, 1 mg/kg SC, PO q12–24h.** Food and water restriction should only be considered in severe cases of galactostasis at peak lactation and furosemide should not be given if neonates are nursing.
   d. **Cabergoline 2.5 – 5.0 μg/kg PO q24h** may be given for 4 – 6 days to dogs with galactostasis at weaning.

4. **Mastitis.** Culture milk or abscessed mammary gland and, while awaiting culture results, treat with
   a. **amoxicillin 10 mg/kg PO q12h dogs and cats, OR**
   b. **amoxicillin-clavulanate 12.5 mg/kg PO q12h (dogs), 62.5 mg (cats) PO q12h, OR**
   c. **cephalexin 20 mg/kg q8h or 30 mg/kg PO q12h cats and dogs.**
   d. Administer **away from feeding times** to avoid peak levels in the milk being consumed by the puppies or kittens.
   e. **Common organisms** are *Staph., Strep., and E. coli.*
   f. If the dam is showing only mild-to-moderate systemic signs and is willing to let the neonates nurse, the neonates may be allowed to continue to nurse if they are thrifty. The assumption is that they have been exposed to the organisms in the milk and, if not infected, are not going to become so. This may help resolution of the mastitis. An alternative is to restrict nursing to normal glands, and this will be necessary if a gland becomes abscessed or necrotic. In either case the neonates must be watched closely for the development of diarrhea (due to bacterial enteritis or "toxic milk syndrome").

g. If the dam is moderately-to-severely systemically ill, and/or if most glands are becoming abscessed or necrotic, the neonates will likely need to be hand-reared. **Surgical debridement** is strongly advised in this setting. While awaiting culture results treat with
- **Ampicillin 20 mg/kg IV q6h, OR**
- **Ampicillin-sulbactam 20 mg/kg IV, IM q8h, OR**
- **Cefazolin 20 mg/kg IV q6h**

II. HAND-REARING

A. Environment. Isolate the litter from other animals for the first 3 weeks. Work in a clean area and thoroughly wash hands before handling neonates. A human neonatal incubator is ideal for in-hospital use. At home a clean cardboard box can be used. The box should be lined with clean newsprint, towels or disposable diapers, ensuring that the animals cannot wriggle their way underneath. Material that provides better traction (e.g., rubber-backed short carpeting) should be used once the animals begin ambulating.

1. **Ambient temperature** for **kittens** should be 31 – 33°C (88 – 92°F) week 1, 27 – 29°C (80 – 85°F) week 2, 27°C (80°F) weeks 3 – 4, 24°C (75°F) week 5 and room temperature thereafter. **Puppies** require slightly lower temperatures at 29 – 32°C (85 – 90°F) week 1, 27°C (80°F) weeks 2 – 4, 21 – 24°C (70 – 75°F) week 5 and room temperature thereafter. Temperature reduction from week to week should be gradual. Ambient temperature can be controlled by:
   a. using a **human neonatal incubator**;
   b. using an **infrared heat lamp** positioned 6 feet above an incubator box, illuminating half the area to create a temperature gradient;
   c. placing a **heating pad** (caution with being too hot) **or circulating hot water blanket** secured on top of (preferably, but ensure it will not fall on the neonates) or below the box half-way to create a temperature gradient;
   d. using **hot water bottles** or **heated oat bags** well-insulated with towels;
   e. heating an **individual room.** An inexpensive thermometer obtained from a hardware store can be used to measure ambient temperature. It is also important that the area be draft free.

2. **Relative humidity** should be 55 – 65%. Inexpensive hygrometers are available from hardware stores, however humidity is probably acceptable if the room does not feel dry or muggy. If the air is dry, commercial warm or cold mist humidifiers may be used, a water dish may be placed beside the box, or a damp towel may be partially draped over the box. Dampness should be avoided, and a dehumidifier is recommended if the room is too humid.

3. **Cleanliness.** Bedding should be changed if it becomes soiled. Because the neonates cannot eliminate on their own, the bedding material tends to initially remain fairly clean. Odour of the nest probably provides comfort to the animals, and the bedding usually does not need to be changed more than daily to every other day.

B. Formula. It is difficult to obtain sufficient milk using a breast pump from a lactating dog or cat therefore formula feeding is necessary. A number of commercial milk replacers are available through distributors of veterinary products, pet supply stores and grocery stores; products readily available in Canada are listed below. Bovine milk protein is the protein source in all of these products; fat sources are animal or animal + vegetable. Use boiled or bottled water to make up formulas. Let the formula sit before use to help remove air bubbles, especially if prepared with a blender. Refrigerate or freeze reconstituted powders and opened cans (powders and liquids) as directed by manufacturer. Use canned liquid formulas within 72 hours and reconstituted formulas within 12 – 72 hours as directed by manufacturer (or within 24 hours if no directions), and emergency formulas within 12 hours. Do not store in the same bottle or syringe used for feeding.

1. **Kitten formulas** – CL Queen Replacer (Champion Alstoe), powder; Feline Mammalac (Bioniche Animal Health), powder; Kitten Formula (Vet Solutions), powder; KMR Liquid (Pet-Ag, providing 0.83 kcal/mL); KMR Powder (Pet Ag); Veta-Lac (Vet-A-Mix), powder; Nutrience Transition Kitten Replacement Milk (Hagen), powder; Advanced Care Milk Replacement for Kittens (Hartz), powder.

2. **Puppy formulas** – Canine Mammalac (Bioniche Animal Health), powder; Esbilac Liquid (Pet-Ag, providing 0.82 kcal/mL); Esbilac Powder (Pet-Ag); Klostral Milk Fortified (Champion Alstoe), powder; Puppy Formula (Vet Solutions), powder; Veta-Lac (Vet-A-Mix), powder; Nutrience Transition Puppy Replacement Milk (Hagen), powder; Advanced Care Milk Replacement for Puppies (Hartz), powder..

3. If the caloric density of the formula is not given, assume it is approximately 1 – 1.25 kcal/mL.

4. Multi-Milk (Pet-Ag) is a powdered milk replacer base that may be mixed with KMR or Esbilac to increase fat content and reduce lactose content of the formula.

5. Petlac Powder (Pet-Ag) is intended for intermittent or supplemental feeding for kittens and puppies, but the nutritional content is similar to some other milk replacers.

   If the above are not available, emergency formulas are:
   a. 1 part water, 5 parts evaporated milk, 5 mL (1 tsp) dicalcium phosphate per litre or quart of formula (provides 1.0 kcal/mL);
   b. 240 mL (8 oz, 1 cup) whole milk, 5 mL (1 tsp) vegetable oil, 2 raw egg yolks, 1 drop infant multiple vitamins (provides 1.2 cal/mL).
   c. For puppies, 300 mL (10 oz) goat's milk, 180 mL (6 oz) boiled water, 1 raw egg yolk, 240 mL (8 oz, 1 cup) plain whole fat yoghurt, 30 mL (2 tbs) mayonnaise.
   d. For kittens, 120 mL (4 oz, 1/2 cup) whole milk, 1 raw egg yolk, 1 drop infant multiple vitamins, 3 $CaCO_3$ (Tums) tablets.
   e. Some breeders hand-rear kittens successfully using goat's milk without any additives.
   f. Clinicare Feline Liquid Diet and Clinicare Canine Liquid Diet (providing 1.0 kcal/mL) (Abbott) can also be used until the proper milk replacer is obtained, although the carbohydrate content is not optimal.

C. **Feeding technique.** All feeding equipment should be meticulously clean or sterile. Warm up formula to 37 – 38°C (98.6 – 100.4°F) prior to feeding. Formula is best warmed up in a bottle placed in heated water or in a baby bottle warmer. Microwave heating and/or heating formula in a syringe under running hot water results in uneven heating and may result in super-heated pockets. If microwave heating and/or heating in a syringe is used, the formula should be thoroughly mixed after heating. Regardless of heating method, formula temperature should be tested on the inside of the wrist. Neonates should be fed in sternal recumbency with the head up in a neutral position. Discard any unused formula.
   1. If the animal has a **strong suckling reflex,** use a 2 oz or 4 oz kitten/puppy nursing bottle (several brands, distributors as for formulas), human baby bottles (for larger puppies), a bottle designed for premature human babies (obtain from a hospital, for smaller puppies), or the Catac kitten nursing bottle and nipples. When the full bottle is tipped upside down a drop should form over 1 – 2 seconds. The rate of flow may be changed by piercing the nipple with a hot needle or by adjusting the tightness of the bottle top. Animals may have a learning period and may show preference for different types of nipples. The head should be gently restrained to keep the mouth on the nipple. Some caregivers find it beneficial to lightly wrap the animal in a towel keeping the head exposed; this helps in preventing the animal in using its paws to push away the bottle. If the animal is not using the bottle well, it should not be squeezed forcing liquid into the mouth. Instead, it may be gently squeezed such that a drop of formula comes out, or a finger with formula on it may be placed in the mouth alongside the nipple, and the nipple massaged to promote flow. A syringe or eyedropper can be used when a bottle is not available and the owner cannot perform gavage, but it is essential to deliver the liquid into the mouth slowly to prevent aspiration. Using a syringe does allow for more exact determination of the amount of formula consumed. A Catac nipple attached to a 3 or 6 mL syringe works well in neonatal kittens. Bottle-feeding may be rather time-consuming and require patience.
   2. If the animal **will not suckle** or if more rapid feeding is desired, use a 5 Fr or 8 Fr infant feeding tube for gavage. Measure from the tip of the nose to the last rib and mark the tube. Fill the tube with formula to minimize introduction of air into the stomach, and pass it down the left side of the mouth into the esophagus and stomach. Confirm correct placement by palpating passage of tube in the esophagus and easy passage of tube to the correct level. If the caregiver is not confident with gavage, the tube should be filled with saline and a small amount injected – the animal will cough if the tube is in the trachea or lung. Gently inject the formula at a rate of 1 mL every 2 seconds. Kink the tube prior to withdrawal and withdraw it quickly to prevent aspiration.
   3. **Burp** the animal after feeding by holding at a 45° angle with the head elevated, and gently massaging the stomach and patting on the back.

D. **Feeding schedule:** Neonates should be fed q2h–q4h (they normally nurse q1–3h). The more intensive feeding schedules reduce mortality, but are more difficult to maintain. In setting a schedule note that:
   1. The **first 3 days of life** are the most critical (and neonates should be fed q2–3h);
   2. **Weak neonates and neonates with low birth weight** require more intensive feeding than strong and normal size neonates;
   3. **Kittens** require more intensive feeding than puppies.
   4. A **practical compromise** is during the 1st week (after the first 3 days) to feed q2–3h during day up until midnight, and then at 4:00 and 8:00 AM. If all is going well, feeding may be reduced to q4h during the 2nd week, and to q5–6h during the 3rd–4th weeks. The exact schedule will vary with the amount the animal takes

in at each feeding and its state of health. The animals may need to be fed more often if they are crying for food. Ideally the neonates should not be disturbed when sleeping, but it is more important to maintain a regular feeding schedule, and neonates that appear to be sleeping may be weak and may not cry for food.

E. **Feeding quantity.** Several guidelines may be followed.
1. Manufacturer's recommendations are provided with each commercial product.
2. The daily ration may be calculated from caloric density of the formula and calorie requirements. Caloric requirements are 13 – 20 kcal/100 g body weight/day during the first week of life, 15 – 22 kcal/100 g week 2, 18 – 28 kcal/100 g week 3, and 20 – 30 kcal/100 g week 4. It is best to begin at the lower end of each range (the tendancy is to overfeed).
3. Stomach capacity is approximately 5 mL/100 g and this can be used to help determine feeding volumes – e.g., for a kitten, 1 – 3 mL (maximum 5 mL) per feeding should be given on the first day, and the volume increased by 0.5 mL/feeding/day or by 1 – 2 mL/feeding every other day to a maximum of 10 mL per feeding. A guideline for kittens is a:

> 75 g kitten (2.5 oz) receives 2.4 mL q3h
> 135 g (4.5 oz) – 4.2 mL q3h
> 150 g (5 oz) – 4.7 mL q3h
> 158 g (5.25 oz) – 6.56 mL q4h
> 210 g (7 oz) – 8.8 mL q4h
> 225 g (8.5 oz) – 10.6 mL q4h

4. The signs that the stomach is full from feeding are the abdomen becoming slightly distended and/or the animal turning its head away from the bottle and squirming.
5. The animal should be gaining weight each day. If there is no other explanation for poor weight gain, the ration should be increased by 10% or another formula considered.
6. **Overfeeding** will result in diarrhea. If this occurs either –
   a. reduce volume to previous level if it appears to be too much; or
   b. keep volume the same to ensure adequate water intake, and dilute concentration by 25%.

F. **Stimulate elimination** after each feeding using cotton balls soaked in warm water to wipe the caudal abdomen and anogenital region, and then dry gently. Wipe down the entire animal with a slightly damp, warm face cloth or soft nail brush 1 – 2 times per day. Voluntarily elimination and self-grooming begin after about 3 weeks. Note that littermates may suckle on each other, and that suckling on the anogenital region will result in elimination.

G. **Weaning.** A commercial weaning formula (various brands), a homemade weaning formula, or a human baby cereal can be added to formula in week 3, and the animals can be introduced to lapping gruel of neonatal or weaning formula and cereal, kitten/puppy food, or adult food at 3 – 4 weeks. This is typically a messy process. A litter box with non-clumping litter should be introduced to kittens at the same time. Animals can usually be weaned off support by weeks 4 – 6.

Kitten weaning formula "Kitten Glop"
Dissolve 1 package Knox gelatin in 1 cup boiling water. Mix well 30 mL (2 tbs) plain whole fat yogurt, 20 mL (2 tbs) whole mayonnaise, 2 raw egg yolks, 240 mL (1 cup) condensed milk or preferably goat's milk, and 5 mL (1 tsp) clear Karo (corn) syrup. Pour this mixture into the gelatin and mix well. The formula may be stored refrigerated for 5 days or apportioned, frozen, and warmed as needed.

H. **Socialization.** Neonates are typically reared as a group, but may be reared individually for the first 3 weeks if this is necesary to prevent suckling on littermates and to promote cleanliness. The intensity of hand-rearing will result in frequent handling during this period. At 3 weeks the critical socialization period begins and lasts until 9 weeks in the cat and 12 weeks in the dog. Keep the litter together and handle the animals frequently during this period in between feedings. If the animal is alone, try to introduce it to other animals that will not pose a health threat.

I. **Failure of Passive Transfer.**

1. Cat milk (and probably dog milk) contains similar quantities of immunoglobulins as colostrum, such that immediate fostering of neonates may result in acceptable levels of passive transfer.
2. Some nursing formulas contain bovine colostrum. While the antibodies will likely be absorbed, the quantity in the formula may be too low and functional benefit is not proven.

3. Commercially available **purified equine IgG** may be given PO or SC (preferably) (Suggested Reading 3). The antibodies are as well absorbed as feline IgG, but they may not function adequately. The lyophilized preparation is reconstituted in sterile saline to a concentration of 200 mg IgG/mL. The **dose** is 400 mg (2 mL) within 6 hours of birth followed by another dose of 400 mg 4 hours later.
4. **Adult species-specific serum** may be given PO, SC, or IP. In the research reports (Suggested Readings 1, 5, 7) serum was obtained from 6 – 15 adult animals, pooled, and frozen in 5 – 8 mL aliquots. This approach may be considered for a clinic with a large pediatric caseload, but it is impractical in most clinics for occasional therapy. An alternative is to obtain serum from a healthy vaccinated mature animal that is suitable as a blood donor. Aseptic technique should be used as with collection of other blood products for transfusion. The phlebotomist's hands are washed thoroughly and the collecting vein is clipped and aseptically prepared. The blood may be collected by vacuum draw into red top (clot) tubes, where the tops of the tubes have been cleansed with alcohol. Alternatively, the blood may be collected in a syringe and aseptically transferred to red top tubes or sterile plastic tubes. Care must be taken to avoid contamination of the tip of the syringe, tubes and stoppers during transfer of the blood. The blood is allowed to clot (this process may be accelerated by incubation of the tubes in 37°C [98.6°F] water. The tubes are centrifuged at the standard speed used to separate serum, and the serum is aseptically drawn off with a needle or open-end tom-cat catheter and syringe, making sure not to collect any of the red cells or buffy coat. The serum is warmed to 35 – 37°C (95 – 98.6°F) prior to administration.

   The optimal treatment protocol is not known, in part because the optimal target levels of immunoglobulins in the blood are not known.

1. The **doses** reported in **puppies** were approximately 20 mL/kg PO at birth (± another treatment 12 hours later), 20 mL/kg SC at birth, and 40 mL/kg SC at birth. This resulted in approximately 10% of the peak IgG levels during the first 2 days post-partum achievable with colostrum, but nearly equivalent IgG levels after the first week of life. The highest peak levels of serum immunoglobulins were achieved with 40 mL/kg SC.
2. The dose reported in **kittens** was 50 mL/kg IP/SC at birth and again at 12 and 24 hours post-partum. This protocol achieved serum IgG levels nearly equivalent to that achieved with colostrum.
3. The **oral route** limits the quantity of serum that can be administered compared to **SC and IP routes** and may interfere with the feeding of milk replacers. (Stomach capacity is at the very most 50 mL/kg, and neonatal puppies usually consume about 80 mL/kg colostrum during the first 24 hours). It should also be noted that maximum intestinal absorption of immunoglobulins occurs in pups at 8 hours post-partum, and this may be the best time if a single oral treatment is to be given. The SC route is slightly more effective than PO. The injection must be given slowly to minimize pain and it results in an obvious pocket of SC fluid.

PHARMACOLOGY

1) **Metoclopramide** is a central-acting dopamine antagonist, which stimulates prolactin secretion in addition to its antiemetic effects.

2) **Acepromazine** is a phenothiazine, which also stimulates prolactin secretion in addition to its tranquilizer effects.

3) **Prolactin** is not commercially available as a therapeutic agent.

4) **Oxytocin** is a hormone of the posterior pituitary gland that is normally released during labor to stimulate uterine contractions and during nursing to promote milk letdown. It is available as an injectable product and as a nasal spray.

5) **Cabergoline** is a dopamine agonist that inhibits prolactin.

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INTRODUCTION

All patients with respiratory problems must be dealt with immediately as the transition from respiratory insufficiency to failure can occur within minutes. Note the respiratory pattern, facial expression and work involved with the respiratory effort and attempt to locate the problem area. Dyspnea is a term used to describe an abnormal breathing effort as assessed by respiratory rate, rhythm and character and altered behaviour. This may occur in paroxysms, after exercise, or continously. Dyspnea may be associated with respiratory or non-respiratory problems. If heart failure is the cause of dyspnea *see Acute Congestive Heart Failure p. 149*. Note that animals with known chronic disease can develop acute on chronic symptoms (e.g., asthma, chronic bronchitis, pulmonary edema of heart failure). Pneumothorax can occur spontaneously, as can hemothorax. Pulmonary edema can be present in patients without cardiac disease. Crackles and wheezes can occur in situations other than heart failure, for example, chronic bronchitis, or neurogenic pulmonary edema. Diaphragmatic hernias can be congenital in origin or secondary to trauma. They may be acute or chronic. Refer to Burns and Smoke Inhalation *p. 682* for this injury.

DIAGNOSIS

History/Signalment

- **Himalayan cats** tend to be over-represented for pericardio-diaphragmatic hernias, although any breed of cat or dog may have this congenital lesion. Often a second problem (e.g., asthma, pleural effusion) may be the reason for presentation.
- **Pyothorax** tends to be the most common septic problem in cats.
- **Puppies and kittens** are more likely to have infectious disease.
- **Brachycephalic breeds,** especially English and French bulldogs, Pugs, Boston terriers, tend to develop upper airway 'obstruction' secondary to the small nares, redundant pharyngeal mucosa and eventual everted laryngeal saccules, and/or hypoplastic trachea. In hot weather or with excitement, these animals become severely compromised and dyspneic.
- **Large,** older dogs tend to develop laryngeal paralysis, while the **smaller** breeds (e.g., Pomeranian, Yorkshire Terrier) tend to develop a collapsing trachea. Rarely, cats may develop laryngeal paralysis.
- West Highland White Terriers, and other small breed dogs may be predisposed to **pulmonary fibrosis.**
- Upper airway problems are rare in cats, however nasopharyngeal polyps and upper airway neoplasms are possible.
- **Larger breed dogs** tend to be more free-roaming and therefore, succumb to motor vehicle injuries, which frequently involve the respiratory system, pulmonary contusions and hemo/pneumothorax.
- Some smaller dogs, but predominantly larger dogs, especially those involved in hunting, tend to develop fungal disease due to the 'nose-to-the-ground' activity. In the author's experience, Golden Retrievers appear to be over-represented (blastomycosis in Southern Ontario), although fungal respiratory disease may occur in any animal.
- **Pneumonia** may be acute if associated with aspiration or sub-acute to chronic. Pneumonia may be bacterial, viral, parasitic, mycotic or rickettsial in origin. Recent history of boarding, hunting, etc., concurrent illness or immunosuppressive medication is helpful in diagnosis. Pneumonia occurs more frequently in dogs than cats.
- **Asthma** is not uncommon in cats. Question the owner regarding coughing. Some owners mistake coughing for vomiting (especially hair balls)/gagging. It may be helpful to question the owner about the presence of smokers in the house.
- **Allergic pneumonitis** can result in acute obstructive airway disease after exposure to the allergen, in both cats and dogs. There may be a chronic history of allergic lung disease but with an acute exacerbation. Question the owner regarding environmental condition (i.e., renovating an old house).
- **Neoplasia in both cats and dogs.** Frequently animals living in a "smoker's" home may have primary lung pathology. Metastatic lung disease occurs with many different tumour types and locations.
- Lymphoma of the respiratory system occurs more frequently in cats than dogs.
- Young animals are more prone to electric cord bite injuries than older animal. Question the owner regarding potential exposure to electric cords and subsequent non-cardiogenic pulmonary edema
- Dogs predisposed to **hypothyroidism** (*p. 285*) may also acquire laryngeal paralysis, megaesophagus and secondary aspiration pneumonia.
- **Neuromuscular disease** (e.g., peripheral neuropathies, myasthenia gravis *p. 494*) can affect the respiratory muscles. These patients have a progressive (may be subtle) history, of at least 2 – 3 days. Question the owner regarding a history of recent bite injury (polyradiculoneuritis/Coonhound paralysis), tick exposure, or garbage/compost ingestion (botulism). The immediate concern is respiratory failure due to muscle weakness and an inability to ventilate. Megaesophagus may be present in patients with generalized or focal myasthenia gravis, which predisposes to aspiration pneumonia.

- **Smoke inhalation injury** (*p. 682*) can be present without associated skin burns. The animal may not be presented immediately as smoke inhalation injury tends to get worse over time (24 – 48 hours). The injury may be restricted to the larynx and trachea (direct heat injury, laryngeal spasm and edema), or continues to involve small airways and lung. Carbon monoxide and other toxic gases and particulate matter can be carried to the lower airways causing direct injury or bronchospasm/constriction after exposure. This, in addition to reduced ciliary activity, predisposes the patient to pneumonia. In severe cases, pulmonary edema and atelectasis occur. **Note:** neurological deficits may occur hours to days post smoke inhalation (*see Burns & Smoke Injury p. 682* for management).
- **Medical history**. May include asthma, heart disease, seizure activity, recent onset of lethargy, depression, vomiting with possible aspiration. If a puppy or kitten is presented, how are the littermates?
- **A rare association with hypertrophic osteodystrophy in puppies** is a diffuse pneumonitis, alveolitis.
- **Whether free-roaming.** Road injury, kicked by a horse, access to toxins, etc. Is there a recent or past history of trauma?
- **If in your clinic.**
  - Consider fluid overload if the patient has received fluids (may still be seen with conservative fluid administration in patients with underlying heart disease).
  - Could the patient have aspirated, after anesthesia, because of weakness and recumbency, or megaesophagus? Is the animal being force-fed which may also have caused aspiration pneumonia?.
  - **If immune-mediated disease** (*p. 411*) with acute respiratory distress, consider pulmonary thromboembolism.
  - If infectious or other inflammatory diseases present, consider **acute respiratory distress syndrome.**
  - **Evacuation of a large volume of pleural fluid** (present for >3 days), **or repair of a diaphragmatic hernia** can rarely lead to re-expansion pulmonary edema either immediately, or delayed by 4 – 24 hours.
  - Upper airway obstruction, post-extubation laryngospasm, or other potential problems.
- **Non-cardiogenic or neurogenic pulmonary edema** may occur due to the following:
  - **Electric cord bite.** May result in varying degrees of non-cardiogenic pulmonary edema. Note if oral burns present.
  - **Head trauma.**
  - **Cardiac Arrhythmia,** continuous or transient also referred to as 'flash' pulmonary edema.
  - **Near drowning** results in non-cardiogenic pulmonary edema due to:
    - **Laryngospasm** and increased negative pressure at onset of drowning.
    - **Inhalation of non-salt water** – increases surface tension within alveoli with subsequent alveolar collapse.
    - **Inhalation of salt water** results in alveolar flooding due to fluid shift into alveoli.
    - **Potential increased intracranial pressure** (*see Neurological Examination in Head Trauma p. 698*); serum sodium abnormalities (*see Hyper/Hyponatremia p. 381*); hypothermia (*see Accidental Hypothermia p. 291*).
  - **Generalized convulsive seizure activity** can lead to fulminating pulmonary edema.
  - **Strangulation** while tethered at groomers, in the yard, or walking on the leash, grabbed by the neck, etc.– **Upper airway obstruction** (i.e., choking on food, airway foreign body).
  - **Violent coughing.**
  - **Ethylene glycol intoxication** (unknown seizures occurred?).
  - Active blocking of the nares while holding the muzzle.

Clinical Signs/Physical Examination

TABLE 1. Definitions and Disease Associations of Respiratory Effort

Term	Definition	Disease Association
Dyspnea	Abnormal breathing effort on inspiration/expiration. Assess by rate, rhythm, character, altered behaviour. Described as a 'panic' sensation in people. May claw at face.	Respiratory or non-respiratory severe disorders or both.
Tachypnea/ polypnea	Increased respiratory rate	Normal after exercise, excitement; otherwise associated with most respiratory problems and neuromuscular, vascular, metabolic, hematologic disorders.
Orthopnea	Difficulty breathing except in upright position	Severe respiratory or cardiac disease (due to pulm edema).
Hyperpnea	Abnormal increase in depth and rate of respiratory movements	Frequent in acidemic patients, trying to blow off CO_2.
Bradypnea	Low respiratory rate	May be associated with alkalosis, CNS disorders or sleep.
Apnea	Cessation of respiratory movements	May occur under general anesthesia or very heavy sedation. Pre-terminal event.

Figure 1. Summarizes the localization of lesions according to the respiratory pattern.

Things to note are:

- Is there more effort on inspiration or expiration (or do both require effort)? Where more effort is required, this phase is longer.
- Is it noisy or quiet?
- Is it rapid and shallow?
- Is the work of breathing excessive for the amount of chest wall movement? Does the thorax have minimal excursion? If the thorax is increased in size (i.e., barrel shaped, separation of the ribs) – consider tension pneumothorax or severe effusion.
- All acutely hypoxic animals (PaO_2 <60 mmHg, oxygen saturation <90 %) present with a 'sense of panic and air hunger' (dyspnea). These animals appear oblivious to their surroundings as they are so focused on breathing; forelimbs may be abducted.
- During the physical examination, note **abnormalities** such as smell of smoke, indicating smoke inhalation, or dirt or gravel indicating traumatic injury, or the presence of abdominal fluid, possibly indicating low circulating blood volume, etc.
- Note **mucous membrane colour** while examining the head and neck area. Cyanosis indicates significant desaturation. Red may indicate hyperthermia due to the work of breathing, or carbon monoxide, acetaminophen or cyanide toxicity. Pale mucous membranes indicate anemia with or without blood loss. Pale gray, indicates poor perfusion (e.g., severe blood loss *p. 619*, pericardial tamponade *p. 145*, gastric dilation-volvulus *p. 59*). Jaundice and pale usually occurs with hemolytic anemia (*p. 411*).
- Look in the mouth for burn wounds usually seen on the mucosa covering the hard palate or at the commissures of the mouth when associated with electric cord bites.
- **Cough** may indicate mitral valve heart disease with enlarged left atrium (compression of the mainstem bronchus), or tumour causing compression. Asthma and infectious diseases noted below also cause coughing.
- Cough on **palpation of trachea** may indicate tracheobronchitis. As this may be *Bordetella bronchiseptica,* or canine adenovirus; observe isolation technique (*see Nosocomial Infection p. 600*).
- If ocular and nasal discharge present, ± cough, or pneumonia suspect an infectious cause (e.g., *Bordetella bronchiseptica,* distemper virus, canine adenovirus, feline leukemia or calici virus). Wear gown and gloves to avoid transmission to other animals. Isolate the patient until proven not infectious (*see Nosocomial Infection p. 600*).
- If **extrathoracic obstruction** evident examine the head [asymmetry of the nose or eyes may indicate nasal pathology (stertorous breathing)]. Look in the mouth for blood clots, vomitus, foreign body (FB), mucous, palpate and examine the neck area for wounds, crepitus, swelling, esophageal FBs (*p. 54*), or a mass. Collapsing trachea produces a 'honking' sound and obstructs the airway during collapse. Auscultate the neck to aid the localization of the lesion within the pharynx, larynx, trachea and thoracic inlet.
- If **intrathoracic 'obstruction',** shave the neck and examine the jugular veins; are they distended (congestive heart failure (*p. 149*), cardiac tamponade (*p. 145*), severe pneumothorax), pulmonary artery thrombosis (*p. 198*)? Other conditions to consider are intrathoracic tracheal collapse, or obstruction (i.e., intraluminal or extraluminal mass, external compression by esophageal FB [*p. 54*]) where jugular veins may not be distended.
- **Auscultate the trachea (cats and dogs).** If loud sounds heard here then pathology is within the upper airway, when auscultating the thorax these sounds will be referred and should not be interpreted as lung pathology.
- **Auscultate the thorax** bilaterally, start dorsally (cranial to caudal), mid-region (cranial to caudal), then ventrally (cranial to caudal). Repeat any area that seemed abnormal. Are there increased breath sounds? These can be present with increased effort without lung pathology (e.g., exercise, hypovolemia,) or due to lung pathology (e.g., neoplasia, pneumonia, contusions, edema, pulmonary hemorrhage).
  - If lung sounds are present ventrally but absent or **reduced dorsally**, with increased resonance on percussion, pneumothorax is present.
  - If lung sounds are present dorsally but absent or **reduced ventrally,** pleural effusion, a space occupying mass, or large volume pericardial effusion is likely present.
  - If a localized area of reduced lung or heart sounds, or displaced heart sounds are noted, a thoracic mass or diaphragmatic hernia may be present. A thoracic mass and effusion frequently coexist. Mediastinal masses may cause a pleural effusion, edema of the head and neck and forelimbs and paraneoplastic signs (polymyositis or myasthenia gravis). Compress the cranial thorax in cats; reduced compressibility may indicate a mediastinal mass. With tumour invasion of vessels, esophagus or trachea, there may be air, blood or exudate within the mediastinum.

FIGURE 1. Localization of Lesion by Respiratory Pattern

EFFORT ON INSPIRATION

Noisy (stertorous or wheeze)

Slow, deep breaths

Open-mouth breathing

Flared nostrils

Commissures of the lips pulled back

Extension of the head and neck "sucking" in at thoracic inlet.

EXTRATHORACIC OBSTRUCTIVE DISEASE

Nose – *obstruction, injuries

Pharynx – elongated soft palate, *obstruction, injuries

Larynx – laryngeal paralysis, edema, *obstruction, trauma

Cervical trachea – collapse, trauma, *obstruction, esophageal *obstruction

PARENCHYMAL DISEASE

cardiogenic and non-cardiogenic pulmonary edema, pneumonia, aspiration, infectious, parasitic, neoplastic infiltrates

CARDIAC DISEASE

congenital and acquired, arrhythmias

NEUROMUSCULAR DISEASE

VASCULAR DISEASE

thromboembolic disease of pulmonary vessels

ANEMIA – ACUTE

EFFORT ON EXPIRATION

Noisy (grunt or wheeze)

Normal or slow, deep breaths with active abdominal component.

INTRATHORACIC OBSTRUCTIVE DISEASE

Intrathoracic trachea – trauma, obstruction, collapse, esophageal *obstruction

Bronchi – *obstruction, collapse, trauma

Small airways – *obstruction, asthma

RAPID AND SHALLOW

Usually quiet

Almost like panting, as condition worsens, the chest excursions become more shallow as the respiratory difficulty increases.

TENSION (usually) PNEUMOTHORAX

With no excursion, barrel-chested, increased intercostal spaces, gasping for air.

RIB FRACTURE

Paradoxical pattern (associated with rapid, shallow breathing) a portion, or whole hemothorax if multiple rib fractures, **moves inward with inspiration and outward with expiration**

RESTRICTIVE DISEASE

Pleural space – blood, exudate, transudate, chyle, air, mass, diaphragmatic hernia

Thoracic wall – fractured ribs, pain

Parenchymal disease – pulmonary edema, pneumonia, neoplasia, fibrosis

NEUROMUSCULAR DISEASE

Minimum **THORACIC** excursion and extreme diaphragmatic effort

EFFORT ON INSPIRATION AND EXPIRATION

Quiet if not associated with fixed airway *obstruction or small airway disease

Respiratory effort could be described as any of the obstructive and/or restrictive types of respiratory pattern but the rate tends to be higher than normal.

COMBINATION OF OBSTRUCTIVE, RESTRICTIVE, OR VASCULAR DISEASE

Fixed airway obstruction – intra- extra-luminal tracheal stenosis tracheal collapse

PARENCHYMAL DISEASE

cardiogenic and non-cardiogenic pulmonary edema, pneumonia, aspiration, infectious, parasitic, neoplastic infiltrates

VASCULAR DISEASE

thromboembolic disease of pulmonary vessels

NEUROLOGICAL DISEASE

head trauma, inflammatory disease

LOW CIRCULATING VOLUME

shock, hemorrhage, sepsis, anaphylaxis

CARDIAC DISEASE

congenital and acquired, arrhythmias

ANEMIA – ACUTE

NEUROMUSCULAR DISEASE

METABOLIC DISEASE

uremia, diabetic, ketoacidosis, severe acidosis, heat stroke

Note: *Obstruction = foreign body, tumour, blood, mucous, debris, purulent material, collapse or edema.

- **In cats** lung sounds may still be heard in the presence of pneumothorax and pleural effusion, but may be almost absent with acute obstructive airway disease ("status asthmaticus"). In this instance, if the animal is unstable for immediate radiographic examination, consider respiratory pattern and history to convince you of pleural space disease or small airway disease (if unstable for radiographic examination.) With severe **small airway disease,** coughing, dyspnea (inspiratory and particularly expiratory) with increased abdominal effort, wheezing, tachypnea, open-mouthed breathing, cyanosis and frantic (air hungry) behaviour are usually noted. Debilitation may be present with cardiac, neoplastic or chronic asthmatic disease.
- With **pneumonia,** dyspnea, cough, pyrexia, depression, anorexia, weight loss and dehydration, serous or mucopurulent nasal discharge may be present. On auscultation there are increased breath sounds with crackles and wheezes. There may be reduced sounds in areas of consolidation. If lung sounds are absent on one side, differentials include a completely consolidated lung lobe or the pleural space may be completely affected, for example, an obstructed mainstem bronchus
- While auscultating, palpate and examine the thorax for wounds, penetrating foreign bodies, or fractured ribs (flail chest).
- **Auscultate heart sounds** (or lack of!), note murmurs and locations. If normal heart sounds are located in an abnormal position this may suggest displacement by a mass. No heart sounds, normal lung sounds ± distended jugular veins suggests pericardial effusion.
- **Non-cardiogenic/Neurogenic pulmonary edema.** The degree of edema is dependent on the degree of pulmonary vessel hypertension experienced following the catecholamine surge in neurogenic/hypoxic situations. An increase in hydrostatic pressure alone will resolve; a more severe increase in hydrostatic pressure with 'stretch' of endothelium with increased 'gap' will result in ongoing edema for a period of time; extreme increase in hydrostatic pressure with endothelial 'tearing' results in hemorrhage and confers a poor prognosis as this is unlikely to resolve. Sanguinous fluid is expelled from the lungs. Auscultation may reveal crackles and increased breath sounds, with the dorso-caudal areas being affected. Where inflammation and subsequent capillary leak occur, the lesion is not localized to the dorso-caudal area but tends to be diffuse.
- Patients **with neuromuscular disease** are weak, recumbent and may present with a shallow, ineffective respiratory pattern, without thoracic expansion, extreme respiratory effort with exaggerated movement of the commissures of the mouth. Terminally, there is only a diaphragmatic component to ventilation. The temperature is usually elevated and occasionally above 42°C (107.6°F). Patients with myasthenia gravis may also have aspiration pneumonia. PaO_2 and PCO_2 may be within normal range, however, the work of breathing required to maintain this contributes to the patient's demise. The work of breathing should be the guide to mechanically ventilate the patient, not the blood gases.
- Does the patient have **inflammatory disease or capillary leak syndrome** (e.g., sepsis, pancreatitis, vasculitis, pneumonia, DIC, IMHA) possibly causing acute respiratory distress syndrome (ARDS) or pulmonary thromboemboli (*p. 198*). Harsh breath sounds with crackles and increased respiratory rate may be auscultated.
- **Pulmonary neoplastic disease** may be primary or metastatic. A primary tumour elsewhere may be identified on physical exam. Weight loss suggesting chronic disease may be evident. On auscultation, increased breath sounds, crackles and wheezes may be heard, or displaced heart sounds due to a mass.
- **Coagulopathies** as a result of thrombocytopenia (*p. 451*), or rodenticide anticoagulant toxicity (*p. 639*), hemorrhage (*p. 619*), can result in pleural, airway or parenchymal hemorrhage.
- **Low circulating blood volume** of any cause (shock); the lung sounds will be normal to slightly increased due to increased rate and depth of breathing. Examine the patient for evidence of vomiting and diarrhea (water and electrolyte loss), peritonitis, pleuritis, liver disease, etc., severe burns (plasma loss) or hemorrhage (coagulopathies, trauma).
- **Pulmonary contusions/hemorrhage** may be diffuse or patchy. Crackles may be heard, or areas of reduced or no sounds if consolidated with hemorrhage.
- **Temperature and pulse.** With **primary respiratory disease,** pulses are easily palpable, regular and increased in rate; rarely bradycardia may be present. Temperature is normal or elevated. Infectious and inflammatory diseases and an extreme effort in the work of breathing, cause a marked elevation in temperature. **Cooling must be addressed immediately** (*see Hyperthermia p. 297*). In **cardiac disease or in shock,** femoral pulses are weak and dorsal pedal pulses are frequently absent. In congestive heart failure pulses may be irregular and increased in rate and the temperature may be below normal.

FIGURE 2. Radiographic Patterns in Respiratory Emergencies

PLEURAL SPACE OPACITY

MEDIASTINAL OPACITY

(junction of dorsal & mid-third thorax)

LUNG PARENCHYMA

INCREASED PULMONARY OPACITY

DECREASED PULMONARY OPACITY

Do not confuse with pleural space decreased opacity!

DECREASED OPACITY

INCREASED OPACITY

AIR
Partial/total (tension) lung collapse, heart elevated

FLUID
Increased density ventrally, leafing of lung lobes
Pleural fissure lines

DECREASED OPACITY

AIR
Trachea, esophagus, aorta, pulmonary artery outlined

AIR TRAPPING (ASTHMA)
Expanded lung field
Displacement of diaphragm caudally
Peribronchial cuffing ± right middle lung lobe collapse (occasionally other lobes)

PULMONARY THROMBO-EMBOLISM
Truncated pulmonary arteries
Patchy alveolar infiltrate (not always)

HYPOVOLEMIA
Small heart elevated off sternum
Poorly visible blood vessels
Narrow vena cava

MASS
Localized areas of increased density

INCREASED OPACITY

FLUID OR MASS
Reduced definition of mediastinal structures

ALVELOR PATTERN

MIXED ALVEOLAR AND INTERSTITIAL

Early Stage

INTERSTITIAL PATTERN

BRONCHIAL PATTERN

PNEUMONITIS
Loss of fine detail

ASTHMA
(early)

BRONCHITIS

PULMONARY CONTUSION

PULMONARY EDEMA

NEOPLASIA
Any Lobe(s)

PNEUMONIA

PNEUMONIA
(Viral/Rickettsial)

BRONCHOPNEUMONIA
with alveolar pattern

CARDIOGENIC
Dog: Perihilar, extensive if severe

Cat: Distribution anywhere

Dog/Cat: Air bronchogram

NON-CARDIOGENIC
Dorsal lobes, or Florid with air bronchograms, or Total opacity if severe

ASPIRATION
Typically right middle lobe, but may be cranial with ventral distribution

INFECTION
Distribution any lobe (s)

Laboratory/Imaging Data Base

Stat

- Only attempt blood collection after you have the respiratory problem under control. Take blood from the IV catheter at the time of insertion. As there are many etiologies of respiratory disease (**Fig. 1 & 2**), it is difficult to advise as to specific tests and results for each. The history and physical examination findings will better guide the appropriate tests, however, basic 'stat' tests recommended below are essential.
- **PCV, TS** to evaluate hydration status and hemorrhage (coagulopathy), sepsis (hypoproteinemia).
- **Stick BUN, creatinine** to evaluate degree of renal involvement and hydration status.
- **Glucose** (hypoglycemia) where sepsis may be an underlying cause of respiratory failure.
- **ACT** to screen for coagulopathy and possible inflammation.
- **Platelet count** if coagulopathy or sepsis is suspected.
- **Serum electrolytes** as part of an overall assessment.
- **CBC** if suspect infection to identify leukocytosis or leukopenia, and assess platelet numbers.
- **Venous CO_2** to assess ventilation if arterial blood gases cannot be obtained. CO_2 may be:
    - low due to hyperventilation with mild-moderate lung involvement;
    - normal if hyperventilating with moderate to severe lung involvement;
    - high when hypoxemic with severe lung involvement.
    - If $PvCO_2$ >45 mmHg with increased respiratory effort, ventilation is compromised.
- **Oxygen saturation** (pulse oximetry) to evaluate ability to oxygenate. If <92%, oxygenation is compromised.
- **Arterial blood gases** if you can obtain without stressing the patient.
- **Metabolic status** using total serum CO_2, serum bicarbonate and adjusted base excess (<-4 indicates non-respiratory acidosis).
- **Cytology and gram stain** on all aspirated effusions and culture and sensitivity where infection suspected (bacteria seen on gram stain, neutrophils present, see Table 2).
- **Chest radiographs,** when stable, to identify lesions or monitor therapy. For interpretation of radiographic findings of individual problems see **Fig. 2.** Lateral view of cervical and intra-thoracic trachea, while **head and neck are in normal position,** may reveal area of >50% collapse in patients with suspect collapsing trachea. To confirm, obtain one view on inspiration (cervical collapse) and on expiration (intra-thoracic collapse).
- **Laryngeal examination** under **light** sedation, i.e., Propofol in 1 – 2 mg/kg increments, preserving jaw tone and the gag reflex, to identify:

    - laryngeal paralysis where the arytenoid cartilages and vocal folds do not abduct on inspiration; in severe cases these structures are literally sucked into the airway with attempts at inspiration. These structures may also be very 'flaccid' and edematous. Should the findings here be equivocal administer **doxopram 1.0 mg/kg** and observe for these signs.
    - laryngospasm in cats following extubation.
    - elongated soft palate is visualized as edematous mucosa protruding into the laryngeal opening.
    - other oropharyngeal obstruction such as neoplasms, foreign bodies, nasopharygeal polyps.

- **If pneumonia or neoplasia** is suspected and the patient is stable, perform transtracheal wash (TTW) **or bronchoalveolar lavage** (BAL), **or fine needle aspirate of most affected area of lung** (cytology, culture and sensitivity), prior to antibiotic therapy. Frequently neoplastic cells do not exfoliate during TTW or BAL resulting in a negative cytological diagnosis. Submit a fecal sample for fecal flotation if parasitic pneumonia suspected. A Baermann fecal test may also be indicated.
- **Biochemical profile** is required for overall assessment of the patient.

Extended Data Base

- Specific tests as indicated based on history, physical examination and potential etiology.
- Fluoroscopy or bronchoscopy to identify area of collapsing trachea.
- Broncho-alveolar lavage to obtain specimen for cytology and culture for definitive diagnosis. In patients with respiratory compromise, BAL will exacerbate the underlying respiratory disease, consider pretreatment with terbutaline at 0.01 mg/kg SC or salbutamol (albuterol) 4 μg/kg IV (diluted), SC.
- Thyroid panel to identify hypothyroidism (*p. 285*). Where possible, perform a fT4 by equilibrium dialysis (instead of TT4) to decrease the influence of sick euthyroid syndrome.
- Acetylcholine receptor antibody titre to identify myasthenia gravis (*p. 496*).

TABLE 2. Evaluation of Aspirated Effusions

EFFUSION	CHARACTERISTICS		ETIOLOGY
TRANSLIDATE	Colorless, clear Protein <30 g/L Cells <0.5 x 10⁹/L (monocytes, non-degenerative neutrophils, mesothelial cells)		Effusion of hyproteinemia Feline heart disease Congestive heart failure
MODIFIED TRANSUDATE	Pink to red, ± slightly turbid Protein 30 – 50 g/L Cells <5 x 10⁹/L (Erythrocytes, macrophages, non-degenerative neutrophils, mesothelial, occ. eosin and lymphs.)		Diaphragmatic hernia Thoracic neoplasia (i.e., lymphoma) Feline infectious peritonitis Lung torsion
	White to pink, turbid Protein >30 g/L Cells >5 x 10⁹/L Small lymphs, some non-degen. neuts Triglycerides > serum level		Chyle
	White, turbid Protein >30 g/L, Cells >5 x 10⁹/L Triglyceride < serum level		Chylous – lymphoma – feline heart disease
	Protein 30 – 60 g/L Cells <10 x 10⁹/L ± malignant cells		Lymphatic obstruction (carcinoma)
	Clusters of malignant mesothelial cells		Mesothelioma
EXUDATE	White, yellow, pink, turbid Protein >30 g/L Cells >3 x 10⁹	Neutrophils non-degenerative:	Non-septic exudate: feline infectious peritonitis sterile foreign body
	Fluid turbid, yellowish or pink/red	Neutrophils degenerative (may be normal if antibiotics used)	Septic exudate
	Odor ± micro-organisms, ± foreign body material	Neutrophils predominate	
HEMORRHAGE	Free-flowing, non-clotting blood, PCV >5% Upon standing supernatant clears		Recent hemorrhage (within hours) (tumour, trauma, bleeding disorder)
	Red-brown, purple Distorted erythrocytes, hypersegmented leukocytes, Upon standing supernatant xanthochromic or pink		Long-standing or resolving hemorrhage (tumour, trauma)

I. GENERAL CONSIDERATIONS

Oxygen administration is essential. If available, heliox (helium 70% and oxygen 30%) administration may be more effective in airway obstruction (intra- or extraluminal) and asthma. Heliox can be administered by the same methods as oxygen. Refer to *p. 577* if mechanical ventilation is being considered in any respiratory emergency.

A. Chemical Restraint

It may be necessary to sedate patients with respiratory compromise (who may have **cardiovascular disease**) in order to perform minor tasks such as blood collection, intravenous (IV) catheter placement or radiographic/ultrasonographic examination. The decision to sedate, and then with what, can be difficult. However, struggling with an animal in heart failure can be more dangerous than the potential adverse effects of the appropriate drug. **Short-acting, reversible sedative regimens are preferred.** Avoid using drugs and dosages that will cause respiratory depression or increase susceptibility to arrhythmias. Blood pressure monitoring should be performed. The IV route of administration is advisable as the dose can then be titrated to effect. However, intramuscular (IM) dosing, starting with a low dose, will have to suffice if there is no IV access. Opioid and benzodiazepine derivative drugs either alone or in combination are preferred.

Severe respiratory compromise, can progress rapidly to respiratory and cardiac arrest and therefore must be dealt with immediately. Calming the animal will facilitate therapy in mild situations, but anesthesia may be necessary for immediate treatment of severely distressed patients. In these situations advanced preparation for intubation and ventilation should be carried out (equipment and drugs available, doses calculated) and personnel managing patients briefed on monitoring these patients and the need to respond quickly and efficiently if deterioration should occur. It is better to sedate than to resuscitate. Always use the **lower end of the dose range** in geriatric or severely compromised animals.

1. **If no IV access** present and the patient is **frantic** or **struggling,** administer
    a. **Acepromazine 0.01 – 0.05 mg/kg IM** (if not hypotensive situation) OR,
    b. **Butorphanol 0.05 – 0.2 mg/kg IM,** followed by
    c. **Midazolam 0.2 – 0.5 mg/kg IM** if further sedation is required. (**If cardiac disease** suspected, especially hypertrophic cardiomyopathy [HCM] the lower dosage is suggested initially; see cardiovascular disease below for further information).
    d. **Ketamine 0.2 mg/kg IM** for sedation may be indicated as ketamine has potential bronchodilator properties as well. Slightly higher dosages may be used.
    e. If **heavier sedation to anesthesia is required,** administer **midazolam 0.2 – 0.5 mg/kg with ketamine 2.5 – 10.0 mg/kg IM.** Diazepam IM hurts! .
    f. If **you cannot get near them (especially cats), spray the mucous membranes of the mouth with ketamine 5 – 10 mg/kg (cats – lowest dose if cardiac disease may be present so as to avoid tachycardia,** add a sedative as soon as possible.
    g. **In dogs,** an alternative is **pentobarbital 10 mg/kg IM** or more to effect (wait 15 min before repeating), and **butorphanol 0.05 – 0.2 mg/kg IM.** This could take several minutes.
    h. **Isoflurane or sevoflurane** is recommended for the worst cases of status asthmaticus. In addition go to **II Intrathoracic Lesions D 1 (*p. 567*) below.**

2. **If IV access** present in any patient (caution in cats with HCM, see cardiovascular disease below), administer:
    a. **Diazepam (5 mg/mL) plus ketamine (100 mg/mL) mixed 1:1 by volume and given at 0.05 – 0.15 mL/kg IV in cats and dogs** (author's preference). Anesthetic induction may be attempted immediately if required. Diazepam/Ketamine combination is chosen for the advantage of safe, slow induction to effect. These animals may be very sensitive to the dose used, especially if a degree of hypoxia has been produced. Titrate to effect using 1/4 – 1/5 of typical induction doses (0.02 mL/kg diazepam/ketamine); repeat in 15 – 20 sec intervals until intubation is possible. OR
    b. **Propofol 1.0 mg/kg,** titrated slowly to effect IV, is an alternative. **Diazepam 0.2 mg/kg IV** can be given to reduce the dose of propofol required and possibly the resultant adverse cardiovascular effects (hypotension from vasodilation). Once airway management has been secured, diagnostic or therapeutic procedures can be performed.
    c. *See Chemical Restraint for Respiratory Emergencies p. 100 for further instruction.*

3. If sedation required for calming or **to perform minor procedures** (IV catheter placement, ultrasonagraphic/echocardiography).
   a. **Butorphanol 0.05 – 0.2 mg/kg IM** is the opioid of choice, however,
   b. **Morphine 0.2 – 1.0 mg/kg IM, IV** (very slowly), dose to effect, may be selected in dogs and cats. Morphine may cause vomiting, and dysphoria in cats if administered too quickly or at too high a dose. It is advised to carefully titrate the dose.
   c. **Fentanyl 2 – 4 μg/kg.**
   d. **Meperidine 3 – 5 mg/kg IM** can also produce reasonable sedation and may be used instead of butorphanol.
   e. Can add diazepam or **midazolam 0.2 – 0.5 mg/kg IV, IM OR** to above opioids for additive effect
   f. **If HCM** is suspected in cats, maintain lower heart rates, using an opiate (usually butorphanol). Very low dose ketamine may be used for sedation, however, induction of anesthesia with ketamine should not be used due to the potential for higher heart rates and enhanced output obstruction; mask induction with isoflurane is recommended.

4. Where upper airway disease is suspected, sedation with **butorphanol 0.05 – 0.2 mg/kg or acepromazine 0.005 – 0.05 mg/kg IV, IM** is recommended.

5. **Due to work of breathing,** the body temperature is increased. Temperature should be obtained as soon as possible. If >39.5°C (102°F), cool with cold wet towels and a fan. *See Hyperthermia p. 297* if further guidance required due to temperature >40.5°C (105°F).

B. Airway/Breathing

1. If **unconscious or acutely apneic** (about to lose consciousness), intubation is necessary. Perform this gently and avoid touching the perilaryngeal structures to avoid possible vagally mediated cardiac arrest. Do not elevate the head too much, perform intubation in either sternal, horizontal or recumbent horizontal position, or in dorsal recumbency. Ventilate with 100% oxygen. Verify correct placement by observing thoracic excursion and auscultate both sides of the chest for lung sounds. Be prepared to perform emergency tracheotomy (*see Respiratory Emergency Procedures p. 582*). If intubation is required due to **small airway disease,** place a 19 gauge (8" or 12" jugular) catheter, through the endotracheal tube – no further than the carina – and give one ventolin (salbutamol) puff into the catheter hub. A puff directly into the ET tube may be helpful. In small airway constriction gentle compression of the thorax on exhalation may help to expel trapped air.

2. If **cyanotic** (non-responsive to oxygen or heliox), and intubation not possible due to tracheal obstruction, quickly clip the hair below obstruction, infiltrate skin, SC down to trachea with 1 mL 2% lidocaine and place a 19 gauge through the needle, 8" or 12" IV catheter through the cricothyroid ligament (oral or phayngeal obstruction) or between the tracheal rings below the level of tracheal obstruction. A 14 – 16 gauge IV catheter is an alternative but these may kink. Attach oxygen delivery tubing. Stabilize catheter around the neck as you would an IV catheter in the limb. Avoid kinking at the hub-catheter interface. Oxygen should be delivered to achieve normal thoracic excursion (30 – 50+ mL/kg). Do not allow the lungs to hyperinflate, remove oxygen line for normal exhalation through the IV catheter if total obstruction present. Be prepared to perform a tracheotomy (*Respiratory Emergency Procedures p. 582*).

3. If **conscious** and able to move some air through the airway, pre-oxygenate with >200 mL/kg 100% oxygen (if airway obstruction, try Heliox if available) prior to any maneouvre; this will calm the animal and allow a little more time to correct the problem before dangerous desaturation occurs. Hold the nozzle of a large tube (e.g., Bain's circuit, oxygen tubing) up to the nose; place a clear plastic bag over the patient's head and insert oxygen tube; or place an Elizabethan collar with plastic wrap over it and insert the oxygen tubing under the loose collar (caution with CO_2 and heat accummulation). Our preference with small animals is placement of a plexiglass 'hood' over the head and shoulders of a small cat or dog (*see Fig. 1 Oxygen Supplementation p. 577*), and nasal prongs in medium to large dogs. If not critical, an oxygen cage may suffice to allow a reduction in the anxiety level.

4. If **oropharyngeal obstruction** due to blood, mucous, vomitus in mouth or pharynx, lower the head and neck, wipe out and suction with an endotracheal tube (larger diameter) as a tip or a Yankauer suction tip. Do not elevate the head. Continue to oxygenate with tube at mouth/nose level or transtracheally. If unable to remove the obstructive material be prepared to intubate and suction or perform tracheotomy (*p. 582*).

C. Circulation/Fluid therapy requires individual consideration. One-half maintenance rate fluids (*p. 366*) should be instituted to maintain patency of the IV catheter which is required for the administration of various medications. Aggressive fluid administration is absolutely contraindicated in most respiratory emergencies. Where fluid resuscitation is required, refer to various sections for guidance (i.e., *see Hemorrhage p. 624 Sepsis/Septic Shock p. 588, Fluid Therapy p. 351*). If PCV<25%, administration of blood or packed cells is advised to improve oxygen delivery to the tissues as oxygenation is already compromised in these animals. Calculate volume to achieve a PCV 30% (*see Transfusion Therapy p. 682*).

II. SPECIFIC CONSIDERATIONS

EXTRATHORACIC LESIONS

A. If **foreign body (FB) within the trachea,** and unconscious, (while getting an assistant to prepare supplies for tracheotomy), rapidly oxygenate (*see B 1 above*), place in sternal position, with head and chest down and hind legs raised, compress chest and abdomen in an attempt to expel the FB. If unsuccessful perform tracheotomy (below obstruction), or go to B below. If conscious, forcibly compress the sternum or thorax laterally (**Heimlich manoeuvre**) while in head down, hind limbs up position; in large dogs, straddle them (your front to the dog's back), compress the sternum; having an assistant raise the hind end to facilitate FB expulsion with gravity. **Sedation** (*see I A above*) may facilitate FB expulsion due to relaxation. Alternatively, place on tilt table if available and compress thorax bilaterally. Anesthesia and bronchoscopy may be required for retrieval. An esophageal FB may also result in respiratory distress (*see Esophageal Foreign Bodies p. 54*). Anesthetize the patient, intubate with long, small-diameter tubing to bypass FB followed by a thoracic tracheal intubation, ventilate, and remove the FB via endoscopy. Emergency thoracotomy may be required.

B. If **fixed obstruction,** intra- or extraluminal (tumours, collapsed trachea) administer oxygen or Heliox in I B above by the method most appropriate for the situation. Definitive therapy is required in these cases. Transtracheal passage of an IV catheter to beyond the obstruction may help the emergent patient. Otherwise anesthesia (*p. 114*) and bronchoscopy to pass a catheter beyond the obstruction might be lifesaving until definitive treatment can be performed.

  1. If **brachycephalic breed (upper airway syndrome) or laryngeal paralysis,**
     a. Oxygenate (*see Breathing above*) and
     b. Administer **acepromazine 0.005 – 0.05 mg /kg IV** or IM (contraindicated if hypotensive) **OR butorphanol 0.05 – 0.2 mg/kg IV, IM** and
     c. **Dexamethasone sodium phosphate 0.25 mg/kg IV, IM.**
     d. **Take temperature.** If >39.5°C cool with wet towels and fan.
     e. Put the dog, with oxygen, and owner in a quiet place and let them both relax!
     f. Occasionally, definitive correction, or tracheotomy has to be performed as an emergency (*p. 582*) if severe obstruction due to soft palate, everted saccules, collapsed arytenoid cartilage or laryngeal paralysis is present.

  2. **Collapsing trachea** can cause severe distress and inspiratory dyspnea initially with inspiratory and expiratory dyspnea in very severe cases.
     a. Follow as **1 above** for upper airway problems.
     b. Add **terbutaline 0.01 mg/kg SC,** followed with **oral dosages of 1.25 – 5 mg/kg/dog** q12h–q8h **OR salbutamol 4 µg/kg IV (diluted), SC.**
     c. **Suppress cough with hydrocodone 0.22 mg/kg PO q4–8h,** OR **butorphanol 0.5 – 1.0 mg/kg** PO q8–12h may be helpful in isolated tracheobronchitis. Do not use if pneumonia present.
     d. **Auburn University Elixir** (*see Pharmacology below*)
     f. **If life-threatening** and deciding what to do, anesthetize with:
        i. **Propofol 2 – 6 mg/kg IV,** followed by 0.5 – 1 mg/kg CRI, OR
        ii. **Ketamine/diazepam I A 2 a above,** followed by CRI to effect

  3. **Tracheal tears or acute laryngeal trauma** from animal fights or other traumatic incidents may be small or the trachea could be completely transected. The patient's condition dictates therapy.
     a. If oxygen supplementation alone aids the respiratory distress, commence judicious fluid resuscitation if required and stabilise the patient prior to definitive treatment.
     b. If emergent airway management is required to correct the disrupted airway, anesthetize the patient. Oropharyngeal intubation should be attempted while palpating the tracheal injury and guiding the endotracheal tube.
     c. Alternatively, approach the trachea as for tracheostomy. Place endotracheal tube through the defect if large enough. Avoid contaminating the airway. If necessary, go below the lesion and perform tracheotomy (*see Respiratory Emergency Procedures p. 582*). Intra-thoracic tears/avulsion may require repair via emergency thoracotomy, unless stable due to bridging by tracheal adventitia and repair can be planned.
     d. Surgery is required for definitive therapy. Tracheal resection is frequently required.

4. **Tracheobronchitis** mainly affects trachea and bronchi, but occasionally pneumonia may be present. Coughing can be very debilitating. In younger animals *Bordetella bronchiseptica* and viruses are main causitive agents. Mycoplasma sp may also be isolated.

    a. **Doxycycline 5 mg/kg q12h** is recommended for *Bordetella bronchiseptica* for 7 – 10 days. Tetracycline is not recommended in puppies and pregnant animals due to discolouration of teeth; administration of q8h frequency and avoidance of medication 2 hours prior to, and 4 hours after feedings makes it impossible to treat!

    b. **Trimethorprim-sulfonomide 15 mg/kg PO q8h** 7 – 10 days.

    c. Cough suppressants: **hydrocodone 0.22 mg/kg PO q4–8h, OR butorphanol 0.5 – 1.0 mg/kg PO q8–12h** may be helpful for relief in isolated tracheobronchitis. Do not use if pneumonia present.

    d. Corticosteroid, **prednisone 0.25 mg/kg q12–24h** as an anti-inflammatory may be useful in severe cases without pneumonia, for 1 – 2 days.

INTRATHORACIC LESIONS

A. **Congestive Heart Failure or Cardiac Tamponade** (*see Congestive Heart Failure p. 149, Cardiac Tamponade p. 145*).

B. Pleural Space Pathology

    1. **Tension pneumothorax.** Intubation and ventilation prior to thoracocentesis will **worsen** the situation. Intubate if unconscious. These patients die of hypotensive shock due to poor venous return to the heart. Tension pneumothorax requires immediate attention.

        a. Perform **immediate thoracocentesis at 7th intercostal space at the junction of upper and middle thirds if in sternal recumbency, or 7th intercostal, highest (mid) point if in lateral recumbency (*p. 574*).** If collapsed place 14 – 16 gauge IV catheter directly into pleural space to relieve tension (remember here pleural pressure is higher than ambient pressure – tension). If time permits, quickly pull skin cranially, clip and prep with alcohol, inject 1 mL 2% lidocaine into skin, SC, muscle and pleura. Make a 5 mm incision through the skin. Push a teat cannula into the chest and allow the air to evacuate rapidly, OR, then aspirate with syringe and stopcock. A large bore chest drain will have to be placed with continuous suction. Alternatively, attach a Heimlich valve (Bard-Parker, Becton Dickinson, Lincoln Park, NJ) to the chest drain. This is recommended for transportation to a continuous care facility. Continuous suction is preferred as this will permit contact of visceral and parietal pleurae, forming a seal.

        b. **Rarely,** incision into the chest (mini thoracotomy), following one 'swipe' of the clippers and a 'squirt' of chlorhexidine or betadine is required in unconscious patients. Exploratory thoracotomy and lavage of the thorax is necessary.

        c. **Exploratory thoracotomy** is required to identify, and definitively correct the problem.

    2. After correction of tension pneumothorax and prior to attending to the following, go to **D 5,** Non-Cardiogenic Pulmonary Edema associated with evacuation of pleural space.

    3. **Non-tension pneumothorax** can be treated with needle thoracocentesis (*see Respiratory Emergency Procedures p. 574*). Measure the amount of air removed. If repeat thoracocentesis is required and the volume of air is reduced at each time, a chest tube may not be required. Should frequent thoracocentesis be required (>3x) with no reduction in volume removed, a chest tube is necessary (*see Respiratory Emergency Procedures p. 575*). Pneumothorax may be secondary to trauma or spontaneous (e.g., bullae, abscesses, FBs). Spontaneous pneumothorax rarely resolves without surgical intervention. Traumatic pneumothorax is almost always self-limiting.

    4. **Pleural effusion.** Diagnostic thoracocentesis should be performed to grossly identify the fluid (Table 2). Needle thoracocentesis is performed at the 7th intercostal space at the costochondral junction (*see Respiratory Emergency Procedures p. 574*). If blood is aspirated and trauma is known or suspected, consider autotransfusion of removed blood (see Transfusion Therapy *p. 680*). If large volumes of fluid are suspected, removal should be performed with a teat cannula (*p. 574*). An IV catheter or butterfly catheter can be used but is time consuming in large dogs. Butterfly catheters may not be long enough in large dogs. All non-blood effusions should be submitted for cytological, biochemical, ± culture and sensitivity, unless due to confirmed heart failure. **Aerobic and anaerobic culture is most important** where infection is suspected as chronic therapy with appropriate antibiotics may be required. While waiting for C&S results *see C3 p. 567/597* for antibiotic selection. Consider fungal cultures if this is a potential problem. Milky effusions are usually chylous, although less 'milky' pseudochylous effusions may occur; odiferous, flocculent or purulent are infectious; serosanguinous or serous may be associated with neoplasia, heart failure or chronic diaphragmatic hernia and liver entrapment; straw-coloured in cats suggest feline infectious peritonitis. If pyothorax diagnosed, place a thoracostomy tube on affected side(s) (*p. 575*) and remove fluid. Ultrasonographic examination is required to determine if an abscess(es) is present and surgical management indicated. Medical management consists of

suction and lavage with ~10 mL/kg body temperature sterile saline q8h. Continuous suction is recommended where possible.

5. **Diaphragmatic hernia.** If traumatic, pneumothorax, hemothorax or entrapment of abdominal organs may also be present. Remove air and blood by thoracocentesis. Congenital diaphragmatic hernias should be suspected in the exotic breeds of cats (i.e., Himalayans), which may also be in association with small airway (allergic lung) disease. Treat small airway disease if applicable prior to surgical correction of the hernia. A diaphragmatic hernia may be identified during laparotomy for a non-related cause, or a pneumothorax may occur as a complication after abdominal surgery (e.g., ovariohysterectomy) in a patient with unknown or history of previous trauma and undetected hernia. (Obtain IV access; support the patient with cautious fluid and oxygen therapy while preparing for surgical correction).

6. **Thoracic mass.** As this is frequently associated with a pleural effusion, removing the fluid will relieve the immediate respiratory difficulty. Occasionally, very little fluid is aspirated as the bulk of the obstruction is the mass, or the fluid is compartmentalized. Submit fluid for cytology. Perform fine needle aspirate of the mass with 12 mL syringe and 22 gauge needle, submit for cytological examination.

C. Mediastinal Pathology

1. **Mediastinal masses** may be lymphoma in cats, thymomas, heart base tumours, enlarged lymph nodes, etc. compressing the trachea. (*see thoracic mass II B. 6 above*). Perform thoracocentesis to remove pleural effusion if present. Aspiration of the mass may be difficult due to depth and large vessels.

2. **Pneumomediastinum.** Spontaneous, after airway or esophageal trauma, occasionally after transtracheal wash, pulmonary parenchymal injury or disease, with visceral pleura intact where the leaking air travels along bronchovascular tissue to mediastinum. Also reported in dogs and cats after tracheal intubation (tracheal trauma from stylet, high cuff pressures, transmitted vibration of ultrasonic scaler to endotracheal tube during dentistry, closed pop-off valve on anesthetic machine). Usually self-limiting, but may progress through thoracic inlet and travel subcutaneously throughout the whole body. If subcutaneous air collection is severe, the air should be evacuated from a large pocket with an 18 gauge needle. A body wrap may be required, however, respiratory compromise may occur. Requires constant observation. Rarely, tension pneumomediastinum may occur; thoracocentesis or chest tube placement is necessary. Here the large volume of air displaces the mediastinal pleura towards the chest wall and presents as if it were a pneumothorax. Oxygen therapy for 24 hours may assist in reabsorption of the air.

3. **Mediastinum** may occur with lymphadenitis, migrating porcupine quills or after esophageal rupture. A FB may still be present in the esophagus, passed into the stomach or recently removed. The FB should be removed. The surgical approach is indicated with esophageal rupture.

   a. Obtain IV access, calculate fluid deficit and administer isotonic crystalloids (*see Fluid Therapy p. 347*).

   b. Administer **clindamycin 10 mg/kg IV q12h and enrofloxacin 5 mg/kg q24h (dogs & cats)***
   [*Do not use enrofloxacin in small dogs <8months, or large breeds <18 months unless absolutely necessary]; OR

   c. **cefoxitin 20 mg/kg IV q6h (dogs) q8h (cats)** OR

   d. **trimethaprim-sulfadiazine 15 mg/kg SC, IV (diluted) q12h and metronidazole 10 mg/kg IV over 1 h CRI q8h** cats and dogs.

   e. Obtain samples for culture and sensitivity where possible prior to antibiotic therapy. However, do not risk the patient's life by delaying treatment.

D. Parenchymal Pathology

1. **Small airway disease ("asthma"), bronchoconstriction.**

   a. If unable to ventilate, anesthetize with **isoflurane or sevoflurane,** mechanically ventilate (go to g iii epinephrine and c below). Caution with cardiac arrhythmias.

   b. Administer **Heliox or oxygen.** Assisted exhalation, by compressing the thorax very gently may help; stop if the cat becomes distressed. As various recommendations exist as to methods of treating feline 'asthma', initial emergent, 24 hour treatment only is presented.

   c. For **anti-inflammatory therapy,** initially, administer **dexamethasone S-P 0.5 – 1.0 (once if severe) mg/kg,** repeat **0.25 mg/kg in 12h IM or IV; OR prednisolone sodium succinate 2.0 mg/kg, followed by 1.0 – 2.0 mg/kg in 12h IM or IV.**

d. For **bronchodilation,** administor **Ventolin® (salbutamol puffer),** one puff (no more due to compound effect within the chamber) into preferably an 'aerokat' chamber (used for cats with a one-way inhalation valve), or an aerochamber (used for children), or face mask and let the cat (or dog) take one breath; repeat with another puff if required every 30 minutes for up to 4 hours; stop should muscle twitches occur. Do not use if epinephrine (*g below*) is considered.

e. **Salbutamol 4 μ/kg IV diluted,** repeat in 15 min if required, increase dose to **8 μ/kg** if required.

f. **Terbutaline 0.01 mg/kg SC,** repeat in 15 min if no sign of relief.
   i. **Terbutaline and salbutamol** are beta2- adrenergic agonist- bronchodilators; relief of asthmatic symptoms in cats may occur in 15 – 30 min. This can be repeated if little or no response. Check heart rate first, if 240 bpm (cats) then the drug is absorbed, the medication should not be repeated. A respiratory rate or effort that drops by ≥ 50% suggests a beneficial effect. Suggest demonstrating SC injection to the owner for at home emergency treatment in cats with bad disease. Do not use if epinephrine (*g below*) is considered.

g. The following treatment for bronchodilation is not ideal but is suggested if the above medications are not available to you and bronchodilation is deemed necessary.
   i. **aminophylline 2 – 4 mg/kg IM use the lower dose with corticosteroids;** OR
   ii. if **non-responsive and dying, and cardiac disease is not a differential, isoproteranol 0.1 – 0.2 mL SC of a 1:5000 solution;** repeat in 5 min if no improvement. OR
   iii. **epinephrine 0.5 mL/cat of 1:10,000 (1 mL of 1 mg/mL in 10 mL saline) IM.** This has not been used by the author but has been recommended in per-acute, non-responsive situations. Repeat hourly if necessary. Caution if salbutamol or terbutaline used.

h. If injectable formulations are **not** available to you, the situation is not emergent and it is possible to administer oral medication.
   i. **terbutaline, one-eighth to one-quarter of a 2.5 mg tab**/CAT q12h. OR
   ii. **sustained release theophylline 25 mg/kg q24h at night** in cats (this is a published dose, however, the author has not used this dose but on occasion uses 25 mg per CAT which may be appropriate for bronchodilation). These doses should be reduced by half after 48h to avoid side effects. Reassess the patient at that time for chronic therapy.
   iii. **Dogs may** present with small airway disease/bronchoconstriction; oral medications to consider **terbutaline 1.25 – 5.0 mg/DOG** PO q8h, OR **sustained release theophylline 20 mg/kg q12h (Theo-Dur).**

i. In refractory cases where euthanasia may be considered, treat the emergent situation and add **cyclosporin 10 mg/kg PO q12h** to attain whole blood levels at 300 – 500 ng/mL.

2. Acute aspiration pneumonia

a. Hold the head down, remove particulate matter if present. Oxygenate.

b. You may have to sedate/anesthetize to remove particulate matter from airway. Suction airway if a large volume of fluid was aspirated. Oxygenate.

c. If a small amount of fluid was aspirated, this should be of little or no consequence.

d. Do not administer steroids or antibiotics routinely. Tracheal and bronchial secretions will neutralize the aspirated contents. Antibiotics should only be administered if infection occurs and the organisms identified OR large volume aspirated. Initial antibiotic of choice for large volume aspiration is cefazolin at 22 mg/kg IV q6h (dogs) q8h (cats).

e. Supportive care is recommended (*see pneumonia below*).

3. Pneumonia (infection)

a. Obtain IV access, replace fluid deficits carefully, and deliver maintenance fluids at maintenance plus 10%/each degree above 38.5°C (101.5°F) (*see Fluid Therapy p. 366*). Caution is advised with fluid therapy as pulmonary edema may develop easily, however maintaining a non-tenacious mucous is also important.

b. Perform TTW or BAL and obtain samples for cytology, culture and sensitivity (very important prior to empirical therapy). Examine gram stain immediately.

c. If TTW contraindicated or if **critical situation administer**

   i. **clindamycin 10 mg/kg IV q12h, combined with cefotetan, or cefoxitin 20 mg/kg IV q6h (dogs) q8h (cats) or enrofloxacin 5 mg/kg IV q24h** if adult, and streptococcus is definitely not suspect, OR only if non-responsive to previous antibiotics and the patient's condition is deteriorating.
   ii. **imipenem 5 mg/kg IV q8h (cat and dog)** as a 1h CRI (may cause seizures in young animals), OR
   iii. **meropenam 20 mg/kg IV q12h, 8 mg/kg SC q12h (dogs & cats).**

    d. If **Gram +ve cocci** administer
      i. first generation **cephalosporin 20 mg/kg IV q6h (dogs) q8h (cats),** OR
      ii. **trimethoprim-sulfadiazine 15 mg/kg SC, IM, IV (confirm formulation) q12h**

    e. If **gram -ve rods,** administer
      i. **trimethoprim-sulfadiazine 15 mg/kg SC, IM, IV (confirm formulation) q12h** OR
      ii. **enrofloxacin 5 – 10 mg/kg IV** (over 30 min dogs only), **IM q24h OR gentamicin 8 mg/kg IV, IM, SC q24h. Do not administer more than 5 mg/kg SC, PO in cats q24h.**

    f. If a history consistent with *Bordetella* infection,
      i. **gentamicin 9 mg/kg IV, IM, SC q24h (dogs & cats),** do not use in animals that are dehydrated or have pre-existing renal disease, OR
      ii. **doxycycline 5 mg/kg IV, PO q12h for 48h, then 5 mg/kg q24h** OR
      iii. ***chloramphenicol 50 mg/kg IV, SC, PO q8h (dog) consider the human risks, such as myelosuppression/aplastic anemia, prior to using this drug.** Gloves must be worn during handling and administration, and hands washed after gloves removed.

    g. Select drug for treatment of parasitic infection based on specific identification.
      i. **Rickettsia** administer **doxycycline 5 mg/kg IV, PO q12h or *chloramphenicol 40 – 50 mg/kg IV, IM, PO q8h (dog); 12.5 – 20 mg/kg IV, IM, PO q12h (cat)**
      ii. **Toxoplasma** administer **clindamycin 10 mg/kg IV, PO q12h.**

    h. **Fungi**
      i. **itraconazole 5 – 10 mg/kg IV, PO q12h.** (*see iii*) OR
      ii. **fluconazole 8 – 10 mg/kg IV q24h.** (*see iii*)
      iii. Where **pulmonary involvement is florid** as opposed to one or two discrete lesions, it is recommended that the lower dose of itraconozole or fluconazole be used initially, plus **1.0 mg/kg prednisone** be administered 1 hour prior to therapy to reduce edema associated with killing of organisms. Prednisone 1 mg/kg q24h therapy combined with antifungal therapy may be required for several days if respiratory effort worsens. A reduction to 0.5 mg/kg q24h if the patient is improving, is suggested for up to one week. In the author's experience severe morbidity and mortality may occur when severe pulmonary fungal infections and CNS infections are treated without prior prednisone treatment. Administration of anti-inflammatory doses of prednisone reduces morbidity (not contributes to it) when used with appropriate antifungal therapy and for a short time (i.e., 2 – 7 days).

    i. **Supportive care** should consist of aerosol nebulization therapy with 0.9% sterile saline. Sterility is very important, otherwise the nebulization will carry bacteria deep into the lung. Physiotherapy after nebulization helps mobilize secretions. If able to walk, this should be encouraged, otherwise coupage (cupping of the hands while "hitting" the chest wall), or electrical massager to the thorax.

    j. Occasionally, **nebulization of gentamicin 8 mg/kg q24** (3 – 5 days) for susceptible organisms (especially, difficult to treat *Bordetella*), in addition to other appropriate systemic antibiotic, may expedite recovery. This intravenous dose plus 3 mL sterile 0.9% saline is nebulized over 10 – 15 min. The caregiver should wear a mask. Patients tolerate this well. Antibiotics with strong odour cannot be used (penicillins, cephalosporins). Consult your local human Medical Supply house for rental of equipment.

    k. Maintain good hydration but avoid over-hydration. Oxygen supplementation if needed. Antitussives and antihistamines are contraindicated, as is furosemide as these "dry up" the secretions. Furosemide will exacerbate nephrotoxicity of aminoglycosides (gentamicin).

4. **Pulmonary edema – Non-cardiogenic (for cardiogenic** s*ee Congestive Heart Failure p. 149).*
   Increased capillary hydrostatic pressure
    a. **Fluid overload.** Stop fluids or blood if this could be the cause. Oxygen supplementation. **Intubate** if critical. If frothing in the airways, intubate, oxygenate, suction with postural drainage (dump); **± nebulize** with 20% – 50% ethanol (suggested in the literature, but has never been used by the author). Administer **furosemide 2 mg/kg** IV, (dogs and cats). If necessary repeat in 30 – 60 min. Repeat again at 0.25 mg/kg if needed. Occasionally a CRI of 0.2 mg/kg/h furosemide may be more beneficial than bolus therapy.
    b. **Neurogenic, Cerebral Hypoxia**
      Strangulation, electrocution, seizure, head trauma, cardiac arrhythmia, coughing, choking, or other causes of increased intracranial pressure or cerebral hypoxia. The inciting cause has been removed and systemic pressures are probably normal.

i. A **single** dose of **2 mg/kg furosemide (dog and cat) IV,** may help; do not continue furosemide to reduce edema as this may result in dehydration and reduced arterial pressure.

ii. Treat the underlying cause (i.e., *seizure activity p. 458 Cat, p. 462 Dog*; oral burns if due to electric cord bite *p. 682*).

iii. Positive pressure ventilation if the conservative measures do not relieve the situation The translocated pulmonary fluid/RBC takes time to resolve.

iv. **Avoid** synthetic colloids.

v. Monitor blood pressure and maintain MAP 80 – 100 mmHg OR systolic 100 – 120 mmHg. If systolic pressure >120 mm Hg or MAP >100 mm Hg, consider **nitroglycerine paste** (*see Congestive Heart Failure p. 149*).

vi. **dopamine (2 – 5 μg/kg/min *p. 233*), or isoproteranol (0.1 μg/kg/min)** may increase alveolar fluid absorption and is suggested in severe situations. Blood pressure monitoring is essential.

5. **Re-expansion of lungs after evacuation of large volumes of fluid, or acute upper airway obstruction or laryngeal paralysis** can cause an acute, short-lived change in transpleural pressures and subsequent increase in pulmonary hydrostatic pressure and vascular injury. **Treat as for Neurogenic or Cerebral hypoxia (D 4b above).**

6. **Near drowning** due to laryngospasm or non-salt water aspiration. Treat as **D 4b** above and be prepared to ventilate. If serum sodium is abnormal refer to Hyper/Hyponatremia for fluid therapy guidelines. If neurological abnormalities see Neurological examination in Head Trauma *p. 698*.

7. **Ethylene glycol intoxication** as D 4b above. Etiology unknown but may be due to un-witnessed seizure activity. Be prepared to ventilate. Treat for ethylene glycol toxicity (*p. 655*).

8. **Increased capillary permeability: capillary leak/vasculitis/ARDS.** Treat the underlying disease. Maintain normal blood pressure, fresh frozen plasma may be beneficial. Fresh whole blood if PCV <25%. 25% human serum albumin if hypoalbuminemic, albumin in combination with furosemide may improve outcome in ARDS. Assisted ventilation may be required. The prognosis is dependent on the underlying cause.

9. **Neoplasia.** Supportive oxygen therapy until definitive diagnosis and treatment or euthanasia. Remove pleural fluid if present.

10. **Pulmonary inflammatory disorders** (e.g., Pulmonary Infiltrates of Eosinophils). A diffuse lesion is usually present when the dog is presented as an emergency. TTW usually rewarding and reveals many eosinophils. Bronchial-alveolar lavage may be required if TTW unsuccessful to rule out fungal disease, but caution is required as massive release of intracellular mediators may occur causing florid pulmonary edema requiring mechanical ventilation. Pre-treat with terbutaline or salbutamol. **Dexamethasone 0.25 mg/kg IV, IM q24h OR prednisone 1 mg/kg q12h** for first 2 days, then assess and taper.

11. **Pulmonary hemorrhage.**
    a. Contusions may be mild or extensive. Oxygen via nasal cannula or mechanical ventilation may be required. **Fluids should not** be administered unless evidence of volume loss. Mild to moderate contusions are usually self-limiting but patients with moderate to severe contusions may require mechanical ventilation.
    b. If severe bleeding into the airways, prognosis is grave. Intubate, hold 'upside-down' to drain majority of fluid, suction as necessary.
    c. Identify area of hemorrhage and place that side down.
    d. If caused by trauma, surgical removal of the lobe may be necessary.
    e. If thrombocytopenia (*p. 451*) or rodenticide toxicity (*p. 639*), fresh blood products (need RBCs, plasma and platelets) and Vitamin K1 (rodenticide toxicity) are required (*see Hemorrhage p. 619*).
    f. Oxygen support. Assisted ventilation may be necessary (*p. 577*).
    g. Caution with fluid therapy (*p. 358*).

12. **Pulmonary thromboembolism** (*see Thromboembolic Disease p. 198*) is difficult to diagnose but highly suspicious with concurrent predisposing disease (i.e., protein-losing enteropathy or nephropathy, IMHA).

13. **Acute respiratory signs associated with hypertrophic osteodystrophy** in medium to large breed puppies and has been described as a pneumonitis. There is a generalized increase in overall lung radiodensity. At necropsy, one puppy had marked and diffuse congestion of the lung; alveolitis and bronchiolitis with hemorrhage was diagnosed on histology (personal communication Dr. S. Gary Brown). Oxygen, mechanical ventilation if condition dictates (*see p. 577*) and general supportive care.

E. Thoracic wall injuries

Pain management. Analgesics are **mandatory** to reduce pain and permit normal lung expansion. Pain prevents expansion of the thorax with reduced ventilation. Butorphanol, hydromorphone, morphine or fentanyl, CRI and/or intercostal nerve blocks are advised (*see p. 229, 125*).

1. **Penetrating objects** should only be removed during surgical exploration where direct visualization of the point of penetration can be made. The object may be lodged in the lung or a vessel and preventing hemorrhage or pneumothorax. Removal without compression or repair, would result in fatal hemorrhage. Debridement and lavage is also required. Stabilize with fluid and oxygen support while preparing for surgical intervention.

2. **Bite wounds or traumatic wounds** frequently have extensive underlying trauma, with lung lobe laceration/herniation that is not visualized on radiographs. Bite wounds will permit air and contaminants to enter the pleural space.

   a. Place a sterile dressing (gauze or laparotomy sponge) with sterile petroleum-based ointment around the periphery over the wound to prevent further air from entering the pleural space.
   b. Perform thoracocentesis (*p. 574*) to remove the air while stabilizing (IV access, fluid and oxygen support) the patient.
   c. Place a chest drain if frequent thoracocentesis required (*p. 575*).
   d. Refer to a specialty continuous care facility for immediate exploration, removal of FBs, debridement, partial or total lung lobectomy if necessary and extensive lavage.

3. **Flail chest** predisposes to laceration of intercostal vessels, results in hypoxemia and increased work of breathing, and pain.
   a. Place a light wrap to prevent excessive motion and reduce pain.
   b. Place the affected, flail side down to decrease unwanted motion.
   c. Acute, fatal hemorrhage and lung laceration can occur with these injuries especially with displacement of fractured ribs. Stabilization with bandage, external or internal fixation is necessary to prevent hemorrhage and lung laceration. Apply external stabilization using a frame secured to the patient with circumcostal sutures adjacent to and in the flail segment where moderate to severe displacement exists.
   d. Analgesics are required due to severe pain
      i. **Oxymorphone OR Hydromorphone 0.025 – 0.1 mg/kg IV, IM q4h** OR CRI/4h (*see Hydromorphone Infusion Chart p. 243*).
      ii. **Morphine 0.2 – 0.4 mg/kg IV, IM q4h** or CRI/4h (*see Morphine Infusion Chart p. 251*).
      iii. **Fentanyl 4 – 6 μg/kg IV followed by 4 – 6 μg/kg/h CRI**
   e. **Fractured ribs** (not flail) are usually managed conservatively if not displaced. A light bandage is usually sufficient. Displaced fractures should be stabilized for the same reasons as flail segments. Analgesics as in c above.

F. Neuromuscular disease. (*see Weakness p. 491*) Oxygen supplementation is required. Once oxygen is supplemented, oxygenation is easily achieved however ventilation and removal of CO_2 remains compromised. Rule out aspiration pneumonia in addition to respiratory muscle weakness. Identify underlying disease. If patient has noticeable work of breathing with fatigue, mechanical ventilation is required. Normal blood gases are often maintained until close to death due to fatigue.

G. Hypoventilation associated with or CNS etiology may respond to **caffeine at 5 – 10 mg/kg IV** slow infusion to increase respiratory drive in dogs and puppies. millophylline, etamyphylline still need to check this

III. ONGOING MONITORING and NURSING

Ongoing monitoring will depend on the underlying cause of the respiratory emergency.

A. If **anxiety** is worsening any of the above conditions, administer **morphine 0.05 – 0.1 mg/kg q3min until achieving desired effect IV** (or more if appears to help). Avoid rapid administration as hypotension will occur. Extrapolate the effective dose over 4 hours (*see Morphine Infusion Chart p. 251*) OR, **repeat q4–6h prn IM, SC if preferred (dogs and cats).** Although some texts state morphine is contraindicated in neurogenic pulmonary edema, this does not appear to be a problem once the inciting cause is removed and is recommended to alleviate anxiety and increase capacitance of pulmonary veins. Administer a sedative if needed.

B. For **bronchodilation,** see II D 1 d – f above.

C. Respiratory rate and effort should be assessed constantly. Do not allow the work of breathing to fatigue these patients. Increase oxygen flow, add another nasal cannula and administer oxygen from a second source. Re-assess underlying disease and respiratory effort.

D. **Temperature** should be monitored q 15 – 30 min if increasing or at least q1h with **increased work of breathing** (*not just increased rate*). The work of breathing, as well as infectious causes, can raise the temperature to >41.5°C. If the temperature exceeds 39.5°C (103°F) due to work (not pyrogen-induced), cool the patient with a fan or wet towel (*see Hyperthermia p. 297*).

E. If pyrogen-induced rise in temperature, ($\geq$41.5°C [106.5°F]) administer once if corticosteroids not being administered.

1. **acetaminophen drops (dogs only 10 mg/kg)** OR
2. **dipyrone 10 – 15 mg/kg IV (dogs and cats)** OR
3. **meloxicam 0.05 – 0.1 mg/kg (cats and dogs)** OR
4. **carprofen 1 – 2 mg/kg (dogs)**
5. plus appropriate antibiotics.

F. **Assisted/mechanical ventilation must be considered when:**

1. **PaO_2** <60 mmHg (acute) or 50 – 60 mmHg (chronic) or O_2 saturation of 90% cannot be achieved initially with the highest oxygen flow rate that can be delivered by your facility,
2. An elevated $PaCO_2$ or $PvCO_2$ alone is not an indication for ventilation. Some animals normally have an elevated $PaCO_2$ or $PvCO_2$ (e.g., the author's observation in brachycephalic breeds) and live quite happily with this. Probably the most important criteria for placing an animal on the ventilator is **work of breathing.** In the face of respiratory distress with an elevated respiratory rate, a "normal" $PvCO_2$ 40 – 45 mmHg is higher than expected, therefore, **work of** breathing becomes much more critical to evaluate. Often oxygen and carbon dioxide can be maintained within normal limits, but the work to maintain this is exhaustive. Animals can decompensate rapidly if not ventilated.
3. Normal blood gas measurements, or O_2 saturation >90%, cannot be maintained with an FIO_2 $\leq$0.5 (50% inspired oxygen) after receiving an FIO_2 >0.8 for the preceeding 24 hour period **without signs** of improvement. The patient is working very hard to maintain these measurements and appears distressed, hyperthermic and is weak (e.g., peripheral neuropathies, spinal injuries, severe pulmonary disease).
4. **Arterial blood gases** (or venous for CO_2 measurements) should be monitored to assess response to therapy. The frequency is determined by the severity of disease. Alternatively, pulse oximetry and total CO_2 can be used to assess oxygenation and ventilation.

G. **Nursing care.** Keep the nares patent. Clean nasal crusts to allow easier breathing. If in lateral recumbency, roll patient q4h. Maintain sternal recumbency where possible. **Place in an area with good air flow, out of a cage is preferred. Place a fan in the area to enhance air flow.**

H. **Serum electrolytes** should be measured daily until the patient is stable.

I. **Nutritional support** (*p. 499*) enteral or parenteral, is mandatory in these patients.

PHARMACOLOGY

1) **Heliox** is a 70% helium and 30% oxygen mixture. This mixture is much lighter than air or oxygen and because of the laminar flow characteristics of helium it can pass through very small openings, overcoming frictional resistance and oxygen can be delivered to the alveoli. Helium will also transport CO_2 from the alveoli to be exhaled. The work of breathing is dramatically reduced. This mixture has been lifesaving for patients at the OVC (unpublished data).

2) **Salbutamol, albuterol (Ventolin®)** produces bronchodilation through stimulation of beta2-adrenergic receptors in bronchial smooth muscle. A measurable decrease in airway resistance occurs by 30 min with peak improvement after 2 – 3 h. Bronchodilator activity may persist for 6 h. **Do not use with epinephrine.** Hypokalemia may result with excessive use.

3) **Theophylline/aminophylline** is a bronchodilator, which directly relaxes smooth muscle. **Corticosteroids and cimetidine will increase theophylline blood levels.** The dose should be reduced with concomitant use of these drugs. It is advised that cimetidine not be used with theophylline. There are many drug interactions and adverse effects. Enrofloxacin will decrease theophylline blood levels.

4) **Terbutaline** produces bronchodilation by stimulation of the beta2- adrenergic receptors in bronchial smooth muscle. Terbutaline also produces a decrease in airway and pulmonary resistance. Available as an inhaler. Use with caution in patients with a history of seizures. Hypokalemia may result with excessive use.

5) **Dopamine and Isoproteranol.** During hydrostatic pulmonary edema, active Na($^+$) transport and alveolar fluid reabsorption are decreased. Dopamine (DA) and isoproterenol (ISO) have been shown to increase active Na($^+$) transport in rat lungs by upregulating Na($^+$)-K($^+$)-ATPase in the alveolar epithelium. Studies suggest that DA and ISO increase alveolar fluid reabsorption in a model of increased left atrial pressure by regulating active Na($^+$) transport in rat alveolar epithelium. The effects of DA and ISO are mediated by the activation of dopaminergic D(1) receptors and the beta-adrenergic receptors, respectively.

6) **Auburn Elixir.** Phenobarbital Elixir 96 mg (24 mL), Isoproteranol 1 mg injectable (5 mL), Ephedrine 200 mg (4 mL of 50 mg/mL or 8 mL of 25 mg/mL), Theophylline 720 mg (135 mL), SSKI (potassium iodide) 2,400 mg (2-4 mL), Karo Syrup 60 mL. Dilute with water to 240 mL. Dose: 0.2-04 mL/kg q8h as needed. Monitor heart rate – do not allow to exceed 160 bpm.

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NOTES

THORACOCENTESIS

Indications

Diagnostic and/or therapeutic removal of air or fluid from pleural space. Continuous accumulations require chest drain placement.

Materials

19 gauge Butterfly catheter or
Over-the needle catheter 20, 18, 16 gauge or
Teat cannula (Pointed tip)
3-way stopcock or
Extension and 3-way stopcock
Large syringe (35 or 60 mL)

Procedure

a. Butterfly catheter technique.
 Attach 3-way stopcock to catheter and syringe. The skin is clipped centered over the 7th intercostal space and surgically prepped. Local anesthetic is not necessary, however, sedation may be necessary to perform this procedure in any difficult to handle animal. Aseptic placement of catheter wearing sterile gloves is mandatory. The needle is placed into the thorax with bevel down, and immediately directed parallel to the ribs. Place dorsally to remove air, or at the costochondral junction, to remove fluid.

b. Over-the-needle catheter technique.
 Once into the chest advance catheter and remove the needle, attach extension with stopcock and stabilize at catheter hub to avoid kinking while aspirating the pleural space. May be sutured in place for repeat aspairation. A 'needle' (PRN) adaptor is placed on the catheter.

c. Teat cannula technique.
 For large volume, single thoracocenteis i.e., pneumothorax, fluid accumulations due to cardiac insufficiency, thoracic duct disease/injury, trauma, hemorrhage. Requires more extensive skin prep. Pull skin forward. Infiltrate 1% lidocaine from skin to the pleura, dorsally or ventrally. Make a 2 mml skin/subcutaneous incision. Advance teat cannula into the chest. Attach extension tubing with 3-way stopcock. Wrap chest when completed.

Note: In an emergency, if the patient is dyspneic and auscultation of the chest suggests air or fluid is in the pleural space, thoracocentesis should be performed prior to radiographic exam. In chronic effusions, such as chylothorax, laceration of the visceral pleura may occur due to pleural pathology. Re-expansion pulmonary edema may rarely occur after evacuation of a large volume present for >3 days.

TRANSTRACHEAL CATHETER PLACEMENT (oxygen delivery, aerosolized bronchodilator, or sample aspiration)

Indications

1. Oxygen delivery in upper airway obstruction.
2. Retrieval of tracheobronchial samples for cytology, culture and sensitivity.

Do not attempt in uncooperative patients (after sedation) or patients with coagulopathies.

Materials

8" – 12", 14 – 19 gauge intravenous catheter (oxygen delivery or sample aspiration)
OR   3", 14 or 16 gauge intravenous catheter (oxygen delivery)
12 to 35 mL syringe
Nonbacteriostatic saline in 3 – 10 mL aliquots (for transtracheal wash [TTW])
Lidocaine 1% 1 – 2 mL
Sedation is usually not required, if necessary 0.025 mg/kg acepromazine (for TTW). The patient is required to cough for this procedure.
Butorphanol or oxymorphone if procedure for oxygen delivery

Procedure

Shave the area over the larynx and extended to the 5th tracheal ring and to each jugular vein. Perform a surgical prep of the area. Restrain with head extended for transtracheal wash or if there is NO debris or foreign body in the oral/pharyngeal area.

Place 1 mL 1% or 2% lidocaine through the skin to the trachea at the level of the cricothyroid membrane (transtracheal wash) or between the tracheal rings distal to the suspected obstruction. Wait 5 – 10 min. The trachea is stabilized, the point of catheter placement is located and the needle introduced at a 45° angle with the bevel of the needle against the ventral (anterior) wall of the trachea. Advance the catheter into the trachea. Remove the needle out of the trachea (place the guard over the needle where the needle cannot be removed) leaving the catheter in place.

If required for:

i. **Oxygen delivery,** attach an IV extension set to the long or short catheter which is attached to the oxygen line. Set oxygen flow at 30 – 50 + mL/kg and observe the chest for normal excursion. Do not over inflate the lungs. Reduce or increase flow as necessary. You may need to remove for exhalation if complete obstruction. If ventilation required using an Ambu bag, place the adaptor from a size 2 or 3 mm endotracheal tube into the IV extension set.
ii. **Delivery of bronchodilator,** attach the adaptor from a 2 or 3 mm endotracheal tube directly into the catheter hub and deliver one puff.
iii. **Transtracheal wash** attach the appropriate size syringe with sterile saline (12 mL syringe and 3 mL saline, to 10 mL saline in 35 mL syringe) directly onto the long catheter. Flush into catheter and aspirate immediately. Only a small portion of instilled fluid will be aspirated. Repeat instillation is usually required. Total volumes of saline for wash ~ 3 – 5 mL for cats and small dogs and 10 – 20 mL for larger dogs. All aspects of this procedure and fluid collection must be STERILE. Coupage the patient and encourage coughing. Less than 20% of fluid will be retrieved. Repeat two to three times as necessary to obtain a diagnostic sample (flocculent, mucous, purulent material). Remove the catheter while applying pressure to the insertion site. Cover the site with betadine or furacin ointment and a gauze square. Wrap. Observe for at least two hours.

Complications

Rarely, laceration to the trachea or lower airway with hemorrhage, pneumomediastinum or pneumothorax may occur. Dyspnea or subcutaneous emphysema occur slightly more often, especially in the smaller patient.

ENDOTRACHEAL WASH TECHNIQUE

Light anesthesia with laryngeal intubation using a sterile endotrachea tube is required. A laryngoscope with sterile blade, is required to ensure direct placement to avoid contamination of the endotracheal tube. Do not connect to anesthetic circuit prior to sampling. Oxygen can be delivered by high flow close to the tube. A sterile tube is placed through the endotracheal tube and into the trachea, beyond the endotracheal tube. Introduce carefully so as not to injure or perforate the trachea. The syringe with saline is attached to this tube and saline instilled into the trachea in aliquots and aspirated. A tight hold of the catheter is required during instillation and aspiration to avoid slipping and migration into the trachea. Several aliquots to a a total of 3 – 5 mL saline in cats and small dogs and 10 – 20 mL in larger dogs may be required.

PLACING A THORACOSTOMY TUBE (CHEST DRAIN)

Indications

When continuous suction is required to evacuate the pleural space i.e. tension pneumothorax, several thoracocenteses required to control pneumothorax, pyothorax, chylothorax, or pleurodesis. NOTE: There is usually time to perform sterile, surgical technique. However if there is tension pneumothorax (barrel chest), then rapid placement is required. Even a small opening into chest is adequate as an emergency procedure to relieve pressure.

After placement, the patient requires constant supervision or guaranteed "animal-proof" protection from patient removal.

Materials

The largest-bore chest tube that can comfortably fit between 2 ribs to allow for thick viscous fluid or clots. However, for **pneumothorax** the smaller size tube (12-16 Fr Fr) or over-the-guidewire 7 Fr or 14 gauge central venous catheters (Mila International, Arrow International) can be placed dorsally into the pleural space. The dilator is not required.

Cats & dogs <7 kg	14 Fr chest tube	
dogs 7 – 15 kg	16-18	Fr chest tube
dogs 16 – 30 kg	18-22	Fr chest tube
dogs >30 kg	22 Fr chest tube	

Types of Tubes

Polyvinylchloride, red rubber, silicone. Silicone rubber is least likely to become occluded; red rubber tubes are the least desirable due to irritation and are non-radiopaque. Fenestrations in these tubes should be limited to the distal one-third. Pre-place the clamp and stopcock onto the end of tube if a stylet is not used.

Adaptor to fit the chest tube
Extension set with clamp and 3-way stopcock
60 mL syringe
Tape or orthopedic wire to secure adaptor and extension set
2-0 non-absorbable suture on a cutting needle.
Furacin ointment, gauze square and bandage material

Procedure

There are numerous techniques for placement of the tube, this is one. Choose the side with significant pathology. However, as the mediastinum is fenestrated, with bilateral pathology, either side will do. An exception is pyothorax, here bilateral drains are recommended. Clip hair from shoulder to last rib and dorsal to ventral midline. Surgically prepare the skin.

Where possible, general anesthesia is recommended for placing large-bore tubes in cats; opioid and local anesthesia is suitable for dogs (*see Chemical Restraint for Emergency Procedures p. 100*). Local anesthesia is adequate for over-the-guidewire catheter placement in cats and dogs.

Oxygen supplementation must be administered. The animal is placed in lateral or sternal recumbency. Drape for tube placement if possible.

A gloved assistant grasps the skin behind the elbow and pulls cranially for fluid drain or caudally for air removal. 1 – 3 mL 1% or 2% lidocaine infiltrated in skin down to pleura at 7th intercostal space at junction of upper 1/3 and lower 2/3 of chest wall. Wait at least 2 min. **(1) Catheter placement**, the guidewire is inserted into the pleural space through the accompanying needle, remove the needle, pass the catheter over the guidewire and remove the guidewire. Suture the catheter to the skin with accompanying clamp. **(2) For tube placement,** the skin incision should be approximately the same size as the tube. Dissect down through subcutaneous tissues and intercostal muscle with Mayo scissors. Penetrate pleura (away from caudal aspects of rib). Pass tube with stylet, Kelly or Carmault or curved hemostatic forceps – directing anterior ventral for fluid, and posterior-dorsal for air removal. Clamp tube as stylet is removed. Release skin which automatically migrates over the tube forming a tunnel preventing air entering pleural space. Place adaptor and extension, aspirate immediately if necessary. Otherwise, secure the tube to the chest wall (in the tunneled area) by a deep suture. A purse string suture and friction knot (Chinese handcuff) is also used to attach the tube to the skin. Secure the adaptor to the chest drain with orthopedic wire, or 'barber pole' the tape (stretch and 'spiral' around, not wrap horizontally) over the chest drain, adaptor and onto the extension set. Furacin antibiotic ointment and gauze are placed over the insertion site. Comfortable bandage is applied. The extension and clamp, Heimlich valve or continuous suction is connected to the tube. All connections are adequately sealed with tape to prevent leaks/disconnection. Secure the bandage at the cranial and caudal aspects, to the body, with sticky tape to avoid slipping.

Tube Maintenance

Dressing change and skin cleansing with warm sterile saline is recommended as needed. We do not feel this should be routine as it is usually not warranted. The bandage should be examined several times/day and changed when necessary or every 48 h. The patient should be adequately supervised to avoid tube dislodgement/disconnection. The tube is removed when no longer needed (fluid and/or air accumulation has cleared – fluid <2 mL/kg/24h). Chest tube irritation and lymph fluid accumulation can produce fluid at approximately 2 mL/kg/24h. When removing, place gauze sponge and antibiotic ointment over thoracostomy site and tube, remove tube with rapid motion. Circumferential bandage should be applied for 24 – 48h to prevent pneumothorax.

INTRODUCTION

Any patient with acute respiratory distress and PaO_2 <70 mmHg on room air will benefit from supplemental oxygen. If the respiratory problem is longstanding, a PaO_2 of 50 – 60 mmHg may be acceptable if the patient appears comfortable. The administration of oxygen (flow rate) should be titrated according to the PaO_2 or oxygen saturation value (SpO_2). A simple method is to monitor the SpO_2 while adjusting the oxygen flow. The oxygen flow that gives a consistent SpO_2 reading of 92 – 94%, is adequate. Observe patient comfort at this level, should this deteriorate an increase in oxygen flow and patient assessment is indicated. Response to therapy (patient comfort, effort and respiratory rate) should be used as a guideline for titration. A $PaCO_2$ or $PvCO_2$ >50mmHg (hypoventilation) should not be extrapolated to hypoxemia requiring oxygen therapy unless the patient is obviously in respiratory distress. Increased CO_2 values may be normal or harmless in some animals; it has been the author's observation that brachycephalic breeds may normally have an elevated $PvCO_2$ and this should not be considered necessary to treat when discovered 'accidentally' on a blood gas analysis. Where oxygen supplementation has been used in these dogs, hypoventilation is worsened and CO_2 values increase dramatically.

The devices recommended to deliver supplemental oxygen do not supply the entire inspired volume, therefore part of the tidal volume must be supplied by room air. The inspired oxygen concentration depends on the flow of oxygen in the unit and the tidal volume of the patient. The fraction of inspired oxygen (FIO_2) in each breath is important to keep in mind. Prolonged exposure (beyond 18 hours) of greater than 80% oxygen concentrations can cause alterations in lung function secondary to oxygen toxicity. In most clinical settings it is difficult to measure inspired FIO_2. The information in Table 1, suggested oxygen flow rates for supplemental nasal oxygen, was obtained from tracheal cannulation in small to large dogs receiving nasal oxygen at the various flow rates noted; data for very large dogs was derived by calculation (Mathews unpublished data). This information is used as a guideline for oxygen flow rates at the Ontario Veterinary College. The only accurate way to titrate oxygen delivery is based on arterial blood gas analysis or oxygen saturation measurements.

Indications for Assisted Ventilation

While various arterial blood gas parameters have been suggested, no absolute guidelines can be used due to patient variability and interpretation of results. However, assisted ventilation must be considered when:

A. A patient is working very hard to oxygenate and ventilate and appears distressed; hyperthermia and weakness (e.g., peripheral neuropathies, severe pulmonary disease) are other parameters to assess. Frequent recording of respiratory rate, effort, degree of fatigue and temperature are mandatory in managing these patients. In the author's opinion, the work of breathing is the **most important** component of assessment for mechanical ventilation. Energy expenditure for the 'normal' work of breathing is ~ 2% of total energy expenditure; where effort is required, this can reach 50%. Oxygen consumption in this situation far exceeds that which is gained from supplementation and mechanical ventilation is necessary.

B. Keeping (A) above in mind, if a PaO_2 >60 mmHg (acute setting) or 50 – 60 mmHg (chronic setting), or 0_2 saturation of 90% cannot be achieved initially with the highest oxygen flow rate that can be delivered by your facility, and/or a $PaCO_2$ >50 – 60 mmHg (acute) OR $PvCO_2$ 55 – 65 mmHg (chronic), assisted ventilation is advised. In the face of respiratory distress with an elevated respiratory rate, a "normal" $PvCO_2$ 40 – 45 mmHg is higher than expected, therefore, **work of** breathing becomes much more critical to evaluate. Often oxygen and carbon dioxide can be maintained within normal limits, but the work to maintain this is exhaustive. Animals can decompensate rapidly if not ventilated. Also, the $PaCO_2$ values must be considered in light of the underlying problem (e.g., opioid overdose) where this can be corrected, and in the absence of respiratory distress.

C. Where a PaO_2 >60 mmHg (acute setting) or 50 – 60 mmHg (chronic setting), cannot be maintained with an FIO_2 <0.5 (50% inspired oxygen) after 24 hours of receiving an FIO_2 0.8 – 1.0. The concern here is with oxygen toxicity.

Oxygen Administration (See Table 1 for flow rates)

A. **A face mask** can be used for rapid, temporary delivery of oxygen. In order to avoid accumulation of exhaled air in the mask reservoir that might be rebreathed, the oxygen flow should be at least 100 mL/kg/min using a well-fitting mask; however not a tight fit as CO_2 and heat has to escape. If a large, poorly-fitting mask is used, flows of 300 mL/kg/min may be necessary.

B. Plexiglass hoods (Fig. 1) can achieve and maintain an oxygen concentration of 80 – 100% with flows of 1 – 5 L/min into a small, medium or large sized hood accommodating a 1 – 8 kg cat or dog. The oxygen concentration can be measured by placing an O_2 analyzer probe approximately 5 cm from the O_2 inlet. The hood can be custom fitted by securing a piece of plastic to the back of the hood with an area cut out to fit over the caudal thorax and abdomen of the patient. There should be sufficient gap between the patient and the hood to allow carbon dioxide to flow out, flushed by the oxygen. The temperature should be monitored q2h as the temperature under the hood can increase significantly, especially with low oxygen flows and a larger patient.

C. Nasal cannula.

1. 5 Fr nasal cannula (5 Fr feeding tube). This is the biggest nasal cannula that can be placed in cats and small dogs. Oxygen flow up to 0.5 – 0.75 L/min can be delivered. Flow rates higher than this generate too much pressure and will alarm or blow the tube off the delivery system.
2. In dogs >10 kg (occasionally can fit smaller breeds) a 10 FR nasal cannula (human nasal oxygen cannula) usually fits comfortably. These cannulae are preferred as they have many very small holes allowing the oxygen to 'diffuse' into the nares rather than a single hole which can be uncomfortable and traumatic with higher flow rates. Oxygen flow can be delivered at 5 – 10 L/min with the 10 Fr nasal cannula, depending on the size of the patient (at higher flow rates it may be uncomfortable in dogs <25kg). A 5 Fr feeding tube can be used in smaller animals.
3. Oxygen flow of 2 – 3 L/min can be maintained through a shortened 8 Fr feeding tube, However, the closed end of the tube should not be cut as this can traumatize the nasal mucosa.
4. Red rubber feeding tubes of various sizes may also be used but with a flow from 0.5 – 5 L/min depending on the size of the patient.
5. Brachycephalic breeds. Due to the variation in anatomy of these dogs, nasal cannulae from 8 – 10 Fr frequently are suitable but a hood may be required for smaller animals.

Delivered oxygen should always be humidified. Plastic bottles with distilled water and an attachment for the flow meter are typically used

Placement of a nasal cannula

Desensitize the nasal mucosa prior to inserting the nasal cannula by placing **4 – 6 drops of ophthalmic local anesthetic, or 0.5 – 1 mL 2% lidocaine,** into the ventral meatus and allow it to run along the ventral floor. Wait 5 min. **Pre-measure the tube** to the medial canthus and mark the tube at the level of the planum nasale. Direct the tube ventro-medially, advance beyond the medial canthus of the eye (as though passing a feeding tube), to ensure proper placement (not in the dorsal meatus). Do not place into the dorsal meatus as this creates turbulence, mucositis and trauma and doesn't do much good! Retract to the medial canthus, the mark on the tube should be at the planum nasale. If the patient is severely compromised, **two catheters** can be placed. If you have problems passing the tube in dogs, press up on the planum nasale (stretching in a dorsal direction) and place the tube ventro-medially. **To secure the tube** in place, apply a small bleb of Krazy glue or tissue glue on the lateral aspect of the planum nasal/hair junction. Direct the tube underneath a neck collar, securing the tube with a small bleb of Krazy glue or tissue glue in 2 spots along its course along the muzzle. Butterfly tape may also be used around the tube which is then sutured to the skin. The **site of fixation** must be at the exit of the nares otherwise the tube will work its way out.

NOTE: Where two catheters are placed, two separate oxygen sources delivered to each cannula is required to gain twice as much oxygen than that through a single cannula (i.e., two flowmeters delivering 5 L each to separate nasal cannulae will deliver a total of 10 L). However, if a large flow is to be reduced based on patient discomfort (i.e., 10 L flow required) this can be divided by using a Y adaptor on the two catheters using the single oxygen source tubing at the 10 L flow.

D. Human nasal prongs fit medium to giant sized dogs. These are very useful, they attach behind the ears and do not require deep insertion into the nares. They are well tolerated. It may be necessary to glue these to the lateral aspect of the planum nasale as you do the nasal cannula. A 6 – 8 litre flow rate will be tolerated. The FIO_2 achieved using the prongs will be less than with a cannula due to the superficial placement.

TABLE 1. Suggested Oxygen Flow Rates For Supplemental Nasal O$_2$

Weight	FIO$_2$ .50	FIO$_2$ .80	FIO$_2$ ~0.9
2.5 kg	0.3 L	0.5 L	0.7 L
5.0 kg	0.6 L	1.25 L	1.5 L
10.0 kg	1.0 L	2.0 L	2.9 L
15.0 kg	1.7 L	3.2 L	4.3 L
20.0 kg	2.2 L	4.3 L	5.7 L
25.0 kg	2.8 L	5.3 L	7.2 L
30.0 kg	3.5 L	6.5 L	8.6 L
35.0 kg	3.9 L	7.5 L	10.0 L
40.0 kg	4.4 L	8.7 L	NA
50.0 kg	5.5 L	10.0 L	NA
60.0 kg	6.5 L	NA	NA
70.0 kg	7.7 L	NA	NA
80.0 kg	8.8 L	NA	NA

Note: Flow rates greater than 10 L/min delivered via one oxygen cannula may cause trauma to the nasal mucosa. However, if a feeding tube is used, trauma will definitely occur. Bilateral cannulae with each flow from a different source will deliver twice as much oxygen as a single cannula.

FIO$_2$ = Fraction of Inspired Oxygen. NA = Not achieved with a single cannula.
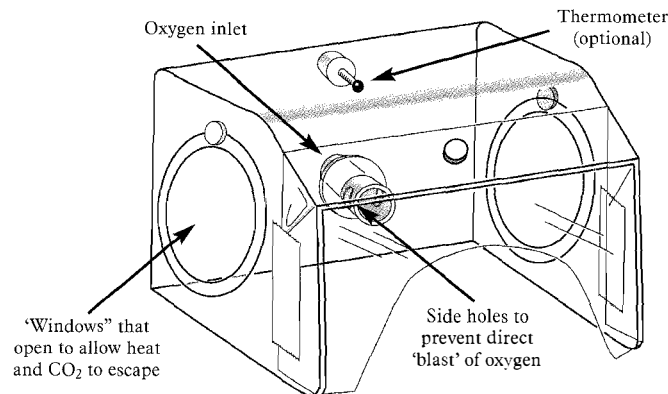
FIGURE 1. Modified plexiglass hood for oxygen supplementation. A range of sizes (15 cms ht x 22 cms w x 22 cms dp; 20 x 25 x 25; and 22.5 x 30 x 30) accommodate most cats and small dogs. Further adjustment for patient size is made with the plastic film cut to shape around the patient's caudal thorax or abdomen, and taped to the back of the hood. Sufficient gap is left to allow CO$_2$ to be flushed out. The thermometer measures temperature in the hood.

Various methods exist to monitor and assess a patient's oxygenation and ventilation. The more common methods are discussed. Each technique has advantages and disadvantages and gives a different piece of information.

ARTERIAL BLOOD GASES

Measurements of arterial blood gases is the gold standard for assessing oxygenation and ventilation. While difficult and costly to perform in most veterinary practices at the moment, the introduction of handheld devices will make blood gas measurements a reasonable monitoring tool in the very near future. The partial pressure of oxygen (PaO_2) in normal, healthy young adult animals under ideal conditions, breathing room air, is considered to be about 95 – 100 mmHg. The PaO_2, the amount of dissolved oxygen in blood, although only a fraction of oxygen content of arterial blood, determines the functional capabilities of the lungs and determines the rate at which oxygen can enter the tissues. Oxygen content (mL O_2/100 mL blood) = ([Hb] x 1.34 x %SaO_2) + (PaO_2 x 0.003). The partial pressure of carbon dioxide ($PaCO_2$) usually provides an excellent index of the adequacy of overall ventilation of perfused alveoli. If the $PaCO_2$ is greater than normal (35 – 45 mmHg) one can assume that the ventilation of perfused alveoli is reduced or carbon dioxide production is increased. If the $PaCO_2$ is lower than normal, one can usually assume that the alveolar ventilation is increased or carbon dioxide production is decreased. An elevated $PaCO_2$ in the presence of alkalosis usually indicates a compensatory effort to restore arterial pH towards normal. Hyperventilation frequently occurs in the presence of metabolic acidosis. As a rule of thumb, with adequate ventilatory compensation for a metabolic acidosis, the $PaCO_2$ should be equal to or less than the last two digits of the pH i.e., pH of 7.35, the $PaCO_2$ should be equal to or less than 35 mmHg. Patients with pulmonary insufficiency may initially be hypoxemic and hypocarbic (mild involvement), hypoxemic and normocarbic (moderate involvement) or hypoxemic and hypercarbic which generally indicates severe pulmonary insufficiency.

VENOUS BLOOD GASES

The carbon dioxide measurements of venous blood ($PvCO_2$) can be used for assessing ventilation with a normal range of $PvCO_2$ being ~5 mmHg higher than $PaCO_2$ values. While PvO_2 measurements are not valid in assessing oxygenation, a central vein (jugular or vena cava) or mixed venous measurement is extremely useful. Normal utilization of oxygen results in a central measurement of 40 – 50 mmHg, but >60 mmHg without oxygen supplementation may be present; the ideal goal with supplementation is 70 mmHg. Central venous values <30 mmHg (SvO_2 be <50%), requires investigation and correction as increased demand or inadequate oxygenation is occurring; values <20 mmHg requires immediate attention. The base deficit (negative base excess) is calculated from the measured pH and $PvCO_2$ included in all blood gas measurements, and provides the clinician with a nonspecific marker of perfusion and lactate production and therefore, anaerobic metabolism and oxygen debt. The base deficit represents the mEq/L of bicarbonate required to restore the total buffer base of the extracellular fluid to normal. Normal base deficit is ±4. A worsening of the base deficit frequently correlates with reduced oxygen delivery or utilization indicating a deteriorating patient or inadequate resuscitation or other therapy. Therefore, measuring the base deficit is a rapid, practical way to estimate ongoing cumulative dysoxia throughout resuscitation in injured or ill patients.

PULSE OXIMETRY

Pulse oximetry (SpO_2) is a non-invasive method of measuring the percentage of oxygen bound to hemoglobin (hemoglobin saturation) in arterial blood (SaO_2) and can be performed in any animal. SpO_2 measures functional oxygenation more accurately than the partial pressure of oxygen (PaO_2) since oxygen bound to hemoglobin is a primary determinant of arterial oxygen content. It is possible to measure oxygen saturation continuously without blood sampling, which is a great advantage in veterinary practice where the patients are small and blood gases are costly. The more practical unit is a hand-held device with a 'probe' (clip-like or wrap around), which is placed on the tongue, toe web, ear, vulva or prepuce. The probe is placed on hairless, non-pigmented skin or mucous membrane, preferably of 0.25 – 1.0 cm thick, which is shaded from fluorescent lighting (can interfere with light absorption). The light emitting diode on one arm of the probe is positioned directly opposite the sensor on the other arm of the probe where both arms 'sandwich' the tissue being measured. This is not uncomfortable but appears to be annoying when placed on the tongue of a non-depressed or non-anesthetized animal. Reflection probes are slightly different in that the photodetector is next to, and not opposite, the light-emitting diode. This probe is designed for rectal use, however, in our experience, the readings are not reliable. The pulse oximeter displays pulse rate and some display the strength of the signal. The pulse rate displayed should equal that obtained directly from the patient in order for the saturation to be **considered** accurate, although this does not guarantee accuracy. Many causes of inaccurate readings, or inability to obtain a reading are

listed in Table 1. As a low SpO_2 may be due to poor perfusion of the area 'sampled', hypoxia requiring oxygen supplementation should not necessrily be assumed. When trending a particular patient, periodic arterial blood gas analysis should be performed to verify the SpO_2 readings.

The SpO_2 correlates with the partial pressure of oxygen in arterial blood (PaO_2) and when <100% can be used as a guide to the actual PaO_2. For example, it is recommended that the SpO_2 remain above 92% to ensure that the PaO_2 is at least approximately 65 – 70 mmHg. As an SpO_2 reading >98% could be a PaO_2 >100 mmHg, it is not necessary to maintain the SpO_2 >95%. Oxygen toxicity can potentially occur when administered at concentrations >50% for >24 hour. Therefore, the goal in hypoxemic patients is to supplement with oxygen to maintain a PaO_2 between 65 – 75 mmHg (~SpO_2 92%) on the lowest possible concentration of oxygen. This author has found the SpO_2 very useful for titrating oxygen therapy. Where readings are > 100%, slowly reduce the oxygen flow rate until SpO_2 reading is ~94%. As an SpO_2 reading >100% could reflect a PaO_2 reading from 110 – 500 mmHg, it is not a sensitive tool in detecting desaturation when oxygen is being administered i.e., under anesthesia where 100% oxygen is administered, desaturation from 500 mmHg to 110 mmHg would not be detected and yet severe compromise is occurring.

If a pulmonary artery catheter is in place, the SvO_2 (saturation of mixed venous blood) can be measured which is an indicator of oxygen utilization. With the SpO_2 and the SvO_2 the balance between oxygen delivery and consumption can be measured. This is termed pulse oximetry and duel oximetry. Pulmonary shunt can be estimated by calculating the ventilation perfusion index (VQI). $VQI = 1\text{-}SpO_2/1\text{-}SvO_2$ which closely approximates intrapulmonary shunt fraction. With adequate hemoglobin and arterial oxygen saturation, a drop in mixed venous oxygen saturation alerts the clinician of the patient's increased oxygen demand (increased metabolism due to sepsis) or decreased oxygen delivery to the tissues (decreased or inadequate cardiac output to meet tissue demands).

TABLE 1. Trouble-shooting Problems with Pulse Oximetry

Problem	Solution
Movement artifact such as shivering	Calm or warm the patient
Tissue too thick or	Alternate site if too thick
too thin	Increase with single layer of dry paper towel
Poor perfusion and low blood pressure	Unreliable until pressures improve
Cold extremities	Place on tongue and warm patient
Compressed tissue (probe placed for long periods)	Place in another area
Pigmented tissue	Place in another area
Increased carboxyhemaglobin (falsely elevated reading)}	Suspect from history and physical exam
methemoglobin reduces the oxygen saturation reading }	and confirm with co-oximetry of arterial
blood gases	
Fluorescent light	Shade from artificial light with a towel
Dirty probe can alter the reading	Clean with warm water after each patient
Damage to the probe hinge (too loose)	Probes are very expensive, appropriate care of equipment is necessary to prevent damage

END TIDAL CAPNOGRAPHY

For **intubated** patients, continuous capnographic display of end tidal CO_2 ($ETCO_2$), is very useful in monitoring mechanically ventilated patients. Once stable, and a comparison of $PaCO_2$ with the $ETCO_2$ has been made, this can assist the clinician in determining changes in ventilation without continual arterial blood gas measurements. $ETCO_2$ may be used as an assessment of $PaCO_2$ which is usually ~5 mmHg higher than $ETCO_2$ in a normal lung and in an otherwise stable patient. A change from normal to high signals a deterioration in the patient's status. A high $ETCO_2$ indicates hypoventilation which is present in inadequate ventilation for CO_2 production, i.e., malignant hyperthermia, increased metabolic rate, physical or functional airway obstruction, pulmonary thromboemboli. However a normal to low value may be difficult to interpret in a patient with moderate to severe pulmonary disease or poor cardiac output as there can be a large $PaCO_2\text{-}ETCO_2$ gap due to poor pulmonary diffusion of CO_2. In this case, the low $ETCO_2$ cannot be relied upon and blood gases with direct measurement of CO_2 is necessary. Venous blood gases are sufficient to detect abnormalities in CO_2 (but definitely not O_2). Conversely, in a resuscitative situation such as cardiac arrest, high $ETCO_2$ confirms successful cardiac compressions and effective circulation as CO_2 is being circulated to the lungs, exhaled and detected on the monitor. A low $ETCO_2$ is indicative of poor response, or esophageal intubation, as a high $ETCO_2$ is expected initially.

There are three methods and situational settings involving tracheotomy tube placement. The first two methods are always performed in life-threatening emergent situations when seconds count. The third is an elective or urgent method when there is an endotracheal tube in place.

Indications
1. An unconscious or nearly unconscious cyanotic patient that cannot be intubated due to obstruction of the glottiss requires a **slash tracheotomy.**
2. The conscious patient with respiratory distress poorly responsive to oxygen supplementation most often associated with severe pulmonary edema, intrapulmonic hemorrhage, or pneumonia; and significant partial airway obstruction associated with many conditions may require an **awake tracheotomy** to allow tracheal access for ventilation, suctioning and nebulization.
3. The anesthetized patient with an endotracheal tube already in place with progressive pharyngeal, glottic or sublingual edema or hemorrhage occurring and of the appearance that if the tube were removed the obstruction would be life-threatening. This requires an **elective tracheotomy.**

Materials
1. Two (one on hand should the first one abstruct acutely) appropriately-sized tracheotomy tubes (one size smaller than a regular endotracheal tube selected for your patient). The human endotracheal tubes have an inner 'tube' which can be removed and replaced while leaving the outer tube in place (Shiley™) This makes tube changing much simplier, and are preferred by some. However, the conformation of these tubes are not ideal for all sizes and breeds of dogs, or cats. Also, they are expensive and potentially not available on an emergent basis in all veterinary practices. They may also become occluded regardless of routine cleaning of the inner cannula.
2. An endotracheal tube one size smaller than that routinely selected for your patient.
   - **'Homemade tracheotomy tube'.** If the ET tube inserted into your patient appears appropriate in size another similar tube, one size smaller, is manufactured into a homemade tracheotomy tube. These are preferred to the use of commercially available human tracheotomy tubes as they conform to the straighter and longer anatomic orientation of the cat and dog trachea. The plastic connector of the ET tube is removed and the tube is split while preserving the cuff-inflation line and the ends attached to two sections of pieces of IV tubing. (Fig. 1). The author has placed more than 300 of these without complication. The second prepared E-T tube is immediately available should the first (one inserted) becomes clogged acutely; however they should be interchanged every 8 hours regardless.
3. Where no E-T tubes or tracheotomy tubes are available, a cut end of an IV administration drip chamber can be used to access the airway with the fluid openings widened with a hemostat. A cap of a hypodermic needle with the end cut off can also be used in smaller patients.
4. An 11 blade and 18 g needle.
5. Analgesia/anesthesia (*see below*)

Anesthesia, Analgesia and Sedation
1. Flow-by oxygen is immediately delivered at 5 L/min with the oxygen line placed within 10 – 15 cm from the patient's nose and mouth. This may calm the patient. If the patient exhibits open-mouth breathing and gasping, the oxygen is provided at 5 – 15 L/min with the nozzle in the mouth directed towards the pharynx.
2. All emergency tracheotomies will cause pain. The only time this will not need to be addressed pre-surgically is if the animal is completely **unconscious or semiconscious with impending respiratory arrest.** Here the time taken to effect anesthesia/analgesia will result in death. *See 3 below* as an alternative approach In these cases the procedure is performed immediately without placement of an IV catheter, or local anesthetic. In all other situations, a local anesthetic (2% lidocaine) is quickly infiltratrated at the incision site (*see 5 below*).
3. A needle-catheter tracheotomy and bag-valve mask assisted ventilation is a stop-gap procedure that may be effective while preparing for the tracheotomy procedure. A 14g IV over-the-needle catheter is inserted into the trachea, between tracheal rings or through the cricothyroid membrane. A 3mm E-T tube is attached to the catheter hub once the catheter has been inserted into the trachea. Rapid ventilation with the bag mask valve (120/min) is performed while the final tracheotomy is being completed.
4. If the patient is so anxious that rapid IV catheter placement would be too stressfull a mixture of **ketamine 1 – 3 mg/kg, butorphenol 0.1 – 0.2 mg/kg, and acepromazine 0.01 – 0.02** is given (by the same syringe) deep into the epaxial muscle. In those with cardiovascular compromise the lower end of the dose is initially used. In extremely anxious animals, the higher end of the dose may be required.

5. The **local anesthetic,** 2% lidocaine without epinephrine and 0.1 mL (1 mEq/mL) sodium bicarbonate added to each 1 mL lidocaine, is used to infiltrate the skin and subcutaneous tissue. Analgesia is effective within 5 min. lasting ~ 2 hours. The sodium bicarbonate reduces the sting of the local anesthetic. T reduce the extreme sensitivity of the trachea, 1 mL per 5 – 10 kg body weight of a similar ratio of sodium bicarbonate to **0.25% or 0.5% bupivicaine** may be injected into the trachea using a 25 g needle. Bupivicaine is effective within 15 min but the duration of analgesia is much longer than lidocaine, frequently lasting from 12 – 36 hours. However further analgesia may be required and is patient dependent (*see Pain Assessment & Management p. 117*). Initially, at the very minimum repeated dosing, or a CRI (ideally) of an opioid analgesic should be instituted in all patients that have invasive indwelling tubes present, including a tracheotomy tube.

    *   Intravenous or intraosseous vascular access is mandatory, at least in the initial stage of managing the tracheotomy tube. Manipulation of the neck in the hypoxic and acidemic patient may induce a vasovagal response that could be life-threatening (causing extreme and rapid hypotension, with or without a profound bradycardia), and other complications may occur requiring rapid administration of analgeiscs, sedatives or anesthetics.
    *   Rare **vasovagal response treatment.** Ventilation with 100% oxygen must be instituted. Atropine 0.03 – 0.05 mg/kg IV bolus (a higher than prophylactic dose to avoid further bradycardia). Occasionally **epinephrine 0.001 mg/kg IV** bolus may also be required if the hypotension and bradycardia are not reversed after a second atropine dose is given, 2 – 3 minutes after the first. All injections must be followed with a rapid flush infusion of several mL saline.

Technique

*   The **slash tracheotomy** is performed without clipping hair or performing a surgical prep. However, long hair should be cut with a single pass of the clippers to allow visualization of the skin and easier palpation of the deeper structures. Preparation should only take seconds to complete. The 'slash' tracheotomy should be performed in the 'sitting' position in a semi-conscious patient as respiratory and cardiac arrest may occur when placed on its back. This position also allows a more effective way to assist ventilation with a bag valve mask as the tracheotomy is being performed. The **slash (unconscious patient) and elective tracheotomy** is performed with the patient positioned as in Fig. 2. The patient is placed in dorsal recumbency preferably on a V-tray. Duct tape or other material is used to pull the front legs caudally, a piece is applied around the front feet and pulled caudally and fixed to the end of the table The neck is hyperextended by placing a firm object under it. A second piece of tape is used to hold the chin toward the surface of the table and then attached to the sides of the table.
*   The **awake and elective tracheotomy** is performed after clipping the ventral neck and applying a rapid surgical prep. The **awake tracheotomy** is performed with the patient positioned as in Fig. 3, sitting on an examination or surgery table with the head held upwards by an assistant, preferably with flow-by oxygen being given. The operator is positioned sitting down preferably with a headlight on to provide adequate visualization.

Both techniques are performed in a similar fashion

*   The operator stands to the side (Fig. 2), or in front (Fig. 3) of the patient and the non-dominant hand is used to palpate the larynx and trachea while the dominant hand is used to mark and cut.
*   The skin incision is made on the midline for a minimum of several cm in the cat and 8 cm in large dogs. This is performed using a scalpel, by sweeping an 18 g needle across the skin (Fig. 4), or by 'tenting' and lifting the skin and cutting it with Mayo scissors (Fig. 5).
*   A curved scissors or Carmalt hemostat (Fig. 6), or 2 curved hemostats of appropriate size (Fig. 7) are used to separate the cervical strap muscles (sternothyroideius-sternohyoideius) exposing the ventral surface of the trachea.
*   Using the fingers to stabilize and partially elevate the trachea , a transverse incision is made between rings (3 – 6) with either an 18 g needle in a sweeping fashion, a No. 15 scalpel blade, or the tip of the scissors. The opening should be approximately 40% of the circumference of the trachea (Fig. 8).
*   In very small animals, a longituidal incision through the tracheal rings may be considered, with a 'T' if needed, to avoid >50% separation of tracheal rings. However author preference is the incision between the rings and partial repair of trachea later should a >50% separation occur.
*   An appropriate sized endotracheal tube is inserted (Fig. 8) and intermittent positive pressure ventilation (IPPV) commenced with an AMBU bag with ~100% oxygen via the AMBU reservoir bag attached.
*   Traction sutures are placed immediately cranial and caudal to the tracheotomy incision (Fig. 8). Two separate lengths of suture material encircle 1 or 2 tracheal rings tying a knot 5 – 8 cm away from the rings. The sutures are placed lateral to the incision where a longituidinal between the rings was made. DO NOT TIE THE KNOT ONTO THE TRACHEAL RING, otherwise these are difficult to remove. Traction on these sutures opens the ostomy to facilitate removal and replacement of the tracheotomy tube.

- Plastic tape tab is attached to each loop and identified with an ink or Sharpie pen as the head (H) and chest (C) loops for orientation, or (R) and (L) (allowing easy opening of the tracheotomy incision for replacement of the tube following its removal for cleaning (required every 8 hours or more frequently as needed, *see below*).
- **Tracheotomy Dressing.** A 4 x 4 gauze square is cut to the middle of the square (appearance of a 'pair of pants') and placed on the surgical opening and around the tracheotomy tube as it exits out of the neck **OR** the gauze is folded in a 'pair of pants' fashion and draped over the tracheotomy tube (Fig. 9). Folding the gauze prevents cut cotton fibres entering the tracheotomy site. The tube is NOT sutured to the skin and the skin incision is left open. The incision will granulate closed after tube removal this allows tracheal healing prior to skin healing preventing formation of subcutaneous emphysema.
- **Securing the tracheotomy tube.** The IV tubing or umbilical tape attached to the two split ends of the tracheotomy tube is brought around the patient's head and tied in a bow to allow rapid release and tube removal. A right-angle or 'elbow' adaptor can be placed onto the tracheotomy tube to prevent occlusion when the patient sleeps. (Fig. 9 insert).
- **Where the IV drip chamber or cap of the hypodermic needle is used,** an 11 blade or 18 g needle is used, in a sweeping fashion, to cut the skin and muscle and penetrate the trachea, and to make a small transverse opening. The tip of the drip chamber or the open needle cap is then inserted into the tracheal opening. An Ambu bag can be attached to the cut end of the drip chamber directly and IPPV commenced. IPPV is best delivered with 100% oxygen .

Care of the tracheotomy patient (rules to follow)
- **Never** leave the patient with a tracheotomy tube alone! One cough expelling exudate against the internal tip of the tracheotomy tube can cause complete airway occlusion.
- **Always** tie the umbilical tape or 'IV tubing' placed through the tracheotomy tube and around the neck (back of head) with a bow to allow rapid removable of the tube. Never suture the tube to the skin. Always keep the access opening into the trachea large enough for removal and replacement of the endotracheal tube.
- Change the tracheotomy tube every 8 hours even if its "sounds" and "looks" OK. Exudate may accumulate inside the tip (single or double-lumen tube). This author is concerned that a double-lumen tube may lead to a false sense of security in that the outer tube is clear and free of exudate as the inner tube is frequently changed. This is not always so as the exudate may still accumulate at the tube tip-trachea interface.
- Ideally provide continuous heated humidified air. This is especially important in patients with pneumonia. Enlist the help of local respiratory therapy personnel at the local human hospital. Frequently, they are helpful in supplying the heat coil and humidification chamber, large tubing and tracheotomy bowl. If this is not available, instill **sterile saline (1 mL/5–10 kg BW (1–5 mL total) into the trachea every 2 – 8 hours).** The frequency depends on the volume and presence of a tenacious exudate). This is followed immediately by coupage, postural drainage for a few minutes then tracheal suctioning (*see below*).

Suctioning protocol
a. Instill the saline, coupage and provide postural drainage.
b. Provide flow-by oxygen, or IPPV as needed.
c. Observe for vasovagal responses and oxygen desaturation. Treat accordingly.
d. Instill another dose of saline and suction. (Use a tracheal suction cannula). Clamp off the vacuum tube attached to the cannula, slide the tube as far as possible until it stops. Activate the suction tube by releasing the clamp or placing the thumb on the hole of the suction cannula. Exhale your breath while beginning the suction (high flow) and gradually twist and pull out the suction cannula as the breath is used up. When the breath is used up the suction should be out of the tracheal stoma.
e Repeat a-d until breath sounds are clear and free of 'rattling and gurgling'. This may take several rounds of oxygenation/ventilation, saline instillation, coupage and suctioning.
f. Remove the tube and replace with the clean one if the exudate removed was quite thick.
g. Re-oxygenate/ventilate again with IPPV breaths using the AMBU bag and reservoir.

Changing the tube
a. Set up equipment
  1. AMBU bag with reservoir attached to oxygen.
  2. Sterile dressing.
  3. Sterile saline and bowl.
  4. Sterile (new or cold sterilized, or at least hot water and soap cleaned) replacement tracheotomy tube. The author frequently washes the tracheotomy tubes with hot water and a bactericidal soap then rinsed well in hot water and shaken "dry" tube.
  5. Sterile powder free gloves.

b. Preoxygenate for one minute of IPPV breaths using the AMBU bag and reservoir.

c. Have the clean replacement tube ready (best to always keep one at cage side).

d. Remove the old dressing and tube while an assistant holds the ostomy site open with the traction sutures. In cases of severe lung injury, edema, etc., flow-by oxygen to the ostomy site is continued during the procedure.

e. Gently clean the ostomy site tissues and skin area with sterile saline and soft gauze sponge.

f. Replace the tracheotomy tube using freshly washed hands or sterile gloves.

g. Re-oxygenate/ventilate with IPPV breaths using the AMBU bag and reservoir if needed.

h. Apply a new 4 x 4 gauze dressing folded or slit to wrap around the tracheotomy tube and cover the wound site.
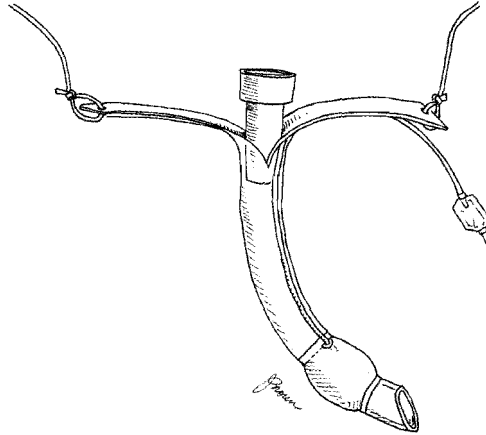
FIGURE 1.
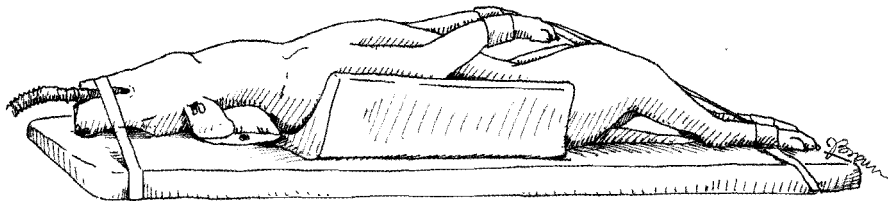
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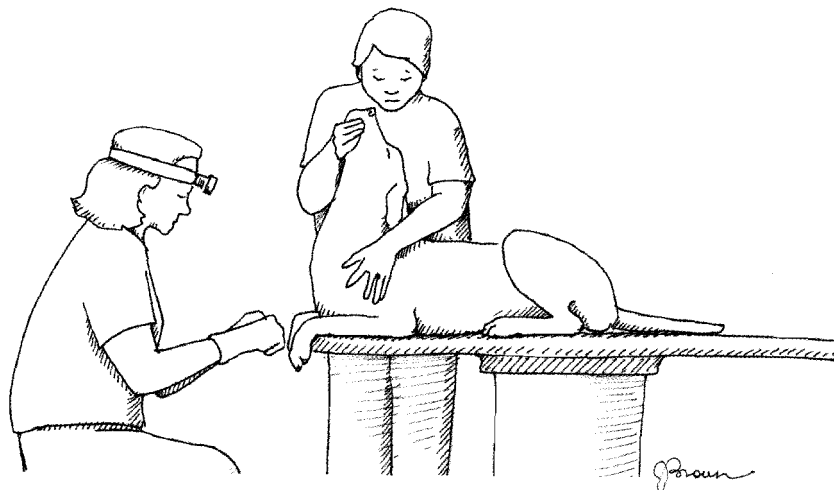
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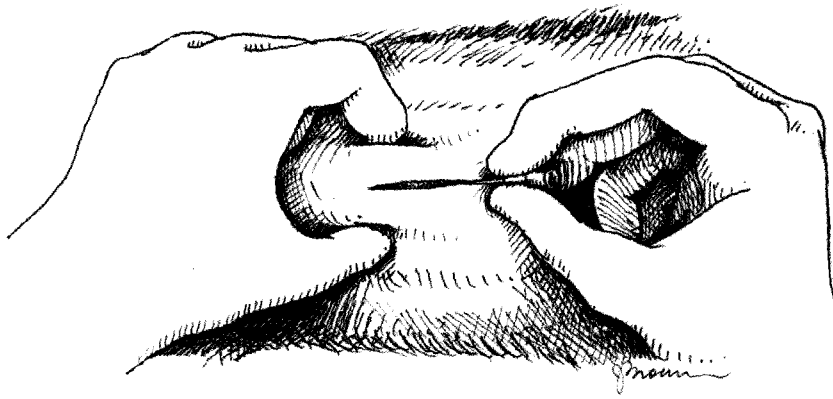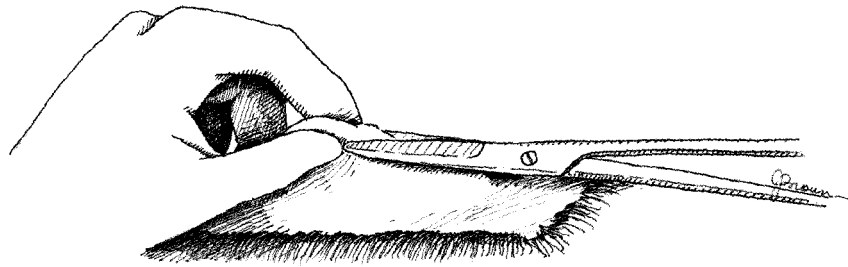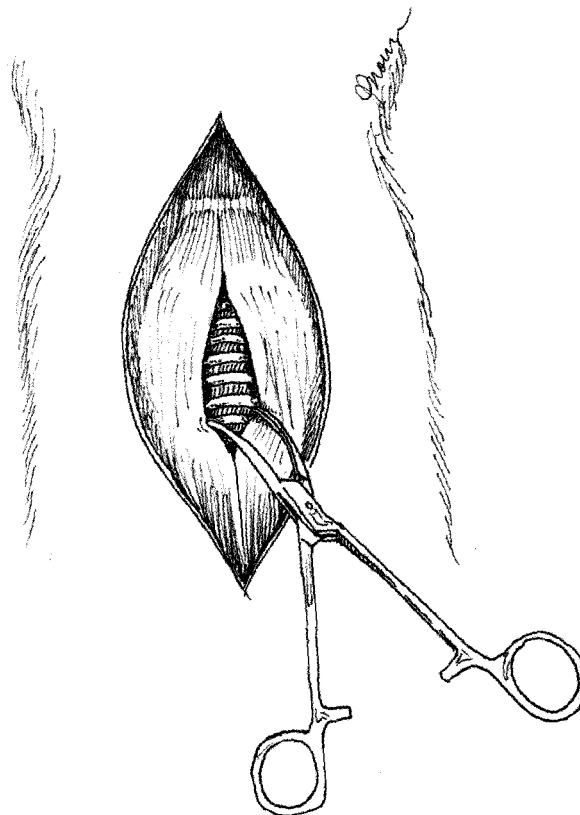
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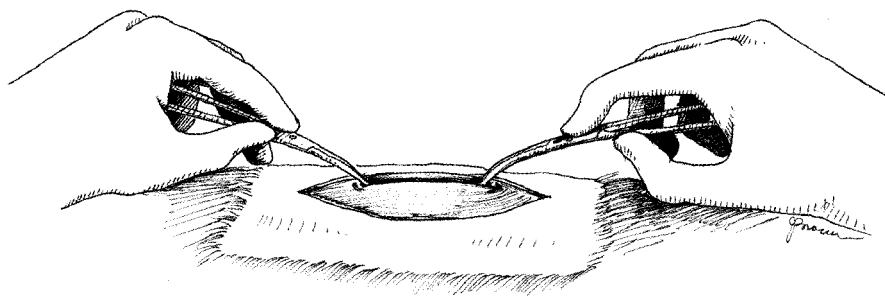
FIGURE 5.

FIGURE 6.

FIGURE 7.
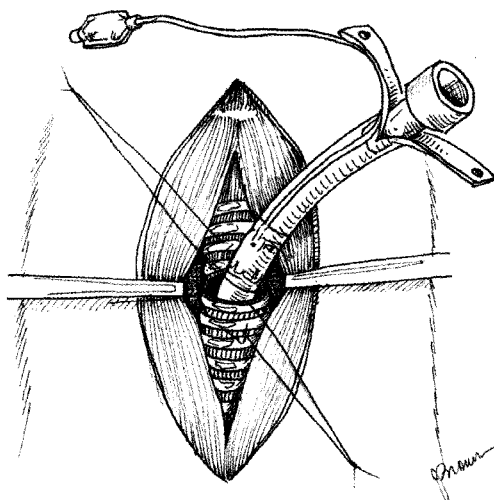
FIGURE 8.
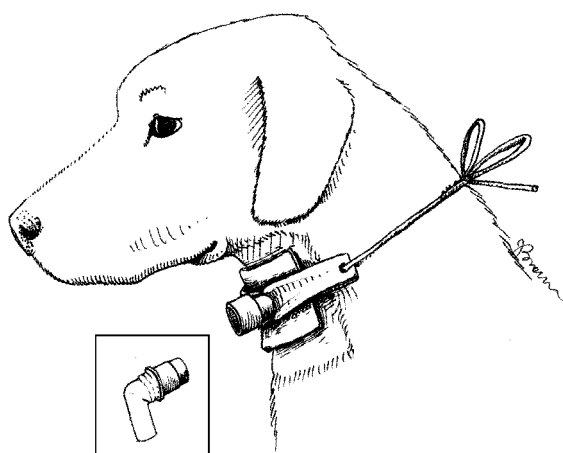
FIGURE 9.

INTRODUCTION

The inciting stimulus of sepsis is a microorganism (bacteria, virus, fungi, protozoa, rickettsia or spirochette), its cell components or toxins. Sepsis can occur with any infection originating in any part of the body. Systemic inflammation is a direct response to these organisms. As the pathophysiological mechanisms involve both the direct and indirect (host's response) effects of the microorganism, sepsis has been further defined to include the host's response as this is what influences morbidity and mortality risk. **Sepsis in critical illness,** is defined as 'the clinical syndrome that embodies the systemic host response to microbial invasions', and is a dynamic interplay between these organisms, or their components, and the endogenous response of the host. The endogenous response includes the acute phase response, the complement and coagulation cascades and the response of various and many cytokines (e.g., tumour necrosis factor [TNF], interleukin-6 [IL-6]) termed the systemic inflammatory response syndrome (SIRS). *See Table 1 below for SIRS criteria for cats and dogs.* However, as these criteria may be present in a non-SIRS setting, a high level of suspicion of an inflammatory focus must be present. Sepsis differs from simple systemic inflammation. To differentiate graded degrees of illness severity, **severe sepsis** is defined as sepsis progressing to the multiple organ dysfunction syndrome (MODS), and **septic shock** defined as sepsis associated with hemodynamic collapse a combination of hypovolemic, distributive and cardiogenic shock with hypotension (systolic BP <90 mmHg or a reduction of more than 40 mmHg from baseline in the absence of other causes for hypotension) despite adequate fluid resuscitation, together with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients receiving inotropic or pressor support may not be hypotensive at the time that perfusion abnormalities are measured, however would still be classified as septic shock.

To define the problem further, a consensus conference in human medicine proposed a system where many factors could be considered and potential biomarkers identified that would facilitate diagnosis and potential targets for treatment. This is the **PIRO** proposal. **P**redisposition (genetic, biological, cultural), which can certainly be applied to our different breeds of cats and dogs. **I**nsult (microbial and site of infection, non-infectious insults such as trauma). **R**esponse of the patient to the insult (physiologic, biologic and biochemical), which may be difficult to define as this could be due to an anti-(not enough) or pro-(too much) inflammatory response, or adrenal insufficiency. But coagulopathies, and extent of concomitant **O**rgan dysfunction, can be identified.

A systemic inflammatory response may also be generated by non-microbial stimuli such as pancreatitis, trauma, snake venom, heat stroke, large or pansystemic neoplasia. Once this cascade is in process, regardless of the iniating cause, the clinical syndrome is similar. It is difficult initially to know whether the patient is septic or not but should this should be assumed so until definitively diagnosed.

TABLE 1. Criteria for Systemic Inflammatory Response Syndrome Manifested by Two or More of the Following Criteria

Clinical parameters	Dogs	Cats
Heart rate	>120 beats/min	<140 or >225 beats/min
Respiratory	>20 breaths pm or PaCO$_2$ <32 mmHg	>40 bpm
Temperature	>39.7° C (103.5° F) or <37.8° C (100° F)	>39.7°C (104°F) or <37°C (100°F)
Neutrophils X10^9/L	>18,000, <5,000, or >10% bands.	>19,000 or <5,000, or >10% bands

With permission. Brady CA, Otto CM. Systemic inflammatory response syndrome. Sepsis, and multiple organ dysfunction. Vet Clin N Amer: Sm Anim Pract. 2001;31(6):1147-1162.

While the above criteria may assist with a diagnosis of SIRS, any two of these could be normal, therefore, an inflammatory process must also be suspected.

The most important aspect of resuscitation in human patients with severe sepsis is early and rapid (within 6 hours) restoration of mixed-venous (cranial vena cava) oxygen saturation to 70%. This would be a reasonable goal to aim for in veterinary patients. Currently, there are no clinical trials investigating the fluid of choice for treating animals with sepsis or SIRS. However this author considers the severity of illness and to categorize this into **capillary leak** (i.e., inflammatory conditions), or **non-capillary leak,** when selecting a fluid regimen. **Non-capillary leak** conditions are categorized into assumed, or measured **low oncotic pressure** (e.g., hypoalbuminemia), or **normal oncotic**

pressure. Selecting the appropriate "fluid", volume and rate of administration, for each problem can be considered as the 'prescription' for correcting the hypovolemic state. Capillary leak is due to an alteration in the endothelium in animals with inflammatory conditions which may have a vasculitis or increase in 'endothelial gap' due to action of cytokines. These animals are more predisposed to edema. Patients with inflammatory conditions may be severely hypotensive, especially with a septic process causing distributive and hypovolemic hypotension. These patients frequently require crystalloid, fresh frozen plasma (*Transfusion Therapy p. 667*) and may also benefit from 25% human serum albumin or a cautious titration of synthetic colloid.

DIAGNOSIS

History/Signalment

Question the owner on behaviour associated with various organ systems and recent events.

- Stranguria, hematuria in intact males may indicate prostatitis (*p. 742*).
- The time frame from the last heat cycle in an intact female may suggest pyometra (*p. 756*).
- Is the patient a diabetic? Diabetic animals are predisposed to infection.
- Is there a recent history of teeth cleaning or extraction? Bacteremia and endocarditis may occur following this procedure.
- Was there a recent traumatic incident (*possible urinary p. 727, biliary or gastrointestinal injury p. 21*)?
- Is this a field working dog? These dogs are exposed to soil fungi or foreign body injuries.
- Previous exposure to wildlife (i.e., porcupine attack, bite wound) or, neighbourhood animal fights?
- Is the cat or dog known to chew on foreign objects? Chewing on sticks, or ingestion of any foreign bodies, may result in penetration through the pharynx, esophagus, or gastrointestinal tract.
- Is the patient receiving immunosuppressive or chemotherapeutic drugs?
- Always have a high index of suspicious for streptococcal infection/myositis/fasciitis with a rapid onset illness and progressive pain, especially where the pain elicited is far worse than expected for the visible lesion. This lesion will progress rapidly making it obvious why the animal is painful.
- Is there a current or very recent situation where reduced splanchnic perfusion occurred (i.e., hypovolemia due to any cause, hypotension due to any cause) with potential for bacterial translocation through alterations in gut mucosa to the intestinal lymphatic/ blood vascular system.
- A recent history of diarrhea and weight loss prior to illness, and the presence of peritonitis, especially in a cat (and rarely in the dog) may suggest perforation of the gastrointestinal tract due to lymphoma.

Clinical Signs/Physical Examination

Patients in septic shock can present in the early or hyperdynamic phase, through to the late, hypodynamic phase; the physical findings are quite different. During the physical examination keep in mind that major areas of infective foci are the reproductive tract in intact males and females, urinary, respiratory and gastrointestinal tract, abdominal (especially in dogs) and thoracic cavity (especially cats), teeth and gums and heart valves.

- **In the early phase,** the mucous membranes may be 'brick' red with a capillary refill time <1 sec, the pulses are bounding and tachycardia is present. Tachypnea or hyperpnea is usually present at this stage also. The animal is warm to touch, depressed but may be agitated.
- Cats most commonly tend to be hypothermic or normothermic and may be bradycardic. This may be the response of cats to sepsis or that they tend to be referred in a later stage of sepsis than dogs.
- Icterus in both cats and dogs may indicate cholestasis which occurs with sepsis, or hepatobiliary pathology. Associated IMHA (*p. 411*) may also be a possibility. The patient may also be icteric in advanced stages of sepsis, or if underlying liver disease is present.
- **In the later phase,** pulses may be difficult to palpate, the capillary refill time is >2 sec and the mucous membranes may be cyanotic, dusty pink, gray or pale with cool extremities. While examining mucous membranes, examine the mouth, and sub-lingual area for string caught and anchoring around the tongue with the remainder passing through the gastrointestinal tract.
- Patients receiving immunosuppressive or chemotherapeutic drugs may present in hypotensive shock with minimal findings associated with infection; they may be febrile, however (*see Oncological Emergencies p. 443*).
- Auscultate the heart for abnormal rate and rhythm. Murmurs are suspicious for endocarditis, which may be the primary or a secondary cause of sepsis. Muffled lung and heart sounds may indicate pyothorax and a careful examination of the skin and body wall is necessary to identify possible puncture wounds. Often this is caused by migrating FBs such as porcupine quills or grass awns. Coughing with crackles and wheezes may suggest pneumonia (*see Respiratory Emergencies p. 555*), or acute respiratory distress syndrome (ARDS).

- Examine the patient for a septic focus, heat, swelling and pain. Not all wounds are apparent. Palpate over the whole body looking for entry wounds of foreign bodies or bites, abscesses, areas of pain and joints for swelling. **Fasciitis, myostitis, cellulitis** may not be seen in long-haired animals but is identified by swelling, heat and pain which may involve any area of the body. **Virulent streptococcal infections,** similar to the fatal streptococcal infections seen in human patients occurs in dogs and rarely in cats. In addition to signs of sepsis, these patients may be extremely painful, much more than one would expect with the lesions present. These lesions are reapidly progressive and do not always have a predisposing injury. This history may not fit with the clinical findings.
- Perform a rectal examination to assess the prostate in males and other abnormalities including enlarged lymph nodes.
- Palpate the abdominal wall to identify wounds that may have penetrated into the abdomen. Include all four quadrants with palpation of internal organs for enlargement, masses, fluid and pain.
- A neurological examination may elicit a stiff, painful neck that may indicate meningitis (*p. 468*) and a focal painful area along the spine may suggest discospondylitis (*p. 468*) as a focus of infection.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV** may be increased relative to the **TS** if there is capillary leak or third-spacing of fluid; TS will be low in these settings, occasionally very low 20 g/L (2.0 g/dL) especially in the later stages of sepsis in both cats and dogs. PCV may be low if anemia is due to infection (especially in cats), or hemorrhage is present.
- **Stick BUN, urea or creatinine** as an estimate of renal function or presence of pre-renal azotemia.
- Glucose may be norml or low. If a diabetic then hyperglycemia will be present. Cats tend to exhibit a transient hyperglycemia when stressed but hypoglycemia frequently occurs if septic.
- **ACT** using grey top (silica) tube is usually increased in DIC, and sepsis from our observations (normal 70 – 120 secs in dogs, 60 – 90 secs in cats using deep axilla (under the 'white coat') or heating block. The ACT is very useful for trending during therapy. ACT may be used instead of PT/PTT.
- **PT/PTT** in addition to ACT, or instead of but for the same reasons. Normal values are generated for each laboratory.
- **Urine,** collected by cystocentesis, for urinalysis, and culture and specific gravity.
- **Serum electrolytes** may be altered in hypovolemic and abnormal metabolic states. Assessment of acid-base status also requires this information (*p. 406*). Correction of abnormalities is necessary. Hypokalemia is not uncommon in sepsis and may be associated with cardiac arrhythmias. Decreased ionized calcium has been documented in septic cats. See chapters on the specific electrolyte abnormality.
- **Venous blood gases (or total CO_2)** is necessary for assessment of the metabolic status of the patient (*see Acid-Base Assessment p. 406*). Sepsis frequently results in a significant base deficit, the value of which reflects the perfusion deficit. Trending of these values is important in management.
- **Systemic blood pressure** may be normal in compensated shock, or low, systolic blood pressure (SBP) <90 mmHg, mean arterial pressure (MAP) <60 mmHg in septic shock. SBP is important to document as it will identify the severity of the patient's condition and direct therapy. Trending is essential during therapy.
- **ECG** findings are frequently those of a sinus tachycardia in dogs, or bradycardia or tachycardia in cats. Ventricular (*p. 179*) or supraventricular (*p. 170*) tachycardias are not uncommon in sepsis.
- **Biochemical profile** is necessry to assess the patient's general condition and identify organs affected in the MODS. Bilirubin is frequently elevated as is creatinine.
- **CBC** to identify criteria for SIRS or sepsis (*Table 1 above*).
- **Lactate** is extremely useful in assessing perfusion status and for trending. Normal is <2.5 mmol/L in dogs and <1.5 mmol/L in cats (*see Acid-Base Assessment p. 406*).
- **Diagnostic imaging** is essential to diagnose the primary problem in most septic animals.
- **Gram stain and cytology of effusions** to help with selection of antibiotics until definitive diagnosis received from clinical pathologist (*see Acute Abdomen p. 30 and Respiratory Emergencies p. 562 for interpretration*).

Extended Data Base

Although the following may be considered in an extended data base, they are necessary for diagnosis and therefore should be performed.

- Submit **samples of** aspirates from abscesses, muscle (e.g., fasciitis), etc, or **abdominal** (*see Acute Abdomen p. 28 for diagnosis*) **or pleural effusion** (*see Respiratory Emergencies p. 562 for diagnosis*) and submit for Gram stain, culture and antibiotic sensitivity and cytology. *See Suggested Readings 2 – 5 below* also for specific therapy based on laboratory results.

- **Blood culture and sensitivity.** Blood should be collected from two separate veins consecutively, after surgical preparation of the skin. It is not necessary to wait an hour as previously recommended.
- **Arthrocentesis** of all suspicious joints, or if no obvious focus of infection is found, or the history suggests possible septic arthritis.
- **Prostatic wash** is advised if prostatic disease is suspected (*see Prostatic Disease p. 742*).
- If **meningitis** (*see Neck Pain p. 468*), or **discospondylitis** perform a CSF tap, and spinal radiographs and fine-needle aspirate of suspicious disc area.
- If underlying illness cannot be identified, (*see Fever of Unknown Origin p. 422*).
- Further individual tests based on history and physical examination may be required.

MANAGEMENT

After all samples have been collected for cytology, gram stain, culture and sensitivity, and fluid therapy has been initiated, antibiotic therapy should be administered (*see H below p. 593*).

A. **Oxygen** supplementation in all cases. An arterial oxygen saturation >92% is required. *See p. 577* for specific techniques.

B. **Obtain IV access,** cephalic is easier initially. Jugular catheter is also advised as frequent blood sampling is required for trending purposes, and parenteral nutrition is advised in most patients. More than one IV access is also required for the many infusions these patients need.

C. **Fluid Therapy.**
1. **Hypotensive** with **moderate to severe hypoproteinemia (TS <45 g/L [4.5 g/dL]),** and/or **suspect capillary leak** judicious fluid management is required to avoid pulmonary edema.
   a. Commence a **balanced electrolyte solution (BES)** (Plasma-Lyte® 148 or A, Normosol® R, or lactated Ringer's). Administer in 1.5 – 2.0 mL/kg/min boluses (90 – 120 mL/kg/h) dog; 1 mL/kg/min (60 mL/kg/h) cat initially. Monitor response as in 5 below (*p. 592*). If poorly responsive after 10 minutes consider reducing crystalloid volume by ~20 – 40% and ADD
   b. Aliquots of **synthetic colloids (6% Hetastarch, 6% Pentastarch, dextran 70) at 5 mL/kg (dog) or 2.5 mL/kg (cat),** monitor response to each aliquote [to a maximum of 20 mL/kg (dog), 10 mL/kg (cat)] while monitoring BP as in 5 below (*see Synthetic Colloids in Fluid Therapy Discussion p. 364* for details). Go to e. below.
   c. If MAP <60 mmHg, TS <30 g/dL) where albumin is, or assumed to be <15 g/L [1/5g/dL] prior to fluid administration, and capillary leak situations. **25% Human Serum albumin (HSA) 0.5 mL/kg** (*see Hypoalbuminemia p. 431 and Fluid Therapy Discussion p. 363* for details prior to administration). Administration by slow push is suggested while monitoring blood pressure. Repeat 0.5 mL dose if no effect. Reduce rate by 25% as pressure increases. Discontinue bolus dosing and continue as a CRI at 0.3 – 1 mL/kg/h when pressures are adequate or optimal, see 5 below. Dosages up to ~4 mL/kg in 24 hours have been administerd by the author. Go to e. below.
   d. Fresh frozen plasma **10 – 20 mL/kg (dog & cat)** may be beneficial in sepsis (*see Transfusion of Blood Products p. 667*), however thawing time precludes its immediate use but may be administered as soon as thawed. Both plasma and 25% HSA may be administered concurrently.
   e. Continue to monitor q5min (*see 5 below p. 592*). Go to D below if poorly responsive to fluid therapy.
2. **Hypotensive not hypoproteinemic.**
   a. Rapid volume resuscitation using a BES as described in 1 above. Monitor as in 5 below *p. 592*. Reduce fluids based on improvement in systemic or central venous blood pressure. If no improvement
   b. Follow with and IV bolus of **synthetic colloid** 5 mL/kg in dogs and 2.5 mL/kg in cats. Monitor q5min as in 1 above, and repeat bolus of synthetic colloid to a maximum of 20 mL/kg in dogs and 10 mL/kg in cats (if given rapidly, it may induce vomiting). The BES is then given to complete the resuscitation.
   c. If blood pressure doesn't increase, go to D below.
   d. Fresh frozen plasma is recommended if ACT is prolonged (*see F below p. 593*).
3. **Not hypotensive.** Administer a BES based on physical examination (*see Fluid Therapy p. 349*).
4. **Pediatrics.** Dehydration and hypoglycemia can occur rapidly in puppies and kittens (*see Hand-Rearing Puppies & Kittens p. 551*).
   a. Administer **1 mL/30 g** Plasma-Lyte® 148 or Normosol® R or lactated Ringer's with **dextrose** (add 1 mL of 50% dextrose/10 mL crystalloid).

    b. Give as a bolus via jugular vein (easily accessible with 20 ga peripheral IV catheter), or intraosseous.

    c. Do not administer subcutaneously.

    d. Repeat bolus as needed based on response. Re-check glucose prior to repeat dosing.

5. **Monitor q5min initially** to assess **response** (i.e., improvement in cap refill time, pulse rate and character, mucous membrane colour and respiratory rate) (*see End-Points of Resuscitation in Fluid Therapy p. 352*) and prevent problems associated with fluid overload (*see Fluid Therapy p. 358*). A slight but consistent increase in respiratory rate can be an early clue to fluid overload and development of pulmonary edema. A slight but consistent reduction in **oxygen saturation (SpO$_2$)** over a few minutes as detected by pulse oximetry may be another indication of pulmonary edema. **Ideal arterial pressures** to optimize oxygen delivery to the tissues are **MAP 100 mmHg and systolic 120 mmHg.** However, where **capillary leak and pulmonary edema** is a concern (e.g., ARDS), adequate resuscitation goals of **MAP 70 – 80 mmHg, systolic pressure 100 mmHg** are acceptable if a lower fluid volume and hydrostatic pressure reduces fluid loss from the intravascular space preventing edema. Capillary leak occurs when hydrostatic pressure is increased and colloid osmotic pressure decreased. Once resuscitation goal is reached, maintain fluids at twice maintenance initially and adjust according to the patient's needs (*see Fluid Therapy p. 355*). CVP (*see Fluid Therapy technique p. 371*) is a useful measurement to assist with rate and volume of fluid administration especially in geriatric patients and those with cardiac insufficiency. If adequate fluid therapy has been administered and hypotension is still a problem, go to D below.

6. **Furosemide 0.25 mg/kg IV** should be administered where pulmonary edema has occurred due to fluid overload. A **CRI of 0.1 – 0.2 mg/kg/h** may be required until resolution.

D. **Vasopressors and Inotropes** are required if hypotension persists after adequate fluid resuscitation (*calculate as in Fluid Therapy p. 352*).

1. **Dopamine 5 μg/kg/min (cats and dogs)** and increase by 1 μg/kg/min ~ every 2 min (max 15 μg/kg/min) until **target blood pressure** (MAP 70 – 100 or systolic 100 – 120 mmHg) is reached. (*see Dopamine Inotropic Infusion Chart p. 233*). Stop if tachycardia develops. If vasopressor effects are inadequate at this rate, discontinue and try

2. **Norepinephrine 0.05 – 0.5 μg/kg/min** increase as for dopamine (i.e., increase by 0.1 μg/kg/min q2min) (*see Norepinephrine Infusion Chart p. 253*), higher doses may be required. OR

3. **Dobutamine 5 μg/kg/min (dogs), 1 – 2 μg/kg/min (cats)** [CAUTION in cats as seizures may occur] if more inotropic effect is warranted.

4. If only **epinephrine** is available and pressor support is necessary, try **0.1 – 1.0 μg/kg/min** (*see Epinephrine Infusion Chart p. 235*) starting with the low dose and increasing every 2 – 3 min to effect, or the highest dose.

5. Gradually reduce pressor support over several hours, or more rapidly if tachycardia or hypertension develops.

6. Refer to *Hypoadrenocorticism p. 274* if non-responsive.

E. **PCV and TS** must be monitored q15min with high volume, high rate crystalloids and synthetic colloid administration.

1. If **TS <50 g/L** prior to fluid resuscitation, plasma is recommended as this will be significantly diluted after resuscitation (plasma takes up to 45 min to thaw).

2. If **TS <40 g/L at any time,** fresh plasma or fresh-frozen plasma is recommended.

3. If **PCV <25% and TS <40 g/L or albumin <20 g/L,** whole blood transfusion is required.

4. If **PCV >45%,** red cells may stick to the injured endothelium in the capillary bed resulting in microthrombosis and poor tissue oxygenation. Keep the fluids going to maintain PCV between 30 – 45%.

5. If **PCV <30%,** rule out dilutional change vs hemorrhage. If it is dilutional and SBP is within normal limits, slow down the infusion and the fluids should equilibrate within a few hours; don't dehydrate to achieve normal PCV.

6. If **PCV <25%** and hemorrage is identified, give fresh blood, or packed cells (use cells <15 days old to avoid abnormal deformability and pluging of the microcirculation) if plasma transfusion is underway. Ascertain source of blood loss (i.e., intra-abdominal, gastric hemorrhage) and treat appropriately. YOU MUST CALCULATE THE AMOUNT OF BLOOD REQUIRED FOR TRANSFUSION TO AVOID POLYCYTHEMIA AND MICROTHROMBOSIS (*see Transfusion Therapy p. 673*). Rheology is important for optimal oxygen delivery to tissues; a PCV of 25 – 30% has been suggested as being close to optimal, therefore blood transfusions are not required to raise the PCV >30%.

F. In septic shock and SIRS, **fresh/fresh-frozen plasma** may be useful to maintain not only plasma antithrombin and albumin levels (both available in stored blood) but also coagulation factors, anti-cytokines, alpha macroglobulins and antiproteases. Administer **10 mL/kg over 1 – 2 hours and an additional 10 – 20 mL/kg during the remaining 22 – 23 hours as a 6 – 10 mL/kg infusion over 2 – 3 hours.**

G. **Pain control** is very important.

1. **Butorphanol 0.2 – 0.4 mg/kg q2h** can be tried initially for mild to moderate pain and continued as a **CRI 0.1 mg/kg/h** or to effect. Stop the CRI for 30 – 60 minutes if appears overdosed and reinstitute at one-half the previous dose. If butorphanol is not adequate, then
2. **Oxymorphone or hydromorphone 0.025 – 0.1 mg/kg** q3 – 4h, or to effect. This dose may be given as a CRI over a 3 – 4 h period (*see Infusion Charts p. 243*). You may have to increase the dose of oxymorphone or hydromorphone if butorphanol has already been administered due to its antagonistic effect.
3. **Morphine or methadone 0.2 – 0.4 mg/kg very slowly IV,** followed by CRI (*see Morphine Infusion p. 251*) is also effective.
4. **Fentanyl 4 – 6 μg/kg IV bolus** followed by **4 – 6 μg/kg/h CRI** in dogs and cats (*see Infusion Charts p. 237*). This is the author's preference for severely painful animals, especially cats (cats really like fentanyl!)

Pain activates the sympathetic nervous system which causes vasoconstriction and therefore poor splanchnic perfusion (especially pancreas and this, in itself, can cause pancreatitis).

H. **Antibiotic therapy** should be instituted as soon as **all the samples have been obtained for culture** and fluid therapy is commenced (*see M below p. 595*). **CAUTIONARY NOTES:** It is advised not to use enrofloxacin in puppies <8 mos (small breeds), <18 mos (giant breeds) however, if required based on severity of illness, assess for joint pain and stop treatment immediately. Enrofloxacin at high dosages IV may cause seizures when administered as a bolus. Imipenem may also cause seizures. Metronidazole may rarely cause seizures. Do not use tetracyclines in animals prior to eruption of adult teeth. If using combination antibiotics, or other medications with similar toxicity, administer at different time intervals. Combination therapy is indicated in most septic patients. Where chloramphenicol is prescribed, owners must be informed of the potential for aplastic anemia to develop in humans; gloves and handwashing when handling is necessary. Aminoglycosides are effective against gram -ve organisms but bacterial resistance occurs. Also, if renal function is questionable or if furosemide may be required, the nephrotoxicity of aminoglycosides increases. If an aminoglycoside is selected, tobramycin is recommended as the nephrotoxicity and resistance is less than amikacin or gentamicin. The choice is directed towards potential pathogens possibly associated with the underlying problem. Enteric bacteria and staphylococci are highly represented in sepsis of pulmonary, abdominal, renal and reproductive origin within both cats and dogs. Anaerobes are identified in pulmonary and abdominal infections a little less frequently in both dogs and cats. Pasteurella is isolated from pulmonary and renal infections more commonly in cats than dogs.

1. As prophylactic against **gastrointestinal and hepatic organisms** that may have translocated during the hypotensive state, and in known hepatic and gastrointestinal infections or translocation, **cefoxitin or cefotetan 40 mg/kg IV** initially and continued at **20 mg/kg IV q6h (dog) and IV q8h (cat)** are **recommended** for their anaerobic and gram negative spectrum.
2. If in **septic shock** and the offending organism is unknown, administer a broad spectrum antibiotic with little known resistance until the culture and antibiogramme is obtained such as
   a. meropenem 20 mg/kg IV q12h (dog and cat)   OR
   b. imipenem 5 – 8 mg/kg q8h (dog and cat) over 1-h infusion.
3. Where the patient is **not in shock** and a **mixed or completely unknown** population of bacteria may be present use
   a. clindamycin 10 mg/kg IV q12h and enrofloxacin 5 – 10 mg/kg q 24h (dogs); 5 mg/kg SC q24h (cats).
4. For neutropenic (*p. 435*), immunosuppressed chemotherapy patients (*p. 443*), see respective chapters for specific guidelines.
5. If **pseudomonas** suspected based on lack of response to previous antibiotic use, empirically administer
   a. tobramycin 9 – 14 mg/kg IM, SC q24h (dogs); 5 – 8 mg/kg IV, IM, SC q24h (cats), OR
   b. amikacin 15 – 30 mg/kg (dogs), 10 – 14 mg/kg (cats) IV, IM, SC q24h combined with ceftazidime 30 mg/kg IV, IM q6h (dogs and cats), SC dogs only. CRI: loading dose of 4.4 mg/kg followed by 4.1 mg/kg/h delivered into IV fluids, OR
   c. ciprofloxacin 10 mg/kg IV, PO q12h (dogs & cats), OR

d. **imipenem 5 – 8 mg/kg IV q8h (dogs & cats)** over 1h infusion, OR
e. **meropenem 20 mg/kg IV q8h (dog) and 8 mg/kg SC q8h (cat).** May be given SC when IV access no longer required.
f. **enrofloxacin** is less efficacious due to development of resistance. However, if selected a dose of **10 mg/kg** (dogs only) **IM, IV q24h.** Enrofloxacin **5 mg/kg SC q24h** in cats.

6. If **gram +ve cocci** suspected administer
   a. **cefazolin 20 mg/kg IV,** PO q6h, OR
   b. **trimethoprim-sulfadiazine 15 mg/kg SC, IV q12h** (check formulation) OR
   c. **clindamycin** if streptococcal infection suspected.

7. If **gram -ve rods** suspected,
   a. **trimethoprim-sulfadiazine 15 mg/kg SC, IV q12h** (check formulation) OR
   b. **enrofloxacin 5 mg/kg q24h in (dogs & cats).**

8. If a history consistent with *Bordetella* infection (*p. 566*),
   a. **doxycycline 5 – 10 mg/kg q12h for 48h IV CRI** over 1h, then 5 mg/kg PO q24h once the patient can take medication orally OR
   b. **enrofloxacin 5 mg/kg q24h** OR
   c. **chloramphenicol 50 mg/kg IV, SC, PO q8h** (hospital personnel and owners must be warned about potential bone marrow suppression when handling chloramphenicol; gloves must be worn and handwashing is mandatory)

9. **Meningitis** (*p. 468*) requires drugs that cross the blood-brain barrier.
   a. **trimethoprim sulfadiazine 15 mg/kg SC, IV q12h** (check formulation) OR
   b. **cefotaxime 30 mg/kg IV q6h** OR
   c. **chloramphenicol 50 mg/kg IV, IM q8h (dog), 50 mg/cat q12h** is recommended (hospital personnel and owners must be warned about potential bone marrow suppression when handling chloramphenicol; gloves must be worn and handwashing is mandatory).

10. **Prostatic infections** (*p. 751*).
    a. **enrofloxacin 5 mg/kg q24h or trimethoprim sulfadiazine 15 mg/kg SC q12h** has been recommended for Gram –ve infections.
    b. **trimethoprim sulfadiazine 15 mg/kg SC q12h** for Gram +ve infections.
    c. **chloramphenicol 50 mg/kg IV, IM q8h** has been recommended for gram -ve, +ve and anaerobes.

11. If septic after a **dental procedure**
    a. **clindamycin 10 mg/kg IV q12h** OR
    b. **ampicillin 20 mg/kg IV q6h** (dogs) **q8h** (cats) is recommended.

12. If anaerobic infection suspected **metronidazole 10 mg/kg IV 1 h CRI q8h.**

13. Select drug for treatment of **parasitic infection** based on specific identification.
    a. **doxycycline 5 mg/kg IV, PO q12h** for *Ehrlichia canis* or *Rickettsia rickettsii* (*see Tick-Borne Diseases p. 307*).
    b. **clindamycin 10 mg/kg IV q12h** for *Toxoplasma.*

14. **Fungi;** antimicrobial therapy to be selected on identification but start with
    a. **itraconazole 5 mg/kg PO q12h (for blastomyloses in dogs) –24h, 5 mg/kg q12h (cats)** OR
    b. **ketoconazole 10 – 15 mg/kg IV (dogs), 5 – 10 mg/kg (cats) IV q8–12h** if cannot take medication orally,
    c. **fluconazole 10 – 20 mg/kg q24h IV, PO (dogs); 50 mg/CAT q12–24h PO.**

If the fever, patient's status, white blood cell count, or appropriate band count **does not improve after 36h** at the most, consider changing antibiotic (call the laboratory for an update on the possible organism cultured), consider possible anaerobic or fungal infection if the antibiotic selected does not cover these organisms. Reassess for continuing focus of infection and remove if possible. The key to recovery is removal of the septic focus.

I. **Non-respiratory (metabolic) Acidosis** usually resolves after fluid resuscitation; sodium bicarbonate should not be administered routinely. Sodium bicarbonate may be considered if the venous pH remains <7.2 and base deficit is >- 12, or bicarbonate or total CO_2 is <12. (Note: Total CO_2 levels may be low if tubes are transported or allowed to sit open prior to test). Dose HCO_3^- (mEq/L) = BWkg x (12 – patient HCO_3^-) x 0.3. Give over 1 hour. Empirical dose HCO_3^- = 0.5 – 1.0 mEq/kg. Give over 1 hour. If lactate levels can be measured, this may better assess adequate tissue perfusion and acidosis. A lactate concentration ≥2.5 mEq/L(dog), 1.5 mEq/L (cat) indicates abnormal lactate acumulation (*see Acid-Base Assessment p. 406*).

J. **Urine output** should be measured to assess adequate renal (splanchnic) perfusion. The goal is 1 – 2 mL/kg/h with urine specific gravity ~1.020, and when weaning off fluids, no less than 0.5 mL/kg/h with normal to high urine specific gravity (ensure increased water intake here). Failure to achieve this indicates further fluid is required or possible renal injury has occurred (*see Acute Renal Failure p. 709*). Examine urine sediment daily for casts during the crisis situation. Should these appear, stop anminoglycoside therapy and ensure diuresis.

K. **Serum electroylytes** should be monitored q2–4h initially as alterations in acid-base status with fluid resuscitation may significantly alter the serum potassium levels (*see Hypo/Hyperkalemia p. 394*). Magnesium levels should be measured and supplemented at 30 mg/kg as a CRI over 4 hours if levels are <0.7 mmol/L. This may be repeated three times in 24 hours to a maximum of 125 mg/kg/24h (*see Magnesium p. 403*), unless serum Mg levels can be measured and hypomagnesemia is present (*see Magnesium p. 403*). Serum potassium should be monitored with magnesium administration as magnesium reduces potassium loss.

L. **DIC** can be expected in septic and SIRS patients. Refer to DIC *p. 417*.

M. **Definitive therapy** is based on the underlying problem which should be sought through physical examination, laboratory and radiographic findings. The underlying problem (pyometra, GI accident, abscess, myositis, fasciitis etc.) must be surgically drained or removed immediately after fluid resuscitation (hopefully within 1 – 2 h) as this focus will prevent resolution of the SIRS. If laparotomy is performed consider placement of a feeding tube (*see Nutritional Support p. 503*).

N. **Ulcer prophylaxis/treatment** is necessary if vomitus contains blood or the patient is ulcer prone (i.e., history of corticosteroid treatment) commence,
1. **Famotidine 0.5 mg/kg IV (diluted) q12h** (dog & cat) OR
2. **Omeprazole 0.7 mg/kg PO q24h**
3. **Sucralfate 0.5 – 1.0 g** should be given if significant gastric bleeding is present (*see Gastrointestinal Hemorrhage p. 69*).

O. **Acetylcysteine** may improve organ function during sepsis. In treatment or prevention of multiple organ dysfunction in septic patients, the author has used
1. **Acetylcysteine 150 mg/kg in D5W** administered IV over 30 minutes, followed by **10 mg/kg IV q12h** until 'out of the woods', with no apparent ill-effects.
2. Wide ranges of doses have been used in human patients.

P. **Nutritional support** is absolutely necessary in these patients (*see Enteral and Parenteral Nutritional Support p. 499*). If abdominal surgery is required for underlying problem, consider placing a gastrostomy tube.

Q. **General nursing care** is very important. Dogs and cats get very upset when soiled. Keep them clean and comfortable. Turn q4h, and keep the bandages clean and dry. Check the IV catheter site frequently throughout the day and remove the catheter and culture if appears contaminated (infected site).

R. **Antiemetic therapy.** Vomiting (*p. 79*) is common in these patients.
1. **Metoclopramide 1 – 2 mg/kg CRI/24h** is frequently used.
2. **Ondansetron 0.1 – 0.18 mg/kg** IV q6–8h if metoclopramide ineffective.
3. Another alternative is to give **chlorpromazine 0.05 – 0.1 mg/kg** slowly IV q4h or **prochlorperazine 0.13 mg/kg** IM (hurts!) or SC q6h. These two drugs can cause hypotension therefore should only be given in the normotensive re-hydrated patient.
4. A **nasogastric tube** should be inserted with intermittent aspiration of gastric fluid in the patient with refractory vomiting.

S. **Synthetic colloids 20 mL/kg/day as an 0.8 mL/kg/h CRI** may have to be continued for 2 – 3 days. Caution with capillary leak (*see Fluid Therapy p. 364*).

T. **Plasma or 25% Human Serum Albumin** may also be required for 2 – 3 days if hypoalbuminemia and capillary leak is present (*see Hypoalbuminemia p. 431*).

U. **Tender loving care** given by you and the owners. Reduce the noise level, turn down the lights and let them rest. When not continuously monitored, attempt to have treatments done in batches so there is time between treatments for sleep.

PHARMACOLOGY

1) **Metoclopromide** is an antiemetic and promotility drug. In this protocol it is used for its centrally acting antiemetic effects. It may cause drowsiness and lower the seizure threshold in susceptible individuals. Use with caution when administering with epileptogenic drugs. Metoclopromide is a dopinergic antagonist.

2) **Chlorpromazine** is a phenothiazine derivative used in this protocol for its centrally acting antiemetic effects. It may cause hypotension and frequently produces sedation.

3) **Prochlorperazine** is similar to (2) above but less sedating.

4) **Ondansetron** is a selective antagonist of the serotonin receptor subtype, 5-HT3, located centrally and peripherally. This is the preferred antiemetic however, it is very expensive.

5) **Famotidine** is an H_2 blocker

6) **Sucralfate** – *see Gastrointestinal Hemorrhage p. 69.*

7) **Dobutamine, dopamine, norepinephrine, epinephrine** – *see Shock p. 606.*

8) **Cefoxitin.** Is a second generation cephalosporin with, good gram -ve and anaerobic coverage and some gram +ve coverage.

9) **Cefazolin.** First generation cephalosporin. Good gram +v, some gram -ve and minimal anaerobic coverage.

10) **Clindamycin.** Good gram +ve and anaerobic coverage. Does not cross the blood brain barrier

11) **Enrofloxacin.** Good gram -ve coverage (Pseudomonas too!). Do not use for Gram +ve even if susceptible in vitro; not susceptible in vivo.

12) **Imipenem and meropenem.** Good gram +ve, -ve (including *Pseudomonus*) and anaerobic coverage. Excellent choice for the crashing and burning with unknown infection and the neutropenic, febrile patient. Meropenem is a better choice than imipenem due to no seizure potential and can be given SC.

13) **Metronidazole.** Excellent anaerobic coverage. Antibiotic of choice for anaerobes.

14) **Cefotaxime.** Third generation cephalosporin. Crosses the blood-brain barrier. Some gram +ve, excellent gram -ve and good anaerobic coverage.

SUGGESTED READING

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NOTES

Antibiotic therapy should be used to **treat an identified,** or highly suspected infection **and not to prevent infection,** unless high risk (*see Nosocomial Infection: Prevention and Treatment p. 600*). The purpose of these guidelines is to suggest antibiotic therapy while reducing the potential for further antibiotic resistance and as an attempt to reduce the ever-exploding concerns for multi-antibiotic resistant organisms. While these guidelines are established for the Ontario Veterinary College, their application is suggested in any veterinary hospital. However, general recommendations for empirical selection of antibiotics is difficult as various geographical areas and specific clinical areas have acquired different rates of antibiotic resistance. Therefore, it is wise to be familiar with antibiotic resistance occurring in your practice as an antibiotic with a high resistance rate would not be effective. It is known that culture and antibiotic susceptibility testing may not be routine for the otherwise healthy patient with a first time infection, however, this is **absolutely essential** in the critically ill patient with an infection. The cost of this test is small when compared to the administration of several different classes of inappropriate antibiotics, the increased length of hospital stay due to deteriorating health, and the guarantee of acquisition of multi-drug resistant bacteria, which eventually will require a very expensive course of treatment. The development of resistant organisms will populate your clinical environment, which will continue to plague you and your patients. There is no better investment in a sick patient with an infection than that of the culture and antibiotic susceptibility test and where possible, measurements of minimum inhibitory concentrations (MIC). However, it is important to note that when culture and susceptibility testing is performed, veterinarians use reliable laboratories that perform tests according to published standards. The most widely used standards are those published by the Clinical and Laboratory Standards Institute (CLSI) (formerly known as National Committee for clinical laboratory standards [NCCLS]). If a laboratory is not performing the tests according to recognized standards, large variations and uncertainty in results are possible.

The critically ill patient is predisposed to infection based on a degree of immunosuppression associated with illness, their underlying illness and the invasive devices they require. While antibiotic therapy is essential to treat most infections, routine prophylaxis should be avoided. Administration of antibiotics to prevent infections secondary to intravenous (IV), urinary or arterial catheters should not be entertained, this practice reduces normal flora and allows resistant organisms to flourish.

Periodically new antibiotics appear on the market for human use and frequently we have to wait until pharmacokinetic and pharmacodynamic studies have been performed in the various veterinary species before we can confidently use them in our patients. At the same time resistance to many antibiotics is occurring, therefore antibiotic recommendations are continually changing. Antibiotic administration strategies are being investigated such as constant rate infusions for those antibiotics that are time dependent (e.g., β-lactams) in order to maintain blood levels above the MIC. With these antibiotics, increasing the dosing schedule rather than the dose may be a better strategy. With concentration-dependent antibiotics such as the aminoglycosides and fluoroquinolones, the dose is the important component of therapy with a high once daily dosing. The following guidelines are those of the author's institution. For patients that are neutropenic or being treated for a neoplastic disorder, refer to *Prevention of Nosocomial Infection p. 600, Neutropenia p. 435 and Oncological Emergencies p. 443.* Refer to *Sepsis/Septic Shock p. 588 and Respiratory Emergencies p. 555* for specific suggestions.

As an aid to selection of antibiotics, the following have been recommended: Patients suspected of hepatic bacterial infections, or infections of gastrointestinal origin administer a second generation cephalosporin (cefoxitin or cefotetan). Lower respiratory tract infections may be managed with first or second generation cephalosporins (cefazolin or cefoxitin). Urinary tract infections may be managed with penicillins (amoxicillin). Prostatitis requires an antibiotic with good penetration such as trimethoprim sulpha for gram +ve or –ve bacteria or fluoroquinolone for gram –ve bacteria. For pseuodomonal infections, aminoglycocide or fluoroquinolones. As rate of killing can be detrimental in some instances, clindamycin may be the better choice for streptococcal infections than a first generation cephalosporin. Antibiotic therapy for neutropenic animals requires special consideration (*p. 437*). In these patients a typical response to appropriate antibiotic therapy would be noted within 24 – 36 hours after institution.

1. Principles of antibiotic use
   a. Antibiotics should be used for treatment of infections after careful consideration as to the appropriate selection. They should not be used as a cover for poor surgical technique, for routine procedures or clean procedures with infection rates <2% and should only rarely be used for peri-operative prophylaxis (i.e., prosthetic insertion, specific orthopedic and soft tissue procedures or neurosurgery – review current practice literature) for less than 24h.

b. If a broad spectrum antibiotic has been prescribed prior to culture and sensitivity (C&S) results, discontinue inappropriate medication and change to an appropriate narrow spectrum antibiotic based on antibiotic susceptibility of the organism.

c. Occasionally, *in vitro* results do not reflect the in vivo sensitivity; i.e., enrofloxacin may prove to be effective against *streptococcus* sp *in vitro* but it is not *in vivo*. Therefore, be aware of these shortcomings.

d. When oral medications are prescribed, consider owner compliance with administration. It is difficult to administer medication q8h when two hours away from meals is required (i.e., ampicillin or tetracycline). While these antibiotics may be cheaper on a per pill basis, when increased frequency of administration and poor compliance is considered, the alternative amoxicillin or doxycycline respectively, is preferred.

2. **First choice antibiotic in the absence of, or pending C & S results,** in light of the history, physical findings and potential microorganism causing infection.

   a. Penicillins (Gram +ve, -ve, anaerobic bacteria)
      i. Penicillin G sodium 20,000 U/kg q4h IV, IM (hurts!), SC (cats & dogs)
      ii. Ampicillin parenteral 20 mg/kg IV q6h (dogs), q8h (cats) OR
      iii. Amoxicillin 10 – 20 mg/kg PO q12h (cats & dogs)

   b. 1st generation cephalosporin (Gram -ve, +ve bacteria)
      i. Cefazolin 20 mg/kg IV q6h (dogs), q8h (cats)
      ii. Cephalexin 20 – 40 PO mg/kg q8 – 12h (cats & dogs)

   c. Aminoglycosides (Gram –ve bacteria predominantly)
      i. Gentamicin 9 mg/kg q24h IV, IM, SC (dogs & cats)
      ii. Amikacin 20 mg/kg IV, IM, SC q24h (cats & dogs), only when known gentamicin resistance is known in your institution or previous treatment has failed.

   d. Sulfa combinations (Gram –ve, +ve bacteria, *Bacillus* spp, *Nocardia* spp, *Pneumocystis carinii*, *Toxoplasma* spp). Excellent tissue penetration including blood brain barrier and prostate.
      i. Trimethoprim+sulfa 15 mg/kg IV (check formulation), SC, PO q12h (cats & dogs)

   e. Tetracyclines (Gram –ve, gram +ve bacteria, some protozoal sp, *Rickettsia* spp)
      i. Tetracycline 5 – 10 mg/kg IV (over 10 min), IM q8h (may cause fever in cats, rare hepatotoxicity)   OR
      ii. Doxycycline 5 – 10 mg/kg IV q12h IV over 1 h for 48h (or PO if patient can take oral meds), then 5 mg/kg q24h PO

   f. Lincosamides (Gram +ve and anaerobic bacteria and *Mycoplasma* spp)
      i. Clindamycin phosphate 10 mg/kg IV (over 10 min), PO q12h (cats & dogs)

   g. Nitro-imidazole (Anaerobic bacteria, *Giardia*)
      i. Metronidizole 10 mg/kg IV 1h infusion q8h (cats & dogs), 15 mg/kg PO q12h (dogs), q24h (cats)
      ii. Tinidazole

   h. Anti-fungal agents
      i. Fluconazole 10 – 20 mg/kg IV, PO q24h (dogs), 50 mg/CAT PO q12 – q24h
      ii. Itraconozole 5 mg/kg IV, PO q12h (blastomycoses in dogs) – 24h (cats & dogs)

3. Antibiotics to be used only when justified by C&S results, or in emergent setting (see below)

   a. Piperacillin 40 mg/kg IV, IM q6h (cats & dogs) (Gram –ve including *Pseudomonus aeruginos*, Grame +ve and anaerobes)

   b. i. Amikacin 20 mg/kg IV q24h (cats & dogs) (see 4 B 2 below for highly resistant setting). OR
      ii. Tobramycin 5 – 8 mg/kg IV, IM, SC q24h (cats) , 9 – 14 mg/kg IV, IM, SC q24h (dogs)

   c. Fluroquinolones (see 4a below)

   d. 2nd & 3rd generation cephalosporins:
      i. cefoxitin, cefotetan OR ceftazidime 20 – 30 mg/kg IV, SC q6h (dogs), q8h (cats), OR
      ii. cefotaxime 20 – 80 mg/kg IV, SC q8h (dogs), q6h (cats)

   e. Potentiated broad spectrum β-lactam antibiotics:
      i. ampicillin + clavulanic acid 13.75 mg/kg PO q12h (dogs), 62.5 mg/CAT PO q12h
      ii. ampicillin + sulbactam 10 – 20 mg/kg IV, IM q8h (cats & dogs)
      iii. ticarcillin + clavulanic acid 30 – 50 mg/kg IV, IM q6–8h (cats & dogs)

4. Suggested Empirical **Antibiotic guidelines for emergent situations,** especially if patients are referred to a tertiary care facility with lack of response to various previous antibiotic regimens, those 'do not know what you are dealing with infections' which could be *pseudomonas* and/or multi-bacterial infection; or based on C&S results.

A. Clindamycin + Fluoroquinolones

1. Clindamycin phosphate10 mg/kg IV q12h. Cats & dogs.
2. Enrofloxacin q24h
   Dog: 10 mg/kg IV over 20 min q24h for three treatments, then 5 mg/kg q24h
   Cat: 5 mg/kg max IV (over 30 min) q24h
3. Other more recent parenteral fluoroquinolones may be substituted, especially where there is a high resistance to enrofloxacin in certain States of America.
   Fluorquinolones where appropriate are preferred to an aminoglycoside where furosemide is, or maybe, administered due to potential nephrotoxicity with aminoglycoside + furosemide.

B. Aminoglycoside + Clindamycin (see above):

1. Gentamicin q24h
   Dogs: 8 – 14 mg/kg IV, SC
   Cats: 5 – 8 mg/kg IV, SC
   OR
2. Amikacin q24h, (where high resistance to gentamicin in certain States of America)
   Dogs: 15 – 30 mg/kg IV, SC
   Cats: 10 – 15 mg/kg IV, SC

C. Aminoglycoside (see above) + Cefazolin + metronidazole:

1. Cefazolin
   Dog: 40 mg/kg IV reduced to 20 mg/kg q6h
   Cat: 40 mg/kg IV reduced to 20 mg/kg q8h
2. Metronidazole 10 – 15 mg/kg IV (1 hour constant rate infusion) q12h
   Measure concentration and clearance of aminoglycoside. If impaired, change to another antibiotic.

D. Single agent empirical selection when above combinations have been administered without success

1. Meropenem (Gram –ve, +ve and anaerobic bacteria). The author's preference
   Cat & Dog: 20 mg/kg IV q12h, may be followed by 8 mg/kg SC q12h.
   If Pseudomonous is suspected or confirmed, increase dose and dosing frequency to 24 mg/kg IV q8h or 8 mg/kg SC q8h. Dosage reduction after 3 days may be possible.
2. Imipenem/Cilastin (Gram –ve, +ve and anaerobic bacteria).
   Cat & dog: 8 mg/kg IV (1 hour CRI) q8h. Induction of resistance is not uncommon, therefore treatment for minimum of 5 days is advised. (Do not use if other seizure-potential medications are used).
3. Cefotaxime 20 – 80 mg/kg IV, SC q8h (dogs), q6h (cats) for CNS infection non-responsive to trimethoprim-sulfa and clindamycin phosphate (useful for encephalitis not meningitis).

E. Refer to Sepsis/Septic Shock *p. 588*, Neutropenia *p. 435* and Oncologic Emergencies *p. 443* for specific guidelines.

NOTES

INTRODUCTION

Most community acquired bacterial infections are responsive to the common, first-line antibiotics whereas nosocomial infections are notably resistant to these antibiotics making the infections difficult and expensive to treat. As nosocomial infections are acquired by hospitalized patients, we should focus on eliminating the source of these infections. The treatment of infections can be challenging when the identification of the potential organism is not known. In the emergency and critical care setting, antibiotics are often administered on an empirical basis prior to receiving results of the culture and antibiogramme. The temptation to administer broad-spectrum antibiotics, or those that are recommended for difficult to treat organisms, should be avoided unless the clinical picture or antibiogramme dictates that these antibiotics be used. Refer to Suggested Antibiotic Guidelines (*p. 598*) for empirical selection of antibiotics. The clinical presentation, with indication of infection, the system involved, the age and physical condition of the patient, should all be considered when selecting the antibiotic. In addition to antibiotic therapy, ensure that overall patient management is optimized.

Non-antibiotic sources of nosocomial infection

Hands of medical personnel are one of the **major** sources of infection. This can be due to resistant flora of the individual (e.g., paronychia) or lack of hand washing between patients and associated with personal hygiene. Hospital environmental sources of resistant bacteria are stethoscopes, ultrasound probes, urinary catheters, intravenous catheters, the water bath used for thawing frozen plasma, inadequate washing of food and water bowls, cages, runs, etc. Traffic throughout the hospital is a source of spread. *Clostridium difficile* has been isolated in both general veterinary practice and a veterinary teaching hospital. Widespread contamination of *C. difficile* has been reported in human hospitals at reported isolation rates of 11.7% to 29% associated with increased morbidity and mortality in critically ill patients. A study investigating the rate of intravenous catheter contamination in a small animal ICU identified a source of contamination of *Bacillus* sp as the gauze squares used to cover venipuncture sites after catheter placement. It was also noted that catheters with dwell times greater than 72 hours had a lower contamination rate than those in place for 24 hours. This study, and clinical practice emphasizes that IV catheters not be routinely changed every 72 hours as previously recommended, but only removed where indicated. However, a specific protocol using aseptic technique and violon material catheters (Becton-Dickinson, Sandy Utah), and not teflon, be used. Containers of alcohol, various disinfectants and antiseptics can become populated with resistant organisms and can be a reservoir for nosocomial infection. Nothing is spared. Urinary catheters are a common source of infection with resistant organisms; a variety of organisms are isolated, most commonly gram −ve organisms.

Guidelines for reduction of environmental-induced infection

It is proven that methods for prevention of infection should be instituted at the point-of-care.

1. **Hand washing** with a chlorhexidine-containing soap after handling any patient or their body fluids and feces, and associated with personal hygiene, **drying with disposable paper towels** (not a towel that is re-used) will reduce the spread of infection. The use of gloves and gowns are reported to control the spread of resistant organisms from infected to non-infected patients. However, the gloves and gowns must be removed prior to touching equipment or other patients. A rule of thumb is that when you turn your back on the infected patient for the last time, and after disposing of all contaminated material (bandages, body fluids etc.) remove gloves and gown, dispose of them in a container, **wash hands** and leave the patient area.
2. **Patient isolation** or cohorting is a potential way of containing nosocomial (or other) infection to one area.
3. When placing **intravenous catheters** use aseptic technique as previously described (*Suggested Reading* 7). For **urinary catheter** care, patient and caregiver hygiene can reduce the incidence of urinary tract infections. Sterile technique must be used when placing a urinary catheter. Closed, sterile urine collection systems with frequent cleaning of the external surface of the catheter with tincture of chlorhexidine may reduce infection. To prevent ascending infection from contaminated urine within the collection system, place a clamp on the line which can be closed when moving the animal, this will prevent reflux of urine from the collection bag into the patient's bladder. Alternatively, commercial urinary collection systems have a one-way valve in-line. Do not allow the collection bag to sit on the floor, raise it to just below the patient or place a barrier drape around it (daily change) if it has to be placed on the floor. Institute nosocomial surveillance by periodic culture of urine (upon placement and every 3 days is recommended), and intravenous catheters (especially where infection is suspected).

Colonization or contamination should not be confused with infection. However, should the urine sediment or culture indicate a urinary tract infection then the patient should be treated. The urinary catheter tip should not be cultured as this is of no value at all as contamination from peri-urethral tissue almost always occurs.

4. Should a positive culture of an IV catheter or endotracheal tube be obtained, and there is no clinical evidence of infection, then antibiotic treatment is likely not necessary.

5. **Do not use prophylactic antibiotics** specifically because of **presence of indwelling** catheters.

As mentioned, there are many sources of potential infection. It is recommended that veterinarians take time to study their cleaning protocol (i.e., frequency, disinfectant, water changes in the bucket), hand washing practice, barrier protection especially between infected and non-infected animals and immunosuppressed and non-immunosuppressed patients and all vectors that can act as sources for nosocomial infection. Protocols can be typed up to include cleaning table tops after every patient, a scheduled daily, and more thorough weekly, cleaning programme throughout the hospital. At the OVC a germicidal product is used to clean the ward floors and cages at least once per day. The cages and other soiled areas are cleaned as quickly as possible. The tables are sprayed after each patient. All dishes are hand washed with dishwashing detergent then washed in a dishwasher with a chlorinated dishwasher disinfectant compound at 98°C (200°F). An in-depth discussion of disinfectant and antiseptic use in small animal practice is available (*Suggested Reading 6*).

Discharging patients from hospital as soon as possible will reduce their chance of nosocomial infection. Development of antibiotic-resistant bacteria occurs in the gastrointestinal tract with increased duration of stay in a hospital and the feces may be a source of continuing contamination of the hospital and community environment (unpublished findings Ontario Veterinary College, Ogeer-Gyles J, Boerlin P, et. al.). Patients hospitalized due to community-acquired pneumonia may be successfully switched to oral from intravenous antibiotics within the first three days of hospitalization and discharged home.

Therapeutic interventions influencing patient infection rate

Important considerations to protect patients from infection in the emergency and critical care setting are to ensure appropriate hemodynamic resuscitation, early management of illness or trauma, early removal or open drainage of the septic focus with containment of this fluid, and early introduction to enteral nutrition. For surgical patients, the surgeon is the most important immunomodulating agent; antibiotics cannot replace the performance of a skilled surgeon. Tissue handling, reduced surgical time, attention to detail, realizing limitations of one's ability when considering a procedure, and observing strict aseptic technique, reduces the requirement for prophylactic antibiotics and contamination of the surgical site. Prophylactic antibiotics require CAREFUL consideration and should not be used as a cover for poor technique. Antibiotics should not be used for routine surgical procedures. Clean procedures with infection rates <2% should not receive antibiotics. Exceptions are prosthetic insertion and neurosurgery. For orthopedic surgery, cefazolin or penicillin IV 30 min prior to incision, with repeat if the procedure is longer than 90 min. No further antibiotics should be given. Antibiotic failure may be due to inappropriate selection, inadequate blood supply to the area of infection (i.e., perfusion-rate limited), or the particular areas of infection (i.e., permeability-rate limited such as the blood-brain barrier, prostate, eye, bronchial epithelium), or inappropriate dosing.

Preventing the emergence and spread of resistant bacteria

Most importantly, enforce basic hygiene procedures.

Where possible develop an antibiotic strategy that should be hospital-wide, with consideration for unit specific areas, group-specific patients and antibiotic resistance surveillance. Where possible, designate a person or committee to keep abreast of antibiotic use and culture results, and respond appropriately to their findings. This is a recommendation of the Centre for Disease Control and Prevention (CDCP) where hospitals should attempt to reduce the emergence and spread of antimicrobial resistant pathogens by monitoring antimicrobial use. The emergence of antimicrobial resistance is a major concern. Careful consideration should be given as to whether the patient has an infection. **Antibiotics should not be prescribed just to avoid potential litigation.** Note history, immune status, physical examination to identify a source, high or low temperature, high or low white blood count, examination of urine sediment, cytology, Gram stain and culture of body fluids or other areas that might be infected. If an infection is noted, consider typical community acquired bacterial infections by system. Select a narrow spectrum antibiotic, with known anaerobic or aerobic activity with the lowest minimum inhibitory concentration that will kill the suspected (or cultured) bacteria, reach and concentrate at the site of infection and have low toxicity in any given age group. Secondary, but important considerations, are drug compatibility or effects on metabolism of concurrent medications, owner compliance, frequency of administration and cost. An appropriate work-up and thorough consideration as to the many problems resulting in fever and elevated white count not associated with infection should be considered (*e.g.,*

neoplasia, IMHA p. 411). Where no infection is noted, re-examination can be offered to stable patients seen on an out-patient basis. Where culture and antibiogramme is not performed a trial basis of amoxicillin for a urinary tract infection (diagnosed on Gram stain of urinary sediment), for example, can be tried for 48 hours. Should there be no noticeable improvement after 36 – 48 hours, re-consideration of the therapeutic plan as to other potential causes of the urinary tract problem (i.e., consider anatomical problems, cystic calculi), and culture the urine. Similar considerations should be given to other systems (Selected Proceedings from three scientific sessions held at the 1997 North American Veterinary conference as a Supplement to the Compendium on Continuing Education for the Practicing Veterinarian March 1997; 19[3]). Refer to Suggested Antibiotic Guidelines *p. 598* for first line antibiotics to consider. The fluoroquinolones are not considered first line antibiotics and essentially are only appropriate for Gram –ve bacteria. Where streptococci are shown to be sensitive to fluoroquinolones in vitro this should be ignored, and if administered could be dangerous. Where an anaerobic infection is likely present, metronidazole or clindamycin are appropriate choices.

Patients presented in critical condition, especially if neutropenic or referred from a hospital where an infection due to a resistant organism may have occurred, are not afforded the luxury of time in identifying the cause of the infection and therefore, require a different approach to management. It is essential that samples of urine, blood, abdominal, thoracic or joint fluid, fine needle aspirates of 'lumps' or areas of swelling and cellulitis, lymph nodes and any other suspicious area be collected, prior to institution of antibiotic therapy. These samples should be submitted for culture and sensitivity and cytological examination. The inappropriate administration of an antibiotic can do great harm i.e., fluoroquinolones for streptococcal infections (*Suggested Reading 8*), inappropriate selection based on site of infection or inadequate dosing can also contribute to the demise of the patient. While avoiding the use of 'last resort antibiotics' is recommended, these drugs are appropriate for **patients dying** of their bacterial infection. For these patients the carbapenems (e.g., meropenem) would be a reasonable choice. These are broad spectrum antibioitcs with coverage against anaerobic and aerobic gram +ve, gram –ve bacteria with resistance to bacterial beta-lactamase. **Patients falling between the stable and critically ill categories** are hospitalized patients where there is time for appropriate antibiotic selection based on sound medical judgement with culture and antibiogramme results of various samples collected at the time of presentation (*see above and reference list*). Refer to Suggested Antibiotic Guidelines *p. 598*.

SUGGESTED READING

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INTRODUCTION

This chapter will give a general overview of shock. Management for non-specific causes of hypovolemia will be outlined. Where a specific cause is identified, please refer to the appropriate chapter as guidelines differ depending on the etiology.

Shock has had many definitions. Recently the emphasis has been placed on tissue perfusion in relation to cellular function. Two definitions for shock are: **i) shock** is a syndrome precipitated by a systemic derangement of perfusion leading to widespread cellular hypoxia and vital organ dysfunction, and **ii) shock** is the state in which profound and widespread reduction of *effective* tissue perfusion leads first to reversible, and if prolonged, irreversible cellular injury. *Effective* tissue perfusion may be reduced by either a global reduction of systemic perfusion (cardiac output), or by increased ineffective tissue perfusion due to maldistribution of blood flow, or a defect of substrate utilization at the subcellular level. Various types of shock have been classified based on the pathophysiology (*See Table 1*). More than one form of shock may exist for a given etiology.

TABLE 1. Classification of Shock

Hypovolemic	Cardiogenic	Extracardiac obstructive	Distributive	Metabolic
A. Hemorrhagic: Intravascular volume loss ≥30% traumatic gastrointestinal retroperitoneal intra-abdominal	A. Myopathic cardiomyopathy myocarditis myocardial contusions myocardial depression (sepsis) calcium channel blocker	A. Vena caval obstruction: Impaired diastolic filling: direct obstruction of vena cava (GDV, tumours)	A. Septic or inflammatory toxic shock	A. Heatstroke
B. Fluid depletion: (non-hemorrhage) *External loss*: dehydration vomiting diarrhea polyuria *Interstitial redistribution*: thermal injury trauma anaphylaxis systemic inflammation *Cavitary* pleural effusion abdominal effusion	B. Mechanical: valve failure hypertrophic ventricular septal defect	B. Increased intrathoracic pressure: tension pneumothorax positive pressure ventilation asthma	B. Anaphylactic/ anaphylactoid	B. Hypoxemic (low PaO_2, hemoglobin loss or dysfunction)
C. Venodilation: sepsis anaphylaxis toxins	C. Arrhythmic: bradycardia tachycardia: SVT ventricular atrioventricular block	C. Decreased cardiac compliance: cardiac tamponade constrictive pericarditis	C. Endocrinologic: adrenal crisis	
		D. Increased ventricular afterload right ventricle: pulmonary embolus acute pulmonary hypertension left ventricle: aortic thromboemboli	D. Neurogenic: spinal injury	

After Kumar A., Parillo JE.[4]

HYPOVOLEMIC SHOCK
Systolic BP <90 mmHg
MAP <60 mmHg
CVP <1.36cm H₂0, 1 mmHg
Tachycardia, Bradycardia, Tachypnea

Hemorrhage

Non-hemorrhage

| Coagulopathy | Trauma | Toxicity rodenticide NSAIAs | Post Surgical | Neoplastic anatomic considerations e.g., pericardial splenic | Inflammation Third-space | Vomiting Diarrhea Anaphylaxis Dehydration Drug-induced |

Non-compressible | Compressible

Pulmonary contusions

Non-compressible

Compressible | Non-compressible

Non-compressible

FIGURE 1. Initial Approach to Hypovolemic Shock.

GENERAL SHOCK

History ⟶   ⟵ Diagnostic Testing

Physical Exam ⟶

A. Oxygen supplementation in all cases (*see p. 577*)

B. Obtain IV access, jugular or cephalic where appropriate (*see p. 368*)

C. Commence a balanced, isotonic crystalloid solution

C1. Dehydrated ⟵ Dying before your eyes ⟶ **C 2.** Not dehydrated

Colloids

Hypertonic Saline and Colloids

If hypotension persists after adequate fluid resuscitation

D. Dopamine or norepinephrine or dobutamine

E. If non-responsive to adequate fluid and vasopressor therapy, consider the possibility of hypocortisolism

FIGURE 2. Approach to Treatment of General Shock.

DIAGNOSIS

History/Signalment

A careful history should be sought with regard to:

- Recent trauma (possible injury to biliary, urinary or gastrointestinal tract).
- Dietary indiscretion (e.g., table food, compost).
- Vaccination status.
- Vomiting and diarrhea.
- Weight loss.
- Polyuria or polydipsia.
- Duration of illness.
- An animal with vague clinical signs, which wax and wane, prior to the current illness, may suggest hypoadrenocorticism.
- Inquire about cardiac disease and other potential causes of shock listed in Table 1.

Clinical Signs/Physical Examination

The physical exam should be thorough and include all the above causes (Table 1).

- Clinical signs of shock, other than early septic shock, include tachycardia (HR >150) progressing to bradycardia, (especially in cats), weak to absent peripheral pulses, pale, grey or white mucous membranes, capillary refill time >2 sec, mental depression, and hypothermia and tachypnea are also frequently noted. *See Hemorrhage p. 623* and *Fluid Therapy p. 349* for assessment of volume loss based on physical findings.
- Patients in early septic shock frequently present with bright pink/red mucous membranes and 'bounding' pulses. The pulse rate is increased above normal.
- In addition to clinical signs, shock is also suspected when the central venous pressure is <1.36 cm H_2O (1 mmHg), systolic blood pressure <90 mmHg and a mean arterial pressure (MAP <60 mmHg. It is frequently cited that peripheral pulses are absent at MAP <60 mmHg however, this author has detected a dorsal pedal pulse at a MAP of 45 mmHg (direct measurement). Therefore, the presence of a peripheral pulse should not be relied upon as an indicator of a MAP >60 mmHg. Conversely, the absence of a peripheral pulse does not always indicate a MAP <60 mmHg. The MAP should be considered in conjunction with history and physical findings. It is recommended to measure rather than estimate arterial pressure measurements in this situation, even so accurate measurements are not necessarily obtained.
- Estimate degree of dehydration (*see Fluid Therapy p. 349*) as this amount, in addition to that depleted from the intravascular compartment, may be required to adequately resuscitate the patient.
- Note abnormal physical findings such as gastric dilation, intra-abdominal, and/or intra-thoracic effusion.
- Obtain samples (abdominal, thoracic effusions, urine, blood and any other suspicious foci) for cytology, culture and sensitivity.

Laboratory Evaluation/Diagnostic Imaging

Stat

For rapid trending purposes obtain **PCV, TS, ACT, stick BUN, systemic blood pressure** and **glucose**.

Extended Laboratory Data Base

Unless a definitive diagnosis is made on physical exam, it may be difficult to diagnose the exact cause of shock without a thorough laboratory work-up, which is advised at the outset in order to expedite finding a diagnosis. Based on findings of the following tests, develop a problem list and refer to relevant chapters for guidance.

- **CBC,** serum biochemical profile including electrolytes, lactate, blood gases (or total CO_2), PT/PTT.
- **Urinalysis** and urine specific gravity,
- **Cytology** and biochemistry of abdominal or thoracic fluid if present.
- **Diagnostic imaging.**
- **ECG.**
- Systemic and central venous blood pressure monitoring.
- Further individual tests based on history and physical exam should be ordered.

As specific guidelines for fluid therapy are given elsewhere in this manual for treating shock with hemorrhage *p. 615*, cardiogenic *p. 149*, anaphylactic *p. 90*, burn injury *p. 682*, head trauma *p. 691*, spinal injury *p. 473*, septic/inflammatory *p. 588*, adrenal crisis *p. 274*, hypo/hypernatremia *p. 381* and acute renal failure *p. 709* etiologies, please refer to the appropriate chapter. With regards to fluid therapy, the following general guidelines may be inappropriate for those problems mentioned above. General treatment of non-hemorrhagic hypovolemic shock, is as follows:

A. Oxygen supplementation in all cases. See Respiratory Emergencies for specific techniques (*p. 577*).

B. Obtain IV access, jugular or cephalic, where appropriate (*see Rapid IV Access Techniques at the end of this chapter*).

C. Commence a balanced, isotonic, crystalloid solution (BES) (Plasma-Lyte® 148, Normosol® R or lactated Ringer's), or 0.9% sodium chloride (0.9% NaCl) if alkalemic. As hydration status and intravascular volume must be considered when calculating fluid requirements, *see Fluid Therapy p. 347* for details. Caution is used when delivering fluids rapidly to geriatric patients and those with cardiac disease. Commence fluids at 1.5 – 2 mL/kg/min (90 mL/kg/h dog) or 1.0 mL/kg/min (60 mL/kg/h cat). In **dehydrated patients** a more rapid infusion, or longer duration may be required as a large fluid shift will occur from intravascular to extravascular space monitor q5min. If hypotension persists administer synthetic colloids as in 1 below.

　　1. If **"dying before your eyes"** and dehydrated, deliver BES or 0.9% NaCl at 20 mL/kg bolus crystalloid under pressure or add an IV bolus of pentastarch, hetastarch, or Dextran-70 at 5 mL/kg in dogs and 2.5 mL/kg in cats. **Avoid** Dextran-40, in dehydrated patients until at least half the estimated shock volume of fluids is delivered to avoid renal injury. Monitor q5min. If no, or minimal improvement, repeat a colloid bolus to a maximum of 20 mL/kg (dogs) and 10 mL/kg (cats). Maintain BES at rate in C above. Reduce rate of infusion by 25% as pressures rise. If pressures continue to rise, reduce by a further 25% (*see H below*). If pressures continue to be inadequate *see D below* and if PVC/TS are inadequate *see F below*.

　　2. If **not dehydrated** and **"dying before your eyes"**, bolus with 20 mL/kg crystalloid, and give hypertonic saline at 1 mL/kg/min: **5%** (dogs: 6 – 10 mL/kg) or **7.5%** (dogs: 4 – 8 mL/kg), one-quarter the dose for **cats.** Do not administer more rapidly as respiratory arrest and/or vagoreflex bradycardia may occur (treat with 0.02 mg/kg atropine). Follow with an IV bolus of pentastarch, hetastarch or Dextran-70, **5 mL/kg in dogs and 2.5 mL/kg in cats,** assess q5min; repeat as required to a maximum of 20 mL/kg (dogs) and 10 mL/kg (cats). The total volume should not be given in less that 15 min as rapid administration may induce vomiting. The crystalloid solution is then given to complete the resuscitation. Blood pressure, vital signs and mentation should be assessed q5min. Reduce infusion by 25% as pressures rise. If pressures continue to rise decrease by a further 25% and *see H below*. Measure PCV/TS (*see F below*). If pressures are inadequate, *see D below*.

D. If **hypotension persists** after adequate fluid resuscitation (*review as in Fluid Therapy p. 347*), try the following:

　　1. **Dopamine 5 μg/kg/min (cats and dogs)** and increase by 1 μg/kg/min every 2 – 3 min (max 15 μg/kg/min) until target blood pressure (MAP 80 – 100 or systolic 100 – 120 mmHg) is reached. (*see Dopamine Inotropic Infusion Chart p. 233*). Stop if tachycardia develops and then re-introduce at a lower rate. If vasopressor effects are inadequate, try

　　2. **Norepinephrine 0.1 – 0.5 μg/kg/min** (*see Norepinephrine Infusion Chart p. 253*) **OR**

　　3. **Dobutamine 5 – 10 μg/kg/min** (dog), **2 μg/kg/min** (cats) (*see Dobutamine Infusion Chart p. 231*), if an inotropic effect is warranted.

　　4. If only **epinephrine** is available and pressor support is necessary, try **0.05 – 0.3 μg/kg/min** starting with the low dose and increasing every 1 – 2 min to effect or to the highest dose (*see Epinephrine Infusion Chart p. 235*).

　　5. **Should norepinephrine fail, methylprednisolone at 1.0 mg/kg** loading dose, continued at 0.25 mg/kg q12h, may improve the patient's response to catecholamines with subsequent increase in blood pressure (*see E below*). Only continue if the patient is responsive.

　　6. **Phenylephrine 0.01 mg/kg IV** ~ every 15 min (or as needed) has been suggested if all else fails, although the author has no experience with this.

　　7. Gradually reduce pressor support over several hours, or more rapidly if tachycardia or hypertension develops.

E. If **non-responsive** to adequate fluid and vasopressor therapy, consider the possibility of **adrenal crisis *p. 274***. Where a patient is non-responsive to all of the above resuscitative efforts, low-dose **methylprednisolone or prednisolone sodium succinate 1 mg/kg IV** may be indicated. **Dexamethasone 0.1 mg/kg** is recommended if ACTH stimulation is considered. **Corticosteroids are NOT** recommended for routine use in any shock state other than adrenal crisis. Refer to Hypoadrenocorticism for further guidelines.

F. **PCV and TS** must be monitored q15min with high volume, high rate crystalloids and synthetic colloid administration. If TS <50 g/L prior to fluid resuscitation, **or <35 g/L** at any time, a plasma transfusion is recommended. If **PCV <25% (dog), <20% (cat)** transfusion of packed red blood cells OR whole blood is recommended. If **PCV<25% and TS <40 g/L,** whole blood transfusion is recommended (*see Hemorrhage p. 619, Transfusion Therapy p. 667*). Seek source of hemorrhage.

G. **Antibiotic therapy** is directed towards potential pathogens associated with the underlying problem (*see Septic Shock p. 588*). In shock where inadequate splanchnic perfusion is suspected, this author administers **cefoxitin 30 mg/kg IV** assuming bacterial translocation may have occurred. Otherwise, routine administration of antibiotics is not recommended.

H. **Optimal arterial pressures** are MAP 100 mmHg and systolic of 120 mmHg to optimize oxygen delivery to the tissues. Occasionally, adequate arterial pressures, MAP 60 – 65 mmHg, systolic blood pressure 90 – 100 mmHg is acceptable (*see Fluid Therapy p. 347, Hemorrhage p. 619*). Once reached, maintain fluids according to the patient's needs (*see Fluid Therapy p. 356*). Central venous pressure is a useful measurement to assist with rate and volume of fluid administration especially in geriatric patients and those with cardiac insufficiency (*see technique and interpretation in Fluid Therapy p. 371*).

I. **Acidosis** usually resolves after fluid resuscitation therefore, sodium bicarbonate should not be administered. Rarely, sodium bicarbonate may be considered if the venous pH remains <7.1 and base excess is <-12 or bicarbonate or total CO_2 is <12. (Note: Total CO_2 levels may be low if tubes are transported to an external laboratory, or allowed to sit open prior to testing. (*See Acid-Base Assessment p. 406*). This author does not administer $NaHCO_3$ in shock; however, general published guidelines are: **Dose HCO_3^-** (mEq/L) = BWkg x (12 – patient HCO_3^-) x 0.3. Give over 2 hours. An empirical dose is HCO_3^- 0.5 – 1.0 mEq/kg. Give over 2 hours. If **lactate levels** can be measured, this may better assess whether tissue perfusion is adequate. A lactate concentration >2.5 mEq/L (dogs) >1.5 mEq/L (cats) indicates abnormal lactate accumulation/generation, anemia, hypoxemia or increased muscle activity (*see Lactate p. 400*).

J. Urine output should be measured to assess adequate renal (splanchnic) perfusion. The goal is 1 – 2 mL/kg/h and no less than 0.5 mL/kg/h. Failure to achieve this indicates further fluid is required or possible renal injury has occurred (*see Acute Renal Failure p. 709*).

K. Serum electrolytes should be monitored q2 – 4h initially as alterations in acid-base status with fluid resuscitation may significantly alter the serum potassium levels. (*see Hyper/Hypokalemia p. 394*). Magnesium levels should be measured and supplemented if levels are <0.7 mmol/L (or empirically if levels not available) (*p. 403*). Serum potassium should be monitored with magnesium administration as magnesium reduces potassium loss. A reduced dose of magnesium is required in renal failure.

L. **Definitive therapy** is based on the underlying problem which should be sought through physical exam, laboratory and radiographic findings. *See Suggested Reading.*

Monitoring General Shock Patients

F. PCV and TS must be monitored q15min with high volume, high rate crystalloids and synthetic colloid administration

If TS <50 g/L (prior to fluid resuscitation)	If TS <35 g/L (at any time)	If PCV <25%	If PCV <25% and TS <40 g/L
Colloid transfusion	Colloid transfusion	Transfusion of packed RBC's OR whole blood	Whole blood transfusion
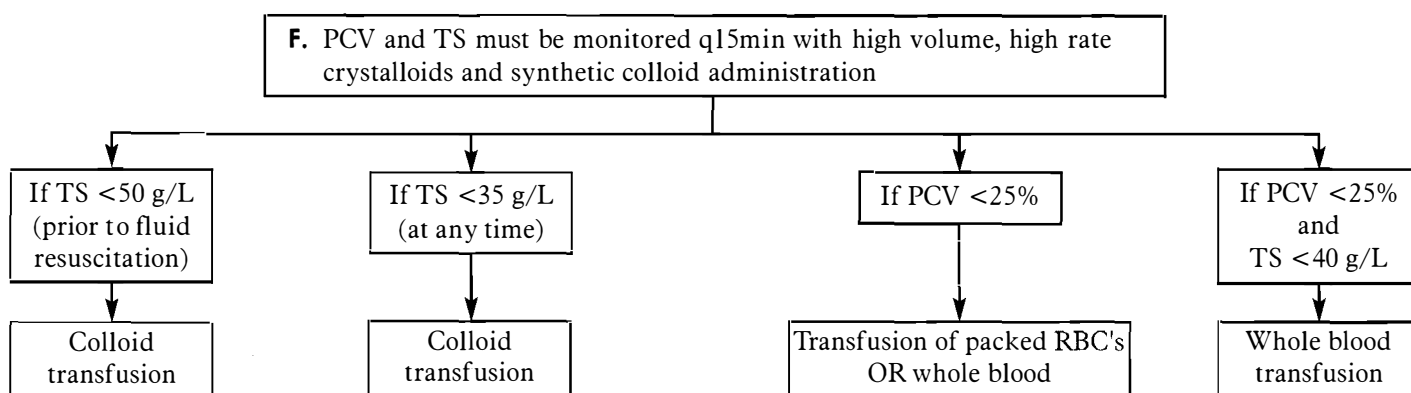
PHARMACOLOGY

1) **Dopamine** is the initial vasopressor of choice in all forms of circulatory shock. It is a central and peripheral nervous system neurotransmitter and the biological precursor of norepinephrine. Dopamine stimulates cardiac beta-1 and vascular alpha receptors.

2) **Dobutamine** has beta, and weak alpha, agonist activity. Dobutamine's inotropic effect is due to a direct action on myocardial contractility and its afterload reducing effect. This in combination with an alpha-mediated venoconstriction in small capacitance vessels, results in augmentation of venous return and cardiac output.

3) **Norepinephrine and epinephrine** exert both inotropic (cardiac alpha and beta-1) effects and peripheral vasoconstriction (alpha effects).

4) **Antibiotics.** *See Septic Shock p. 588.*

SUGGESTED READING

1. Ettinger SJ. Feldman EC. (eds). Textbook of Veterinary Internal Medicine 6th ed. St. Louis, MO. 2005 (see appropriate sections for definitive therapy).
2. Kumar A. Parrillo JE. Shock: Classification, pathophysiology, and approach to management. In: Critical Care Medicine, Principles of Diagnosis and Management. Parrillo JE, Dellinger RP. (eds). Toronto, Mosby; 2001:371-420.
3. Slatter D. (ed). Textbook of Small Animal Surgery, 2nd ed. Philadelphia: Saunders, 2003 (see appropriate sections for definitive therapy).

NOTES

INTRODUCTION

This simple technique "facilitates" the placement of all peripheral and central catheters by cutting the skin over the top of the vessel using the bevel of an 18 g hypodermic needle. This technique allows easier placement of the catheter, especially when teflon catheters are used as these tend to form a 'burr' at the tip, especially in dehydrated patients, and those in shock. As less force is required to pass the catheter through the subcutaneous tissue and into the vein, this also allows the operator to "feel" the insertion and advancement of the catheter into the vessel. This maneuvre is less painful for the patient and therefore, reduces the chance of the patient moving from noxious stimuli at a very critical time in catheter placement. The facilitative maneuver lessens the chance of bacterial contamination of the catheter as the catheter is not passed through the dermis where bacteria may still reside following the surgical preparation.

INDICATIONS

1. When the vessel cannot be seen or palpated (i.e., hypovolemic or hypotensive, edematous or obese patients).
2. Dehydrated or geriatric patients.
3. Optional all vessel catheterizations, peripheral or central.
   (*Editor's note:* tapered catheters constructed of a violon [Becton-Dickinson] are easily placed into a vein)

CONTRAINDICATIONS

Lesions over the venipencture site.
Hematoma at the venipuncture site.

MATERIALS

1. Latex rubber, or other, tubing as a "tourniquet" (optional)
2. Supplies for surgical prep
3. 18 g (20 g preferred by some) hypodermic needle
4. Sterile gauze pad
5. Curved mosquito hemostats
6. IV catheter of choice
7. Tape to secure the catheter in place
8. Bandaging material
9. Antiseptic ointment (*see footnote*)
10. Analgesics
11. T-port extension set
12. Heparin saline flush

TECHNIQUE

- In most cases pain relief with a pure mu agonist (hydromorphone 0.02 – 0.05 mg/kg IM) is recommended for the emergency patient. An alternative selection, especially in frightened or uncontrollable patients sedation with butorphanol 0.1 – 0.2 mg/kg mixed with ketamine 1 – 3 mg/kg and acepromazine 0.01 – 0.03 mg/kg in the same syringe administered into the epaxial muscles, is preferred by the author. The dose selected is dependent on the individual's level of pain and anxiety, but is usually administered to effect. Several minutes are required for full effect to be appreciated. This allows the procedure to be performed without undo stress and heightened pain. If the situation is emergent, the topical application of ethyl chloride or ice, or pinching the skin prior to cutting the skin may also confer pain relief. As these are ill or injured patients, flow-by oxygen is recommended throughout the procedure.
- The hair is clipped with a No. 40 or 50 blade around the entire leg and several cm proximally and distally from the intended placement sight of the catheter.
- A surgical prep is performed. The author recommends a product that is rapidly bacteriocidal, is safe for open wounds without causing discomfort. (TechniCare Topical Antiseptic• - Microbicide Surgical Srub which contains 3% chloroxylenol and 3% cocamidopropyl PG, dimonium chloride phosphate as the active ingredients)[a].
- An 18 g (20 g preferred by some) hypodermic needle is held like a short pencil by the thumb, index and middle finger with the bevel of the needle aligned with the operators line of vision.
- The skin of the vessel is moved slightly to the side of the vessel and held there by an assistant or the opposite hand of the operator (Fig. 1). The author prefers to incise directly over the vein using the presumed anatomical location when not visualized.

- Using the intrinsic muscles of the thumb, index and middle finger the bevel of the needle is drawn over the skin cutting for several millimeters. The cutting is repeated until the dermis is completely divided. Care is taken not to cut the vessel below the dermis, which may occur if the skin in not moved to the side of the vessel before cutting (Fig.2). The skin is allowed to retract back over the top of the vessel if it was pulled to the side initially.
- Further careful dissection of the tissues on top and to each side of the vessel may be required to visualize the vessel. This is recommended in hypovolemic states where the vessel has minimal blood (Fig. 3).
- The catheter is then inserted through the small opening that is centered over the top of the vessel (Fig. 4).
- Should greater visualization be required, the skin incision is extended and a small curved hemostat is used to dissect the vessel further. The tips of the hemostat are inserted lateral and ventral to each side of the vessel separating it from the surrounding tissue (Fig. 5). The tip of a curved mosquito hemostat is then inserted under the vessel where it isolates the vessel. By placing traction on the hemostate, the vessel is 'straightened' and elevated towards the operator (Fig. 6). Traction on the hemostat stablizes the vein preventing 'counter' traction of the vein as the catheter-needle unit penetrates the vessel wall. The catheter is then inserted and advanced into the taught, stable retracted vessel (Fig. 6). This "minicutdown" is very effective and recommended in severely hypovolemic, hypotensive patients. It allows for direct, full visualization of the vessel and the retraction affords a clean entry into the vessel and advancement of the catheter, which would otherwise not be possible, or very difficult, due to lack of vessel filling. Some may prefer to close the incision proximal and distal to the catheter site using staples or sutures.
- The catheter is then secured by rapid taping over sterile gauze covering the incision. The topical antiseptic ointment may be placed onto the incision prior to taping. To help the tape stick to the catheter and skin ando secure it well, the author recommends I.V. Prep (Smith & Nephew, Inc.)[b], or a similar product that provides a sticky base. It is applied topically on the catheter and the intact skin in the area of the exit site.
- A T-port connected to the catheter is recommended to facilitate bolus injections and secure catheter placement.
- The catheter is flushed with heparinized saline and further bandaging is placed from the toes proximally to avoid limb swelling distal to the catheter.

a. TechniCare Microbicide, Care-Tech Laboratories, St. Louis, MO
b. I.V. Prep Antiseptic Wipe, Smith & Nephew, Inc., Largo, FL
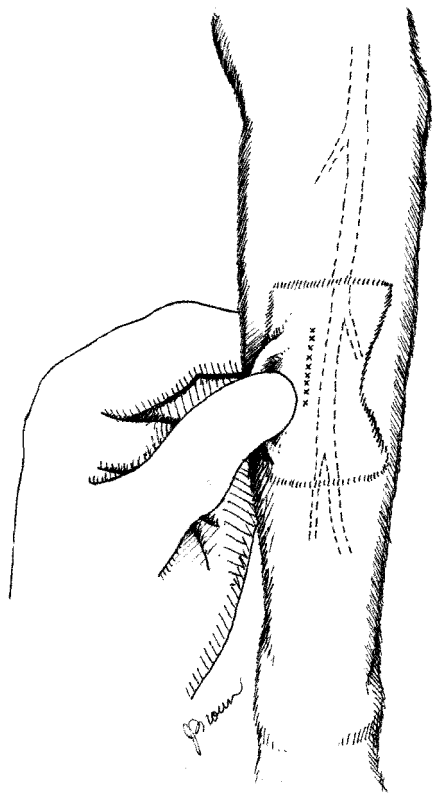
FIGURE 1.
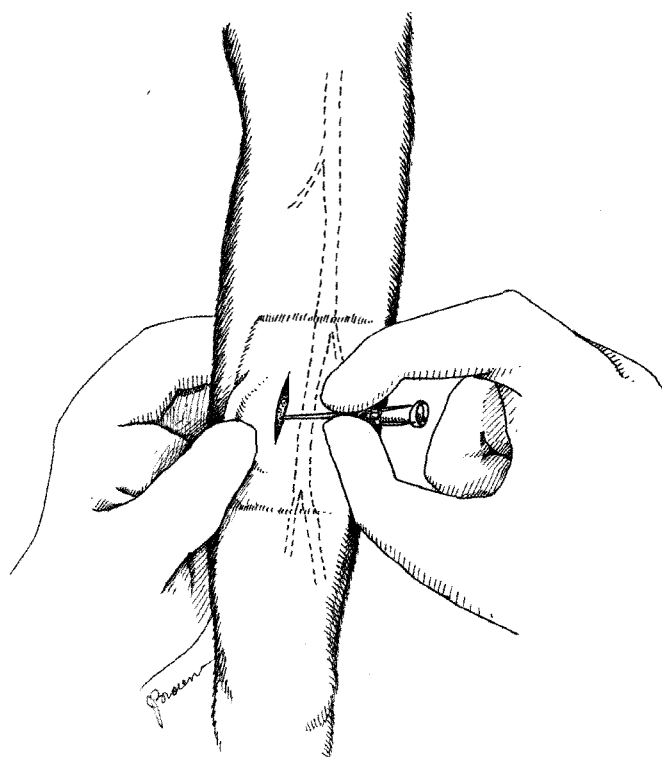
FIGURE 2.
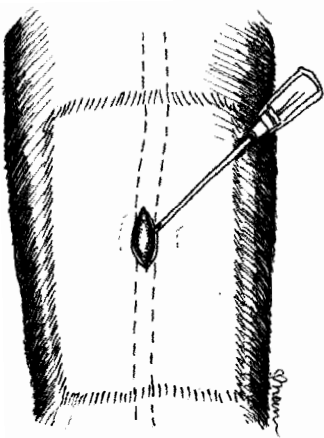
FIGURE 3.
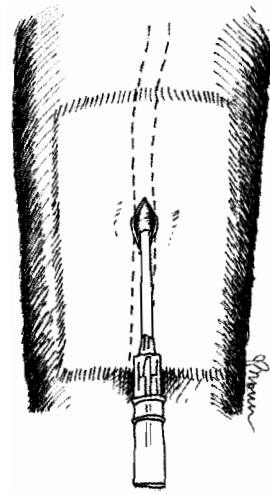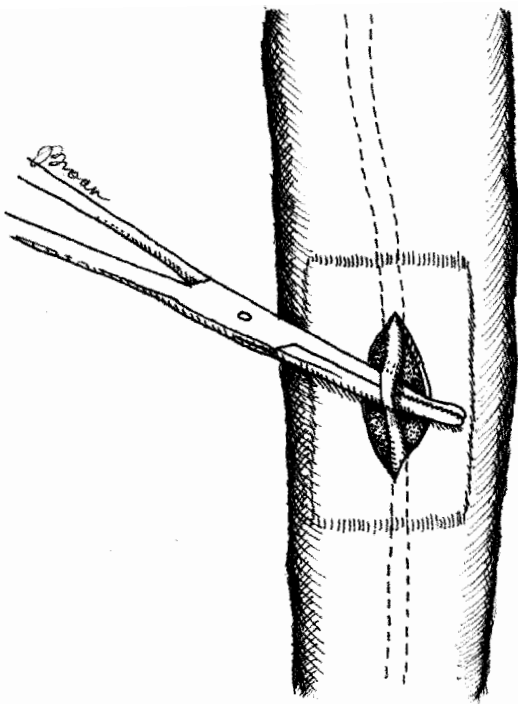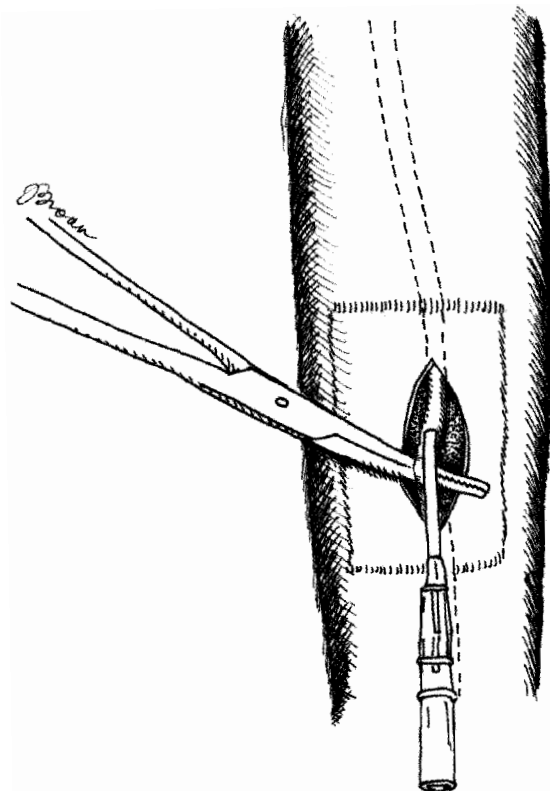
FIGURE 4.

FIGURE 5.

FIGURE 6.

1. A SHORT IV CATHETER USED AS AN INTRODUCER OF A LARGE BORE FEEDING TUBE INTO THE CENTRAL VEIN (DONE PERCUTANEOUSLY OR BY CUTDOWN).

2. PEEL-AWAY TECHNIQUE.

3. A LARGE BORE FEEDING TUBE PLACED DIRECTLY INTO A VEIN THROUGH A VENOTOMY AND ADVANCING THE TUBE INTO THE CENTRAL VEIN.

CENTRAL CATHETERIZATION INDICATIONS

Central vein access is practical and often life-saving as fluids and drugs may be delivered more rapidly than that through a peripheral vein, and blood can be drawn easily for analysis. Central venous pressure (CVP) can also be measured which can guide the delivery of fluids. Central catheters are also economical as they frequently function for the duration of the patient's stay in the hospital where peripheral catheters may have to be replaced. *See Fluid Therapy p. 370* for further indications for central catheter placement. Normal CVP is 2 – 6 cm H_2O. Those that are lower generally indicate hypovolemia, or relative hypovolemia where vasodilation has occurred. Those higher than 10 cm H_2O generally indicate volume over-load, or obstruction in venous return (e.g., pneumothorax, pericardial tamponade, pericardial – diaphragmatic hernia, heart base tumor, positive pressure ventilation).

Central catheters access the thoracic or abdominal vena cava. Access to the vena cava is typically achieved via the external jugular or femoral vein; however, access may also be obtained via the cephalic or saphenous veins.

1. A short intravenous (IV) catheter used as an introducer for a large bore feeding tube into the vena cava.

MATERIALS

1. 20 gauge needle with tip removed. This is then placed into the proximal, cut end of the 3.5 Fr feeding tube where IV fluids can be attached.
2. 3.5 French pediatric feeding tube cut to length based on 3 – 4 cm cranial to skin exit to the 2nd rib (1 – 3 kg patient). Introducer is a 2" 16 gauge over-the-needle catheter.
3. 18 gauge needle with tip removed. This is then placed into the proximal, cut end of the 5 Fr feeding tube where IV fluids can be attached.
4. 5 French feeding tube cut to length based on 3 – 4 cm cranial to skin exit to the 2nd rib. Introducer is a 2" 14 gauge over-the-needle catheter. Pre-flush with sterile saline leaving syringe attached.
5. 3-way stopcock.
6. 50% dextrose or sterile packet variety K-Y jelly (glycerin).
7. Suture material.0
8. #11 scalpel blade.
9. Small curved surgical needle.

TECHNIQUE

The technique described below is for placement of a central catheter via all other access veins (jugular, femoral, lateral saphenous vein in the dog, and the medial saphenous vein in the cat) described in this chapter. The cephalic vein can be accessed but it is often more difficult to insert the catheter centrally, and to prevent occlusion of the catheter when the elbow is flexed. The jugular vein should be avoided in patients with coagulopathies, wounds or skin diseases near the proposed venotomy site and in head injured patients. The medial saphenous vein is recommended for patients with a coagulopathy.

GENERAL APPROACH FOR CATHETER PLACEMENT

Strict aseptic technique is required. The neck or medial side of the thigh is clipped and surgically prepared. Gloves should be worn and the site draped. The animal typically is placed in lateral recumbency for both jugular or saphenous access. The sternal position may be easier in overweight or thick-necked dogs for jugular vein access. An assistant extends the neck and occludes the vein proximally using digital pressure at the thoracic inlet. If the jugular vein does not distend with pressure, the assistant occludes the jugular veins bilaterally. The right jugular vein is easier to catheterize than the left as it takes a straighter course to the heart. If the jugular vein cannot be easily palpated due to obesity or excessive skin folds its location lies along a straight line from the thoracic inlet to the angle of the mandible.

The medial saphenous vein lies on the medial aspect of the thigh. It is often used in cats as less restraint is required when this vein is accessed as compared to the jugular vein. An assitant extends the hind limb with digital occlusion at the femoral canal region. If the patient is cold a mildly warm compress applied to the skin for a few minutes often distends the vessel sufficiently to be visualized.

If the access vessel cannot be readily visualized, perform a mini-cutdown as described for the facilitative maneuvre. This often is needed in volume contracted states.

When placing the catheter via the jugular vein, pre-measure it to the level of the fifth intercostal space, which will ensure placement of the catheter at the junction of the jugular vein and the right atrium. A suture tied around the central catheter at the desired level is a means of keeping track of where the predetermined point is. This avoids placing the tip of the catheter in the heart, which can be irritating and may lead to arrhythmias. Ensuring placement within the thoracic cavity is also preferrable for accurate central venous pressure measuring.

If the saphenous vein is used the tip of the catheter is measured caudal to the heart (where it will then lie in the caudal thoracic vena cava).

A rapid acting surgical bacteriocidal prep solution Techi-Care (Care-Tech Laboratories, St. Louis) is recommended. The active ingredient is 3% chloroxylenol. It does not cause skin, open wound, or eye irritation.

Prior to accessing the vein a small facilitative maneuver is performed (*see Intravenous Facilitative Maneuvre p. 609*). This allows the vein to be entered more easily with the "access" catheter to be used to advance either a feeding tube, wire or central catheter itself into the vein. Because the jugular vein is fairly mobile and often "rolls" away from the needle as the needle is inserted through the skin this facilitative maneuver also provides better and more accurate penetration of the catheter into it without it slipping off and coursing along side the vein. It also helps avoid creating a hematoma.

FEEDING TUBE – PERIPHERAL CATHETER INTRODUCER TECHNIQUE

Feeding tubes used as the central vein catheter can consist of various types materials. Silicone, polyurethane, red rubber, and polyvinyl chloride are materials commonly used in the manufacture of sterile feeding tubes. Feeding tubes are more flexible than the typical polyethylene intravenous catheter manufactured for central line placement in veterinary medicine. Costs vary from a few dollars to over ten, generally in reverse order than listed. Silicone has the advantage of being the least reactive and the most antithrombogenic. It has the disadvantage of requiring a woven wire or nylon stylet placed within its lumen to provide the stiffness needed to pass the tip of the catheter to its desired locations without kinking or twisting back on itself. The most common feeding tubes used are the polyvinyl chloride nasogastric feeding tubes used for infants and children. A 3.5 French feeding tube can be passed through most 16 gauge over-the-needle catheters. A 5 French feeding tube can be placed through most 14 gauge over-the-needle catheters. The feeding tubes should be passed through the 16 or 14 gauge short peripheral intravenous catheters prior to placement in the patient to make sure the feeding tube passes through the peripheral venous catheter selected.

A 3-way stopcock is attached to the distal end of the feeding tube and the feeding tube is filled with saline. The feeding tube is premeasured to the desired level. The 2-inch catheter is placed into either the jugular or saphenous vein percutaneously through the opening in the skin made by the facilitative maneuver. The exterior of the feeding tube is lubricated with sterile 50% dextrose or sterile packet variety K-Y jelly (glycerin) and inserted through the catheter to the desired location. The percutaneous catheter is removed from the vein and slid as far proximally along the length of the feeding tube as possible. It is not necessary to remove the peripheral catheter from the feeding tube. Pulling it out of the vein and leaving only the feeding tube in place will cause some additional hemorrhage at the vein puncture site but this is easily controlled with digital pressure.

The feeding tube with the short peripheral catheter at its neck is secured in place using tape taps and anchored to the skin with suture or staples A sterile dressing is placed.

These 'tubes' have been left in place over two weeks without any adverse complications. Studies looking at the reaction caused by the use of these feeding tubes in patients central veins have revealed less reaction that that occurring with the plastic polyethylene venous catheters.

If anchored to the periosteium of the wing of the Atlas the central venous catheter will not move. The immobilized catheter reduces intraluminal movement of the catheter reducing inflammation, infection and thrombus formation.

PEEL-AWAY TECHNIQUE

This technique is useful when the access vessel is large enough to accommodate an introducer catheter that is "over" the outside of the central catheter. Various companies such as Cook Veterinary Products and Luther Medical supply kits that provide the peel-away introducer catheter and the central catheter. The peel-away catheter is inserted into the vein; when the 'flash back' is observed, the catheter is advanced slightly and the needle ('stylet') is removed. Immediate digital coverage of the catheter is required to prevent air from entering the vein. A large breath, generating negative intrathoracic pressure, may lead to aspiration of air into the vein and a subsequent airlock within the heart. Death may occur following the airlock. This is a rare occurrence. The central catheter is then passed down through the peel-away catheter into the vein and advanced to the predetermined location indicated on the catheter.

Following placement of the central catheter the peel-away outer catheter is pulled apart and removed. Skin and fascia fixation of the catheter and dressing is the same as for the other catheters.

VENOUS CUTDOWN (OPEN VENOTOMY) AND INSERTION AND ADVANCEMENT OF A FEEDING TUBE OR CATHETER INTO THE CENTRAL CIRCULATION

This technique is particularly effective in the severely hypovolemic patient and larger patients, when the jugular vein is flat and can not be visualized from the skin's surface. With this technique an incision is made over the anatomic area of the jugular vein. A curved hemostat is pushed into the soft tissues in the area of the jugular vein, and the tips spread. This is repeated until the vein is visualized. The hemostat is then inserted into the tissues immediately adjacent to the vein and the tips spread. The procedure is repeated on both sides of the vein. The tip of hemostat is advanced from one side of the vessel to the other until the vein is held over the top of the hemostat's handles.

Two suture loops are passed under and around the vein proximally and distally. With traction the vein is slightly stretched while a number 11 scalpel blade is used to penetrate the middle of the vein. The blade is then turned 90 degrees (at a right angle to the length of the vein) and brought outward making a controlled venotomy involving approximately 50% of the diameter of the vein. A commercially available venous introducer or a blunt end of a small curved surgical needle is then inserted into the vein opening, lifting it in such a way as to act as a "shoehorn" to keep the venotomy open and visible. The feeding tube is then inserted into the vein and advanced toward the heart. The needle is then removed and the two vascular loops are tied around the vessel and catheter to prevent bleeding, and to secure the catheter in place.

The wound is closed by use of skin staples or sutures and the catheter anchored to the skin and superficial fascia. A sterile dressing is then placed as for other central catheters. In this technique it is mandatory that the catheter NOT be removed if there is a coagulopathy unless an approach is made to the vein and the vessel ligated as the catheter is removed.

SELDINGER TECHNIQUE

The Seldinger technique employs a guidewire to help with placement of the central catheter and is described in *Fluid Therapy p. 370.*

FOR ALL CATHETERS DESCRIBED HERE

Once the catheter is placed and secured by sutures, a layer of triple antibiotic ointment is placed over the venotomy site followed by sterile gauze. A light padded bandage is placed over the top of the catheter. The outer layer should be water repellant and secured such that the venotomy site is never exposed. The bandage should be checked on a frequent basis as neck movement can cause the bandage to constrict leading to airway and circulatory compromise. The bandage should be changed daily and the site monitored for infection. When walking dogs with jugular catheters the leash should be placed around the head and under a forelimb (not around the neck) to prevent strain on the bandage and catheter. When the catheter is removed direct pressure should be applied to the venotomy site for 5 minutes. A sterile dressing should be placed for a further 24 hours. The tip of the catheter always should be cultured if infection is suspected.

RADIOGRAPHIC VERIFICATION OF CATHETER LOCATION

A lateral chest radiograph is taken after catheter placement to verify that it is in the proper location (cranial thoracic vena cava for jugular or cephalic access sites and the caudal intrathoracic vena cava for the saphenous access sites). If a radiograph cannot be taken an alternative approach is to measure CVP and note a 'pulling' of the water column when the patient begins a normal breath (inspiration). The catheter when properly positioned should also allow the sampling of venous blood very easily by simply aspirating with a syringe

INTRODUCTION

The classic anaphylactic reaction represents a type I immune response and is also referred to as an immediate hypersensitivity reagin-dependent, or cytotropic response. A series of interactions involving an antigen (allergen), and immunoglobulin of the IgE class (reagin) and specific effector cells (mast cells and basophils) are implicated in mediator synthesis and release. Anaphylactoid reactions are clinically identical to classic anaphylactic reactions but there is no evidence of participation by IgE. An anaphylactoid reaction may follow exposure to agents such as radiocontrast dyes, opiates etc. This type of reaction usually occurs in individuals with multiple allergies. Idiopathic anaphylactoid reaction in an allergic individual is the apparently spontaneous development of symptoms resembling anaphylaxis. This is very rare in animals.

A variety of antigens are known to cause anaphylactic/anaphylactoid reactions. These include: penicillins and cephalosporins, tetracyclines, chloramphenicol, erythromycin, vancomycin, foreign proteins (antitoxins etc.), exogenous ACTH, TSH, insulin and oxytocin, vaccines, penicillinase, procaine, benzocaine, tetracaine, lidocaine, salicylates, antihistamines, tranquilizers, iodinated contrast media, vitamins, heparin, stinging insects, snake venoms, food and allergens (hypersensitization and skin testing), blood and blood product transfusions, and some chemotherapeutic agents such as asparaginase.

DIAGNOSIS

History/Signalment

> While treating the patient, obtain a history with regard to exposure to any of the above or other potential allergens (i.e., any drug therapy).

Clinical Signs/Physical Examination

- The most common signs are restlessness, urticaria, diarrhea, vomiting, circulatory collapse, epileptiform seizures, coma and death. These signs usually occur within minutes of exposure to the antigen.
- Circulatory collapse, due to pooling of blood in the splanchnic circulation, is associated with hypotension, tachycardia, weak to absent peripheral pulses and pale mucous membranes.
- Temperature should be obtained.
- Rapid assessment of respiratory pattern and rate should be made.
- A similar episode may occur approximately 6 – 12 hours after successful treatment of the initial reaction (late phase reaction); therefore, careful monitoring is required.

Laboratory Evaluation/Diagnostic Imaging

Stat

When time permits before or after stabilization, obtain:

- **PCV,** which may be increased due to loss of plasma volume from increased vascular permeability resulting in hemoconcentration.
- **TS** may be lower than normal due to loss of plasma volume.
- **Stick BUN** to identify potential pre-renal azotemia.
- **Blood glucose** levels may reflect stress hyperglycemia
- **Blood pressure** is essential to identify severity of hypotension and monitor response to therapy.
- **ECG** monitoring may reveal associated arrhythmias; *see Ventricular Arrhythmias p. 179, Supraventricular Arrhythmias p. 170, Bradycardia p. 164* for management of those identified.

Extended Laboratory Data Base

Further laboratory investigation will depend on the history and physical findings.

Stop all potential inciting causes (ie any of the above, other medications).

A. Maintain a patent airway, intubate and administer oxygen if necessary.

B. Obtain IV access

1. **IF PERACUTE** reaction, administer **epinephrine 0.01 mg/kg (0.1 mL/kg of 1:10,000) IV** [prepare by taking **1.0 mL epinephrine 1:1,000 (1.0 mg/mL)** and diluting in 9 mL saline]. Volume in milliliters to be given equals body weight in kilograms divided by 10.

2. **If unable to obtain IV access** and patient is unconscious or intubated, administer
   a. into the tongue vein or parenchyma,
   b. via a urinary catheter into an endotracheal tube to the level of the carina, OR
   c. transcutaneously into the trachea (may need to double dose if no response).

3. **IF SEVERE** reaction, administer **0.1 mL/kg of 1:100,000 IV, IM** [prepare by taking **0.1 mL epinephrine 1:1,000 (1 mg/mL)** and dilute in 9 mL saline]. Volume to be given in milliliters equals body weight in kilograms divided by 10 as a bolus and titrate more to effect.

4. If indicated, **repeat in 20 – 30 minutes,** or earlier if necessary.

5. **IF MILD to MODERATE** reaction and normotensive go to (E) and (F) below.

C. **Fluid therapy** at 1.5 – 5mL/kg/min (90 mL/kg/h dog), (50 mL/kg/h cat), or to effect.

D. If **hypotension unresponsive** to above volume, add a colloid. Pentastarch or hetastarch in 5mL/kg (dog), 2.5mL/kg (cats) bolus to 20 mL/kg (dog), 10 mL/kg (cat) over 15 mins. Monitor blood pressure, and physical response (i.e., improved mentation, pulses), to guide further therapy.

E. Antihistamine –

1. **Diphenhydramine 0.5 – 2.0 mg/kg** (max total dose 50 mg) IM q8h (never give IV due to hypotension and vomiting) or

2. **Tripelennamine HCl, 1 mg/kg IV** or IM q12h.

F. Rapid-acting corticosteroid should be administered IV once at least half of the above fluid has been administered,

1. **Prednisolone sodium succinate or methylprednisolone sodium succinate at 2.0 mg/kg IV over 15 – 20 minutes (OR IM).** No faster as this may cause vasodilation and worsen the shock state. OR

2. **Dexamethasone sodium phosphate** 0.25 – 0.5 mg/kg IV slowly, IM, SC.

   Corticosteroids may be helpful in controlling ongoing anaphylaxis if there is persistent mediator release. However, their benefit in reversing the life-threatening situation is questionable, and therefore should not be used until most of the IV volume is re-established as corticosteroids may cause hypotension. Higher dosages are not indicated.

G. If **hypotension persists** after all above, try:

1. **Epinephrine 1 mL/kg/h CRI** by adding 4.0 mg epinephrine to 1 litre of saline (preferred to dopamine, *see Pharmacology p. 618*). Titrate to effect. Or calculate at **1 – 10 μg/kg/min** (*see Epinephrine Infusion Chart p. 235*), OR

2. **Dopamine 2 – 10 μg/kg/min CRI** (*see Dopamine Infusion Chart p. 233*); start at low end.

3. Titrate to effect by monitoring blood pressure and heart rate. Effect is rapid, therefore if no response after 15 seconds, increase rate. Once blood pressure increases and heart rate decreases, slow down the infusion. If heart rate increases immediately after transfusion is begun slow down infusion. Once the patient is stabilized gradually decrease the infusion while maintaining patient stability. Do not terminate the infusion abruptly, unless necessary due to overdose, to avoid acute hypotension.

H. **PCV and TS** should be monitored after fluid or colloid administration, to assess effect on hemodilution.

I. If necessary, due to **respiratory distress** (ascertain), administer

1. If **due to bronchconstriction** administer **salbutamol IV.** Monitor heart rate and pulse pressure. Stop if pulse pressure drops and/or heart rate increases.

2. If due to **pulmonary edema** administer **furosemide 0.5 mg/kg IV.**

J. **Famotidine 0.5 mg/kg q12h** if gastric ulceration suspected after resuscitation.

A. Maintain a patent airway, intubate and administer oxygen if necessary.

B.1 Peracute
Epinephrine **0.01 mg/kg IV, IM**

B.2 Severe Reaction
Epinephrine **0.001 mg/kg**

B.5 Mild to Moderate Reaction

0.1 mL/kg of **1:10,000** IV epinephrine – [1 mL of 1 mg/mL + 9 mL saline]

0.1 mL/kg of 1:100,000 epinephrine
[0.1 mL of **1:10,000** + 9 mL saline]

E. antihistamine e.g., Diphenhydramine
0.5 – 2.0 mg/kg IM
Max total 50 mg

C. Establish IV access.
Isotonic fluids –
Dogs: 90 mL/kg/h
Cats: 50 mL/kg/h (cat)
Give to effect.

D. If hypotension persists titrate synthetic colloid.
Dog: 5 mL/kg (max 20 mL/kg)
Cat: 2.5 mL/kg (max 10 mL/kg)

F. Prednisolone Sodium Succinate Or methylprednisolone 2 mg/kg over 10 min OR Dexamethasone S-P 0.5 mg/kg IV.

G. If hypotension persists titrate to effect.
Epinephrine CRI starting at 1 mL/kg/h (add 4.0 mg epinephrine/L saline).

H. Respiratory distress due to bronchoconstriction – salbutanol 4.µg/kg IV or terbutaline 0.01 mg/kg SC. If due to pulmonary edema – furosemide 0.5 mg/kg.

Monitor heart rate, blood pressure and respiratory effort.

PHARMACOLOGY

1) **Epinephrine,** in this instance, causes a decrease in intracellular synthesis, and release, of mediators via an increase in intracellular cAMP. In addition, due to epinephrine's alpha effects, peripheral vasoconstriction occurs with increased systemic vascular resistance and increased arterial blood pressure. The beta effect relieves bronchospasm and may increase cardiac output through a positive inotropic and chronotropic action.

2) **Aminophylline** also causes a decrease in intracellular synthesis and release of mediators. It also causes relaxation of bronchial smooth muscle.

3) **Famotidine** is an H2 blocker. See Gastrointestinal Hemorrhage

4) **Diphenhydramine (Benadryl®)** is an anti-histamine and anti-emetic, has atropine-like action and is contraindicated in bronchial asthma.

5) **Tripelennamine HCl (Vetastim®).** Similar to diphenhydramine. Available in the USA.

6) **Dopamine.** See Pharmacology of CPR.

SUGGESTED READING

1. Cohen RD. Systemic anaphylaxis. In: Bonagura (ed) Kirk's Current Veterinary Therapy XII Small Animal Practice, Toronto: Saunders; 1995:150–152.

NOTES

INTRODUCTION

Common causes of hemorrhage in veterinary patients are listed in Table 1.

TABLE 1. Common Causes of Hemorrhage

Trauma
Coagulopathy
    rodenticide toxicity
    thrombocytopenia
    hepatic failure
    specific factor deficiences
Diseases of the gastrointestinal tract
    ulceration due to
        non-steroidal anti-inflammatory analgesic ingestion
        neoplasia
        stress ulceration
    Addisonian crisis
    Uremia
Surgical procedures
Rupture of tumour or abscess
Leptospirosis
Vitamin K deficiency (non-rodenticide)

When presented with any patient with paler than normal mucous membranes, always assume the animal is bleeding from somewhere. Physical examination, history and laboratory tests will confirm if anemia is present. If anemia is present, determine if this is due to **whole blood loss** or limited to **red cell loss** (*see Immune-mediated Hemolytic Anemia p. 411*). If an area of hemorrhage is suspected but cannot be readily identified (*non-compressible hemorrhage*) assume pleural space, mediastinum, trachea, lungs, abdomen and retroperitoneal space, pelvis, fracture site or cranium as potential sites for ongoing hemorrhage that may be identified in time. Hemorrhage due to a **coagulopathy** of any etiology can occur **anywhere.** Determine if hemorrhage is present and to what degree based on clinical signs, physical examination and continual trending with respect to further ongoing blood loss. Resuscitation will depend on the severity of injury and blood loss.

The goal of therapy is to ensure oxygen delivery to the tissues by attaining/maintaining adequate perfusion pressure without predisposing the patient to worsening of the hemorrhage. **Potential deleterious effects of aggressive fluid therapy** used to treat patients with *non-compressible hemorrhage,* before full assessment, can increase morbidity and mortality. Crystalloids, synthetic colloids, hemoglobin-based oxygen carrying solutions (HBOCS), or blood products should be administered, at calculated rates, based on clinical signs, physical examination findings and laboratory data. A careful and skilled approach to volume resuscitation must be conducted in these patients, while maintaining adequate perfusion pressure to avoid an elevation in blood pressure that will displace a delicate clot formed over an area of hemorrhage (i.e., fractured liver or spleen, intercostal vessel), or increase hemorrhage due to other causes (e.g., rodenticide toxicity). Twenty to 30 minutes is required for a fibrinous clot to form over a laceration. Unnecessary aggressive fluid therapy prior to this time can prevent clot formation, and beyond this point could raise blood pressure and disrupt the clot. Crystalloids and synthetic colloids can contribute to a coagulopathy. Where external hemorrhage is identified (*compressible hemorrhage*), immediate compression should be performed. These patients can then be resuscitated to optimum as hemorrhage is controlled. However, trauma patients may also have **pulmonary contusions.** Aggressive fluid therapy in these patients may cause pulmonary edema, therefore, pulmonary status must be evaluated and monitored. If **pulmonary contusions are noted, judicious fluid administration** to adequate end points should be carried out. It should not be assumed that patients with pulmonary contusions are hypovolemic. On many occasions, IV fluid therapy is not required, therefore, the need for fluid therapy must be assessed on an individual basis.

The fluid volumes suggested in this protocol to facilitate resuscitation, are merely a guide; more or less may be required. As a reminder, fluid requirements for cats are less than dogs. Continual examination as outlined is required to meet appropriate requirements.

Urine output may be used as a guide of splanchnic perfusion. If renal blood flow is adequate assume so is cardiac output in these patients. Similarly, mental status is a good indicator of cerebral perfusion. A change in mentation can indicate a change in cardiac output. Note, *gloves should be worn initially when attending to animals where visible blood is present, as this may be blood of a caregiver bitten while assisting the dog or cat. This is a caution against human to human blood borne diseases.*

DIAGNOSIS

History/Signalment

- While examining the trauma patient obtain a history with regard to the immediate period post-trauma (i.e., was the patient ambulatory, has there been a deterioration).
- Always enquire about the previous medical history (cardiac problems, epilepsy, diabetes, etc.).
- Medications administered (e.g., non-steroidal-anti-inflammatory analgesics, chemotherapy [*see Oncological Emergencies p. 443*], methimazole rarely induces a PIVKA (protein induced Vitamin K antagonism) resulting in hemorrhage.
- Previous episodes of hemorrhage (i.e., following neuter, minor traumatic incidents, eruption of teeth). Breeds predisposed to platelet function deficiencies are Doberman Pinschers, Shetland sheepdogs, Old English sheepdogs, Golden Retrievers. German Shepard dogs and Golden Retrievers are highly represented in factor VIII deficiency.
- Free-roaming with potential exposure to toxins, or toxins (rodenticides *p. 650*) in the home environment. Ask owner for the container as duration of therapy depends on toxin ingested.
- Travel history.
- Specific geographical areas associated with disease predisposing to hemorrhage.
- History of chronic diarrhea may be related to malabsorption and associated Vit. K loss. History of hematochezia due to neoplasia or trauma, or melena which may be nasal or gastric in origin.
- Vomiting may be due to biliary tract disease/obstruction and subsequent Vit K deficiency. Hematemesis may be associated with gastric ulceration or coagulopathies.
- History of illness pre-disposing to DIC.
- Puppy and kitten anemias are discussed in *Fading Puppy and Kitten p. 540*.
- Ill animals may also be infested with fleas and become extremely anemic.
- Direct further questions to the potential causes listed in Table 1.

Clinical Signs/Physical Examination

While performing a physical examination the degree of blood loss must be assessed. Of importance is to note whether the patient is in shock. If a coagulopathy is suspected, gentle handling of the animal is imperative to avoid further injury and hemorrhage. See Table 2 below (*p. 623*) for assessment of blood loss.

- **Shock** is generally defined as a mean arterial pressure (MAP) less than 60 mmHg or systolic pressure less than 90mmHg with accompanied tachypnea, tachycardia, or bradycardia (end-stage shock or in cold patients).
- **Compensated shock** (hypovolemia) can be accompanied by near-normal, normal or increased blood pressures; **in this instance tachycardia and tachypnea remain even after analgesics are administered** and the patient appears comfortable; an additional benefit of administering analgesics allowing the clinician to rule out pain as the cause for tachycardia, tachypnea.
- **Sympathetic (catecholamine) response** to a traumatic incident results in tachycardia, tachypnea, weaker than normal pulses (vasoconstriction), paler than normal mucous membranes (vasoconstriction), and capillary refill time ≥ 2 seconds (vasoconstriction), even without blood loss or very little blood loss. The term 'shock' is frequently used to describe such a patient and a reflex response is to administer aggressive fluid therapy. This in turn enhances hemorrhage. However, patient may be in compensated shock (*see above*).
- **Mentation** is an important part of the assessment, in fact it is the key to assessing degree of blood loss. If the patient has depressed mentation of varying degree but without known brain injury, and associated with physical findings also associated with blood loss, this suggests clinically important blood loss and shock. If however, the patient still is alert, the physical findings may be the result of a sympathetic response due to pain and fright, and not necessarily associated with blood loss.
- **Pain** results in tachycardia and tachypnea which masks these clinical signs as a potential reponse to hypovolemia; analgesic administration does not worsen the situation but unmasks the volume status of the patient. Tachycardia and tachypnea will still be present if hypovolemia is present. Hydromorphone, oxymorphone or fentanyl, titrated to effect will not compromise the cardiovascular response to hypovolemia. One must consider the potential role of the neuroendocrine response in producing these clinical signs with or without blood loss. As an example of relating blood loss to clinical signs, a 30 kg blood donor normally donates 450 mL blood (i.e., 20% of blood volume) without obvious clinical signs.

Upon presentation, establish the following:

- **Mental status** (i.e., bright, alert and responsive, depressed, stuporous, comatose). With depression or stupor and coma, head injury must also be suspected, however in this case the blood pressure may be normal or high (*see Head Trauma p. 691*). Without head injury, the mentation is important in determining the degree of blood loss (*see MANAGEMENT D 1 below p. 624*).
- **Heart rate,** which is most commonly increased either due to blood loss alone, or in combination with pain and anxiety, or respiratory compromise.
- **Pulse rate** simultaneously with heart rate to assess if pulse deficits are present. Pulse pressure should be assessed for strength. Absent to weak peripheral pulses are frequently observed with moderate to severe blood loss, and when associated with femoral pulses, indicates severe to massive blood loss. Normal to increased 'strength' may indicate no blood loss, or compensatory response. Assessment of pulse pressure must be made in conjunction with other vital signs and mentation.
- **Capillary refill time** is >2 seconds with significant blood loss and/or moderate to severe pain (Table 2).
- **Mucous membrane** colour may be white, to pink (Table 2). Petechiae or ecchymoses are usually present in thrombocytopenia/pathia, leptospirosis. Icterus signals liver disease *p. 70*; or IMHA *p. 411*, this may be pale yellow, with significant blood or red cell loss; or biliary tract obstruction.
- **Temperature** is important to obtain as hypothermia will result in a low systemic blood pressure (SBP).
- **Systemic blood pressure** should always be measured. SBP <90 mmHg and mean artrial pressure (MAP) <60 mmHg requires immediate fluid therapy (*see Management below p. 623*), especially if associated with depressed mentation. SBP ≥90 mmhg, MAP ≥60 mmHg requires cautious fluid administration until location of hemorrhage and pulmonary status is assessed. Normal and high SBP does NOT rule out significant blood loss.
- **Respiratory rate and pattern** to identify pulmonary problems. Tachypnea may also be present in low volume states. If severely dyspneic, auscultate the chest and determine if pneumothorax, pulmonary contusions or pleural effusion is present. Assess coagulation prior to performing thoracocentesis (*p. 574*). Mediastinal hemorrhage may be difficult to identify, assess jugular venous distension. Increased breath sounds and crackles are associated with pulmonary contusions or hemorrhage. Total absence of lung sounds to an isolated area may indicate hemorrhage with total consolidation of a lung lobe(s).
- **Upper airway** obstruction (*p. 565*), with stridorous breathing, occurs with pharyngeal, laryngeal hemorrhage. This may progress to marked dyspnea, as can tracheal hemorrhage. This may be a presenting sign of rodenticide toxicity.
- If **heart sounds are reduced or absent** but lung sounds are audible, cardiac tamponade may be present and pericardiocentesis (*p. 147*) is warranted. This is confirmed if pulsus paradoxus is present.
- **Jugular distension** may indicate cardiac tamponade (*pericardial effusion p. 145*), hemothorax or pneumothorax.
- Cover all open wounds with a sterile (or clean) towel.
- **Palpate limbs** for fractures and monitor for expanding hematomas at the fracture site. If the femur is fractured, place the fractured side down if possible to aid in tamponade. Palpate joints for hematomas if coagulation factor deficiency suspected.
- **Assess the abdomen** for size and tenderness. It takes 40 mL/kg of fluid or blood to noticeably distend an abdomen, so don't wait until you see this to confirm your suspicions before treating! Bruising around the umbilicus has been reported to indicate abdominal hemorrhage but this is not consistently present. Ventral abdomen and inguinal areas may have petechial hemorrhages if thrombocytopenia present.
- Examine **prepuce or vulva** for hemorrhage. Consider all causes for this secondary to trauma or other primary problems (*see Male Urogenital Emergencies p. 736, Vaginal Emergencies p. 759, Pyometra p. 756, Dystocia p. 751*), or coagulopathies and oncological *p. 443* or urologic *p. 731* hemorrhagic cystitis.
- **Rectal examination** should be performed to identify rectal hemorrhage following all traumatic incidents or where a history of hematochezia is reported.

Laboratory Evaluation/Diagnostic Imaging

Stat

Avoid using the jugular vein for obtaining blood where a coagulopathy or thrombocytopenia is present, due to difficulty with adequate compression at this site.

- **PCV and TS.** Initially to assess baseline values and severity of red cell loss. The PCV may be artificially elevated relative to total solids (protein) due to splenic contraction in hemorrhage. TS is normal in immune-mediated anemia due to red cell loss alone. Careful and frequent monitoring of these parameters will assist in diagnosing ongoing hemorrhage, or hemodilution after fluid administration.

- **Agglutination** should be assessed where anemia without blood loss is suspected (*see IMHA p. 411*).
- **Platelet count should** always be performed, but especially if thrombocytopenia (*p. 451*) is suspected. Normal range for dogs is 179 – 483 x 10³/L (10 – 25 on high power field) and cats 201 – 523 x10³/L (15 – 40 on high power field). Always observe feathered edge for platelet clumping prior to diagnosing thrombocytopenia.
- **ACT, PT/PTT** as routine baseline, but especially if coagulopathy suspected based on history and physical findings. Required also for trending purposes. For the ACT test, add 2 mL whole blood immediately to the grey top tube with silica (ACT tube), start timing as the blood enters the tube while gently inverting the tube. Place well into your axilla under the white coat, or into a 37°C heat block for 60 seconds, gently rock and observe for beginning of a clot. Replace and observe q10seconds. The ACT is the moment a clot begins to form 70 – 120 seconds in dogs and 60 – 90 seconds in cats. A platelet count <10,000 may prolong clotting time by 10 seconds. The ACT is prolonged in most coagulopathies involving the intrinsic and common pathways, the extrinsic system may also be involved.
- **PIVKA test** to measure coagulopathy associated with Vitamin K deficiency/loss. Useful for trending Vitamin K therapy. If this test is normal 48 hours after discontinuing Vitamin K therapy, treatment can be permanently discontinued.
- **Venous blood gases or total CO_2,** may reveal a non-respiratory acidosis due to poor perfusion, or hypoxia if pulmonary parenchymal injury or hemorrhage are also present.
- **Arterial blood gases** or oxygen saturation (pulse oximetry) will determine if acid-base abnormalities are due to inadequate oxygenation secondary to respiratory compromise.
- **Lactate** concentrations >2.5 mmol/L in the dog and 1.5 mmol/L in the cat indicates perfusion impairment if the patient was not struggling during collection (*see Lactate p. 400*).
- **Systemic blood pressure** measurement should be performed as a baseline to establish severity of hemorrhage and guide therapy.
- **ECG monitoring** to identify arrhythmias associated with ischemia or trauma (*see Ventricular p. 179 and Supraventricular Arrhythmia p. 170*).
- **Radiographs** of abdomen and chest should be performed to rule out diaphragmatic hernia, hemorrhage into the retroperitoneal space and other potential problems not detected on physical examination, or if the integrity of the pleural space is questionable. Expanding the radiographic field to include the spine, pelvis, femurs, scapulae and distal limbs in smaller patients, is advised to assess the presence of other injuries. The technique used however, should be directed towards optimizing thoracic or abdominal detail. Retroperitoneal hemorrhage is recognized by increased fluid density adjacent to the kidney and following ureters. Hemorrhage may depress the kidney ventrally. Unless there is free peritoneal hemorrhage, the abdomen has a normal detail.
- **Abdominocentesis or thoracocentesis** where indicated. **PCV/TS** on the fluid should be compared to the peripheral blood sample. **Abdominocentesis** can be performed by inserting a 20 or 22 g needle immediately to the right of the umbilicus to confirm if hemorrhage is present and an estimate of loss. If free flowing blood, that does not clot, is obtained, a large volume of blood is present (>5 mL/kg). If the blood clots, inadvertent aspirate from the spleen may have occurred. Suction applied to a syringe may result in a negative centesis due to omental plugging. Remove syringe, twirl the needle and allow for free flow. Needle/catheter thoracocentesis is performed at the 7th intercostal space at just dorsal to costo-chondral junction.
- **Stick BUN and/or creatinine, glucose and potassium** should be performed on abdominal fluid to identify concurrent uroperitoneum (*p. 727*) or sepsis (confirm with history). Cytology should be considered if ruptured bowel is a possibility (*p. 30*).

Extended Laboratory Data Base

- **CBC,** is necessary to identify various anemias based on red cell number and morphology (*see IMHA p. 411*). Acute hemorrhage will not have time to be regenerative, whereas chronic blood loss >3 – 5 days should be regenerative. Schistocytes may suggest DIC but are not consistent for this. Leukocytosis may be suspicious of an infectious cause (e.g., Leptospirosis). Thrombocytopenia may be immune-mediated or secondary to consumption due to leptospirosis, Ehrlichiosis infection, or DIC, for example.
- **Buccal mucosal bleeding time** is a fairly insensitive test of platelet function, however in dogs if >4 min is highly suspicous and >5 min, it is considered prolonged. In cats <3 min is normal.
- **Biochemical profile** is required for general assessment and to rule out all the above potential causes of hemorrhage.
- **Urinalysis** and cytological examination of sediment to identify red cells vs hemoglobin/myoglobin and potential neoplastic cells.
- Further tests for confirmation of etiology should be ordered based on history, physical examination and laboratory findings (i.e., specific coagulation factors).
- **Imaging studies** to locate potential neoplastic, or other sources of hemorrhage.

TABLE 2. Assessment of Degree of Blood Loss

Attitude	Membranes	CRT	Pulse	Mean Art. Pressure	Systolic Pressure	Blood loss	Hemorrhage Class
Depressed Stuporous	pale/v. pale	slow	weak to absent	<60mmHg	<90 mmHg	35 – 50%	IV Life-threatening
Depressed	pale	>2 sec	weak	<70 mmHg	<90 mmHg	25 – >35%	III Severe
Anxious Alert Responsive	pink to pale pink	2 sec	pressure slightly decreased	>70 mmHg	>90 mmHg	20 – 25%	II Moderate
Alert	bright pink to pink	<2 secs	normal pressure	>70 mmHg	>100 mmHg	<10 – 15%	I Mild

NOTE: MAP AND SBP may be normal or increased with signficant blood loss.

MANAGEMENT

The author finds it useful to build an algorithm when managing patients with suspected hemorrhage. If there is *hemorrhage, is this compressible or non-compressible?* If **compressible** (i.e., laceration that can be bandaged), then manage the patient to an **optimal goal of resuscitation:** systolic pressure 120 mmHg, MAP 80 – 100 mmHg. If **non-compressible,** then resuscitate to **adequate perfusion:** a systolic blood pressure of ~90 – 95 mm Hg, MAP ~60 mmHg (*see D below*). After hemorrhage is controlled blood pressure can be optimized. *Is this **hemorrhage with pulmonary contusions?*** Resuscitate to **adequate perfusion** (*see below*). *Is surgical intervention required?* Resuscitate to **adequate perfusion** and proceed to optimal when hemorrhage controlled.
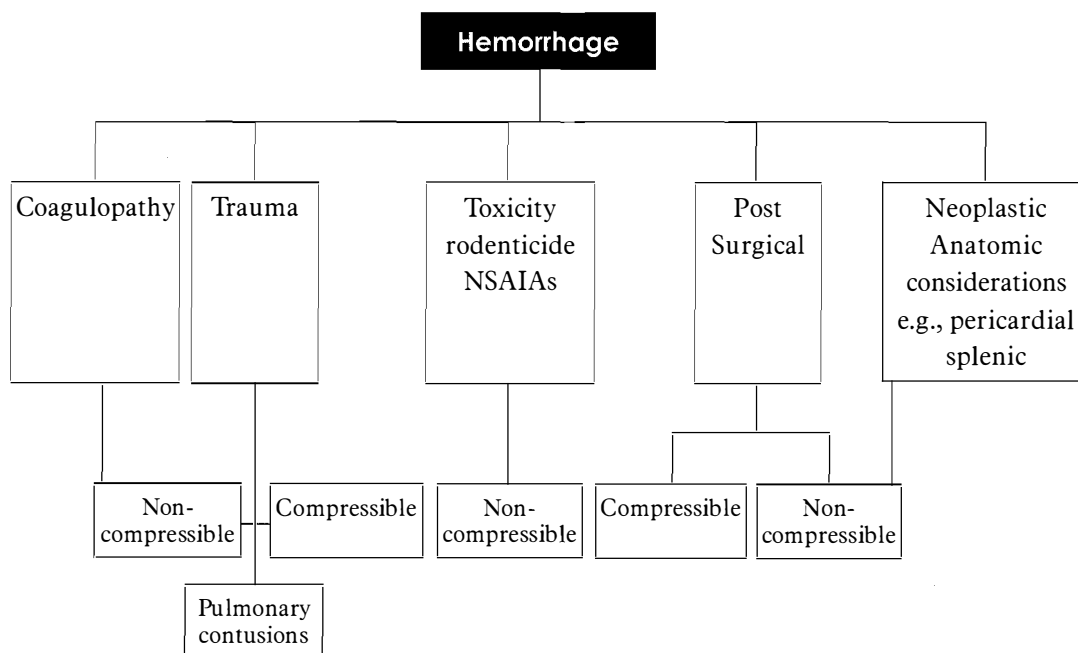
A. Airway/Breathing

1. Administer oxygen by mask and ensure there is a clear airway.
2. Suction the pharynx if hemorrhage is interfering with breathing. If not painful, sedation with **butorphanol 0.2 – 0.4 mg/kg (dog), 0.4 – 0.6 mg/kg (cat)** may facilitate this.
3. **Intubate** if necessary. Sedate with **oxymorphone** or **hydromorphone 0.025 – 0.1 mg/kg IV and midazolam or diazepam 0.2 – 0.5 mg/kg IV.**

4. Ascertain from physical examination whether pleural space (including diaphragmatic hernia), or pulmonary parenchymal injury is present. If pneumothorax or hemothorax is a possibility, and patient is dyspneic, perform thoracocentesis (*see Respiratory Emergencies p. 574*). If a diaphragmatic hernia is causing serious respiratory compromise, immediate surgical correction may be required.

5. Pericardial tamponade should be treated immediately via pericardiocentesis (*see Pericardial Effusion/Tamponade p. 145*). Submit blood from pericardial effusion for blood gases (or observe colour) to ascertain right or left sided cardiac hemorrhage (if due to trauma and surgical correction is required). Hemorrhage may also be due to a ruptured tumour, or idiopathic.

B. Control External Hemorrhage (lacerations, fractures, etc.)

Use direct pressure over the hemorrhaging area and pressure points proximal to the injured tissue immediately (*see 1 and 2 below*). **Address internal hemorrhage (i.e., abdomen, retroperitoneal space, pleural space, epistaxis (*E below p. 627*),** after intravenous catheter placement and fluid resuscitation (*D below*) has commenced.

1. **Direct pressure** can be placed over external wounds with gloved fingers or gauze pad. The wound can be packed with sterile cotton umbilical tape, gauze or laparotomy pads. Sterile towels can be used to pack large wounds. Leave in place for several hours or until definitive surgery can be performed. If bleeding through the towels occurs, add additional wrap over the previous wrap and apply a little tighter than the first. Sterility is important to avoid infection (especially nosocomial) and complications. The purpose of pressure wraps is to reduce the hemorrhage and allow stable clots to form in the injured tissue and vessels. Packs and/or wraps should remain in place and not disturbed for several hours for this to occur. However, other concerns may preclude this duration of pressure. When finally removing the bandages, do so gradually over several minutes/hours to avoid rapid changes in pressure, which could cause bleeding to recur.

2. **Pressure points** to consider, are brachial and femoral arteries for hemorrhage of the limbs. Pressure to the maxillary artery tributaries located deep, ventral and directly adjacent to the angle of the mandible, will control bleeding to the head, nose and oral cavity. Avoid compressing the jugular veins. Blood pressure cuffs can be placed proximal to or directly over the hemorrhaging wound and inflated 20 – 30 mmHg higher than measured arterial pressure. The inflated cuff can remain in place for 2 – 4 hours. However, frequent examination should be made to ensure ischemic injury does not occur. **Narrow tourniquets are not** recommended unless the limb is to be amputated. Bands 5 – 10 cm wide can be used safely up to 30 minutes.

3. **Vascular loops**, clamps or ligatures can be applied directly to blood vessels where direct pressure is not controlling the bleeding. This should be followed by a surgical approach to definitively correct the problem.

C. Pain Control. Analgesics must be administered to all trauma patients that are conscious and aware, or are anxious. Where the patient is depressed, or stuporous/comatose administer an opiod, as the patient begins to respond to volume resuscitation, at the lower dosage recommended. A further dose is administered as required.

1. Initially, **butorphanol 0.2 – 0.4 mg/kg IV** or IM may be adequate for mild pain and anxiety. Later, once the patient is stable and the neuroendocrine response is down-regulated, the patient may appear in more pain (*see 2. below*).

2. For moderate to severe pain, administer **oxymorphone or hydromorphone at 0.025 – 0.1 mg/kg** IV, IM, or more if required. Titrate the opioid to effect to avoid panting. Panting will only occur if the patient is less than moderate to severely painful. Should panting occur, reverse the unwanted effects of the opioid by titrating 1 mL mixture of 0.1 or 0.25 mL (0.4 mg/mL) naloxone, depending on size of the patient, in 5 – 10 mL saline until the patient is comfortable.

3. If **morphine 0.1 – 0.5 mg/kg** is selected, give IM, or IV slowly (dogs & cats) to avoid potential hypotension, or **methadone 0.1 – 0.5 mg/kg IV, IM.**

4. Pain can result in an elevated heart rate and blood pressure, pale mucous membranes and slow capillary refill time. When pain is controlled, these parameters should improve; if not, then the patient is hypovolemic and resuscitation should continue. If they improve after administration of analgesics, alter fluid therapy accordingly.

D. Volume Resuscitation. Determine the degree and cause of hemorrhage by physical examination.

1. Life-threatening hemorrhage (Class III or IV, 35 – 50% blood loss).
2. Severe blood loss (Class III >25% <35% blood loss).
3. Moderate hemorrhage (Class II *20 – 25% blood loss). *Note: 20% blood volume removed for blood donation.
4. Mild hemorrhage (Class I 10 – 15% blood loss).

Place an intravenous catheter in all trauma patients even if fluid therapy is not required (*see Rapid IV Access Techniques p. 609 in Shock*). Then, if during the observation period, the patient deteriorates due to occult hemorrhage, intravenous access is available. Fluid resuscitation should be occurring at the same time as hemorrhage control. It is important to assess the patient as carefully as possible in deciding rate and volume of fluid administration. An in-line burette should be placed when treating cats and small dogs. A known volume should be placed in the burette and closed off at the bag to prevent fluid overload (*see Fluid Therapy p. 347*).

1. **LIFE-THREATENING HEMORRHAGE (Class IV, 35 – 50% blood loss) see Table 2.** This translates into blood loss of **28 – 40 mL/kg in dogs** and **23 – 32 mL/kg in cats. Mentation is the key in this setting as the patient is markedly depressed to comatose. Goal of therapy is SBP 90 mmmHg, MAP 60 mmHg.**
   a. **If "dying before your eyes":**
      i. **Hypertonic saline 5% (6 – 10 mL/kg max), OR 7.5% (4 – 8 mL/kg max) at 1 mL/kg/min** for dogs, **quarter of this for cats,** [respiratory arrest and/or vagoreflex bradycardia may occur, which can be treated with 0.02 mg/kg atropine]. Volume depends on how quickly donated blood can be obtained. Follow with crystalloids in 2. below. Follow hypertonic saline with blood. If HBOCS available this may be preferred to hypertonic saline; go to iii.blood and crystalloids below.
      ii. **Whole blood ~10 – 20 mL/kg (dogs & cats); there is no time for a test dose** OR, if blood not available, go to iii. or iv. Otherwise go to 2 below.
      iii. **HBOCS 10 – 30 mL/kg (dogs), 5 – 14 mL/kg (cats),** is an excellent alternative to blood. Although these dosages are empirical, response to therapy should decide total volume. Administration should **not exceed 10 mL/kg/h or total dose 30 mL/kg in dogs,** and **4 mL/kg/h or total dose 14 mL/kg in cats.** As these patients are severely hypovolemic, overload is usually not a problem with these guidelines. However, titration to an **adequate endpoint** is advised until hemorrhage is stopped. The PCV will no longer be a reliable method of monitoring the animal; hemoglobin content and improved clinical signs will have to be used to monitor progress. Several biochemical tests will be altered using colorimetric methods of analysis (*see package insert for details*). Whole blood may be required at some point. If 1. i–iii not available, consider finding a donor for immediate blood collection and begin.
      iv. **Synthetic colloids 10 mL/kg (dog), 5 mL/kg (cat)** initially with crystalloids at 2+mL/kg/min. Repeat colloid bolus if needed and follow as in 2a and b below.
      v. **Goal is SBP 90 mmHg, MAP 60 mmHg if hemorrhage is ongoing. If no response** in the trauma patient, **cross-clamping of the aorta** should be considered.
      vi. Refer to End-points of Resuscitation in C Management in *Fluid Therapy p. 352.*

2. **SEVERE HEMORRHAGE (25%>35% blood loss) see Table 2. Patient is depressed.** This is ~23 – 28 mL/kg (dogs, 19 – 23 mL/kg (cats) blood loss. **Goal of therapy is SBP 90 mmHg, MAP 60 mmHg.**
   a. **Balanced electrolyte solution** (BES) rapidly (2 – 4 mL/kg/min is a starting point), while obtaining **whole blood, HBOCS, or synthetic colloid,** at which time crystalloids should be reduced to 40 – 60 mL/kg/h (0.75 – 1.0 mL/kg/min) (dog) or 20 – 40 mL/kg/h (0.5 – 0.75 mL/kg/min) (cat). Further adjustments may be necessary. There won't be enough time for the 'test' dose of blood (*see Transfusion Therapy p. 674*). MUST determine if A or B blood is required for a cat. Approximately half of the above estimated lost volume of blood will be required. As assessment of blood loss may be over-estimated, continuous blood pressure monitoring with pulse strength and heart rate monitoring q5min is very important. As blood pressure increases reduce the rate of infusion otherwise hemorrhage will increase due to displacement of the blood clots.
   b. **If whole blood not available packed cells + crystalloids or colloids** may be used as plasma is being thawed. **Colloids** should be administered in **2.5 mL/kg boluses at up to 10 mL/kg over 15 min (cat) up to 20 mL/kg (dog)** to an **adequate endpoint SBP ~90 mmHg, MAP ~60 mmHg in** *non- compressible hemorrhage.* Synthetic colloids reduce the volume of crystalloids required for resuscitation by ~40%.
   c. After hemorrhage is controlled MAP can be optimized to 80 – 100 mmHg, with systolic pressure of 100 – 120 mmHg.
   d. **Where coagulopathies are the cause of hemorrhage**
      i. Packed cells + fresh frozen plasma (must be obtained), or preferrably whole fresh blood if a donor is available.
      ii. Synthetic colloids will reduce the coagulation factors, however if death is imminent, initiate therapy until fresh blood is obtained.

     iii. Add e or f below.
- **e. Where rodenticide toxicity or liver failure is diagnosed add** Vitamin K$_1$ 5 mg/kg SC divided into several sites using a 25 ga needle, followed in 6 – 12 hours by 1.25 – 2.5 mg/kg PO q12h with a fatty meal, or SC if not eating. *See* J *below p. 630* for continuing therapy.
- **f. Where von Willebrand's disease is diagnosed**
  - **i.** Fresh whole blood (from DDAVP boosted donor) is preferred as platelets are required.
  - **ii.** Platelet-rich plasma or platelet concentrate where available is also recommended (*see Transfusion Therapy p. 667*).
- **g. Assess response q5min** as assessment of blood loss may be less than estimated. Note return or improvement in peripheral pulses, an improvement in CRT and mucous membrane colour, an increased level of consciousness or improved response to the caregiver and a reduction in heart rate. Lactate concentrations should decrease. **The fluid rate should be reduced to one-half at this point.**
- **h.** Continue to monitor and adjust fluid/colloid administration to maintain patient stability. Avoid SBP >95 mmHg or MAP >65 mmHg if ongoing hemorhage is present. Monitor lactate to ensure that perfusion is adequate (<2.5 mmol/L – dogs, 1.5 mmol/L – cats). Monitor heart and respiratory rates; tachycardia and tachypnea, with adequate analgesia, suggest further volume resuscitation is required. Caution, if hemothorax is present, binding of the abdomen will lead to increased hemorrhage into the thorax. Continue to monitor PCV and TS. Further blood products are required if PCV decreases to <25%. Give plasma or whole blood if TS <40 g/L. Refer to End-points of Resuscitation in C of Management in *Fluid Therapy p. 352.*
- **i. Pain management** must be considered as patients are resuscitated (*see pain control C above p. 624*).
- **j.** If not yet done, go to *E below p. 627* for control of internal hemorrhage.
- **k. Assessment of initial therapy**
  - **i.** A rapid response to bolus therapy, where the patient is stable indicates a blood loss of <20% and/or there is a major component of vital signs noted due to anxiety and pain. After reduction of fluids to maintenance rate, continue to monitor vital signs and administration of analgesics.
  - **ii.** A transient response to bolus therapy with deterioration following reduction in fluid/blood/colloid therapy indicates inadequate resuscitation, or continuing hemorrhage. Depending on PCV < 25 and TS <40, whole blood or packed cells + plasma are indicated. Failure to stabilize requires surgical exploration.
  - **iii.** Minimal or no response suggests >40% blood loss. Rule out cardiac tamponade, massive pleural hemorrhage, pneumothorax and other underlying reasons for poor cardiac output. Surgical intervention is required for traumatic thoracic or abdominal injuries or ruptured neoplasm.
  - **iv.** If trauma with catastrophic abdominal hemorrhage, thoracotomy and cross-clamping of the aorta, followed by blood administration to enhance perfusion to heart, lungs and brain, prior to laparotomy, has proven beneficial in controlling abdominal hemorrhage and increased survival. Acute blood loss >30% often requires surgical exploration.
3. **MODERATE HEMORRHAGE (Class II, 20 – 25% blood loss)** *see Table 2.*

   AGGRESSIVE FLUID THERAPY IS CONTRAINDICATED.
   - **a.** Start BES fluids at 1 mL/kg/h (dog & cat), (one-half maintenance) until the patient is fully assessed. With this degree of blood loss, it is unlikely that SBP would be <90 mmHg and MAP <60 mmHg. This measurement may be obtained in patients with this degree of blood loss if they are hypothermic or extremely vasoconstricted due to pain and anxiety.
   - **b.** Re-assess heart rate, CRT, mucous membrane colour and SBP, MAP q5min to detect any deterioration immediately. If not yet done, go to E below.
   - **c. Administer analgesics** C above *p. 624* immediately if associated with trauma as pain may be contributing to abnormal vital signs.
   - **d.** Trending at 30 – 60 min after stabilization is very important to confirm that there is no ongoing hemorrhage. Go to K above for assessment of initial therapy.
   - **e.** Reduce fluids to maintenance rate and continue monitoring vital signs.
   - **f. If condition deteriorates, go to D2 above.**
4. **MILD HEMORRHAGE (Class I 10 – 15% blood loss).**
   - **a.** Fluid therapy not necessary but IV catheter placement is recommended while blood pressure is normal in case blood loss is identified during trending.
   - **b.** Trending is important to confirm that there is no ongoing hemorrhage.
   - **c.** See **pain control C above** *p. 624*.

E. INTERNAL HEMORRHAGE CONTROL

1. **Abdominal hemorrhage**
   a. If estimated **blood loss into the abdomen or thorax is >40%,** surgical intervention is advised. Thoracotomy and cross-clamping of the aorta followed by blood administration to enhance perfusion to heart, lungs and brain, prior to laparotomy, has proven beneficial in controlling abdominal hemorrhage and increased survival. Blood loss 30% >40% often requires surgical exploration.
   b. Autotransfusion of blood due to ruptured neoplasm should not be performed. Frequently, previous hemorrhage has occurred, and transfusion of this material will result in DIC. Following trauma, rupture of the gastrointestinal tract and contamination of the free abdominal blood is always a concern.
   c. **Conservative management with ≤30% blood loss** (*see e below*).
   d. There is a 50% false negative rate, a negative centesis does not rule out abdominal hemorrhage. A four quadrant abdominocentesis or DPL is not really necessary as experience indicates that if there is difficulty retrieving blood, severe blood loss is not a concern at the time, or it is irretrievable in the retroperitoneal space. **Retroperitoneal hemorrhage will result in a negative centesis.** If a diagnostic peritoneal lavage (DPL) is elected to rule out ruptured viscous (*see Acute Abdomen p. 21*) it should be performed after attempts at resuscitation and stabilization .
   e. For **abdominal or retroperitoneal hemorrhage,** apply external counterpressure to abdomen, pelvis and pelvic limbs (indirect pressure to abdominal organs). The bandage essentially reduces the compliance of the abdominal wall. Fold towels (small or large varying with the size of dogs or cats) and place in the inguinal and ventral abdominal area and between the hind limbs extending to the hocks (important, to avoid pooling of blood in the limbs). Avoid "lumps". Wrap around the towels, from the feet toward the diaphragm, with tensor bandage. Apply some pressure, but do not wrap too tightly and increase intra-abdominal pressure to the point where compression of ureters occurs with reduction of urine flow. Avoid tight (tourniquet-like) areas. Do not compromise expansion of the diaphragm. The wrap should look smooth like a good Robert Jones bandage. You should be able to place a finger easily between the bandage and skin. This will not stop arterial bleeding but appears to control low flow, venous hemorrhage from splenic or liver fractures.
   f. **Things to look for:** If ventilatory effort is increasing, check tightness of bandage and assess if thoracic or pericardial hemorrhage is occurring. An abdominal bandage will increase thoracic and pericardial hemorrhage and must be removed. Examine toes for temperature (coolness), swelling and cyanosis, these are all signs of excessive pressure. The counterpressure wrap should be released from abdomen to hock slowly. If mean blood pressure or systolic pressure drops by 5 mmHg or greater, re-establish the wrap. If the pressure is not stabilizing, maintain counterpressure and take the animal to surgery.
   g. If conservative measures do not control hemorrhage, surgical exploration is necessary.
2. **Thoracic hemorrhage**
   a. An altered ventilatory pattern with dullness noted ventrally on thoracic auscultation is suggestive of hemothorax. Diagnostic thoracocentesis will confirm if blood is present. Remove the abdominal wrap if one was placed.
   b. Blood should be removed if ventilation or venous return is impaired (note jugular distension).
   c. Large **volumes** of blood can be removed with a teat cannula and **autotransfused** back to the patient (*see Transfusion Therapy p. 680*).
   d. If necessary, place a large bore chest drain (*see Respiratory Emergencies p. 575*). Avoid if a coagulopathy is the cause of hemorrhage.
   e. If vital signs worsen, the patient may be exsanguinating into the chest and exploratory thoracotomy is indicated. Fractured ribs may indicate the source of the hemorrhage.
   f. A dog can resorb up to 30% of its blood volume in 4 days. If blood in the pleural space is not interfering with ventilation or venous return and is self-limiting, it is not necessary to evacuate the chest.
3. **Acute pericardial tamponade** (*p. 145*) is diagnosed on reduced to absent heart sounds with audible lung sounds, pale to grey mucous membranes, severe dyspnea and distended jugular veins. Small complexes on ECG are usually not present in acute pericardial tamponade and the cardiac silhouette may not be noticeably large.
4. **Epistaxis**
   a. Sedatives/analgesics are required for the anxious or active patient (*see C above*).
   b. Apply digital pressure to the maxillary arteries.

c. Instil 2 – 4+ drops of 1:100,000 epinephrine (0.1 mL of 1:1,000 [1.0 mg/mL] and add 9.9 mL saline) **or** neosynephrine spray, **or** 5% solution of cocaine **or** diluted phenylephrine spray into the nasal passage.

d. If necessary pack the nares with vaseline impregnated gauze tape. If gauze not available, Q tips have been suggested. When ready to remove, do so a ½ inch at a time, or one Q tip at a time. (Elizabethan collar required).

e. If **hemorrhage is refractory,** then anesthetize and pass a foley urinary catheter through the ventral meatus to the nasopharynx, inflate the balloon, and retract the catheter up to the nasal passage. Apply local anesthetic into the nares. Pack the nasal passage up to the balloon with vaseline gauze tape. Leave pack in place for 24 – 48 h.

f. If the patient is **anxious** and is

    i. **not hypotensive or painful,** then sedate with **acepromazine 0.03 mg/kg IV, IM.** If the patient is in pain go to iii.

    ii. **hypotensive or not,** mild analgesia and sedation with **butorphanol 0.2– 0.4 mg/kg, dog; 0.2 – 0.6 mg/kg, cat IV, IM** may be required.

    iii. **painful** administer **oxymorphone or hydromorphone 0.025 – 0.1 mg/kg, or morphine 0.1 – 0.2mg/kg + diazepam 0.2 mg/kg combination or fentanyl 2 – 4 μg/kg/h CRI** for moderate to severe pain.

    iv. Selecting drugs for **heavy sedation or anesthesia:** Trauma patients are all potentially hypovolemic and hypotensive. Even if blood pressure is normal, this may be maintained by the sympathetic nervous system induced by pain or hypovolemia. Potential hypotensive drugs such as proprofol and thiopental should be used with caution and titrated to effect carefully (*see Analgesics and Sedatives p. 81*). Ketamine may cause hypotension if the animal's sympathetic nervous system cannot respond to ketamine's hypotensive effects. Acepromazine is also hypotensive. If anesthesia is desired isoflurane (can also cause hypotension) by mask is recommended after the opioid/diazepam has been administered.

F. Surgical Intervention.

If there is no improvement or the patient is deteriorating after instituting C and D above, SURGICAL INTERVENTION IS NECESSARY.

THE KEY AS TO WHETHER SURGICAL EXPLORATION IS REQUIRED IS THE PATIENT'S CONDITION AND LABORATORY DATA. IF THE PATIENT IS DETERIORATING, DESPITE ALL CONSERVATIVE EFFORTS, DON'T WASTE TIME WITH EXTENSIVE DIAGNOSTICS IF YOU CAN LOCATE THE PROBLEM AREA (i.e., hemorrhage from fracture site, abdomen, pleural space). PROCEED TO SURGICAL EXPLORATION/CORRECTION.

TABLE 3. Indications for Exploratory Surgery in Cases of Hemoperitoneum

1. Abdominal expansion clinically more apparent.
2. Vital signs (heart rate, blood pressure) not responding to rapid volume replacement and counterpressure.
3. Relapse of signs of shock following volume replacement and counterpressure.
4. Radiographic signs of pneumoperitoneum, diaphragmatic hernia, or mass effect.
5. Presence of abdominal herniation or penetration.
6. Follow-up sample of peritoneal fluid hematocrit or hemoglobin greater than previous ones by 5% or 1 g/dL, respectively, despite use of counterpressure.
7. Microscopic or chemical analysis of lavage fluid (*p. 30*) suggesting hollow viscous leakage (e.g., urinary bladder, intestine, gallbladder).
8. Radiographic and clinical evidence of continued retroperitoneal space expansion and hemorrhage despite use of counterpressure.
9. Persistent decreasing of peripheral hemoglobin or hematocrit with volume expansion despite use of counterpressure.

G. Corticosteroids should *not* be administered.

H. Antibiotic treatment will depend on the injury sustained.

    1. Skin lesions: **cefazolin 20 mg/kg IV q6h (dogs) q8h (cats) or cephalexin 20 mg/kg PO q8h.**
    2. Abdominal trauma where bowel injury may be present: **cefoxitin or cefotetan 20 mg/kg IV q6h (dogs) q8h (cats).**

I. **Liver disease** causing coagulopathy. *See Hepatic Failure/Dysfunction p. 37* for ongoing treatment for coagulopathy.

J. **Continued therapy for rodenticide coagulopathy Vitamin K$_1$ 1.25 – 2.5 mg/kg q12h PO.**

   1. It is important to identify the potential toxin as treatment duration is based on

      a. Warfarin 7 days

      b. Diphacinone and indanediones 3 – 4 weeks

      c. Brodifacoum and bromodiolone 4 – 6 weeks

      d. Unknown should be assumed to be either (b) or (c) and treated for 3 weeks, followed by e

      e. For (a) – (d) the PT should be tested 48 hours after last Vitamin K treatment. If it is prolonged, continue treatment for a further 2 – 3 weeks and re-test. As a range is suggested, a reduction to the lower dosage may be effective at this time.

      f. Exercise restriction is mandatory until coagulation parameters are normal after discontinuation of Vitamin K$_1$.

K. **Padded cage** and continual careful handling for patients with coagulation disorders (e.g., thrombocytopenia, specific factor disorders, liver disease, rodenticide toxicity).

SUGGESTED READING

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NOTES

INTRODUCTION

Veterinarians will be presented with pets that may be exposed to any number of toxins. It is an impossible task for the veterinarian to be aware of the pathophysiology, toxic doses of, and treatments for all possible toxins. Fortunately, applying general principles of decontamination and supportive care can treat most toxicologic cases appropriately. When presented with an unfamiliar toxin, the veterinarian will need to research the details of the particular agent to guide further management (Tables 1 & 2). Rapid access to this information, as well as having ready access to the materials needed for decontamination and appropriate antidotes, are necessary to provide medical care for toxin cases.

DIAGNOSIS

When presented with a confirmed or reported toxin case, follow the steps outlined below.

Get a detailed history on the telephone or in the clinic
- Signalment?
- Why is toxin ingestion suspected?
- When did it occur?
- Was it witnessed?
- How long will it take for the clients to get to the clinic?
- Are there pre-existing medical problems?
- Have owners performed any first-aid measures?
- Present clinical signs, if any?

Ask clients to bring in container and any vomitus (or remains thereof).

If, after initial assessment of an ill animal presented for another reason, and toxin exposure is suspected or on a rule-out list, see list of questions under "presentation at veterinary clinic," below.

Pre-hospital Advice

If the client must travel to the hospital, suggest support measures to be done en route.
> Supportive measures must be practical and easy to perform. Do not advise procedures which will cause a long delay of arrival to the hospital, or potentially contribute to morbidity due to incorrect assumptions.

A. If seizing:
1. Apply wet, cool towels to the patient
2. Place ice packs (frozen vegetable bags) wrapped in a light towel in the groin and axilla.
3. Travel with a second person in the car.

B. If ingestion of a corrosive agent, and patient remains alert:
1. Offer milk (2 – 6 mL/kg)

C. If comatose:
1. Travel with a second person in the car.
2. Keep head raised to prevent aspiration.
3. Lower head below the body if vomiting occurs.

D. Advise the client on the degree of **urgency needed.**

E. Home management may be necessary if the client cannot come into the hospital at all. See section D under "Management" for options in inducing emesis at home in this case.

Research the potential toxin and its effects prior to patient's arrival.
> Find information on the LD50, the mechanism of action of the toxicant, and any relevant species differences **(Tables 1 & 2).**

On Presentation of the Patient at the Veterinary Clinic

History

Obtain further history while performing the physical examination. If toxin exposure is suspected after initial assessment by the veterinarian, the following questions may help uncover a history of toxin exposure:

- How and when is the animal supervised?
- Does the pet spend its time indoor or outdoors?
- Could it have any access to drugs?
- Were any drugs (including topical medications) given to the patient?
- Are any residents in the house on medications, including topical medication or inhalers?
- Is there access to plants?
- What is the diet, including any recent special treats (onions, raisins, macadamia nuts)?
- Is there access to sugar-free products? (Xylitol used in Atkins diet products can be toxic to dogs)
- Has there been recent access to garbage?
- Is there access to a garden?
- Are garden products used (cocoa bean mulch, metaldehyde, garden compost, insecticides, pesticides)?
- Are carbon monoxide detectors used in the house?
- Has the pet chewed or destroyed anything recently?
- Is there access to garage items?
- Is there antifreeze in the plumbing?
- Have any pesticides been used in the house or on the pet recently?
- What is the vaccine history?

Clinical Signs/Physical Examination

On primary survey ensure
- Airway: patent airway
- Breathing: adequate respiration
- Circulation: normal cardiac rhythm, euvolemia, normotension

Airway, breathing and circulation must be stabilized and seizures controlled (*see Seizures Cat p. 456, Dog p. 460*) prior to initiating decontamination procedures. Administration of the appropriate antidote may be necessary at this point to stabilize the patient (*see Table 4*). Refer to information specific to the toxin being treated.

If toxin exposure is strongly suspected, but the toxicant is not known, proceed with appropriate decontamination procedures while ruling out other illnesses through a diagnostic work-up. *See Table 3* for a list of possible toxicants based on clinical signs.

Laboratory/Imaging Data Base

Stat
Perform quick assessment tests and extended physical examination. If possible, while taking samples for STAT tests, take sufficient sample for an extended data base and toxicologic assessment (see next section). The following tests are suggested to identify a potential toxin and to fully assess patient status:

- **PCV, TS** to assess hydration status (vomiting, diarrhea, hepatic, renal dx) or anemia/hemorrhage (e.g., rodenticide, nonsteroidal anti-inflammatory analgesic toxicity).
- **Glucose** (xylitol-toxicosis results in hypoglycemia).
- **Stick BUN,** urea or creatinine to identify renal involvement.
- **Serum electrolytes** to assess hydration/acid base status and abnormalities associated with specific toxins
- **Venous blood gases** to assess metabolic status (acidosis/alkalosis).
- **Urine dipstick and specific gravity.** Look at urine in a non-plastic container with Wood's lamp if ethylene glycol toxicity is a possibility (urine may fluoresce).
- **Lead II ECG** for rhythm abnormalities.
- **Blood pressure.**
- **Pulse oximetry.**
- **Temperature.**
- **Abdominal radiographs** to estimate volume of ingesta prior to decontamination (*see notes on gastric decontamination, below*).

While specific abnormalities for all potential toxins exposed to cannot be noted here, the findings may be helpful when identifying the causes in Table 3.

- **CBC.**
- **Biochemical profile** to assess renal, hepatic and metabolic status.
- Complete **urinalysis** to assess potential renal injury, ethylene glycol toxicity (calcium oxalate crystals).
- See Table 3 for toxins resulting in organ failure.
- **Thoracic radiographs** to assess potential aspiration in a dyspneic, vomiting dog, or pulmonary hemorrhage associated with rodenticide toxicity.
- Future toxicologic analysis may be necessary.
  - Preserve blood and urine samples in sodium fluoride (gray stopper) tubes.
  - Collect urine and blood in royal blue topped tubes if zinc or element analysis necessary.
  - Collect hair samples if topical exposure to organophosphates or pyrethrin/pyrethroids is suspected.
  - Refrigerate or freeze all samples in separate, air-tight containers until analysis (*see I below*).

MANAGEMENT

A. Stabilize Airway, Breathing, Circulation, Neurologic signs.

1. **Oxygen** (flow by, nasal) if in respiratory distress.
2. Tracheal intubation if extremely weak, semi or totally unconscious. Mechanical ventilation may be necessary. Oxygen therapy is contraindicated in paraquat toxicity.

B. Control body temperature

1. Seizuring animals may be hyperthermic: apply ice packs to inguinal and axillary regions.
2. Dampen coat with cool water and apply a fan.
3. Give cool water enema if temperature >42°C (107.6°F) (*see Hyperthermia p. 297*).

C. **IV access.** If required, based on preliminary lab data and physical exam findings, administer:

1. Balanced electrolyte solution (*p. 362*).
2. 0.9% sodium chloride if alkalemic (*p. 406*)or hypercalcemic (*p. 377*).
3. Blood if hemorrhage with PCV< 25% (dog), <20% (cat).
4. Fresh blood OR packed RBC's and frozen plasma for rodenticide toxicity.

D. Decontaminate the skin (topical toxins).

1. Decontaminate by washing the patient, then go to (**F**).
2. If toxin is a powder, vacuum off prior to washing.
3. Be aware of the toxic potential to the staff. Use gloves and aprons to minimize human exposure.
4. Do NOT attempt to bathe a seizuring animal (control the seizures first).
5. Dishwashing liquid and water is effective in removing most substances.
6. Sticky petroleum-based substances may be removed by solubilizing with mineral or vegetable oil, and then washing with dishwashing liquid.

E. Decontaminate the Stomach (Ingested Toxins)

1. Calculate amount of toxin ingested relative to toxic dose to determine whether decontamination is necessary (*for calculation help, see Table 5*). If not sure of the amount ingested, assume a toxic amount has been consumed and decontaminate the gastrointestinal tract as outlined below.
2. **Emesis and Gastric lavage both present risks to the patient,** may be time-consuming, thus allowing ongoing absorption of ingested toxin, and frequently resulting in incomplete gastric emptying. Current recommendations in human medicine suggest the use of activated charcoal as the sole intervention for gastrointestinal decontamination in most poisoning situations. No studies have been performed in veterinary medicine to assess the efficacy of this approach. However, if the amount of toxin ingested is not life-threatening, and/or the risks to the patient of gastric decontamination by emesis or lavage are high, the sole use of **early** administration of activated charcoal may be justified (*see F below*). If gastric decontamination is warranted, and emesis not contraindicated, (*see Emesis 3 below*) it is recommended **over gastric lavage,** and is toxin and time-dependent:

    a. Generally, the time for ingesta to move completely out of the stomach is variable, taking many hours in some animals if 'bulk-type' material ingested (e.g., composted material or leaves), whereas liquids and small toxins (e.g., tablets) move fairly quickly (within 1–2 hours). Gastric emptying time also varies with the patient, the amount ingested and the toxin. Therefore, radiographic or ultrasonographic assessment of the quantity of stomach contents should be performed prior to considering emesis or gastric lavage.

    b. Gastric lavage or emesis more than **4 hours** beyond ingestion MAY be beneficial in removal of a significant amount of toxin (e.g., chocolate, rotting compost).

    c. Toxins that induce neurologic signs often result in prolonged gastric emptying, and gastric decontamination in these patients may be indicated beyond 4 hours after ingestion.

    d. Lipid-soluble agents are rapidly absorbed (e.g., ethylene glycol, aspirin).

3. Emesis

    a. Contraindications for emesis

       i. Pre-existing vomiting.

       ii. Neurologic signs, including tremors or seizures.

       iii. History of epilepsy.

       iv. Severe cardiac disease.

       v. Recent abdominal surgery.

       vi. Megaesophagus.

       vii. Spinal injury.

       viii. Severe lethargy, debilitation or coma.

       ix. Hypoxia or dyspnea.

       x. Rodent, rabbit or bird patients.

       xi. Ingestion of caustic substances (strong alkali, strong acid), petroleum distillates or other volatile substance.

       xii. Bread dough ingestion.

    Note: Some ingested toxins may prevent emesis: marijuana, phenothiazine tranquilizers, barbiturates, antihistamines, codeine.

    b. Induction of Emesis

    Recommendations for cats:

       i. Medetomidine 20 μg/kg IM, IV

       Atipamezole **(medetomidine reversal)** 80 μg/kg IM

       ii. Xylazine 0.44 mg/kg IM, SC

       Yohimbine **(xylazine reversal)** 0.1 – 0.5 mg/kg IV

       CAUTION: Use of medetomidine or xylazine may result in hypertension or hypotension, bradycardia, hypothermia, and respiratory depression.

       iii. 3% Hydrogen Peroxide 1 – 2 mL/kg, maximum 10 mL orally. Emesis is caused by mild gastric irritation. Repeat only once, if necessary. Further administration may result in hemorrhagic gastroenteritis. Old product is less effective.

       iv. Syrup of Ipecac 2.5 mL (dog), 3.3 mL/kg (cat) PO once. Dilute 1:1 with water for cats. Emesis is caused by gastric irritation and stimulation of the chemoreceptor trigger zone. It is the least desirable emetic, as it is less reliable and has a late onset of action. Onset of vomiting may be 15 – 20 minutes. It may be administered by orogastric or nasogastric tube. DO NOT CONFUSE WITH THE MORE CONCENTRATED and potentially TOXIC EXTRACT OF IPECAC. Hydrogen peroxide may be administered simultaneously with syrup of ipecac for more reliable and faster emesis.

    Recommendations for dogs:

       i. Apomorphine: is the most reliable emetic in dogs

         – **IV 0.03 mg/kg** typically results in immediate vomiting

         – **IM 0.04 mg/kg, SC 0.08 mg/kg** results in vomiting within 5 minutes.

         – **conjunctival tablets 0.25 mg/kg** typically result in vomiting in 5 – 10 minutes, are less reliable, but allow dosing to effect; the tablet is rinsed out of the eye once emesis has occurred.

       ii. Apomorphine reversal with naloxone 0.04 mg/kg IV will reverse the sedative, but not the emetic, effects of apomorphine. If emetic effect persists, consider the use of metoclopramide.

       iii. 3% Hydrogen Peroxide 1 – 2 mL/kg, maximum 50 mL
Emesis is caused by gastric irritation. **Repeat only once,** if necessary. Further administration may result in hemorrhagic gastroenteritis. Old product is less effective.

    iv. Syrup of Ipecac 1 – 2 mL/kg, max 15 mL dogs (*see as for cats above*).
Hydrogen peroxide may be administered simultaneously with syrup of ipecac for more reliable and faster emesis.

CAUTION: The use of salt as an emetic is not advised because it is unreliable and may result in salt toxicosis. Similarly, forcing fingers or large amounts of water into the back of the mouth is an unreliable and potentially dangerous method of inducing emesis, and is therefore not recommended.

Once emesis has occurred, save and freeze stomach contents if toxicologic analysis is necessary (*see I below*).

4. Gastric Lavage
   a. Contraindications for Gastric Lavage
      i.   Unacceptable anesthetic risk
      ii. Volatile hydrocarbon ingestion
      iii. Corrosive agent
   b. Technique
      i.   Place the animal on a raised table.
      ii.   **Anesthetize** the patient if not comatose. The anesthetic protocol will vary with the patient's condition and the toxin ingested. In general (*see Anesthesia p. 114*):
         – Avoid ketamine for seizuring patients.
         – Induce with an opioid and diazepam, OR
         – Cautious titration of propofol, followed by
         – Carefully monitored inhalant anesthesia.
      iii. Place a **cuffed endotracheal tube,** expand the cuff carefully, and place the patient so the head is lower than the thorax. Tilt the table, or elevate the patient's hind quarters. **Aspiration of lavage fluid and stomach contents is a risk**
      iv.   Measure a **large-bore gastric lavage tube** from nose-tip to xyphoid cartilage and mark; lubricate well with KY jelly and pass into the esophagus to the mark.
      v.   Using either a funnel and gravity, or a pump, fill the tube with **tepid water, 5 – 10 mL/kg.** Excess water will increase the risk of aspiration, and possibly increase entry of stomach contents into the small intestine.
      vi.   **Lower** the tube below the level of the patient, and allow gravity flow to empty stomach contents through the tube into bucket. Save stomach contents for **toxicologic analysis** for identification.
      vii. **Gentle ballotment** of the abdomen by an assistant will suspend stomach contents in the lavage fluid.
      viii. **Repeat the lavage** until the effluent is clear. This may take 15 – 20 cycles. The stomach contents may obstruct the tube, if this occurs, pinch off the end of the tube, remove it from the patient, clear the obstruction and replace it.
      ix.   **Empty the stomach** and administer activated charcoal, if indicated (*see F 2 below*), through the lavage tube.
      x.   **Pinch off the tube** prior to removing it to prevent leaking of the contents and **aspiration.**
      xi.   Clear the oropharynx of any material to avoid aspiration.

F. **Administer activated charcoal (topical and ingested toxins):** Activated charcoal is used to adsorb toxicants and thus prevent absorption across the bowel wall. It is available in a variety of preparations; some **combine activated charcoal with sorbitol,** a cathartic. Activated charcoal **does not bind to all substances equally.** It is **less effective** for ethanol, methanol, most heavy metals, nitrate, nitrites, fertilizer, fluoride, ferrous sulfate, mineral acids, and petroleum distillates. However, it does provide binding to some extent to most toxins, therefore is recommended in all toxin ingestions unless there are specific contraindications for its use. **Tablets and capsules** are **not** recommended due to vastly reduced surface area compared to liquid and powder formulations. Activated charcoal is typically administered after oral ingestion of a toxin, but is of help in minimizing the effects of some **dermal toxicants,** probably by adsorbing to toxicants ingested by grooming. Repeat administration, **without sorbitol, every 12 hours for 2 days is recommended in cases of dermal toxicants.**

1. Contraindications for activated charcoal
   a. Confirmed or suspected gastrointestinal perforation.
   b. Severe vomiting.
   c. Caustic substances (they are not absorbed systemically, and the charcoal will make subsequent visualization of burns difficult).

2. **Routes of administration at 0.5 – 2g/kg commonly used, up to 4 g/kg suggested:**
   a. **Offer directly.** Occasionally, dogs will ingest it directly when offered, or will ingest it if mixed with a small amount of canned dog food.
   b. **Place in the gastric lavage tube** after the gastric lavage procedure.
   c. **Administer through an orogastric tube.**
   d. **Give directly by syringe.** This is least desirable, as aspiration is a risk, and a large quantity must be given and many animals find it disagreeable. Avoid extending the neck extensively when administering liquids, because this increases the risk of aspiration.
3. **Repeat the administration** of activated charcoal if indicated for the toxicant. Some toxins have extensive entero-hepatic recycling (e.g., ivermectin), which can be interrupted by repeat doses of activated charcoal every 4–6 hours. **Avoid preparations of activated charcoal with sorbitol for repeat administration.**
   Mix charcoal with 50 – 200 mL water or suitable volume for size of patient (~5 – 10 mL/kg).
4. If the patient is to be discharged shortly after the decontamination procedure, advise the client that the stool will be black and possibly loose.

G. Administer a cathartic: Cathartics are used to speed passage of the toxicant out of the intestinal tract. Sorbitol, present in many formulations of activated charcoal, is a cathartic. The charcoal/sorbitol combination limits the repeat dosing therefore. Charcoal without sorbitol is required if activated charcoal is to be given repeatedly.
   a. **Contraindications for cathartic administration:**
      i. Diarrhea
      ii. Dehydration
      iii. Electrolyte imbalances
      iv. Ileus
   b. **Cathartic agents**
      i. **Sorbitol 70% solution 1 – 3 mL/kg** (available in U.S.A.).
         Sorbitol is a non-absorbable sugar, which has an osmotic effect in the intestinal tract. It is considered the cathartic of choice in human medicine.
      ii. **Lactulose 0.5 – 1.0 mL/kg PO** – no published dose for catharsis.
         Lactulose is also a non-absorbable sugar, and has been suggested for use as a cathartic. It has the advantage of being readily available in most veterinary clinics.
      iii. **Magnesium sulfate (Epsom Salts): 250 mg/kg (1/4 tsp/5 kg).**
         The magnesium is partially absorbed across the intestinal tract and may cause hypermagnesemia with concurrent depression and weakness. Magnesium sulfate is contraindicated in patients with renal disease or in treatment of toxins that may slow gastrointestinal transit time.
      iv. **Mineral oil – not recommended** as it may interfere with charcoal adsorption, may enhance absorption of toxic product, and aspiration will result in pneumonia.
      v. **Monitor hydration** status carefully after administration of a cathartic and supply appropriate fluid therapy as needed to avoid dehydration and hypernatremia.

H. Use an antidote if appropriate and if not already administered during stabilization procedures: The need, type and particulars of antidote use will depend on the toxin ingested. As the presentation of toxicology cases is never scheduled, it is recommended that the veterinarian always be prepared to treat a wide variety of toxin cases. The decision to stock antidotes in the veterinary clinic depends on several factors:
   1. The expense and shelf-life of the drug, the frequency of that particular toxin case.
   2. The time frame of antidote use for successful treatment of the case.
   3. The necessity of use of the antidote for successful treatment of the case.
   4. Availability of the antidote outside of the veterinary clinic.
   5. Emergency clinics, which expect to see more toxin cases than regular veterinary practices, may choose to stock a greater selection of antidotes than a regular practice.
   6. Veterinarians should make advance preparations to treat toxicology cases by making arrangements to obtain antidotes quickly if they choose not to carry them.
   7. Local human hospitals, pharmacies, veterinary pharmacy suppliers and local veterinary emergency clinics may be helpful in providing an antidote that can be accessed quickly.
      Table 4 presents a suggested antidote inventory for the emergency veterinary practice. An excellent and detailed discussion of this topic is found in Current Veterinary Therapy XIII (*see References*).

I. Monitor patient carefully and provide supportive care as required. Poisoned patients will present with a vast array of pre-existing and toxin-induced symptoms. Each patient is unique, and will need symptomatic treatment tailored to its own clinical situation. Careful monitoring of all body systems, repeated bloodwork and anticipation of possible sequelae to the toxicosis are necessary. Refer to other chapters in this book for treatment of seizures (*p. 456/460*), hyperthermia (*p. 297*), acid-base disturbances (*p. 406*), fluid therapy (*p. 347*), arrhythmias (*p. 164/170/179*), electrolyte disturbances (*p. 373/377/381/390/394*), anemia and pain (*p. 117*).

J. Submission of toxicologic samples

1. Consultation with the veterinary diagnostic toxicologist before sample submission is necessary to guide test selection and ensure correct sample submission.
2. The local human hospital may be of help, especially in cases where prescription, illicit or stimulant drug ingestion is suspected.

TABLE 1. Sources of Information

- Compendium of Pharmaceuticals
- Local poison control hotline (look in local phonebook)
- National Animal Poison Control Hotline (888) 426–4435, www.aspca.org:

    This is a veterinary-oriented service, staffed by board-certified veterinary toxicologists. They maintain a large database on veterinary toxins, and will provide information and advice on therapy for individual cases. (Note there is a charge for this service; at time of press it was $50.00 U.S. per case. Payment is expected by credit card at the time of consultation.

- The world wide web is constantly changing, and has become an ever-evolving, excellent resource for toxicologic information. Websites listed here may be outdated or altered at any time. Frequent perusal of the internet for accurate, up-to-date sites and "bookmarking" them for future reference is recommended.

Veterinary Information Network (www.vin.com) (paid members only)

http://ace.orst.edu/info/extoxnet/
Non-corporate information on environmental toxins and lawn care products. Not veterinary-oriented. The site is a cooperative effort of University of California-Davis, Oregon State University, Michigan State University, Cornell University, and the University of Idaho.

http://sis.agr.gc.ca/pls/pp/poison?p_x=px
Canadian Federation of Agriculture website. Comprehensive information on poisonous plants. Lots of veterinary (but usually large animal) specific information on plants. Good links to other resources.

http://www.library.uiuc.edu/vex/toxic/intro.htm
From the University of Illinois. Veterinary-oriented information on poisonous plants, complete with photographs.

www.merckvetmanual.com
Free online access, no registration required. Offers concise, veterinary-specific information on a wide range of toxins.

http://toxnet.nlm.nih.gov/
A cluster of databases on toxins and hazardous chemicals.

http://www.ivis.org
International Veterinary Information Service (IVIS) is a not-for-profit organization established to provide information to veterinarians using internet technology. Free registration required. Provides information on many toxicants, including groupings of toxicants by clinical signs.

Many good toxicology texts are available (*see References at the end of this chapter*). Additionally, many internal medicine texts have information on selected toxins.

TABLE 2. Summary of Toxin-specific Information Available in Selected Textbooks

Current Veterinary Therapy XIII	Current Veterinary Therapy XII
• Treatments used in toxicoses • Rodenticides • Nephrotoxins • Hepatotoxins • Grass, poinsettias, non-toxic plants • Lawn care products • Common household chemical hazards • Toxicities from newer over-the-counter drugs • Flea and tick products	• Toxic ornamental and garden plants • Herbal remedies • Bee and hymenoptera stings • Anticoagulant rodenticide • Antifreeze poisoning • Zinc toxicity • Iron toxicity • Pyrethrin/Pyrethroids • Organophosphates/carbamates • Lawn Care Products • Illicit drug intoxication • Indoor air pollutants
Current Veterinary Therapy XI	**Current Veterinary Therapy X**
• Activated charcoal use • Bromethalin rodenticide toxicosis • Chlorpyrifos toxicosis (cats) • Ibuprofen • Xylazine reversal with Yohimbine • Zinc Toxicosis	• Ivermectin • Cholecalciferol • Lead • Arsenic • Bleaches/antiseptics, disinfectants • Bites and stings
Veterinary Clinics of North America, Small Animal Practice, March 2002	**5 Minute Veterinary Consult**
• Herbal hazards • Plant hazards • Toxic mushrooms • Mycotoxins • Oral medications: SSRI's , benzodiazepines, amphetamines, carprofen, COX-2 inhibitors, pseudoephedrine, calcium channel blockers, baclofen • Topical Preparations: calcipotriene, Vitamins A & D, zinc oxide, 5-fluorouracil, brimonidine, imidazoline, local anesthetics, corticosteroids, antibiotics, salicylates, benzoyl peroxide. • Toxicity of newer pesticides for dogs and cats • Rodenticides	• acetaminophen • aflatoxin • amitraz • arsenic • aspirin • carbamate • carbon monoxide • chocolate • ethanol • ethylene glycol • hepatotoxins • iron • itraconazole • ivermectin • lead • lily • metaldehyde • mushroom • organophosphate • pyrethrin • strychnine

TABLE 3. The following lists, while not comprehensive, may suggest toxins to consider with presentation of the following clinical symptoms.

Seizures	Other neurologic signs	Acute renal failure	Severe Gastrointestinal Signs
• Metaldehyde • Illicit drugs • Chocolate • Tremorgenic mycotoxins (garbage, compost) • Organophosphate or carbamate insecticides • 5-Fluorouracil cream • Local anesthetics • Ivermectin • strychnine • pyrethrin	• Albuterol/salbutemol (asthma inhalers) (weakness, restlessness) • Bromethaline toxicosis (hind-end ataxia, paresis) • Macadamia nuts (hind-end paresis, dogs) • Ethylene glycol • Ethanol/methanol • Bread dough toxicosis • Propylene glycol • Organophosphate, carbamate or pyrethrin/pyrethroid insecticide • Amitraz • Illicit drugs • Ethylene glycol toxicosis • 5-fluorouracil cream • Imidazoline decongestants • Cigarette ingestion • carbon monoxide • xylitol (sugar found in sugar-free diet foods causes hypoglycemia in dogs)	• Easter Lily (cats) • Ethylene Glycol • Non-steroidal anti-inflammatory drugs • Calcipotriene topical ointment • Cholecalciferol rodenticides • Raisins (dogs) • Pine oil or turpentine (cats) • Glyphosate ("ROUND-UP") (pulmonary edema, metabolic acidosis)	• 5-fluorouracil cream • Tricothecene mycotoxins • Amanita (mushroom) • Other gastro-intestinal irritant mushrooms • Autumn crocus • Glory Lily • Flower bulbs (amaryllis, paper whites, spring-blooming crocus, Narcissu, daffodil, iris, tulip. • English Ivy • Non-steroidal anti-inflammatory drugs • Zinc • Iron • arsenic • pyrethrin • snake venom • vitamin D
Dyspnea • Aspiration of petroleum distillates • Anticoagulant rodenticides (pulmonary or pleural hemorrhage) • Paraquat • Smoke inhalation • Carbon monoxide inhalation • Glyphosate ("ROUND-UP") (pulmonary edema, metabolic acidosis)	**Acute Hepatic Failure** • Aflatoxins • Amanita (mushroom) toxin • Idiosyncratic drug reaction • Zinc • Iron • Selenium • Blue-green algae • Phosphorus • Acetaminophen (cats) • Pennyroyal oil (herbal flea control) (dogs)	**Anemia/hemorrhage** • Anticoagulant rodenticide • NSAIAs • Zinc • Onion	

TABLE 4. Suggested List of Antidotes for an Emergency Clinic to Carry

TOXIN	ANTIDOTE	DOSE
Ethylene glycol (dogs)	4 methylpyrazole, fomepizole	Dogs: 20 mg/kg IV, then 15 mg/kg IV q12h x 2 doses, then 5 mg/kg IV at 36h
Ethylene glycol (cats & dogs)	Ethanol (p. 656)	Dogs: 5% ethanol, 10 mL/kg IV q4h x 24h, then q6h x 24h OR CRI at 2.5 mL/kg/h Cats: 5% ethanol CRI of 2.5 mL/kg/h
Acetaminophen, other oxidant injury	Acetylcysteine	140 mg/kg initially, then 70 mg/kg IV q4h x 12–24h
Organophosphatee	Atropine	0.2–0.5 mg/kg: ¼ dose IV, balance IM or SC
Cholecalciferol	Calcitonin (p. 375)	4 – 6 IU/kg SC q2–3h until serum calcium levels are normalized
Zinc, lead	Calcium EDTA	25 mg/kg SC q6h x 2–5 days, diluted in 5% dextrose
Iron	Deferoxamine	10 mg/kg IM or IV q8h for 24h
Metaldehyde	Methocarbamol (injectable)	55 – 220 mg/kg IV: Give half, then administer to effect. Do not exceed 330 mg/kg/day.
Anticoagulant rodenticide	Vitamin K1	2.5 – 5.0 mg/kg SC, PO. Duration and dose variable with the anticoagulant

TABLE 5. Calculation Help

- 1 mL of liquid (water density) weighs 1 g

- If a liquid, the concentration is usually weight/volume (e.g., mg/mL, μg/L)

- If a solid, the concentration is usually weight/weight (e.g., mg/g, mg/kg)
Concentration may be expressed as part per million (ppm), part per billion (ppb), or part per trillion (ppt)
   One ppm = 1000 ppb = 1,000,000 ppt
   ppm = mg/kg for solids
   ppm = mg/L for liquids

- Concentration may be expressed as % (g/100 g or g/100 mL)
  Converting % to mg/g, or mg/mL
Rule of thumb: move the decimal place on the percentage one to the right to get mg/g or mg/mL .
   1% = 1 g in 100 g solid, or 1 g in 100 mL liquid
    = 1000 mg in 100 g solid, or 1000 mg in 100 mL liquid
    = 10 mg in 1 g solid, or 10 mg in 1 mL liquid

- Concentration may be expressed as mg%
   1 mg% = 1 mg/100 g solid, or 1 mg/100 mL liquid
   Given that 100 mL = 1 dL, mg% represents mg/dL

- Concentrations may be in mEq/L
   mg/mEq = (Atomic weight/Valence of element)
   Converting mEq/L to mg/L
   mg/L = (mEq/L x Atomic Weight)/Valence

- Concentration may be in "proof" (alcohol)
   One proof = 0.5% alcohol
   e.g., 100 proof is 50% alcohol

Useful Equivalents

1 oz = 29.6 mL	1 grain = 65 g	1 tbsp = 15 mL	1 mL = 0.034 oz
1 lb = 0.454 kg	1 tsp = 5 mL		1 kg = 2.205 lb

PHARMACOLOGY

1) **Apomorphine** acts centrally at the chemoreceptor trigger zone, through stimulation of dopaminergic receptors.

2) **Medetomidine and xylazine are alpha2 agonists, acting at the chemoreceptor trigger zone.**

3) **Sorbitol 70% solution 1-3 mL/kg** (available in U.S.A.) Sorbitol is a non-absorbable sugar, which has an osmotic effect in the intestinal tract. It is considered the cathartic of choice in human medicine. Do not repeat.

4) **Lactulose 0.5 – 1.0 mL/kg PO.** No published dose for catharsis. Lactulose is also a non-absorbable sugar, and has been suggested for use as a cathartic. It has the advantage of being readily available in most veterinary clinics.

SUGGESTED READING

1. Current Veterinary Therapy, Editions X, XI, XII, XIII.
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4. The 5 Minute Toxicology Consult, Lippincott, Williams & Wilkins; 2000. Oriented for human medicine, but comprehensive data source on many toxins.
5. The 5 Minute Veterinary Consult Canine and Feline, LP Tilley, FWK Smith Jr ,3rd Edition, Blackwell Publishing; 2003.
6. Veterinary Clinics of North America, Small Animal Practice; 2002.

NOTES

INTRODUCTION

This chapter reviews the sources, mechanisms of action, toxic doses, clinical signs, diagnosis and management of specific emergencies encountered in veterinary practice; heavy metals, household food products, insecticides, pesticides and rodenticides, commonly administered over-the-counter and prescription drugs and recreational drugs. Refer to the previous chapter for general approach to known or unknown toxicities, decontamination procedures, poison control contacts and reference material.

I. HEAVY METALS

A. IRON TOXICOSIS

Sources
Human pregnancy supplements containing iron, multi-vitamins, general dietary supplements, and mineral-fortified fertilizers. The oral products are over the counter and sugar-coated and hence, highly palatable.

Mechanism of action
Iron salts are corrosive and cause hemorrhagic necrosis, and can accumulate in high concentrations as they dissolve in the stomach. Free circulating iron penetrates cells of the liver, heart and brain, causing hepatic damage, myocardial failure and seizures, respectively. The cardiovascular system is most profoundly affected. Metabolic acidosis develops from accumulation of lactic acid and release of hydrogen ions during the oxidation of ferrous ion to ferric ion with free radical generation and lipid peroxidation of cellular membranes.

Toxic dose
Amount ingested not the type of iron salt, determines the degree of toxicosis. Doses extrapolated from humans to dogs: <20 mg/kg is nontoxic, 20 mg/kg – 60 mg/kg mild to moderate toxicity, >60 mg/kg severe toxicity and doses >100 – 200 mg/kg are potentially lethal.

Clinical Signs
- Depression, vomiting, hematemesis, diarrhea, bloody stools, tremors, shock and death.
- The clinical signs of acute iron toxicosis are divided into 4 stages:
  - **Stage I:** 0–6h: nausea, vomiting, diarrhea, gastrointestinal hemorrhage.
  - **Stage II:** 6–24h: apparent clinical recovery.
  - **Stage III:** 12–96h: severe lethargy, recurrence of the GI signs, metabolic acidosis, liver necrosis, cardiovascular collapse, shock and occasionally death.
  - **Stage IV:** 2–6 weeks: gastrointestinal ulcerations heal, resulting in scarring and stricture formation and possibly gastrointestinal obstruction.

DIAGNOSIS

- **CBC** and **biochemical profile** may reveal leukocytosis and hyperglycemia.
- **Abdominal radiographs** may reveal ingested tablets.
- **Serum iron concentration and total iron-binding capacity** definitively diagnoses iron toxicosis. Measuring iron concentration at 4 – 6 hours post-ingestion is ideal as the tablets may dissolve at variable rates and the serum concentration may change dramatically in the first few hours because of the kinetics of metabolism.

MANAGEMENT

A. *See Toxicological Emergencies p. 632* for gastric decontamination, as soon as possible after ingestion. Activated charcoal does not bind iron well. Other lavage fluids recommended include sodium phosphate or sodium bicarbonate.

B. Emergency laparotomy and gastrotomy may be needed for removal of large quantities of pills adhered to the mucosa or embedded in a bezoar.

C. General critical care management is required. Chelation with desferoxamine is recommended in severe iron toxicosis. Chelation therapy should be started as soon as possible and given as a CRI IV at 15 mg/kg/h. More rapid infusion can cause cardiac arrhythmias and potentiate or aggravate existing hypotension. Alternatively, administer Desferoxamine IM at 40 mg/kg every 4 – 8h. Chelation for 2 – 3 days of therapy may be required until serum iron levels decrease below 300 mg/dL or the total iron binding capacity, whichever is lower. After the GI tract is cleared of iron, ascorbic acid (Vitamin C) 20 – 30 mg/kg PO 4 – 6 times daily can be given to increase the efficacy of desferoxamine.

D. Monitor for signs of gastrointestinal absorption for up to 6 weeks after ingestion.

B. LEAD TOXICOSIS

Sources
Lead may be present in a variety of sources including paints, old wallpaper, foodstuffs stored in containers with lead base, vegetables grown in lead saturated soils, and is present in discarded batteries, lead weights and lead shots.

Mechanism of action
Mechanisms for the neurotoxic effects include interference with the action of γ-aminobutyric acid (GABA), capillary damage, and neuronal necrosis in the CNS. The gastrointestinal effects may be secondary to neurotoxicity.

Toxic dose
800 – 1000 mg/kg. Toxicity depends on the type of lead salt. Repeated doses can cause acute poisoning.

Clinical Signs
- Acute: vomiting, diarrhea, anorexia and abdominal pain. Subsequent neurological signs: hyperexcitability, seizures, opisthotonus, blindness, lethargy, paralysis. Death can occur in several days.

DIAGNOSIS

- **CBC.** Anemia and basophilic stippling (prominent in dogs). **Abdominal radiographs** may reveal ingested lead objects, **serum lead concentrations** >0.4 ppm suggests toxicity.

MANAGEMENT

A. Gastric decontamination (*see Toxicological Emergencies p. 632*). Emergency laparotomy and gastrotomy may be needed for removal of lead objects. General critical care support. Chelation with **calcium EDTA, 25 – 50 mg/kg dissolved in 0.9% NaCl or D5W** given IV slowly, this dose can be repeated 2 – 3 times daily.

B. A newer chelating agent, **2,3-dimercaptosuccinic acid (DMSA)** or Succimer (Chemet, McNeil Consumer Products) **is preferred** to calcium EDTA as it can be given while lead is still in the gastrointestinal tract. It is also less likely to cause zinc toxicity, has a lesser risk of nephrotoxicity than CaEDTA and comes in an oral form. Recommended dose 10 mg/kg PO q8h for 10 days or per rectum if animal is vomiting.

C. Rebound can occur post-chelation as lead stores are redistributed from bone and tissue in animals with chronic lead poisoning. Repeat therapy for another 10 days, especially if animal is symptomatic.

C. MERCURY TOXICOSIS

Sources
- **Inorganic:** *Elemental mercury* found in thermometers, barometers, small storage batteries and mercurial salts in preservatives, fixatives and ointments (e.g., mercuric oxide)
- **Organic:** *Alkyl mercurials* (e.g., methyl and ethyl mercury) in fungicides and *aryl mercurials* (e.g., phenyl mercuric acetate) found in anti-mildew paints.
- Other sources include mercury in marine fish, burning coal, and sewage sludge containing industrial wastes. Chronic and acute poisoning is rare because of limited availability of obsolete mercurial products; usually ingestion is accidental in dogs and cats.

Mechanism of action
- **Inorganic mercury** can be inhaled or ingested. Mercury vapor is lipid-soluble and absorbed by inhalation. Ingested elemental mercury and mercurial salts are slowly absorbed from the gastrointestinal tract and accumulate in the renal cortex where direct tissue and renal tubular necrosis occurs. Excretion occurs in urine.

- **Organic alkyl mercurials** are lipophilic and highly absorbed by the gastrointestinal mucosa. Excretion occurs mainly in bile and feces. The toxicologic effects are prevention of synthesis of essential proteins leading to cellular degeneration and necrosis, especially in the brain.
- All forms of mercury are teratogenic.

Toxic dose

Toxicity depends on the form and amount of mercury ingested. Continuous toxic exposure occurs with doses of 0.2 – 5.0 mg/kg body weight of methyl mercury.

Clinical Signs

- Acute toxicosis with mercurial salts include stomatitis, pharyngitis, vomiting, diarrhea, dehydration and shock. Death may occur within hours. Oliguria and azotemia lasts 1 – 2 days if animals survive acute mercuric ion toxicosis. Signs seen with alkyl mercurials develop slowly over 7 – 21 days. Early signs include erythematous skin, conjunctivitis, lacrimation and stomatitis. Intermediate signs include depression, ataxia, incoordination, paresis and blindness. Dermatological signs progress over the course of the disease and include dermatitis, ulcers and pustules. Hematuria and melena may also occur. Advanced clinical signs are proprioceptive deficits, abnormal postures, paralysis, blindness, anorexia and slowed respiration rate. Mortality rate is very high in this stage.

DIAGNOSIS

- **Abdominal radiographs, blood and urine mercury concentrations.**
- **Histopathologic lesions include** ulcerative, necrotic enteritis and colitis. Pale, swollen kidneys with renal tubular necrosis.
- Cerebellar hypoplasia in kittens born to cats exposed to mercury.

MANAGEMENT

A. Egg white or activated charcoal to inactivate ingested mercury. Oral sodium thiosulfate (0.5 – 1.0 g/kg body weight) also binds mercury. Saline cathartic or sorbitol promotes clearance from the gastrointestinal tract.

B. (DMSA *see B p. 642*) may be effective in increasing urinary excretion of inorganic mercurials.

C. Supplemental selenium and vitamin E may be protective against methyl mercury toxicosis.

D. ZINC TOXICOSIS

Sources

Zinc nuts from transport cages, zinc plumbing nuts, storage batteries, galvanized bars, pipes and wires, zinc game pieces from board games and American pennies minted after 1982, and zinc oxide ointment (Desitin).

Mechanism of action

Inhibition of specific biochemical enzymes and/or direct damage to cell membranes or organelles. Cells involved in the transport of metals, such as gastrointestinal, hepatic or renal tubular cells are particularly susceptible. Zinc is mainly excreted in the feces, however 25% is excreted in urine.

Toxic dose

Depends on the degree of intestinal absorption, the form of zinc salt and the pH of the gastrointestinal environment. The acidity of the stomach allows gradual release of zinc from objects.
Acute toxicity:LD_{50} of zinc salts is ~100 mg/kg body weight.

Clinical Signs

- Vomiting, anorexia, diarrhea. Severe intravascular hemolysis results in moderate anemia, icterus, hemoglobinuria, hematuria, generalized multiple organ failure and death.

- **CBC.** Increased nucleated red blood cells, basophilic stippling, target cells and polychromasia.
- **Biochemical profile.** Increased urea, creatinine, ALP, ALT and bilirubin.
- **Coagulation panel.** Supportive of disseminated intravascular coagulation, which include thrombocytopenia, prolonged PT/PTT and increased fibrinogen degradation products.
- **Measurement of serum zinc levels.** Be careful to avoid zinc contamination from the syringe or vial. Normal canine serum zinc range is 0.7 – 2.0 μg/mL.

MANAGEMENT

A. General critical care management followed by rapid removal of zinc object by endoscopy or laparotomy. The rate of release and absorption of zinc depends on acidity of the stomach; use an acid-lowering agent e.g., famotidine. Prevention of acute renal failure (*p. 709*). Metal chelators such as calcium EDTA 25 mg/kg (diluted in 5% dextrose to reduce irritation when injected) SC q6h should be given immediately after the diagnosis of zinc toxicity has been made. CaEDTA can be nephrotoxic, so hydration status must be maintained adequately. Duration of therapy may be days to weeks until serum zinc levels normalize.

II. HOUSEHOLD FOOD PRODUCTS

A. ALCOHOL

Sources
Ethanol toxicosis occurs following ingestion of raw dough/sourdough containing baker's or brewer's yeast, and ethanol containing beverages. (Non-edible products such as dermal absorption of ethanol-containing shampoos, methanol in automotive windshield fluid antifreeze and other similar products).

Mechanism of action
Ethanol is metabolized to acetaldehyde by alcohol dehydrogenase and subsequently to acetone by aldehyde dehydrogenase. Methanol is metabolized by alcohol dehydrogenase to formaldehyde initially and to formic acid by alcohol dehydrogenase.

Toxic dose
Dogs: 4 – 8 g/kg ethanol or methanol.

Clinical Signs
- Appear within one hour of ingestion and are similar to those seen with ethylene glycol ingestion (*p. 655*), e.g., depression and ataxia, vocalization and excitability, hypothermia, and respiratory and/or cardiac arrest.

DIAGNOSIS

- **Blood gases** reveal a metabolic acidosis due to acetate or formate formation.
- **Blood alcohol levels** can aid in diagnosis.

MANAGEMENT

A. *See Ethylene Glycol Toxicity p. 655.*

B. HOMEMADE PLAY DOUGH

Sources
A salt-flour mixture used to make ornaments. Approximately 8 g of salt is contained in 1 tbsp of play dough. An estimated toxic dose of salt is 2 g/kg and lethal dose is 4 g/kg.

Mechanism of action
An increase in serum sodium concentration >170 mEq/L results in early signs of toxicity with severe signs occurring at >180 mEq/L. The central nervous system is the most vulnerable. (*see Hypernatremia p. 381*).

Clinical Signs
- Vomiting, diarrhea, polydipsia, polyuria, abdominal pain, fasciculations, tremors, seizures, tachycardia, hyperthermia, dehydration, recumbency, acidosis.

DIAGNOSIS

- *See Hypernatremia p. 381.*

Treatment
Emesis may be induced if ingested within 30 minutes and is asymptomatic for CNS signs. Feeding a small moist meal prior to inducing vomiting may increase the chances of emesis. Emesis may be induced with 1 tsp/2.5kg (~5 lbs) 3% hydrogen peroxide **NOT** to exceed 3 tbsp. Apomorphine is preferred. Activated charcoal is of no value. Offer small amounts of water frequently to those mildly affected. For severely hypernatremic patients *see Hypernatremia p. 384.*

C. XYLITOL

Sources
A sugar alcohol, used in the making of sugar-free products, gums and candies, and baked foods.

Mechanism of action
In dogs, unlike in humans, xylitol produces a rapid, dose-dependent increase in insulin levels and significant lowering of blood glucose.

Clinical Signs
- Vomiting, weakness, lethargy, ataxia, depression, hypokalemia, seizures and coma.
- Liver dysfunction or failure may develop in dogs following ingestion of xylitol.

DIAGNOSIS

- **Blood glucose** is decreased within 30 minutes of ingestion. Hypokalemia (*p. 394*) may also occur.

MANAGEMENT

A. *See Toxicological Emergencies p. 633* for details on inducing emesis. The risk of vomiting and aspiration is higher when signs of hypoglycemia (*p. 280*) are evident. Efficacy of activated charcoal is unknown.

B. Frequent small meals and oral sugar supplementation may be needed for dogs that are not symptomatic.

D. AFLATOXICOSIS

Sources
Peanuts, corn and cottonseed meal. *Aspergillus flavus* and *A. parasiticus* on the food, produce the aflatoxins. Warm temperatures (>30°C) and high relative humidity favors aflatoxin production.

Mechanism of action
Natural aflatoxins are designated as B_1, B_2, G_1, G_2 and M_1, M_2, which can be found in milk of which aflatoxin B_1 is the most potent. Epoxides, highly reactive intermediate metabolites, are produced which react with RNA, DNA and cellular proteins resulting in inhibition of protein synthesis.

Toxic dose
Dogs and cats: LD_{50} 0.5 to 10 mg/kg body weight. Younger animals are more susceptible.

Clinical Signs
- Hepatotoxicity is the most well defined syndrome seen including anorexia and icterus (hepatic lesions can include pale liver, bile duct hyperplasia, acute hepatic necrosis and hemorrhage). Other syndromes such as teratogenicity, immunotoxicity and carcinogenesis can also occur.

- **History** of consumption of suspected contaminated feed and clinical signs.
- **Biochemical profile.** Decreased albumin, increased serum bilirubin, ALP, ALT, AST.
- **Histopathology.** Centrilobular necrosis and bile duct hyperplasia.
- **Chemical analysis.** Mass spectrometry, gas and liquid chromatography, thin-layer chromatography on samples of suspected feed.
- **Tissue analysis.** Liver and kidney have measurable residual levels of aflatoxin.

MANAGEMENT

A. Gastric decontamination, *see Toxicological Emergencies p. 632.*
B. Supplemental **vitamin E and selenium** may ameliorate the effects of aflatoxins. **Hydrated sodium calcium aluminosilicate (HSCAS)** has a high affinity for aflatoxin reducing absorption from the gastrointestinal tract.
C. Symptomatic and supportive care.

E. GRAPE AND RAISIN NEPHROTOXICITY

Sources
Red and white varieties of grape, as well as organic products. Grape crushings, or fermented grapes from wineries have also caused renal toxicity in dogs. Raisins of any kind are also potentially toxic.

Mechanism of action
Ochratoxin, associated with the ingestion of grapes, has been implicated to cause renal failure in dogs. Other potential mechanisms include an inability to process flavinoids, tannins and excessive monosaccharides.

Toxic dose
0.41 – 1.9 oz/kg body weight. Lowest documented dose of grapes is 0.7 oz/kg and 0.11 oz/kg for raisins.

Clinical Signs

- Dogs, cats and ferrets. Vomiting and lethargy occur within 6 hours of ingestion. Anorexia, diarrhea, lethargy and abdominal pain. Oliguria or anuria within 24 – 72 hours. Fatality ranges from 50% – 75%.

DIAGNOSIS

- **Biochemical profile** results support renal failure.
- **Histopathological findings** include proximal renal tubular necrosis with tubular regeneration, metastatic mineralization of numerous tissues, including gastric mucosa, myocardium, lung and blood vessel walls.

MANAGEMENT

A. *See Toxicological Emergencies p. 632* for induction of emesis and gastric decontamination for dogs that consume large quantities of grapes or raisins. Follow with IV fluid diuresis for 48 hours after ingestion.
B. Dogs that become oliguric or anuric (*p. 709*), require peritoneal dialysis (*p. 723*) or hemodialysis.
C. Symptomatic therapy for vomiting and diarrhea.

F. METHYLXANTHINE ALKALOIDS

Sources
Caffeine, theophylline and theobromine are methylated xanthines found in **coffee, tea and chocolate** respectively, and over the counter stimulants containing 100 – 200 mg of caffeine/tablet.

Mechanism of action
Methylxanthines are rapidly absorbed orally and distributed throughout the body. Methylxanthines stimulate the central nervous system and cardiac muscle, promote diuresis and induce smooth muscle relaxation. They inhibit intracellular calcium sequestration resulting in increased skeletal and cardiac muscle activity. Methylxanthines increase sensitivity of the sensory cortex and mental alertness. Larger doses enhance motor activity and responsiveness to normal stimuli.

Toxic dose

Dogs: caffeine and theobromine: 100 – 200 mg/kg; theophylline – 300 mg/kg.
Cats: caffeine and theobromine: 80 – 150 mg/kg; theophylline – 700 mg/kg.

Clinical Signs

- Restlessness, hyperactivity and mild hyperreflexia. Urinary incontinence or diuresis. Vomiting and diarrhea, especially with chocolate toxicosis.
- Later signs: Excessive hyperactivity, muscle twitching, hyper-reflexia, tonic to tetanic convulsive seizures, tachypnea, tachycardia and hyperthermia.

DIAGNOSIS

- History and analysis of stomach contents, serum or urine for the presence of alkaloids.

MANAGEMENT

A. *See Toxicological Emergencies p. 682* for details on emesis followed by activated charcoal and osmotic cathartics. Emesis is contraindicated if the animal is experiencing hyper-reflexia or seizures.
B. Control seizures (*see Seizures in Dogs p. 460 and Seizures in Cats p. 456*). Acidification of urine to promote urinary excretion.
C. Tachycardia can be controlled with lidocaine, or beta-blockers.

G. ONION AND GARLIC (*ALLIUM* SPP)

Sources

Onions, garlic and chives (members of the *Allium* family). All parts of the plants are toxic. Dried and powdered plant material, e.g., onion powder, are also potentially toxic. Garlic is least toxic.

Mechanism of action

Active toxic agent is N-propyl disulfide, which is believed to cause oxidative damage to erythrocytes and hemoglobin denaturation resulting in Heinz body formation and acute hemolysis. Cats are more susceptible than dogs, with Akitas and Shiba Inus more susceptible than other dog breeds.

Toxic dose

Dogs: 5.5 g dehydrated onions/kg body weight and 8.75 g minced onions/kg body weight.
Cats: even a small amount of baby food containing onion powder.

Clinical Signs

- Hemolytic anemia and methemoglobinemia develop within 6–24h. Methemoglobinemia manifests as dyspnea, weakness and cyanosis. Icterus and hemoglobinuria may occur with hemolytic anemia. Low-grade, chronic exposure also results in anemia, with or without methemoglobinemia. Most common clinical signs are vomiting and diarrhea, tachypnea and tachycardia.

DIAGNOSIS

- **CBC** reveals anemia with Heinz body formation.
- **Biochemical profile** shows increased bilirubin and elevated liver enzymes.

MANAGEMENT

A. *See Toxicological Emergencies p. 632* for details on induction of emesis and lavage, followed by activated charcoal.
B. Fluid and electrolyte support.
C. Blood transfusions may be necessary in cases of severe hemolytic anemia.
D. Oxygen support for methemoglobinemia may be needed.

III. INSECTICIDES AND PESTICIDES

A. ANTICHOLINESTERASE INSECTICIDES: ORGANOPHOSHATES & CARBAMATES

Sources
Organophosphate products: diazinon, chlorpyrifos, fenthion, coumaphos, disulfoton and terbufos.
Carbamate products: aldicarb, methomyl, carbofuran, propoxur, and carbaryl.
Formulations. Sprays, pour-ons, oral anthelminthics, baits (fly, ant, roach), flea collars, dips, dusts and powders.

Mechanism of action
Organophosphates and carbamates competitively inhibit acetylcholinesterase (AChE) resulting in accumulation of acetylcholine at the synaptic junction with excessive neurotransmitter activity in the parasympathetic (cholinergic or muscarinic) and neuromuscular (nicotinic) sites. Organophosphates cause irreversible binding and carbamates reversible binding, to AChE.

Toxic dose
1 – 20 mg/kg; cats are more susceptible than dogs. Ingestion of stomach contents from a dead animal can also be toxic.

Clinical Signs
- **Muscarinic signs** include excessive salivation, lacrimation, urination and defecation, vomiting, dyspnea, miosis and bradycardia. Sympathetic stimulation may mask the muscarinic signs and cause mydriasis and tachycardia. Dyspnea is caused by increased bronchial secretions, bronchoconstriction and decreased contraction of the respiratory muscles.
- **Nicotinic signs** include muscle tremors, twitching, weakness and paresis progressing to paralysis. Hyperactivity and seizures occur with ingestion of high dosages of highly toxic compounds such as disulfoton or methomyl. Seizures may occur prior to or without the nicotinic and muscarinic signs.

DIAGNOSIS

- Only interpret AChE activity with a normal reference value from the test laboratory as there are many different methods to test the activity, which also varies among species.

Atropine response test
Crucial if an animal presents with signs suggestive of organophosphate/carbamate exposure but no known insecticide toxicosis. Use a preanesthetic dose of atropine 0.02 mg/kg IV for dogs and cats and monitor the response closely. If tachycardia or mydriasis occurs, then it is likely NOT organophosphate or carbamate toxicosis, as it takes 10 X this atropine dose to resolve the muscarinic signs due to insecticides.

MANAGEMENT

A. Stabilize and control seizures (*see Seizures in Dogs p. 460, Seizures in Cats p. 456*). *See Toxicological Emergencies p. 632* for induction of emesis and administration of activated charcoal and removal of topical insecticides. For highly toxic compounds (methomyl, disulfoton) **do not** induce emesis if the exposure is longer than ½ hour.

B. **To control the muscarinic signs; atropine sulfate 0.02 mg/kg,** give ½ dose IV and other ½ IM or SC. Repeat doses of atropine sulfate as needed, to control bradycardia & bronchial secretions. **Pralidoxime chloride** (2-PAM) **20 mg/kg IM q12h** preferably administered within 24h, forms a complex with the insecticide that is renally excreted and frees the AChE. Carbamate toxicosis does not respond to 2-PAM treatment because of the reversible binding to AChE.

C. **To control the nicotinic signs, oximes, pralidoxime chloride 20 mg/kg IM or SC** are used. Aging of organophosphates increases stability of the phosphorylated enzyme and renders the oximes ineffective. 2-PAM can be used for days after an exposure, but it may be cost-prohibitive.

D. Phenothiazine sedatives can **enhance the toxicity** of organophosphates. Neuromuscular agents such as succinylcholine and curare can **potentiate the nicotinic effects** of organophosphates.

B. INSECTICIDES: PYRETHROIDS

Sources
Natural pyrethrins are found in chrysanthemums and related plants. **Synthetic pyrethrins** are found in insecticidal products: permethrin, allethrin, fenvalerate, cypermethrin.

Formulations: sprays, spot-on products, shampoos and dips, used as insecticides and for flea control.

Mechanism of action
Pyrethrins are lipophilic and rapidly absorbed orally and dermally. Metabolism occurs in the gastrointestinal tract. Pyrethrins slow sodium conductance and suppresses potassium efflux in the axonal membrane of nervous tissue. Alterations of ATPase may also occur resulting in repetitive firing in sensory fibers.

Toxic dose
Great variation in the toxic dose, oral dose is 100 – 200 mg/kg. Highly toxic to cats.
Solvents in the formulations (e.g., alcohols, hydrocarbons) can increase absorption of pyrethins.

Clinical Signs
- Onset of clinical signs is minutes to hours, depending on the route of intoxication. Hypersalivation, twitching, hyperesthesia, lethargy, mild vomiting and diarrhea. Severe toxicosis causes protracted and severe vomiting and diarrhea, depression, ataxia, severe muscle tremors and seizures. Death may occur within 1 – 3 days of exposure.

DIAGNOSIS

- Analysis of urine and plasma to detect exposure, is available for only some pyrethroids.
- **CBC** may reveal a stress leukogram.
- **Biochemical profile** may reveal hyperglycemia.

MANAGEMENT

A. No specific antidote is available.
B. Stabilize and control seizures (*see Seizures in Dogs p. 460 and Seizures in Cats p. 456*). **Methocarbamol, 55 – 220 mg/kg IV, not to exceed 2.0 mL/min and a maximum dose of 330 mg/kg/day** for tremors.
C. Atropine should be avoided as it can increase CNS stimulation in large doses.
D. *See Toxicological Emergencies p. 632* for details on induction of emesis and administration of activated charcoal, and removal of topical products.

C. METALDEHYDE (SNAIL BAIT) TOXICITY

Sources
Snail and slug baits. Metaldehyde is a molluscicide formulated in pellets that can be mistaken for kibble.
Trade Names: Halizan, Meta-Fuel, Metason, Slug Death, Slugit Pellets.

Mechanism of action
Metaldehyde is metabolized to acetaldehyde and other metabolites which decrease GABA, norepinephrine (NE) and 5-hydroxytryptamine (5-HT).

Toxic dose
Dogs: LD_{50} 100 – 1000 mg/kg.
Cats: LD_{50} 200 mg/kg.

Clinical Signs
- Early behavioral signs include vocalization, anxiety and restlessness that progress to incoordination, ataxia, vomiting, diarrhea, mydriasis, salivation, nystagmus, tachypnea, tachycardia, cyanosis, opistothonus and muscle tremors, continuous convulsions with hyperthermia, respiratory and/or cardiac arrest.

DIAGNOSIS

- Analysis of stomach contents and vomitus for acetaldehyde.
- **Blood gases** may reveal metabolic acidosis from the formation of acetaldehyde.

A. Induction of emesis is contraindicated in hyperactive animals, or if any tremor is present as it can induce seizures. Emesis may be induced if toxin ingested within 30 minutes and the patient is asymptomatic. Feeding a small moist meal prior to inducing vomiting may increase the chances of emesis. Emesis may be induced with 1 tsp/2.5 kg (~5 lbs) 3% hydrogen peroxide **NOT** to exceed 3 tbsp. Apomorphine is preferred.

B. Administration of activated charcoal 1 – 3 g/kg plus cathartic therapy (70% sorbitol 3 mL/kg) or combined product, if ingestion was recent once. Repeat one-half of the charcoal dose only q4–8h if able to take oral medication.

C. No specific antidote, mostly symptomatic and supportive care. Muscle relaxants e.g., methocarbamol 55 – 220 mg/kg IV, half the dose given at 2 mL/min followed by the remaining dose, to control severe tremors. Methocarbamol may be repeated should signs re-appear, however do not exceed 330 mg/kg in a 24 hour period.

D. Constant monitoring of body temperature and cooling with fans and wet towels if ≥39.5°C. Signs may continue for several days. Liver enzymes may increase.

D. ANTICOAGULANT RODENTICIDE TOXICITY

Sources
Accidental or malicious exposure to anticoagulant rodenticide bait. Fewer than 10% of cases are exposed to short acting warfarin. Assume, if unable to the verify product, that patient was exposed to 2nd generation, longer-acting anticoagulant.

Mechanism of action
Depletion of active vitamin K_1 and impaired synthesis of active clotting factors II, VII, IX and X. Coagulopathy follows the depletion of active clotting factors, with a lag time of 3 – 5 days (can be as little as 24 hours) from the time of exposure to the time of clinical signs.

Toxic dose
Dogs and Cats: LD_{50} variable depending on the compound.

Clinical Signs
- Hemorrhage from any site: epistaxis, hemoptysis, hematomas, melena, hematuria, petechiation, lameness (hemorrhage into a joint), lethargy / pallor / weakness / dyspnea due to bleeding into the thorax, abdomen or lungs.

DIAGNOSIS

- History of exposure and clinical signs.
- **Coagulation profile.** Markedly prolonged PT (prolonged first) and prolonged PTT or activated clotting time (ACT).
- **CBC.** Anemia +/- thrombocytopenia noted.
- **Biochemical profile.** Hypoproteinemia, decreased albumin and globulin.
- Cross-match.
- **Thoracic radiographs** for evidence of pleural effusion or pulmonary hemorrhage.
- **Abdominal radiographs or ultrasound** for evidence of hemoabdomen.
- Reduction in coagulation parameters 12 – 24 hours after initiating vitamin K_1 therapy.

MANAGEMENT

Differs based on **recent exposure** versus **presentation at time of hemorrhage.**
Recent exposure (within 12 hours of presentation) and no signs of hemorrhage:

A. Decontamination procedures recommended (*see Toxicological Emergencies p. 630*).

B. Initiate vitamin K_1 therapy based on estimate of lag time between exposure and presentation, exposure dose, and success of decontamination procedures.

C. If Vitamin K_1 therapy not initiated, PT should be checked at 24 – 36 hours and again at 96 hours after exposure to ensure normal coagulation.

Presented with signs of hemorrhage:

A. Immediate restoration of clotting factors with fresh or stored whole blood (*see p. 673 for volume calculation*) if significant hemorrhage, especially into a non-compressible space (pleural space, lungs, abdomen), or plasma administered at 10 mL/kg. Whole blood selected if marked anemia noted (PCV <25%).

B. Vitamin K_1, initial dose for 2nd generation anticoagulant rodenticide is 2.5 – 5 mg/kg SC. Significant synthesis of new clotting factors requires 6 – 12 hours from the time of initiating vitamin K_1 therapy.

C. Intravenous crystalloid fluids to maintain cardiovascular support and supplemental oxygen where indicated.

D. Thoracocentesis if hemothorax impairs oxygenation/ventilation. Plasma transfusion is necessary to prevent further hemorrhage due to thoracocentesis.

E. Continued therapy for rodenticide coagulopathy is Vitamin K_1 1.25 – 2.5 mg/kg PO q12h with food. Exercise restriction is mandatory until coagulation parameters are normal after discontinuation of Vitamin K_1. It is important to identify the potential toxin as treatment duration is based on:

    1. Warfarin 7 days.

    2. Diphacinone and indanediones 3 – 4 weeks.

    3. Brodifacoum and bromodiolone 4 – 6 weeks.

    4. Unknown should be assumed to be either 2 or 3 and treated for 3 weeks, followed by 5.

    5. For 1 – 4 the PT should be tested 48 hours after last Vitamin K_1 treatment. If it is prolonged, continue treatment for a further 2 – 3 weeks and re-test. As a range is suggested, a reduction to the lower dosage may be effective at this time. If PT not prolonged, repeat in 96 hours for confirmation.

IV. OVER THE COUNTER AND PRESCRIPTION DRUGS

A. ACETAMINOPHEN (or Tylenol®)

Sources

Most common source is accidental, or intentional ingestion in dogs and cats by owners who are not aware of the toxic effects. Regular strength tablets are 325 mg and extra-strength tablets are 500 mg.

Mechanism of action

Acetaminophen is metabolized to reactive metabolites (N-acetyl-p-benzoquinone) in hepatocytes which cause cellular damage and hepatic necrosis. Oxidizing metabolites accumulate and methemoglobin forms, reducing the oxygenation of blood. Hemoglobin becomes denatured and attaches to the erythrocyte membranes leading to Heinz body formation.

Toxic dose

Cats: 50 – 100 mg/kg

Dogs: 600 mg/kg

Cats are more susceptible than dogs as they have a relative deficiency in glucuronyl transferase and limited ability to conjugate glucuronides.

Clinical Signs

- Initially, nonspecific and include vomiting, diarrhea, anorexia, depression and weakness. Cyanosis develops within 4 – 12 hours because of methemoglobinemia. Edema of face and paws in cats, lacrimation, pruritus, anorexia and depression. Hepatotoxicity develops in severe cases; *see Acute Liver Failure/Dysfunction p. 37.*

DIAGNOSIS

- **CBC.** Chocolate-coloured blood. Heinz body formation and hemolytic anemia, especially in cats.
- **Biochemical profile.** Albumin is decreased, ALP, ALT and serum bile acids are increased.
- **Histopathology** shows centrilobular hepatic necrosis and bile duct hyperplasia.

MANAGEMENT

A. *See Toxicological Emergencies p. 632* for induction of emesis, gastric lavage and administration of activated charcoal.

B. **Antidote** is **N-acetylcysteine (NAC) 280 mg/kg PO or IV** in 5% dextrose. Start at half this dose for less severe cases. Intravenous infusion of NAC is administered over 20 – 30 minutes. NAC reduces oxidative injury to the liver caused by acetaminophen. Additional doses of NAC are administered at 70 mg/kg PO q6h for six additional doses after the loading dose.

C. Ascorbic acid may also be used.

D. General critical care management.

E. Corticosteroids and antihistamines are **contraindicated.**

B. ANTIDEPRESSANTS

Sources

Dogs gain access to these drugs usually by ingesting their owners' prescription medications or their own antidepressant/anxiolytic medications. Four groups exist:

- Tricyclic antidepressants (TCA)
- Monamine oxidase inhibitors (MAOI)
- Selective serotonin reuptake inhibitors (SSRI)
- Atypical antidepressants. The predominant group is the SSRI.

Mechanism of action

- Tricyclic antidepressants – not fully understood, block reuptake of norepinephrine and serotonin at presynaptic membranes, e.g,. amitriptyline (ELAVIL®) and clomipramine (CLOMICALM®).
- Selective serotonin reuptake inhibitors – block reuptake of serotonin at postsynaptic membrane; increase brain serotonin levels, e.g., fluoxetine (PROZAC®), Paroxetine (PAXIL®), Sertraline (ZOLOFT®).
- Monamine oxidase inhibitors – inhibit MAO. MAO normally functions in the catabolism of CNS neurotransmitters, such as serotonin, dopamine and norepinephrine. The main effect may also be on dopamine in the CNS, e.g., selegiline (ANIPRYL®), Phenelzine (NARDIL®).
- Atypical antidepressants – mechanism varies, alteration of neurotransmitter in the CNS, e.g., buproprion (WELLBUTRIN®), buspirone (BUSPAR®).

Toxic dose

- The mechanism of action varies but the clinical signs are similar; at low doses lethargy is seen, while at higher doses CNS stimulation may occur.
- TCAs: very narrow therapeutic range; signs can be seen at therapeutic doses.
- SSRIs: mild depression at lower doses (approx. 1 mg/kg); tremors, cardiac effects, and or serotonin syndrome possible at 10 mg/kg and greater.
- MAOIs: stereotypical behaviour possible after a therapeutic dose, and seen with 3 mg/kg selegiline.
- Buproprion: vomiting and depression at 5 mg/kg.

Clinical Signs

- **SSRIs and TCAs,** in particular, cause serotonin syndrome, which is manifested as central, autonomic and neuromuscular signs. In descending order they include: vomiting, diarrhea, seizures, hyperthermia, hyperesthesia, depression, mydriasis, vocalization, blindness, hypersalivation, dyspnea, ataxia/paresis, disorientation, hyper-reflexia, coma and death. Clinical signs can occur within 30 minutes to several hours, if extended release products are consumed. They can last for 12 to 72 hours in severe cases.
- **MAOIs.** Vomiting, diarrhea, lethargy, pacing, agitation, seizures, hypersalivation.
- **Atypical antidepressants.** Vomiting, diarrhea, hypersalivation, ataxia, seizures, agitation, tremors, hypotension.

MANAGEMENT

A. *See Toxicological Emergencies p. 632* for induction of emesis, followed by activated charcoal. Emesis may be considered for the first 3 – 4 hours if extended release products were consumed. Activated charcoal effectively adsorbs antidepressants, especially the extended release products and TCAs that undergo enterohepatic recirculation. Repeated doses of activated charcoal may be needed if extended release products were consumed.

B. General critical care management.

C. Animals with tremors or muscle rigidity may respond to methocarbamol (*see Metaldehyde above*).

D. Bradycardia, tachycardia or conduction abnormalities (*see appropriate chapter*). Propanolol 0.02 – 0.06 mg/kg IV over 2 – 3 min q8–12h has some serotonin blocking effects and may be useful in animals with tachycardia.

E. CNS stimulation may be managed with diazepam, phenothiazines or other sedatives. *See Seizures in Dogs p. 460 and Seizures in Cats p. 456* if present. Cyproheptadine at 1.1 mg/kg PO (**dogs**) or at 2 – 4 mg PO (**cats**) can be used in cases of suspected serotonin syndrome, to alleviate signs of hyperthermia and CNS stimulation. When the oral route is not feasible (e.g., severe vomiting, coma), cyproheptadine can be crushed in saline and instilled per rectum. Cyproheptadine can be repeated q1–6h as needed until signs have resolved.

Potential complications

Pulmonary edema (*p. 569*), rhabdomyolysis, renal failure (*p. 709*), and disseminated intravascular coagulation (*p. 417*) may occur in severe cases.

Prognosis

Overall, prompt, aggressive treatment should result in a full recovery, usually within 48 hours in uncomplicated cases. Prognosis depends on dose, treatment and exposure to other highly protein bound medications and the underlying health of the dog. Dogs with concurrent liver disease have delayed metabolism of these antidepressants and those with renal disease can have delayed excretion.

V. RECREATIONAL DRUGS

A. COCAINE TOXICITY

Sources

Cocaine is derived from the coca plant, *Erythroxylon coca* or *E. monogynum*.

Freebase is chemically extracted pure cocaine alkaloid. Street cocaine is usually combined with amphetamine, cocaine, lidocaine, quinine or even strychnine.

Mechanism of action

Cocaine inhibits neuronal reuptake of catecholamines and promotes catecholamine release. It is rapidly absorbed from the gastrointestinal tract, mucous membranes and lungs. The half-life is short (about 3 hours) and the parent compound and metabolites are excreted in the urine.

Toxic dose

Dogs and cats: Oral LD_{50} – 50 mg/kg; intravenous LD_{50} is ~12.5 mg/kg.

Clinical Signs

- CNS stimulation alternating with depression. Hyperesthesia, seizures, hypertension, and tachyarrhythmias, ventricular premature contractions.

DIAGNOSIS

- **Biochemical profile.** Hyperglycemia, increased ALT and creatine kinase may be seen.
- **Detection of cocaine metabolites in plasma or urine.** A true history may not be forthcoming and can be misleading or incomplete and can be problematic when making a diagnosis. A high index of suspicion is required.

MANAGEMENT

- **A.** Detoxification is relatively ineffective as the half-life is so short and the drug is rapidly absorbed.
- **B.** Respiratory support may be necessary.
- **C.** Anti-arrhythmic therapy treatment of arrhythmias by **non-selective beta-blockade must be avoided** as coronary vasoconstriction and hypertension secondary to unopposed alpha-stimulation may occur. **Selective beta-1 agents** (e.g., esmolol) or agents with some alpha-blocking activity (e.g., labetolol) are therefore recommended for use. Since lidocaine and cocaine both inhibit fast sodium channels in excitable membranes it is possible that **lidocaine may aggravate cardiac toxicity of cocaine** and may also potentiate cocaine-induced seizures. External cooling and sedation with acepromazine should control hyperthermia.

B. MARIJUANA (*CANNABIS SATIVA*) TOXICITY

Sources

Marijuana is in the dried leaves and flowers of the hemp plant, *Cannabis sativa*. **Hashish** is the resin extracted from the hemp plant. The active ingredient in marijuana is tetrahydrocannabinol (THC). Most common sources are ingestion of the owner's supply intentionally or unintentionally, consumption of baked goods containing tetrahydrocannabinol (THC) and hashish oil.

Other names

Hemp, Mary Jane, grass, pot, weed, and hashish.

Mechanism of action

THC is rapidly absorbed from the gastrointestinal tract and the smoke is rapidly absorbed via the lungs. Enterohepatic recirculation maintains the drug levels and production of hepatic metabolites, which are excreted in ~24 h.

Toxic dose

Dogs are more likely to ingest toxic doses of marijuana than cats.

Dogs: LD_{50} 3 g/kg.

Cats: LD_{50} 200 mg/kg.

Clinical Signs

- Depression, ataxia, incoordination and nystagmus. More dramatic CNS signs include alternating behavioral changes between depression and excitement and hallucinations, manifested as barking and agitation without external stimulation.
- Vomiting, dry mucous membranes, hypothermia or hyperthermia, tachypnea and bradycardia may also be present.

DIAGNOSIS

- History of exposure, clinical signs and detection of THC in plasma or urine. Histories can be misleading or incomplete and can be problematic to obtain accurately.

MANAGEMENT

A. Induction of emesis is not always useful as THC has some antiemetic properties. Administration of activated charcoal and cathartic therapy if ingestion was recent (*see Toxicological Emergencies p. 432*).

B. General critical care.

C. Control excitement or agitation with diazepam.

NOTES

INTRODUCTION

Antifreeze is 95% ethylene glycol (EG) which has a sweet taste. Occasionally owners will leave EG in easy reach of their cat and dog after tending to their cars. Ethylene glycol is also used to prevent freezing of the toilet system in cottage areas and dogs drinking out of the toilet will consume this in the spring when returning to the cottage. Thirsty animals consuming water from puddles may also ingest antifreeze that has been drained from a car.

The median lethal dose of EG is very small, **1.5 – 4 mL/kg in the cat and 4 – 6 mL/kg in the dog.** Ethylene glycol is rapidly absorbed from the gastrointestinal tract and is metabolized, or excreted unchanged in the urine, within 24 hours. Intermediate products of metabolism, especially glycoaldehyde and glyoxylate which are directly toxic to renal tubular epithelium (major cause for renal failure), are also responsible for metabolic acidosis and deposition of oxalate crystals in the renal tubules. The goal of therapy is to prevent metabolism of EG, and production of toxic metabolites, and to enhance its elimination. Where hemodialysis is available, this should be instituted within 5 – 6 hours of ingestion as EG and metabolites can successfully be removed with a single dialysis treatment. Beyond this time, several treatments are required.

Ethanol competes with EG as substrate for alcohol dehydrogenase, while fomepizole (4-methylpyrazole) (4-MP) is an inhibitor of alcohol dehydrogenase. Therefore, either of these two agents will prevent metabolism of EG to the toxic metabolites. The earlier ethanol or 4-MP are administered, the better the prognosis. Ethanol therapy can be administered at home if ingestion was witnessed and the owner is not able to seek veterinary attention immediately (*see Home Therapy below p. 656*). The prognosis varies with time to presentation. If <8 hours in the dog, < 3 hours in the cat, and treated with 4MP, the prognosis is very good to excellent. Duration beyond this with treatment using ethanol will be protracted and expensive. Prognosis is variable, and poor if anuric. It may take several weeks to months for renal function to normalize if azotemia was significantly increased on presentation.

DIAGNOSIS

History/Signalment

- Both cats and dogs of any age may be presented.
- Question the owner with regard to any opportunity of exposure to EG either in their home or anyone elses if the animal is unsupervised at any time.
- The time frame from possible exposure to presentation is important for prognosis as well as therapy.
- If ingestion was witnessed, ascertain volume consumed.

Clinical Signs/Physical Examination

- The clinical signs will vary with volume ingested and time of exposure to presentation.
- Within the first **2 – 4 hours** a sweet odour to the breath may be present or the patient may be 'exhilarated' or 'inebriated'.
- By **4 – 7 hours** central nervous system depression and ataxia are noted. Ataxia, knuckling, muscle fasiculations, nystgmus, head tremours, decreased withdrawal reflexes and righting ability may also be present.
- In dogs CNS signs tend to improve at ~ **12 hours** but recur later. Cats usually remain depressed.
- Seizures may occur which may be witnessed or not. This may be the cause of the very rare pulmonary edema with a non-cardiogenic pattern noted on radiographs.
- If a relatively large volume was ingested, coma and death may occur by **12 hours.**
- Polyuria occurs within hours and persists in dogs; if they are unable to drink they become very dehydrated. Polyuria does not occur in cats.
- Kidneys may be large and painful, especially in cats.
- Patients may be oliguric, or anuric at late presentation.
- Within the **first 12 hours** with low to moderate exposure, nausea, vomiting, polyuria and polydipsia and dehydration (estimate hydration status), may be evident. These events may be transient with clinical improvement over the next **12 – 48 hours** in dogs only to regress when renal failure occurs. This time frame is approximately **12 – 15 hours** in cats.
- Oral ulcers and salivation may be noted.
- Body temperature may be low or normal

Laboratory Evaluation/diagnostic Imaging

Stat

- **PCV and TS** are usually increased due to dehydration. A stress leukogram is frequently present.
- **Biochemical profile** to assess renal function and to obtain calculated osmolality (required for osmolal gap, see Extended Data Base below). The total CO_2 is useful in measuring the anion gap (*see Acid-Base Assessment p. 406*) Urea and creatinine increase with time and renal involvement (~36 hours in the dog and 12 hours in the cat). Hyperphosphatemia develops in the early stage due to absorption from the EG solution and then in the later stage due to renal failure and decreased GFR.
- **Serum electrolytes** and **venous blood gas** (or total CO_2) to calculate the anion gap (*see Acid-Base Assessment p. 406*); an increased anion gap due to metabolites, results in metabolic acidosis within 3 hours and is present for several more hours. $PvCO_2$ or $PaCO_2$ may be low due to hypernea from acidosis. **Hyperkalemia** may be present at the later stage with renal failure, and **hypocalcemia** due to chelation of calcium by oxalic acid and renal failure
- **Blood glucose** is frequently increased due to reduced metabolism of glucose by aldehydes, and the stress response (increased epinephrine and cortisol), however, hypoglycemia may occur.
- **Definitive laboratory diagnosis** may be made with an **Ethylene Glycol test kit (PRN Pharmaceutical Inc., Pensacola, Florida).** This test is only sensitive if EG was consumed within a few hours, peaks 1 – 6 hours after ingestion and measures concentrations >50 mg/dL. Contact your local laboratory and enquire as to EG testing ability. Some laboratories can test for EG up to several hours after consumption.
- **Urinalysis** may reveal calcium oxalate crystals which appear at 3 h post-ingestion in cats and 6 h in dogs; pH is low; cellular and granular casts may be present at the later stage. Woods lamp shone on the urine imparts a fluorescent blue/green.

Extended Data Base

- **Measure osmolality** and if the difference between **measured** (calculated components on profile + EG present in serum) and **calculated** is >10 – 15 mOsm/L (high osmolal gap) and history and physical findings support ethylene glycol toxicity, this is somewhat confirmatory. The difference between the measured and calculated osmolality will not be evident after the EG has been metabolized (~12 hour depending on volume consumed), therefore a difference of <10 cannot rule out EG toxicity. An estimate of ethylene glycol can be made by multiplying the osmolal gap by 6.2. Once EG is metabolized, the gap is normal ~ 10 mOsm/L. This will change later as uremic toxins contribute to the osmolal gap.
  - Calculation of **serum osmolality (mOsm/kg):**
    SI Units: mOsm/kg = $[1.86 \times (Na^+ + K^+)]$ + glucose + urea + 9, all units in mmol/L.
    Traditional units: mOsm/kg = $[1.86 \times (Na^+ + K^+)(mEq/L)]$ + [glucose (mg/dL)/18] + [BUN (mg/dL)/2.8]. Consider hyperosmolar if serum osmolality > 320 mOsm/kg in **dogs** (normal 290 – 310), or >330 mOsm/kg in **cats** (290 – 330).
- **Ultrasonographic examination** reveals hyperechoic renal cortices when calcium oxalate crystals are present in renal tubules. These changes maybe observed within 4 – 8 hours after ingestion. Areas of relative lucency appear at the corticomedullary junction and within the central medullary region giving a 'halo' appearance which corresponds to clinical anuria. The kidneys are often enlarged.
- **Renal biopsy** for confirmation of diagnosis and prognosis.

MANAGEMENT

While keeping in mind that the prognosis for survival after known EG ingestion is very poor if not managed immediately, the following advice may be offered if treatment will be delayed, or 4-Methylpyrazole (4-MP) is not available. Ethanol treatment is required for almost 48 hours to be effective and is associated with CNS depression, increased osmolality, hypothermia, osmotic diuresis, especially so in cats. However, if the alternative is to do nothing, or distance to travel is extensive, then ethanol treatment may save the animal's life.

I. HOME THERAPY

On receiving a call from a client regarding EG ingestion, if EG ingestion is witnessed and there is a considerable distance to travel to a veterinarian, suggest the following:

A. **Induce vomiting** with 1 – 2 mL/kg **hydrogen peroxide (3%).** If vomiting is not induced within 5 min, repeat ONCE. EG is rapidly absorbed, therefore vomiting should only be induced if witnessed within <1 hour of ingestion.

B. **Administer alcohol** e.g., vodka, rum (after all potential for vomiting [above] has subsided; this contains **40%** (40 g/100 mL) **alcohol,** therefore, **give 1.5 mL/kg PO** (for a 0.6 g/kg dose). Diluted 1:1 with water may be a little more palatable, but the larger volumes may be more difficult to administer. Warn about polyuria and dehydration

C. 'Get on the road' immediately.

D. **For those not able to travel right away** (or not willing to see a veterinarian), repeat (B) above: i.e., **1.5 mL/kg of alcohol PO q4h for four times.** If possible, continue at half this dose q4h for a further four times while maintaining the animal's ability to drink (may require lower volumes to maintain this). DEHYDRATION and REDUCED EXCRETION of EG is of major concern here and the owners should be notified of this. Water must be available, and offered/administered, to the animal at all times. Caution regarding potential vomiting and aspiration.

II. GENERAL MANAGEMENT

A. **Place an IV catheter,** obtain blood for above tests and go to B below immediately, commence fluid therapy with an isotonic alkalinizing crystalloid solution (Plasma-Lyte® 148 or A, Normosol® R or lactated Ringer's) based on degree of dehydration and urine production (*see Fluid Therapy p. 347, Acute Renal Failure p. 709*).

B. If ingestion of EG was witnessed, or is strongly suspected, **within 1 hour** of presentation and the patient is not dyspneic, hypoxic, stuporous to comatose, or convulsing; PREVENT ABSORPTION.

  1. **In dogs,** induce vomiting with
     a. **Apomorphine**
        i. **Tablet** placed in the conjunctival sac. Vomiting should occur within 5 – 7 mins. Do not allow to become sedated, remove quickly and flush well.
        ii. **IV IV 0.03 mg/kg** typically results in immediate vomiting.
        iii. **IM 0.04 mg/kg or SC 0.08 mg/kg** results in vomiting within 5 minutes. If apomorphine tabs not available, try
     b. **hydrogen peroxide 1 – 2 mL/kg,** if oral lesions are not present (1 tsp = 5 mL, 1 tbsp = 15 mL).

  2. **In cats**
     a. **xylazine 2 mg** (0.1 mL of 20 mg/mL) **/4 – 5 kg IM;** (20 – 30 mins to effect), is most effective. CAUTION: Use of xylazine may result in hypertension or hypotension, bradycardia, hypothermia, and respiratory depression.
     b. **Hydrogen peroxide 1 – 2 mL/kg** if oral lesions are not present (~ 1 tsp/cat).

C. After vomiting has been induced and has stopped administer,
  1. **Activated charcoal,** of petroleum or vegetable origin only, at **1 – 5 g/kg** at a concentration of 1 g charcoal to 5 to 10 mL of water OR
  2. **Activated charcoal** prepared slurry with sorbitol (Charcodote®, Pharmascience Inc., Montreal, Canada) at same dose.

D. **Fluid therapy** is commenced with a balanced electrolyte solution at twice to three times maintenance until the rate can be more accurately calculated based on hydration status and ability to produce urine (*see Acute Renal Failure p. 709*). **Go to F, G, or H immediately** while establishing the fluid plan. If the patient is polyuric, calculate hydration status and replacement fluid requirements in addition to maintenance and continued urine losses (*see Fluid Therapy p. 347*).

The addition of multiple B vitamins with pyridoxine and thiamine to the maintenance fluids may be beneficial for neuroprotection with ethanol administration, and to reduce formation of calcium oxalate crystals as pyridoxine and thiamine are co-factors in alternate pathways for ethylene glycol metabolism. However, stability in-line with ethanol is not established, therefore, a separate line is required.

E. If recumbent or if urine production is questionable, place an indwelling urinary catheter, aseptically, to obtain urine for urinalysis and to monitor urine output. A urinary catheter must be placed if peritoneal dialysis is performed. If dialysis is deemed necessary and hemodialysis is an option, then refer to the appropriate centre immediately.

K. **Sedation** with **acepromazine 0.01 mg/kg** may be required should the animal become delerius and vocalize. However, caution is warranted regarding hypotension. Reduce the rate of ethanol administration in these patients.

L. Measure PCV, TS, serum electrolytes, glucose, venous blood gases, and osmolality as frequently as indicated by previous results and treatment changes.

M. WEIGH 2 – 3 times daily as a guide to fluid management.

N. Nutritional support is required either enterally, if able to eat, or parenterally (*see Nutritional Support p. 499*).

PHARMACOLOGY

1) **Ethanol** competes with EG for alcohol dehydrogenase. Alcohol dehydrogenase metabolizes EG to toxic metabolites. If alcohol dehydrogenase is not available for EG metabolism, then EG is excreted unchanged. The purpose of continual ethanol administration is to ensure that the alcohol dehydrogenase is preferentially used in ethanol metabolism while all the EG is being excreted. Ethanol causes central nervous system depression and polyuria. Hydration status, urine output and fluid therapy must be monitored carefully. A 20% solution = 20 g/100 mL.

2) **4-Methylpyrazole** is an alcohol dehydrogenase inhibitor and is more effective than ethanol in preventing EG metabolism in dogs. 4MP at doses tested is not very effective in cats. Another advantage to 4-MP is that it will not cause central nervous system depression or polyuria.

3) **Activated charcoal** is used for gastric decontamination. It is an inert, non-toxic adsorbent with a surface area of 3000 m2/g. Due to its poor palatibility, it may be necessary to administer through a nasogastric feeding tube. The sorbitol combined with activated charcoal in Charcodote®, is a cathartic. Continual repeated dosing with sorbitol is not recommended. A second repeat is of no concern, however thereafter activated charcoal should only be used if repeat is deemed necessary.

4) **Apomorphine** tablet, placed in the conjunctival sac is frequently effective in inducing vomiting however, if it is not, remove the tablet after 5 – 7 min. Remove the tablet immediately after vomiting.

5) **Furosemide.** *See Acute Renal Failure p. 713.*

SUGGESTED READING

1. Connally HE, Hamar DW, Thrall MA. Inhibition of canine and feline alcohol dehydrogenase activity by fomepizole. Am J Vet Res. 2000;61(4):450-5.
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4. Cowgill LD, Langston CE Role of hemodialysis in the management of dogs and cats with renal failure. Vet Clin North Am Small Anim Pract. 1996;26(6):1347-78.
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NOTES

INTRODUCTION

The exposure and/or ingestion of toxic plants is not a common emergency in small animal practice. Cats are more likely to sample house/garden plants than dogs. The chart provided here represents common house and garden plants that are known to be toxic to dogs and/or cats, and is not meant to be an exhaustive list.

DIAGNOSIS

History

- The key to diagnosis of toxic plant exposure is the history and identification of the plant. If an owner suspects plant toxicity, it is important that a sample of the plant is brought to the veterinarian for identification. There are many picture references that can be useful in these situations (*see website in Suggested Reading*). In some cases, where plants are not ingested, contact with the plant may induce toxicity.

Physical Examination/Clinical Signs

- These will vary with the toxin exposure and are listed in the table below.

Laboratory Evaluation/Diagnostic Imaging

Stat

- Body weight, PCV/TS, stick BUN, blood glucose and electrolytes should be collected on all patients for baseline assessment and monitoring. The results will vary depending on severity of illness and toxin exposure.

Extended Data Base/Diagnostic Imaging

- Complete blood count, biochemical profile and urinalysis are indicated where the ingested plant is known to be highly toxic. The results will vary depending on severity of illness and toxin exposure.

Treatment

Treatment is usually symptomatic, directed towards the underlying clinical signs (gastrointestinal, cardiac, seizures, etc.). In a few cases, an antidote may be available. Prognosis depends upon the toxin, dose, pre-exisiting conditions and extent of supportive therapy.

A. An intravenous catheter should be placed dependent upon hydration, ongoing losses due to vomiting/diarrhea, and anticipated toxicity (i.e., acute renal failure, hemorrhagic gastroenteritis).
Fluid therapy see p. 347 .

B. Ingestion (General)

1. Induce emesis if ingestion was within the past 60 minutes and the pet is fully conscious (*see p. 632*).
2. Consider gastric lavage if ingestion of a large amount of plant material is not removed via emesis. This procedure may only be indicated when highly toxic plant ingestion has occurred since it requires general anesthesia (*see p. 634*).
3. Administer repeated doses of activated charcoal (*see p. 634*).
4. Catharsis is rarely indicated, but could be performed using sorbitol (3 mL/kg PO) rather than a magnesium-containing product (*see p. 635*).
5. Oral rinsing can be performed using water or milk, if exposed to plants containing oxalates/calcium oxalate has occurred.
6. Analgesics are indicated in cases of moderate/severe oral pain (*see p. 81*).

C. Cardiac: Toxicity of cardiac glycoside-containing plants may include the use of (Digibind®) GlaxoSmithKline (digoxin immune Fab). Dose depends on ingestion. Dosage for animals is unknown. Infants <20 kg receive 1 vial (38 mg) however, recommendations with the drug should be followed. In cases where cardiac abnormalities may be seen, electrolytes (especially potassium) should be monitored carefully and arrhythmias should be treated accordingly (*see p. 164/170/179*).

D. Cholinesterase inhibitors: if symptoms are severe, administer **physostigmine 0.02 mg/kg IV** over 5 minutes. Use repeated doses, as needed.

E. Cyanide toxicity <u>that has been confirmed</u> can be treated with **sodium nitrite 16 mg/kg IV. Sodium thiosulfate** should then be administered **30 – 40 mg/kg** slowly IV. This dosage may need to be repeated. In addition, extra-label use of oxyglobin should be considered in dogs/cats.

F. Glutathione precursors (**n-acetylcysteine** loading dose of 140 mg/kg PO, then 70 mg/kg PO every 4 hours for 3 – 5 treatments, **SAM-e 18 mg/kg PO**) may be useful when oxidative red blood cell injury occurs. Oxyglobin may be used, if needed.

G. Acute liver failure (*see p. 37*).

H. Seizures (*see p. 456/460*).

I. Acute renal failure (*see p. 709*).

J. Contact (General)

  1. Bathing should be performed with the handler wearing gloves. A lubricating ophthalmic ointment should be placed in the animal's eyes. Use warm water and mild pet shampoo. Rinse for at least 15 minutes to ensure the toxic material is removed.

K. Ocular irrigation can be performed using copious amounts of sterile saline for as long as the animal will tolerate the procedure.

KEY TO TABLE 1

1. **Toxin(s)**
   - U= unknown
   - M= multiple
   - **Cardiac glycosides:** toxin that interferes with cardiac muscle Na/K ATP-ase ; leads to arrhythmias and eventual asystole.
   - **Oxalates/calcium oxalate:** plants containing this toxin are able to "inject" the toxin into the tissues upon contact, causing a marked local reaction. If ingested, oxalate may precipitate and cause acute renal failure; however, the insoluble form, unlike the soluble form in rhubarb leaves, likely will not do this but monitoring is advised.
   - **Grayanotoxins:** toxin disrupts cellular sodium channels and allows an influx of sodium.
   - **Solanines:** cholinesterase inhibiting

2. **Signs**
   - GI=gastrointestinal: vomiting, diarrhea; if severe, hemorrhagic gastroenteritis.
   - Cardiac: bradycardia, tachycardia, dysrhythmias, asystole.
   - Oral pain: salivating, pawing at mouth, edema/swelling of the lips, tongue. If severe, upper airway stridor may be seen.
   - CNS = central nervous system: ataxia, seizures, paralysis, coma.
   - MS = musculoskeletal: weakness, trembling, syncope/collapse.
   - Cholinesterase inhibitors= Parasympatholytic:
     a. mild = mydriasis, tachycardia, xerostomia
     b. moderate = urinary retention, dyspnea, ileus, CNS stimulation followed by CNS depression

3. **Treatment**
   - S/S = symptomatic/supportive:

TABLE 1. Toxic Plants, Signs and Treatments

Common	Latin	Toxic part	Toxin(s)[1]	Signs[2]	Treatment/Comments
Chenille plant Jacobs coat copperleaf	acalypha	latex	diterpenes	GI	S/S
Bushman's poison wintersweet	acokanthera	seeds>plant>fruit	cardiac glycoside	GI, oral pain, cardiac	S/S, cardiac
Monkshood Helmet flower	aconitum	whole plant, vase water	alkaloid	oral pain, GI, blind, cardiac	S/S, oral rinse, cardiac
Baneberry, cohosh	actaea	berries, roots	U	oral pain, severe GI, renal, CNS	S/S, oral rinse
Horse chestnut buckeye	aesculus	Nuts/branches > whole plant	M	GI, CNS, death	S/S
Fool's parsley, dog parsley, small hemlock	aethusa cynapium	whole plant	aethusin	GI, CNS, death	S/S
Japan oil tree, tung oil tree, Jamaican walnut	aleurites	whole plant	derivative of phorbol	GI	S/S
Onion, garlic	allium	bulb>plant	disulfides	anemia	S/S, glutathione precursors
Elephant's ear	alocasia/colcasia/caladium	leaves, stems	calcium oxalate insoluble form	oral pain	oral rinse
aloe	aloe	latex	barbaloin	GI, renal possible	S/S
Amaryllis, belladonna lily, naked lady	amaryllis/hippeastrum	bulb	lycorine/alkaloids	GI, hepatic possible	S/S, monitor for liver disease
Pasque flower anemone	anemone	whole plant	protoanemonin	oral pain, severe GI, CNS, death	Oral rinse, S/S
Anthurium flamingo flower	anthurium	leaves, plant	calcium oxalate insoluble form	oral pain	Oral rinse, S/S
prayer bead, rosary bead, precatory bean	arbrus precatorius	seed (must be opened)	abrin	GI, sometimes severe	S/S
Jack-in-the-pulpit, green dragon, dragon tail/head	arisaemai	whole plant	calcium oxalate insoluble form	oral pain	oral rinse, S/S
Solomon's lily, black calla	arum	whole plant	calcium oxalate insoluble form	oral pain	oral rinse, S/S
Asparagus fern	asparagus sprengeri	leaves, berries	U	contact irritant, GI (if berries ingested)	S/S, bathing
Deadly nightshade, belladonna, nightshade	atropa belladonna	whole plant	atropine, belladonna alkaloids	parasympatholytic	S/S, physostigmine

Common	Latin	Toxic part	Toxin(s)[1]	Signs[2]	Treatment/ Comments
mustard	*brassica*	roots, seeds	isothiocyanante	ocular/oral irritation, GI, blindness, contact irritant	S/S, bathing, oral rinse, ocular irrigation
Giant milkweed	*caotropis*	whole plant	cardiac glycoside, vesicant	oral pain, contact irritant, ocular irritant, rare cardiac	bathing, ocular irrigation, S/S, cardiac
Day/night-blooming Jessamine (jasmine)	*cestrum*	fruit, leaves, sap	solanine, saponins, alkaloids, 1,25-dihydroxyvita-min D glucoside	parasympatholytic,CNS, GI, renal failure due to hypercalcemia (*cestrum diurnum*)	S/S, physostigmine, see vitamin D toxicity (p.)
Autumn crocus	*colchicum autumnale*	bulbs>whole plant	alkaloid colchicine	GI, MS, shock, death, renal failure	S/S, monitor for ARF
Lily of the valley	*Convallaria majalis*	Whole plant	cardiac glycoside	GI, cardiac, MS, CNS, death	do not induce emesis, S/S, cardiac
croton	*croton*	seeds	oil of croton	oral, GI, CNS, death	S/S
Sago palm maybe called "false"	*cycas revoluta*	seeds>plant> roots	M	GI, hepatic failure, renal, death	poor prognosis, S/S
Dwarf bay, daphne, lady laurel	*daphne*	whole plant	daphnin, mezereinic acid anhydride	contact irritant, contact exposure can cause systemic signs, severe GI, MS, renal, CNS, death	bathing, S/S
Datura, devil's trumpet, jimsonweed, mad apple	*datura*	seeds>whole plant	atropine, scopolamine, hyoscyamine	hallucination, Parasympatholytic	S/S, physostigmine
Dumbcane	*dieffenbachia*	whole plant	calcium oxalate – insoluble form; proteolytic enzymes	oral pain, GI, cardiac, mydriasis, coma, death	oral rinse, antihistamines, S/S, rare to see severe signs
Foxglove, fairy bells, thimbles	*digitalis*	whole plant, vase water	cardiac glycosides, M	oral pain, GI, cardiac, death	S/S, cardiac
Golden pothos, devil's ivy, variegated philodendron	*epiprenum*	whole plant, roots	calcium oxalate – insoluble form; proteolytic enzymes	oral pain	oral rinsing
Pointsettia, spurge	*euphorbia*	leaves,stems, sap	phorbol esthers	oral pain/irriation, GI	S/S, rare toxicity
English ivy	*hedera helix*	foliage>berries	saponin	GI	S/S
Day lily (also see Easter lily, etc.)	*hemerocallis* (also see *lilium*)	whole plant	U	GI, ARF (see p.)	cats only, S/S, monitor for ARF, high mortality

Common	Latin	Toxic part	Toxin(s)[1]	Signs[2]	Treatment/ Comments
Hyacinth	*hyacinthus*	bulb	U	GI	S/S
Hydrangea	*hydrangea*	whole plant	cyanogenic glycoside	GI, may be severe	rare toxicity S/S
Holly	*ilex*	leaves/berries	U	GI, CNS	rare, S/S
Morning glory	*ipomoea tricolor*	seeds	LSD and others	hallucinogenic, GI, mydriasis	S/S
Black walnut	*juglans*	hulls, shavings	U (possibly tremorgenic mycotoxin)	GI, seizures	S/S
Laurel	*kalmia*	whole plant	grayanotoxin	Epiphora, salivation, nasal discharge, CNS, death	do not induce emesis, S/S
Bean tree, golden chair	*laburnum anagyroides*	pods/seeds>whole plant	cytisine (nicotine-like)	Excitement, incoordination, GI, CNS, MS, death	S/S
Easter lily, Asiatic lily, Japanese show lily, rubrum lily, tiger lily (also see day lily)	*lilium* (also see *hemerocallis*)	whole plant	U	GI, ARF (*see p.*)	cats only, S/S, monitor for ARF, high mortality
Passionflower/fruit, tomato plant	*lycopersicon esculentum*	plant/fruit	solanine	GI, cardiac, collapse	S/S, rare toxicity
Apple	*malus sylvestris*	seeds/leaves	cyanide	cherry-red mm, GI, tachycardia, cns, tachypnea, death	see cyanide antidote S/S
Chinaberry tree	*melia azedarach*	fruit/bark/flowers	alkaloid	GI, CNS, coma, death	S/S
Cutleaf philodendron, mexican breadfruit, hurricane plant, mother-in-law, swiss cheese plant	*monstera*	whole plant	calcium oxalate – insoluble form	oral pain	oral rinse
Daffodil	*narcissus*	bulb>whole plant	alkaloids	GI, rare CNS, death	S/S
Oleander, rose laurel	*nerium*	whole plant	cardiac glycosides	GI, oral pain, cardiac, death	cardiac, S/S
Horsehead, red emerald/princess, cordatum	*philodendron*	whole plant	calcium oxalate – insoluble form	oral pain	oral rinse
Mistletoe	*phoradendron/ viscum album*	berries>whole plant	phoratoxin	GI, CNS, cardiac, shock, collapse, death	S/S
Japanese andromeda	*pieris*	flowers, leaves, nectar	grayanotoxin	salivation, GI, CNS, epiphora, bradycardia, death	S/S

Common	Latin	Toxic part	Toxin(s)[1]	Signs[2]	Treatment/ Comments
Cherry, peach, plum, apricot	*prunus*	seeds, ± leaves	cyanide-like	cherry-red mm, GI, tachycardia, tachypnea, death	see cyanide antidote, S/S, almond odor
Buttercup	*ranunculus*	whole plant (mature only)	protoanemonin	oral pain, blisters, GI if ingested	oral rinse, S/S if ingested
Rhubarb	*rheum rhaponticum*	leaves	calcium oxalate soluble form	GI, ARF possible	milk per os, then induce emesis, S/S, rare toxicity
Azalea, rhododendron	*rhododendron*	whole plant	grayanotoxin	salivation, oral pain, GI, epiphora, bradycardia, MS, CNS, death	do not induce emesis, oral rinse, S/S
Castor bean, castor oil plant	*ricinus communis*	seeds>whole plant	ricin	shock, collapse, death; low dose may see oral pain, GI, ARF (*see p.*)	S/S, monitor for ARF
Black nightshade, Irish potatoe, Jerusalem cherry	*solanum*	plant, roots, fruit	solanine, alkaloids, M	parasympatholytic, or atropine-like signs, oral pain, GI (may be severe), CNS	S/S, physostigmine, be careful with atropine
Bird of paradise	*strelitzia reginae*	seeds, seedpods	U	GI	S/S
Skunk cabbage	*symplocarpus*	leaves, whole plant	calcium oxalate – insoluble form	oral pain	oral rinse, milk per os, induce emesis, S/S
Yew	*taxus*	seeds, leaves, wood, bark	taxines	MS, GI, collapse, seizures, cardiac, death	S/S
Poison ivy/oak	*toxicodendron*	sap, whole plant	urushiol	contact dermatitis, GI if ingested	bathing, S/S
Tulip	*tulipa*	bulb	alkaloids	GI	S/S
Nettle, stinging nettle	*urtica*	hairs on plant	formic acid, acetylcholine, histamine	salivation, MS, paresis/paralysis, death	atropine, oral rinse if ingested, S/S
Calla lily	*zantedeschia*	whole plant	oxalates- insoluble form	oral pain	oral rinse, S/S

PHARMACOLOGY:

1) **Digibind** (Glaxo Wellcome) is an ovine immunoglobulin fragment (Fab). Since this drug has a greater affinity for digoxin than the sodium pump receptor, it is able to bind the digoxin and lower free drug levels. The bound digoxin is then cleared by the kidneys and reticulendothelial system. There are no known contraindications; however, since a foreign protein is being injected, patients should be monitored for anaphylactic and anaphylactoid as well as delayed allergic reactions and fever. The suggested dose is 60 mg/kg IV; repeat doses may be needed.

2) **Physostigmine** is a cholinesterase inhibitor. It is used only as an antidote for cholinergic intoxication, because it has many adverse effects. It is useful in cases with CNS signs because it is able to cross the blood-brain barrier, unlike neostigmine and pyridostigmine. Overdose causes excessive cholinergic effects; use atropine to treat.

3) **Sodium nitrite** (1% solution) is an antidote for cyanide poisoning. It should only be administered if cyanide toxicity is confirmed, otherwise severe, even fatal, methemoglobinemia will result. Give slowly IV to avoid hypotension.

4) **Sodium thiosulfate** (25% solution) provides an exogenous source of sulfur to help with the conversion of cyanide to its nontoxic metabolites. The metablites are then excreted through the urine.

5) **N-acetylcysteine:** (10 or 20% solution) usually given per os for acetaminophen toxicity. N-acetylcysteine reduces methemoglobinemia by restoring glutathione levels.

6) **SAM-e** (Denosyl®) is a nutraceutical that helps to replenish hepatic glutathione levels. The tablet should not be broken or crushed and should be given on an empty stomach.

7) **Sorbitol** (70%) is an osmotic cathartic that can cause vomiting, diarrhea, and dehydration. It should not be used in volume depleted or hypotensive patients.

8) **Oxyglobin** is bovine hemoglobin that is used to treat acute anemias by raising the systemic oxygen content. Its effects are short-lived (approximately 24 hours). Contraindications include advanced cardiac or renal disease, or other conditions where volume expansion may be detrimental. The dose for dogs is 10–30 mL/kg IV at a rate of 10 mL/hour. It should be given at a slower rate if used off-label in the cat. Give at room temperature and do not mix with other solutions.

SUGGESTED READING

1. www.aspca.org/toxicplants
2. Gfeller RW, Messonnier SP. Toxic Plants. In: Small Animal Toxicology and Poisonings, 2nd edition, St. Louis MO: 1994:334-410.
3. Osweiler G. Toxic Plants and their Clinical Signs. In: Tilley LP, FKW Smith eds, The 5-Minute Veterinary Consult, 4th edition, Baltimore MD: 2004:1386-1388.

NOTES

INTRODUCTION

The production of whole blood or blood products has facilitated transfusion therapy in practice. There are successful blood donor programs using clinic or client-owned animals. Blood products commonly used are packed red blood cells; stored, fresh or fresh-frozen plasma; and platelet-rich plasma. Cryoprecipitate is less commonly used. Whole blood, packed red blood cells, stored, fresh or fresh-frozen plasma can be prepared by most veterinary practices and will be outlined here. Indications for use, administration and complications of transfusion therapy are also presented.

I. INDICATIONS

A. Whole Blood

1. A whole blood transfusion is indicated in any condition with rapid loss of both red blood cells (RBC) and plasma volume including: trauma, surgery, anticoagulant rodenticide toxicity, ruptured tumour (*see Hemorrhage p. 619*). Blood transfusion should be considered when the PCV<25% in dogs and <20% in cats.
2. **Fresh,** as opposed to stored blood, is preferred where:

   a. Emergent, acute hemorrhage situations where an associated coagulopathy or severe inflammation (*see C 1 below*) is known or suspected.
   b. Finances are a concern and possibly only one unit will be authorized and optimization of all constituents are required.
   c. The time to collect the blood is quicker than thawing or obtaining the component part.
   d. More than 30% of total blood volume will be required.

B. A Stored Plasma transfusion is indicated:

1. In puppies with severe protein loss due to parvovirus diarrhea.
2. In severe hypoalbuminemic patients (albumin <15 g/L [1.5 g/dL]) requiring volume expansion prior to surgical intervention. 25% human serum albumin is an alternative (*see Fluid/Colloid Therapy p. 347, Hypoalbuminemia p. 431*).
3. Volume resuscitation where TS <40 g/L or normal blood pressure cannot be attained or maintained with crystalloids alone. (25% human serum albumin may be an alternative).
4. As component therapy (with packed red blood cells) for whole blood loss.
5. In rodenticide toxicity as stored plasma contains sufficient quantities of Factors II, VII, IX and X.

C. Fresh or Fresh-Frozen Plasma (FFP)

1. A transfusion of FFP is indicated in any inflammatory process or situation with significant cytokine release (i.e., sepsis, pancreatitis, major trauma, neoplasia, major surgery) where antithrombin, alpha-macroglobulins, various anti-cytokines, anti-proteases, and fibronectin are required. Although many of these substances are relatively stable in plasma and whole blood, they do decrease over time. Using fresh (or fresh frozen) plasma ensures their maximum possible concentration.
2. Some coagulopathies to supplement specifically Factor VIII and von Willebrand's Factor (vWf), and to a lesser extent Factor V.

D. Packed Red Blood Cells (PRBC)

1. PRBCs may be administered to address red cell destruction of any cause (i.e., immune-mediated hemolytic anemia, *Mycoplasma haemofelis* infection [hemobartonellosis]) where:

   a. PCV <20 and volume resuscitation is required due to dehydration.
   b. PCV <18 with ongoing acute destruction.
   c. PCV <15 with clinical signs of anemia.
2. Component therapy for whole blood loss in combination with plasma or crystalloids.

E. Platelet-Rich Plasma (PRP) and Platelet Concentrate (PC)

1. PRP or PC transfusions are indicated for non-thrombocytopenia with petechiae or hemorrhage.
2. As a replacement platelet infusion after stored whole blood transfusion for significant blood loss.
3. For immune-mediated thrombocytopenia therapy with vinca-loaded platelets.

F. Administration of cryoprecipitate is indicated in:

1. von Willebrand's disease
2. Hemophilia A

II. COLLECTION, PREPARATION AND STORAGE OF BLOOD AND BLOOD COMPONENTS

A. COLLECTION & STORAGE

1. **Primary Goals**
   a. Maintain viability and function of constituents.
   b. Prevent physical changes detrimental to constituents.
   c. Prevent bacterial proliferation.

2. **Biochemical changes in blood stored at 1 – 6°C**
   a. Decrease in pH as RBCs metabolize glucose to lactate.
   b. Subsequent decrease in **2,3 diphosphoglycerate (2,3 DPG).** [In vivo, increased 2,3 DPG levels promote more release of O_2 to peripheral tissues at given PO_2; decreased 2,3 DPG would cause oxygen to have a great affinity for the RBC resulting in decreased tissue oxygenation. Following transfusion of blood stored at 1 – 6°C, it usually takes 3 – 8h for severely depleted cells to generate 50% of their 2,3 DPG levels and 24 hours to restore complete function]. This is only applicable to dogs. Concentration of 2,3 DPG in **CPDA-1 (citrate, phosphate, dextrose, adenine)** stored blood is maintained near normal for 12 – 14 days. If immediate O_2 delivery is required CPDA – 1 stored blood less than 12 days is recommended. Patients most affected by decreased 2,3 DPG concentrations are those receiving massive transfusions of stored blood over a short time and with IMHA patients.
   c. Decrease in **adenosine-triphosphate (ATP)** levels. [Dextrose helps maintain adequate ATP by allowing continuation of glycogenic pathway. Blood stored at 1 – 6°C slows the glycogenic pathway, therefore dextrose is consumed less rapidly and intermediary metabolites are not generated as quickly. Adenine provides substrate for RBC synthesis of ATP. Phosphate contributes to adenosine triphosphate to help maintain cell viability].
   d. At 4 or 5 weeks 70 – 80% of the red cells are viable when whole blood is stored in **citrate phosphate and dextrose (CPD)** or CPDA-1, respectively. Red cells become less compliant after 12 days and may block small capillaries. **Blood or PRBCs <12 days** old are not recommended for IMHA and other inflammatory conditions as the endothelium is abnormal and older RBCs cannot 'percolate' through the capillaries.
   e. Citrate prevents coagulation by inhibiting calcium dependent steps of the coagulation cascade. Although not a problem with stored blood, reduced serum levels of ionized calcium can occur with patients transfused with large volumes of blood containing citrate anticoagulant. Thus patients receiving multiple rapid transfusions or those with impaired liver function should be monitored for signs of hypocalcemia. Note that total serum calcium, as measured on a routine serum chemistry analyzer, will remain normal. Ionized calcium must be measured to document this effect.
   f. An increase in potassium (K^+) due to leakage of intracellular K^+ from destroyed red cells is not a problem with stored canine blood (except in the Akita and Shiba Inu) as canine erythrocytes do not have intracellular K^+ concentrations as high as humans.
   g. Bacterial proliferation will occur if there is not strict adherence to aseptic technique in blood collection, storage, preparation and administration.

B. BLOOD DONOR PROGRAMS (see Appendix 5 p. 681 to this chapter)

C. SPECIAL CONSIDERATIONS PRIOR TO BLOOD COLLECTION

1. In **blood collection for fresh plasma** only, where red cells are not required, plan to transfuse the red cells back to the donor or bank them.
2. **If only red cells are required,** it is not necessary to replace the plasma as albumin rapidly equilibrates into the intravascular space. Freeze the plasma for other use.
3. **For patients with Hemophilia A and von Willebrand's disease, desmopressin (DDAVP)** a synthetic analogue of **vasopressin** transiently increases levels of factor VIII and vWF. It has been recommended as an alternative to transfusion for the acute treatment of hemophilia A and von Willebrand's disease.
   a. **Human intranasal DDAVP drops (100 μg/mL)** at a dose of 0.6 μg/kg (diluted in sterile saline for an administered total volume of 1 – 2 mL) is given IV, or undiluted SC daily for 3 – 4 days. If required prior to surgery, and a thiobarbiturate is used for induction of anesthesia, the DDAVP should be given prior to induction as response is suppressed by barbiturates.

   b. **Limitations**
      i.   Effect is transient and maximal 2 – 3 hours, therefore timing for effect must be during surgery.
      ii. Some dogs (particularly hemophiliacs) do not respond.
      iii. Refractoriness develops to repeat treatments.
      iv. DDAVP should not be relied upon as the sole agent to improve hemostasis in dogs with hemophilia or von Willebrand's disease, either in an emergency or prior to elective surgery, but is an adjunctive therapy.
   c. **DDAVP Administration to Blood Donors**
      i.   DDAVP may be given to normal donors to boost plasma vWF and factor VIII activity, 45 minutes prior to blood collection for transfusion.
      ii. **Dose: 0.6 μg/kg diluted in 0.9% saline, 1 – 10 mL; give slowly IV over 10 minutes.** Peak levels occur between 30 and 60 minutes; time donation between these times, OR
      iii. **Administered SC** without diluting it but takes longer to effect.

D. WHOLE BLOOD COLLECTION: Canine donors (*see Appendix 3*), Feline donors (*see Appendix 4*).

E. PREPARATION OF BLOOD PRODUCTS

The rationale for component therapy is to allow multiple use of a single unit and to minimize transfusion reactions by only transfusing needed components. Packed red cells allow multiple transfusions to anemic patients without volume overload. Plasma is stored as fresh-frozen plasma, if separated within 24 hours, or as stored plasma, if collected at the whole blood expiration date. (FFP stored for >1 year is also considered to be stored plasma). Platelets or clotting factors are given without risking erythrocyte transfusion reactions, and without unnecessary wastage of red cells. As these products are available from commercial blood banks (see below for contact information), the techniques described are for the rare occasion where specific blood products are not available to you and you have an urgent need for component therapy. Please be aware that utmost care must be taken to prepare these products in an aseptic manner and NO contamination along the collection or administration process can be accepted.

1. **Plasma Extraction (Plasma and Red Blood Cell Preparation)**
   a. In practice, refrigerate (4°C) fresh anticoagulated blood. Obtain or make (or use a flat object such as a book) an extractor (*see Fig. 1 p. 669*). Hang the bag by the holes which fit the hooks of the extractor, until red cells settle (24 hours, maximum for fresh/fresh frozen). The 24 hours sedimentation prior to separation maximizes plasma yield. Canine Factor VIII and vWf are more stable than human factors and will still have clinically useful levels of these factors at 24 hours. Store in a plastic satellite bag or Transfer Pack Container (for large volumes) or in a large syringe with the hub up (small volumes). Select the appropriate bag system.

   b. **If an extractor is not available,** and red cells are required for transfusion, hang the bag upside down (reverse of above) and when the cells have settled they can be transfused (or transferred to a 300 mL satellite bag). The plasma remaining behind can be frozen. Feline blood in a 60 mL, or two 35 mL syringe, (depending on red cell or plasma requirement), can be stored in an upright position; the plasma or red cells are either transfused or transferred to a 150 mL bag.
   c. **Separate plasma from red cells.** When using the double-plastic-bag blood set, gently express plasma while still upright into the second bag. When using a syringe, plasma is simply injected out of the syringe. Take care to minimize contamination of plasma by red cells.
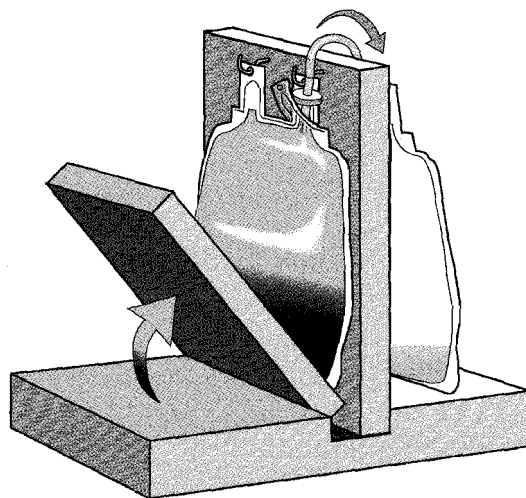
FIGURE 1. Simple blood/plasma separator constructed from three pieces of wood (two 8" x 6" x 1", one 8" x 6" x 2") with two hooks to hang blood bag. After standing to separate, plasma can be squeezed across to separate bag.

d. **At a blood bank or human hospital,** the bag should be centrifuged at 5000 x g for 5 min, or 2000 x g for 10 min. This includes acceleration but not braking time. Braking should be slow to avoid resuspension of red cells.

e. **The plasma is then extracted.** A coupler from a 300 mL Transfer Pack Container is inserted into the outlet port and the plasma expressed. The tubing between the bags [(l) plasma (1) pack RBC] should be permanently sealed.

F. STORAGE OF PLASMA

1. **Stored plasma** is prepared by maximum separation after 24h from 3 or 4 week (CPD or CPDA-1) stored blood, and has a storage life of 5 years in a -20°C freezer.

2. **Fresh or fresh-frozen plasma** is obtained after separation of plasma and packed RBC's up to 24h after collection. The plasma will be platelet poor but provides coagulation factors. The plasma is stored at -20°C or colder for one year (the ideal is -70°C).

3. **If the FFP is accidentally thawed** it may be re-labelled and refrozen and used at a later date as banked stored plasma.

G. STORAGE OF PACKED RED BLOOD CELLS

1. When **separated immediately** after collection, packed red cells are stored at 4°C for 35 days with 100 mL Adsol™, Nutricel™, or Optisol™ (a red cell preservative solution found in a triple bag blood-pack unit). Reconstitution with saline before transfusion is not necessary. For feline blood, Adsol™, Nutricel™ or Optisol™ is added at 12.5 mL/red blood cells from 60 mL whole blood.

2. When **whole blood is separated at the expiration date (35 days),** the red cells are discarded and the plasma is frozen as stored plasma. The total life span of stored red blood cells is 21 days without presrvatives. If plasma is removed during this time, the remaining life time of the red cells is still based on the time from donation.

3. Erythrocyte Storage Viability
   a. Citrate Phosphate Dextrose (CPD)
      i. Dogs and Cats: Whole blood, 21 days stored at 4°C
      ii. Packed cells, not known
   b. Citrate Phosphate Dextrose Acetate-1 (CPDA-1)
      i. Dogs and Cats: Whole blood, 35 days stored at 4°C
      ii. Dogs: Packed cells, 21 days
   c. Adsol™ and Nutricel™ Optisol™
      i. Dogs and cats: Packed cells only, 42 days (should there be 'clumped' material within the bag at this time, do not use)

H. CRYOPRECIPITATE PREPARATION

Cryoprecipitate is a precipitate of fresh frozen plasma and contains Factor VIII, vWf, fibrinogen, fibronectin and Factor XIII and can be purchased from a Veterinary Blood Bank (see below) and delivered overnight. While preparation is not recommended in a practice setting due to inability to control quality of the product, the following maybe useful in the emergent setting.

1. Thaw a unit of fresh frozen plasma in the refrigerator (1 – 6°C), on the extractor (Fig. 1), until it is a slushy consistency.

2. The cryoprecipitate is ready for separation when thawed approximately 90%. The thawed plasma is expressed into a satellite bag (Transfer Pack Container) leaving approximately 10 – 15 mL with the slush (cryoprecipitate). The tubing is sealed between the two bags. Cryoprecipitate can be stored at -18°C or colder for up to one year. The plasma is re-frozen and labelled as cryopoor plasma.

I. PLATELET-RICH PLASMA (PRP) AND PLATELET CONCENTRATE (PC)

1. In practice, PRP, which also contains the buffy coat (unfortunately, some RBCs are also captured), may be prepared by sedimentation of freshly collected blood for up to 15 hours at room temperature (derived from human studies but likely the same for dogs). A 1–2h sedimentation time is required for cat blood. The PRP is transferred to another **non-latex** bag (*see 5 below*). Results of this technique however, have not been reported in dogs and cats. The red cells are stored as packed red cells, preferrably in Adsol™, Nutricel™ or Optisol™ . Unfortunately, what is good for platelets is not for RBCs. Platelets require harvesting at room temperature, while RBCs require refrigeration for optimal viability. The main negative effect of room sedimentation on RBCs is on reduced 2,3-DPG activity. After harvesting the PRP or PC, the PRBCs can be stored in the refrigerator and the plasma frozen as stored plasma. Of course, the potential for bacterial growth is increased during sedimentation at room temperature should the collection be contaminated.

2. Platelet-rich plasma is also prepared by centrifugation of whole blood at 2000 x g, at room temperature, for 3 minutes with an acceleration time of 30 seconds and a braking time of two and one-half minutes. The plasma is expressed into a satellite bag. This bag is then centrifuged again for platelet concentrate.

3. Platelet concentrate is prepared by centrifugation at 5000 x g for 5 min, at room temperature, with an acceleration time of one minute and a braking time of two and one half minutes.

4. The platelet-poor plasma is expressed leaving 40 – 70 mL of plasma and platelets, in the original bag. This is left undisturbed for one hour prior to transfusion. Plasma is frozen and labelled as **'fresh frozen plasma'.**

5. The platelet concentrate is either administered immediately or stored. If stored, plastic platelet satellite bags should be used (CXL, PL-732, PL- 1240). The platelet concentrate is stored at room temperature with constant agitation for 'three' or 'five' (dependent on the bags) days. If not used after this time, discard.

III. ADMINISTRATION OF BLOOD OR BLOOD PRODUCTS

A. Cross Match

Ideally, all donors and recipients should be cross-matched. First transfusion in dogs (*see Appendix 6 p. 681*), is usually safe without cross-matching. Cats have naturally-occurring antibodies to red cells from different blood groups. Therefore, severe incompatibility reactions to a first transfusion can occur, and we have experienced this on rare occasions. A volume (less than 5 mL) of blood can cause an acute, life-threatening reaction. Regionally (southern Ontario) most cats share blood group A. An increased frequency of group B is reported in purebreds and exotics, but we have also noted group B blood in domestic shorthair cats. Australian cats are highly represented by both groups. As a guide, a list of cat (*see Appendix 6 p. 681*) and dog (*see Appendix 5 p. 681*) breed 'potential' blood types are included (*see p. 681*). Cross-matching or blood-typing is recommended for **all cats.** Cross-matching should be performed for all:

1. **High-risk Recipients**

   a. Prior transfusion more than 10 – 14 days previously.
   b. Unknown transfusion history.
   c. Donor blood type is unknown (cats).

2. **Agglutination tests** can easily be performed in general practice. Unfortunately, the cross-match technique that detects hemolysis is not feasible in general practice unless the Coomb's reagent is purchased. The techniques described below only detects agglutination, but are still considered to be valid screening tests for severe incompatibility.

   a. **Rapid method.** Where time is critical, take 1 drop of **donor** blood (EDTA or CPD-1, 1 drop of **recipient** SERUM and 2 drops of saline, place on a glass slide and 'swirl' to mix well. The volumes of each recipient and donor must be the same.

   b. **Blood typing card test** for canine DEA 1.1 +(pos) and DEA 1.1 – (neg) and feline A, B, AB types. (Rapid Vet®-H Blood Group Determination System. DmsLaboratories, Inc., 2 Darts Mill Road, Flemington, NJ 08822, Tel. (908) 782-3353 Fax (908) 782-0832. www.rapidvet.com . dmslabs@aol.com)

   These tend to be reliable for the cat but not as useful for dogs.

   The dog cards are fine for donor selection but should not be used for recipient typing. As the typing cards have a false positive reaction of 10%, i.e., 10% of DEA 1.1 neg dogs will be called DEA 1.1 pos. If the card is used to screen donors, there will be a 10% loss of potential donors, which is not a big a problem. BUT, if used to type your recipients, 10% of DEA 1.1 neg dogs will be called DEA 1.1 pos. IF you then give these dogs 1.1 pos blood, they will be sensitized. Therefore, to avoid reactions in practice, it is advised to use DEA 1.1 neg blood.

   c. **Tube method**
      i. Take two drops of donor whole blood from an EDTA tube (purple top) or CPDA-1 (tubing from blood bag) and mix well with 1 mL of sterile saline.
      ii. Place in a glass or plastic tube (e.g., red top serum tube *without additive*) with two drops of patient's SERUM (do not use plasma as the fibrinogen present may give appearance of agglutination) and centrifuge at very low speed (750 rpm for 15 – 30 seconds; just enough to bring the cells together but not packed tightly.
      iii. Gently shake or flick the tube to resuspend the cells. Hold up to the light to observe any macroagglutination.

   d. **Slide method (most reliable)**
      i. Place 0.5 – 1.0 mL of blood in an EDTA tube (purple top) and 1 – 2 mL in a serum tube (red top) from both recipient and donor (CPDA-1 tubing from blood bag). Label the tubes.

ii. Centrifuge all tubes at about 1000 x g for 5 – 10 min to separate red cells from serum and plasma. If you don't have a centrifuge, allow all tubes to sit at room temperature from 1 – 6 hours to allow separation of RBCs from plasma or serum. Aspirate serum or plasma from tubes with a syringe and 18 gauge needle and place serum in separate tubes. Discard plasma. Label tubes.

iii. An optional step for the slide method to reduce rouleaux formation is to prepare a 4% donor and recipient diluted **red cell suspension (RCS).** Place 0.2 mL packed red cells and 4.8 mL saline in a tube and mix well. Label tubes.

iv. Label 4 glass slides as: a) donor control, b) major cross-match, c) minor cross-match and d) recipient control. Onto each slide place as follows:

    a. donor control – 2 drops donor serum and 1 drop donor RBCs, OR
    1 drop donor serum and 1 drop donor diluted RCS

    b. major cross-match – 2 drops recipient serum and 1 drop donor RBCs, OR
    1 drop recipient serum and 1 drop donor diluted RCS

    c. minor cross-match – 2 drops donor serum and 1 drop recipient RBCs, OR
    1 drop donor serum and 2 drops recipient diluted RCS

    d. recipient control – 2 drops recipient serum and 1 drop recipient RBCs OR
    1 drop recipient serum and 1 drop recipient diluted RCS

e. Interpretation for all techniques, gently rock the slide back and forth and note if there is macroagglutination within 2 minutes. Place on a coverslip and observe under a microscope for microagglutination within 5 minutes.

i. **Agglutination must be differentiated from rouleaux formation.** They are indistinguishable macroscopically. Rouleaux formation may be intense in cats; and in dogs when undiluted cells are used. Microscopically, aggregates of agglutinated cells are rafted together, randomly oriented and superimposed on each other and appear as a 'cluster of grapes' (Fig. 2). Rouleaux appear as stacks of coins (Fig. 3). Small aggregates (Fig. 4) typically appear as a small 'cluster of grapes'. Small aggregates and rouleaux are readily distinguished, but strong rouleaux (rouleaux network Fig. 5) will clump and have a similar appearance to aggregates; however, the edge of the clump helps to distinguish rouleaux (Fig. 5 ↖)from aggregation. After 1 – 2 min in the cat, and 2 – 3 min in dog, dessication of the sample on the slide results in rouleaux formation which is initially identified at the edge of sample.

ii. **A positive for agglutination guarantees incompatibility.** A negative does not guarantee compatibility, but major transfusion reaction is unlikely.

iii. **Patients with immune-mediated hemolytic anemia** have circulating antibodies to red cells, so a major cross-match is often positive, and therefore may be of little value. Preferably, blood from a known DEA 1.1 neg donor should be given. Blood from a donor with 'least positive' cross-match can be used if blood typing is unavailable, but does not guarantee compatible transfusion.
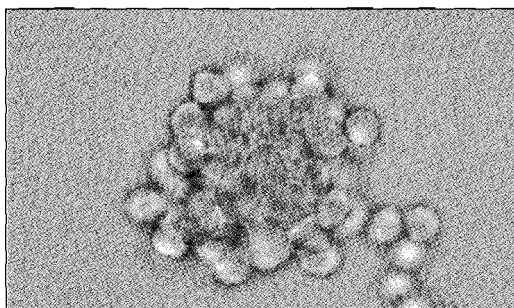
FIGURE 2. Cluster of grapes
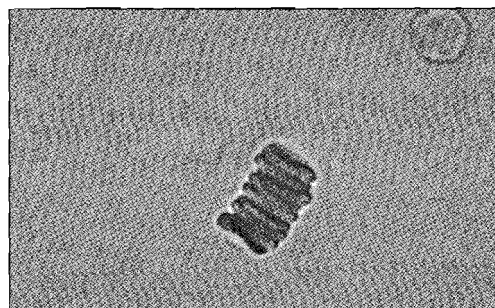
FIGURE 3. Rouleaux
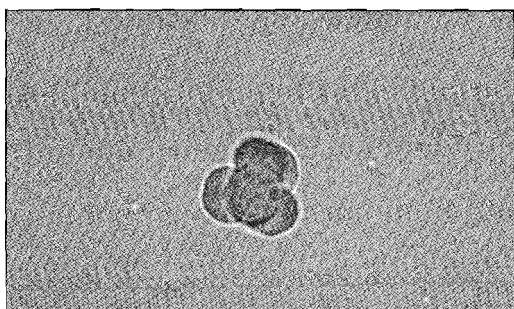
FIGURE 4. Small aggregates
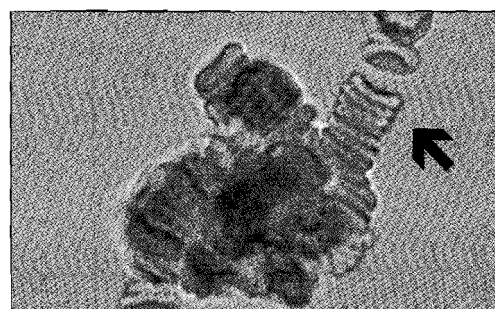
FIGURE 5. Rouleaux network

B. SET UP FOR ADMINISTRATION OF BLOOD OR BLOOD PRODUCTS

1. **Warm refrigerated blood** to room or body temperature prior to transfusion, to avoid hypothermia and possible cardiac arrhythmias.

2. **Deliver transfusions** via commercially made administration sets where in-line filters are present. Filters are designed to retain blood clots, platelet microaggregates, WBCs and fat. Most transfusions of whole blood, RBCs or plasma utilize a 170 μm size filter. Y-component administration sets are advantageous in that 0.9% saline can be given in the fluid administration port to reduce viscosity of RBCs.

3. **Do not administer** lactated Ringer's solution, 5% dextrose in water and hypotonic sodium chloride solution in the same line as the blood transfusion. 5% dextrose in water solution may cause RBC clumping, swelling and subsequent hemolysis as the osmolality is only 252 mOsm/L. Lactated Ringer's contains enough ionized calcium to allow for micro-coagulation to occur.

4. **Platelet administration,** infusion sets should **not contain latex** as platelets will adhere to the latex. Check the filters as occasionally the filter of small blood delivery sets may contain latex.

5. **Small volumes of blood** i.e., for small dogs and cats, can be delivered via an infusion set with a wide arm level connector for a syringe [Blood Component Infusion Set (filter in-line), Baxter Fenwall]. Alternatively, place the blood/plasma in a burette and connect a regular blood filter set.

6. **Administer** via piggy-back of the blood delivery set into an injection port of the fluid line, or connect directly to the IV catheter.

7. **Strict aseptic technique** must be observed when handling all connections. If the existing IV delivery or extension set has been in place >24h it is advised that this be replaced prior to establishing the blood transfusion.

C. TRANSFUSION TECHNIQUE

1. **Whole blood**
   a. **Gently rock and thoroughly mix contents**
   b. Connect the blood bag to commercial blood delivery set with in-line filter.
   c. Open regulation clamp to let blood flow aseptically. Save a few drops of blood from the administration set for PCV. The PCV must be determined before proceeding with the calculations for volume to be transfused. DO NOT ASSUME A VALUE FOR PCV as there is great variability, especially for cats. Connect to patient's catheter or established IV delivery set.
   d. The desired PCV for the recipient is determined by the reason for transfusion. In hypovolemic blood loss a PCV of 25 – 30 (if ongoing blood loss or further crystalloid resuscitation required) is ideal. In immune-mediated hemolytic anemia, a PCV of 20 is adequate and will not suppress bone marrow production of red cells. This equation is usually accurate and is preferred over others.
   e. **Calculation for volume required for red cell replacement:**

$$\text{Donor Blood (mL)} = \begin{matrix} 80 \text{ (Dog)} \\ 60 \text{ (Cat)} \end{matrix} \quad X \quad \text{Weight (kg)} \quad X \quad \frac{\text{Desired PCV – Recipient PCV}}{\text{PCV Transfused Blood}}$$

   A maximum volume of 22 mL/kg/day has been recommended, however the authors have used twice this volume given rapidly without adverse effects. **Volumes greater than this may precipitate hypocalcemic tetany or a hypocoaguable state.**

   f. For active bleeding due to clotting factor deficiency, fresh blood can be administered at 6 – 10 mL/kg two to three times per day for 3 – 5 days or until bleeding stops.

2. **Packed red blood cells** (as for whole blood 1a – e above)

3. **Plasma: stored and fresh-frozen**
   a. Thaw in a 37°C water bath with periodic or continuous agitation.
   b. Connect to a blood delivery set and filter. Connect to patient's catheter/IV line.
   c. **Calculation for volume required for albumin replacement:**

   Volume of donor plasma to be transfused =

   Recipient Wt (kg) x 4.5 x [Desired – Current Recipient Plasma Albumin (g/L)] *

   *Where normal canine plasma volume is assumed to be 4.5% body weight (kg), albumin concentration in the donor bag is assumed to be 25 g/L and the distribution of albumin is assumed to be 40% in plasma. An average unit of canine plasma is 250 mL.

    d. Estimate for volume required

Approximately 22.5 mL/kg plasma is required to raise the recipient's albumin by 5 g/L. The initial dose of plasma for the delivery of clotting factors (e.g., for treating vitamin K antagonist poisoning) and other plasma factors is 10 – 30 mL/kg.

4. Cryoprecipitate

    a. Thaw in a 37°C water bath with gentle agitation.

    b. Deliver via blood delivery set and filter.

    c. Calculation for volume required:

Cryoprecipitate (mL) =

$$\frac{\text{Body wt (kg) X 0.080* X [1–Hct(L/L)] X [Desired – Current Factor level (U/mL)]}}{\text{Factor Level in Plasma Product (U/mL)}}$$

*0.080 x wt = estimated blood volume

    d. Estimate for volume required:

One unit of cryoprecipitate/10 kg q4–12h until bleeding stops. Alternatively fresh-frozen plasma at 20 mL/kg is equivalent to one cryoprecipitate dose.

5. Platelet concentrate or platelet-rich plasma

    a. Connect to blood delivery set with filter that will not trap platelets.

    b. Calculation for volume required

Expected 1-hour Platelet Count x 10^9/L =

$$\text{Plt Count x } 10^9\text{/L before} + \frac{\text{Unit Plt Count x } 10^9\text{/L X Unit vol. X 0.51*}}{\text{Recipient Wt (kg) X 0.080* L/kg}}$$
Transfusion

*0.080 x wt = estimated blood volume and 0.51 corrects for splenic sequestration of transfused plts.

    c. Estimate for volume required:

One unit of platelet-rich plasma or platelet concentrate/10 kg.

    d. Repeat transfusions to maintain the platelet count at 10 – 15 x 10^9/L

D. Rate of Infusion

1. Whole blood and blood components should be warmed by passing tubing through a water bath at temp of 37°C (no hotter otherwise RBCs may lyse), or commercial blood warming device, prior to administration. Initial administration rate should be slow (0.25 mL/kg/h) for the first 15 minutes to allow for observation of reactions. If blood is required for massive hypovolemic blood loss, the initial 0.25 mL/kg/h cautious step is usually omitted and blood is administered to effective endpoint. Maximum rate of delivery is usually 22 mL/kg/h but can be higher in emergent situations. Cardiac arrhythmias may occur at the faster rate therefore monitor ECG. If slight facial twitching is noted, or other evidence of tetany, after administration of large volumes of blood, measure blood/serum calcium as **hypocalcemia** maybe present; administer calcium gluconate 10% solution at 0.5 – 1.5 mL/kg IV over 30 min while monitoring heart rate.

2. Prior to infusion, baseline values should be recorded for: temperature, pulse rate, respiratory rate, mucous membrane colour, PCV and total solids.

3. These parameters should be monitored periodically throughout the transfusion.

4. The transfusion is continued at 5 – 10 mL/kg/h.

5. Volume overload is a significant risk in certain circumstance; congestive heart failure, renal disease, high volume recent transfusions or fluid therapy, normovolemic anemia (i.e., hemolytic or non-regenerative) (*see Fluid/Colloid Therapy p. 347*).

6. Deliver at a maximum rate of 4 mL/kg/h if at high risk of volume overload. Titrate up gradually if no adverse affects noted (i.e., increased respiratory rate and effort, distended jugular veins).

7. **Plasma** may be administered at 5 – 10 mL/kg two to three times per day as required, over 1 – 4h, or as a CRI. Divide volumes such that a bag is not hanging longer than 8h.

8. **Cryoprecipitate** should be infused over 2 – 4h within 6h of thawing.

E. Route of Administration

1. Intravenous

    a. Preferred route; 100% of cells are transfused into the circulation.

    b. Use a 16 – 20 gauge catheter, depending on the size of the animal and circumstances, placed in the cephalic (preferred) or jugular vein. The higher viscosity of blood or RBC's may slow or stop flow if a smaller catheter (22 – 23 gauge) is used.

   c. Flow is improved by diluting blood with 0.9% saline only (calcium-containing, hypo or hypertonic solutions and colloid solutions are incompatible with anticoagulated blood). Peristaltic pumps should not be used as red cells may be damaged.

2. Intramedullary

   a. Efficacy similar to IV; 95% of red cells are absorbed into the circulation within 5 minutes.

   b. An 18 or 20 gauge needle or bone marrow aspiration needle can be inserted into the medullary cavity via the trochanteric fossa, the greater tubercle of the humerus or the tibial crest of neonates or small patients.

3. Intraperitoneal

   a. Poor choice. The rate of red cell absorption is slow. IP route may be useful in puppies and kittens when IV or intramedullary transfusion is unsuccessful. Approximately 50% of cells reach the circulation in 24h and 70% within 48 – 72h. Intraperitoneal transfused cells have a shorter life span.

IV. COMPLICATIONS OF BLOOD COMPONENT THERAPY

Complications can arise from improper component preparation, storage and administration. Transfusion reactions are primarily of two types:

- Immune-mediated
- Non-immune-mediated

A. Immune-Mediated

1. Immediate Immunologic Reactions TO RED CELLS AND PLASMA CONSTITUENTS:

Acute hemolytic destruction of incompatible blood: this is an intravascular event resulting in hemoglobinemia and hemoglobinuria. A more delayed reaction similar to extravascular hemolysis in IMHA can also occur.

Clinical signs associated with hemolysis due to red cell incompatibility and plasma constituents

- Restlessness and anxiety
- Fecal and/or urinary incontinence
- Urticaria/pruritus
- Anuria/renal failure
- Muscle tremors
- Convulsions
- Nausea/salivation/vomiting
- Stretching of legs
- Fever
- Facial edema (angioedema)
- Apnea and/or tachypnea
- Tachycardia

2. Nonhemolytic Reactions

- Urticaria/pruritus
- Anaphylaxis
- Fever
- Facial edema
- Seizures

3. Delayed Immunologic Reactions

   a. Hemolysis due to anamnestic antibody to cell antigen.

     i. Clinical signs similar to A1 above, but usually not as profound.

     ii. Drop in PCV at 2 – 21 days post-transfusion.

   b. Delayed phagocytosis in approximately 7 – 10 days with incompatible transfusion due to antibody formation.

   c. Post-transfusion purpura due to antiplatelet antibodies.

B. Non-Immune Mediated Transfusion Reactions

1. Vascular Overload/Overly Rapid Delivery

- Cough
- Dyspnea
- Vomiting
- Urticaria

2. Fever
3. Non-immunologic Hemolysis
   - Physical trauma to red blood cells:
   - Freezing
   - Overheating
   - Mixing red cells with non-isotonic solutions.

V. TREATMENT OF TRANSFUSION REACTIONS

A. Stop the transfusion at the first sign of reaction. Administer oxygen if dyspneic.

B. If acute anaphylaxis and SHOCK is evident
1. Ensure a **patent airway** and
2. Start rapid infusion of **crystalloid (100 mL/kg) in 20 mL/kg boluses** and assess between boluses.
3. **Epinephrine IV (0.01 mg/kg)** 0.1 mL/kg of 1:10,000 [**prepare** by taking 1.0 mL epinephrine 1:1,000 (1.0 mg/mL) and diluting in 9 mL saline]. The volume in millilitres to be given equals body weight in kilograms divided by 10. If unable to obtain IV access administer into the tongue vein or via a urinary catheter into an endotracheal tube to the level of the carina. Repeat dose if no response. (*see Anaphylaxis p. 615*).
4. **Administer antihistimine: diphenhydramine 0.5 – 2.0 mg/kg (50 mg max.) IM q8h.** NOT IV as hypotension and vomiting may occur OR **tripelenamine HCl 1 mg/kg q12h IV, IM (available in the USA).**

C. Determine the rate and volume received. If **signs are mild** and delivery was rapid, slow the transfusion.

D. If angioedema, pruritus or urticaria present *see Angioedema p. 212.* Remove the blood and examine it. If there is discolouration or unusual appearance, submit a sample for culture and sensitivity, refrigerate and label 'DO NOT USE' (for further testing if needed). If the blood looks normal, refrigerate it and re-start at 25% of the previous rate when reaction has subsided. Should signs recur, discontinue. Administer antihistamine: **diphenhydramine 0.5 – 2.0 mg/kg (50 mg max) IM q8h.** (NOT IV as hypotension and vomiting may occur) OR **tripelenamine HCl 1 mg/kg IV, IM q12h.**

E. Examine the donor and recipient blood for hemolysis **in all cases.** Monitor urine for hemoglobinuria. Cats may have a hemolytic reaction to a blood transfusion without developing hemoglobinemia or hemoglobinuria.

F. If hemolysis has occurred, obtain baseline serum urea or creatinine bilirubin and perform an activated clotting time (ACT).

G. Administer crystalloid fluids at twice maintenance to start. Increase or decrease depending on the severity of the reaction (mild hemolysis vs moderate to severe with hypotension). Fluid therapy and diuresis is essential to avoid renal injury by red cell stroma and hemoglobin. Cautious fluid administration is required for IMHA patients due to increased plasma volume and vasculopathy.

H. Should a significant reduction in urine output occur *see Acute Renal Failure p. 709* .

I. If activated clotting time is 70 <125 sec (dog), 60 <90 sec (cat), OR if massive hemolysis or possible sepsis has occurred, consider treating for DIC (*see p. 417*), administer heparin 75 U/kg SC q8h for as long as is necessary with appropriate monitoring.

J. If sepsis is suspected, collect blood for culture and give **dogs enrofloxacin 5 mg/kg IV q12h** and **clindamycin 10 mg/kg IV q12h** and continue until culture and sensitivity results from blood product are received. For **cats** an aminoglycoside should be substituted for enrofloxacin (*see Neutropenia p. 435*). **Cefoxitin 20 – 30 mg/kg IV q6–8h** and **ampicillin 20 mg/kg IV q6h** may be suitable single-agent alternatives.

K. If a fever develops (>41°C) and is not subsiding, administer **dipyrone 15 mg/kg IV,** OR **dexamethasone sodium phosphate 0.25 mg/kg** (if not contraindicated), or **acetaminophen 10 mg/kg (dog only)** OR **aspirin 10 mg/kg (dog only)** OR **meloxicam 0.1 mg/kg IV, IM, PO,** once.

L. Seizures may occur. If not self-limiting (<60 sec) administer **diazepam 0.5 mg/kg** (*see Status Epilepticus p. 456/460*).

M. **Diarrhea** may occur but rarely requires treatment. If this is a problem administer **famotidine 0.5 mg/kg IV, PO, SC, IM (not IV in cats).**

North American Blood Banks
Animal Blood Bank Hotline www.animalbloodbank.com Tel: 1-800 243-5759
Hemopet www.hemopet.com Tel: 1 714 891-2022
RRC Canadian Animal Blood Bank www.rrc.mb.ca

Eastern Veterinary Blood Bank www.evbb.com 1- 800 949-3822
Midwest Animal Blood Services www.midwestabs.com 1-877 517-6227
Northwest Veterinary Blood Bank www.nwvetbloodbank.com Tel: 1-306 752-5544

PHARMACOLOGY

1) **Adsol™** contains dextrose, adenine, sodium chloride and mannitol. It is supplied in the human blood collection set. Therefore 100 mL of Adsol is in one satellite bag (unit) for canine packed red blood cells. Use 10 mL for feline PRBCs packed red blood cell.

2) **Nutricel™** contains citric acid, citrate, phosphate, dextrose, adenine, sodium chloride. It is supplied as above for Adsol.

3) **Optisol™** contains sodium chloride, dextrose, mannitol, adenine. It is supplied as above for Adsol.

SUGGESTED READING

1. Abrams-Ogg A. Practical blood Transfusion. In: Day MJ, Mackin A, Littlewood JD. BSAVA Manual of Canine and Feline Hematology and Transfusion Medicine. British Small Animal Veterinary Association, Gloucester, UK, 2000:263-303.
2. Kristensen At, Feldman BF eds. Canine and Feline Transfusion Medicine. Vet Clin North Am: Small An Prac. 1995;25(6):1231-1490.
3. Wardrop KJ, Reine N, Birkenheuer A, Hale A, Hohenhaus A, Crawford C, Lappin MR. Canine and feline blood donor screening for infectious disease. J Vet Intern Med. 2005;19:135-142.

APPENDIX 1

CANINE BLOOD DONOR
A good choice would be a Greyhound or any dog >30 kg (lean weight), <8 years with a docile nature, easily accessible venipuncture sites, negative for Dog Erythrocyte Antigens (DEA) 1.1, 1.2 and 7. Female donors should be nulliparous and spayed and male donors castrated. There should be no potential for bacteremia (periodontal disease, surgical implants, skin lesions, wounds or abscesses, systemic illness). Donors should not be receiving any therapy (except heartworm prophylaxis) and should not have had a previous blood or blood product transfusion. Set up a health program as follows. This can also be used as an incentive for private donors.

Health Maintenance

A. Vaccinate annually for distemper, hepatitis, leptospirosis (depending on prevalence of disease in an area), parainfluenza, parvovirus and rabies. Stagger vaccinations of donors as modified live virus vaccines can alter platelet or endothelial function for up to 10 days. Blood donation should wait until at least 2 weeks after vaccination. Vaccination schedule may vary according to current recommendation for any dog.

B. Heartworm negative and on preventative medicine.

C. Resident clinic donors. Every six months perform CBC, biochemical profile, fecal exam, urinalysis, and annual Knotts or, preferably heartworm antigen test.

D. Client-owned donors. Every 12 months, perform CBC, biochemical profile, fecal exam, urinalysis and Knotts, or preferably heartworm antigen test.

E. Donors are bathed and clipped routinely to keep free of ectoparasites.

F. Tests for infectious agents i.e. *Ehrlichia canis, Anaplasma (Ehrlichia) platys, Brucella canis, Mycoplasma haemocanis (Haemobartonella canis), Trypanosoma cruzi, Borrelia burgdorferi* and *Leishmania donovani*, depending on geographic prevalence.

G. Maintain clinic-owned donors on a quality commercial diet. For frequent donors, supplementation with iron, protein, vitamin B$_{12}$, folic acid and pyroxodine are recommended.

H. The amount of blood withdrawn from a dog should not exceed 20 mL/kg every 21 days; client-owned dogs usually donate every 2 – 3 months. Donors to be exsanguinated prior to euthanasia should be in good physical health with normal CBC, biochemistry profile and urinalysis; negative heartworm test; negative tests for blood-borne parasites; and negative to DEA 1.1, 1.2 and 7. An immediate complete necropsy would be optimal.

APPENDIX 2

FELINE BLOOD DONOR

A large (>4.5 kg), lean, young (between 1 and 8 years), friendly, male (size), adult, neutered cat living indoors is preferred. Donor cats should not be fed uncooked meats to prevent *Toxoplasma gondii* infection.

Health Maintenance

A. Vaccinate annually for panleukopenia, calicivirus, rhinotracheitis and rabies or current recommended schedule for the average pet.

B. Examine fecal sample for endoparasites.

C. Annual serum biochemistry and CBC.

D. Test for FeLV, FIP virus, FIV and *Mycoplasma haemofelis/M. haemominutium* (*Haemobartonella felis*). Other infectious agents should be tested for in endemic areas. Serologic testing for *Toxoplasma gondii* is not necessary if cats are raised indoors and fed only a commercial diet.

E. Blood-typing. Cross-matching recommended. See above for methods.

F. Clinic-owned donor may provide 50 mL (no more than 15 mL/kg) blood every 28 days but occasionally 21 days in emergencies. We do not recommend client-owned cat donors as we have had two fatalities associated with anesthesia and blood removal.

APPENDIX 3

WHOLE BLOOD COLLECTION FROM CANINE DONORS

SUPPLIES

- Surgical Prep Solution
- 10, 3 x 3 gauze squares
- Adhesive tape (split lengthwise in half)
- 20 gauge IV catheter
- Clippers
- Sedation 0.05 mg/kg (max usually required is 1.5 mg) hydromorphone or 0.2 mg/kg butorphanol given IM 15 min prior to collection. Regular donors usually do not require sedation.
- Blood Pack with CPDA-1, usually gravity filled (suction may be used).
- Scale to measure 587 g [450 mL blood (470 g) + weight of bag and anticoagulant (117 g)]. Minimum acceptable underdraw for whole blood is 405 mL (429 g) and for packed cells is 300 mL (318 g). Maximum overdraw is 495 mL (525 g); plus 117 g for bag and anticoagulant.

TECHNIQUE (2 persons)

1) Check records – Jugular and cephalic veins are alternated for each donation.
2) Perform TPR, PCV, TS, BUN.
3) Clip area over the jugular vein approximately 4” x 4”.
4) Apply EMLA cream to venipuncture area, wrap and wait for 60 minutes.
5) If sedation is necessary at this point, administer **hydromorphone 0.05 mg/kg** (glycopyrolate 0.005 mg/kg should be given to minimize salivation) or **butorphanol 0.2 mg/kg** may be used instead of hydromorphone. (**Acepromazine** should be avoided if possible to minimize hypotension. If necessary use at **0.01 – 0.03 mg/kg**).
6) Surgically prepare the jugular area.
7) Have an assistant restrain the dog in lateral recumbency with one hand compressing the jugular vein. The neck should be extended slightly.

8) With freshly washed hands or clean gloves, insert the 16 gauge needle into the jugular vein (toward the heart) and collect the 450 mL blood while rocking the bag to disperse the anticoagulant throughout the collection.
9) Set bag on scale when appears full (moderately distended, not tight).
10) Upon completion, hold off vessel to minimize hematoma (5 minutes minimum, by the clock!) Wrap neck to compress venipuncture site.
11) Recover the dog in a cage and observe for any untoward events. Check pulse rate, mucous membrane colour and capillary refill time. Don't forget to give donor a tasty dog biscuit treat!
12) After blood collection, seal the tubing a distance from the bag. Express all blood in the tubing into the bag to allow the blood to go into the bag; hold the tubing. Mix the bag and release the tubing to allow the blood to flow back into the tube. Repeat three times. Seal the tubing close to the bag and at several places up the tube. Cut the tube between the seals (like sausages) to obtain samples. This mixing allows the anticoagulant to mix with the blood so when PCV and TS is obtained it accurately reflects that of the bag.

Blood Bag Label (Dog or cat)

DATE COLLECTED
DATE EXPIRED
PRODUCT

PCV:
TP:

Volume in bag
Unit Number
Donor Name

Record information in the dog's records.

APPENDIX 4

WHOLE BLOOD COLLECTION FROM FELINE DONORS
Prior to blood collection obtain PCV. Must be >28%.

SUPPLIES

- Sedation: see 5 below
- 10, 3 x 3 gauge squares and prep solutions
- 19 gauge butterfly catheters and IV catheter
- Clippers
- 8.4 mL CPDA-1 anticoagulant
- 60 mL syringe (load CPDA-1 in syringe, or split anticoagulant into 2 – 35 mL syringes)
- Artificial tears or ointment for eyes

TECHNIQUE (2 persons)

1) Check records – jugular and cephalic, or medial saphenous veins are alternated for each donation.
2) Perform TPR.
3) Clip area over the jugular vein approximately 2" x 2".
4) Clip and surgically prep cephalic for IV catheter placement. Place catheter and obtain PCV, TS.
5) Surgical prep over the jugular venous access area.
6) **Sedation.** All cats have to be heavily sedated or almost anesthetized. Frequently, a 'pre-medication' is required prior to restraint for further preparation. Depending on the personality of the cat; (i) **butorphanol 0.2 – 0.4 mg/kg IM** alone, (ii) **butorphanol + 0.03 mg/kg acepromazine IM,** or (iii) **butorphanol + acepromazine + 5 mg/kg ketamine IM,** may be required. Acepromazine also useful as an anti-emetic. Blood pressure usually not affected by this dose. Once sedated and IV access obtained, slowly administer ketamine/diazepam 0.5 mL/kg of mixture [1/4 mL ketamine (100 mg/mL) + 1/2 mL diazepam 5 mg/mL) to effect. If not sufficiently sedated, inject a small bolus (0.02 – 0.05 mL/kg) of Ketamine/Diazepam (1:2) IV; if they become light, small boluses of Ket/Val (0.02 – 0.05 mL/kg) IV are given to effect.
7) Administer 90 mL 0.9% sodium chloride, SC.

8) Have an assistant hold the cat in sternal recumbency, with the head up and front limbs hanging over the table top edge; OR in lateral lateral recumbency with head extended and compression applied to the jugular vein.

9) With freshly washed hands or clean gloves, insert the 19 g butterfly needle into the jugular and connect the butterfly tube to the syringe containing the anticoagulant.

10) While collecting 51.6 mL blood slowly (i.e., over 10 min to avoid a drop in blood pressure) remember to mix the 8.4 mL anticoagulant in blood by inverting the 60 mL syringe.

11) Upon completion, remove butterfly from the jugular vein and apply pressure to the venipuncture site for 5 mins, by the clock, to prevent hematoma.

12) Give 60 mL warm 0.9% sodium chloride through cephalic or jugular catheter (this is in addition to 6 above).

13) Recover the cat in a cage in a quiet/dark area.

14) Test blood for PCV, TS without contaminating the blood collected.

AUTOTRANSFUSION

INDICATIONS

- In situations involving large volume blood loss in to the chest or abdomen, autotransfusion can be lifesaving for both cats and dogs.
- Hemorrhage due to trauma or surgery is the most common indication.
- Although blood loss due to rupture of a tumour (i.e., hemangiosarcoma) has been cited as a possible indication for autotransfusion, in the author's (KM) experience this blood is usually discoloured and contains gross particulate matter and autotransfusion is absolutely contraindicated. The recent hemorrhage is possibly one of several and some blood in the chest or abdomen is frequently >24h old which is a contraindication for transfusion due to induction of DIC.

SUPPLIES
- Extension set, 3-way stopcock, luer-lock injection cap, 60 mL syringe, regular blood collection bag with anticoagulant

TECHNIQUE

a) A closed system is made by taking an extension set with a 3-way stopcock, placing an adapter (a luer-lock injection cap) and a 60 mL syringe onto the two arms of the stopcock. The needle of a regular blood collection bag, with anticoagulant, is pushed into the adapter. The stopcock is off to the syringe.

b) The site for thoraco- or abdominocentesis is shaved and surgically prepped. For thoracocentesis, the skin is pulled forward, for abdominocentesis, the skin is pulled slightly to one side.

c) 1 – 2 mL of 2% lidocaine is infiltrated over the site and down to the pleura or peritoneum. Wearing sterile gloves, a 0.25 cm incision is made through the skin and subcutaneous tissue. A sterile teat cannula with a tapered tip is best as it does not kink (alternatively an 18 or 16 gauge IV catheter); secure onto the extension set and pass the cannula into the pleural space or the abdomen (requires a little force).

d) Blood should flow through the tubing into the bag. If this doesn't occur, turn the stopcock to close the collection bag and open the syringe; aspirate via the syringe. Sterile gloves should be worn as the barrel of the syringe will become contaminated with holding and will subsequently contaminate the inside of the syringe. This is only a problem with repeated use of the same syringe. When the syringe is full, close the stopcock towards the patient and gently deliver the blood into the bag.

e) Agitate the bag while the blood is flowing in. Repeat this until the bag is full. For smaller volumes, use 8 mL CPDA-1/60 mL syringe and collect blood.

f) Blood should be administered through a blood filter set and can be delivered rapidly.

g) As with donor transfusion, autotransfusion can result in a hypocoaguable state if transfusion volumes approach 50% or more.

h) The risk of **sepsis** with autotransfusion from a traumatized abdomen is greater than in the thorax. Contamination can also occur in any situation during the collection process. Patients with this degree of blood loss are immunocompromised and are more susceptible to infection. For **thoracocentesis, cefazolin 20 mg/kg IV q6h (dog), q8h (cat)** is recommended, and for **abdominocentesis, enrofloxacin 5 mg/kg IV q24h plus clindamycin 10 mg/kg IV q12h OR ampicillin 20 mg/kg q6h** should be administered. The antibiotic regimen can be reevaluated when the extent of the injuries are known (i.e., whether or not there is a ruptured viscus, etc.) and under what conditions the blood was collected and transfused. Antibiotic therapy should be discontinued once it is established that no infection/contamination is present, 48 hours should be adequate.

APPENDIX 5

General Trends in Blood Types of Dogs in the OVC Blood Donor Program

DEA 1.1/1.2 Negative Breeds (*there are exceptions*):

- ☐ German Shepherd Dogs
- ☐ Hounds (greyhounds)
- ☐ Huskies
- ☐ Boxers
- ☐ Dobermans
- ☐ Mixed Breeds
- ☐ Newfoundlanders

- ☐ Great Danes
- ☐ Nova Scotia Duck Tolling Retrievers
- ☐ Airedale Terriers
- ☐ Mastiff
- ☐ Pitbulls
- ☐ Curly Coat Retrievers
- ☐ Standard Poodles
  (<25 kg, caution with removal of >375 mL)

DEA 1.1/1.2 Positive Breeds (there are exceptions):

- ☐ Golden Retrievers
- ☐ Rottweilers
- ☐ Great Pyrenees
- ☐ Kuvasz
- ☐ Bernese Mountain Dogs
- ☐ German Short Haired Pointers,

  Wire-Haired Pointers

- ☐ Dalmatians
- ☐ Bouviers
- ☐ Chow Chows
- ☐ Rhodesian Ridgebacks
- ☐ Briards
- ☐ Labrador Retrievers (predominantly DEA 1.1/1.2+, but have some DEA 1.1/1.2 -)

APPENDIX 6

FELINE BLOOD TYPE FREQUENCY IN THE UNITED STATES

Breed	Type A (%)	Type B (%)
Abyssinian	86	14
Birman	84	16
British Short-Hair	60	40
Cornish Rex	66	34
Devon Rex	59	41
Domestic Shorthair (by region)		
Northeast	99.7	0.3
North Central	99.6	0.4
Southeast	98.5	1.5
Southwest	97.5	2.5
West Coast	95.3	4.7
Himalayan	93	7
Japanese Bobtail	84	16
Maine Coon	98	2
Norwegian Forest Cat	93	7
Persian	86	14
Scottish Fold	82	18
Siamese	100	0
Somali	83	17
Sphynx	81	19
Tonkinese	100	0

Giger U. Feline Transfusion. Veterinary Technician November/December 1997:747–752.

INTRODUCTION

Exposure to a fire can cause several types of injury: (1) direct thermal injury of the integumentary system; (2) direct thermal, and smoke (inhalational) injury to the upper and lower airways; (3) hypovolemia and hypotension, hypoalbuminemia and multiple organ dysfunction/failure; (4) hematologic injury – coagulation, erythrolysis, DIC; and (5) immediate or delayed neurological dysfunction. Damage to skin and deeper structures is caused by intense heat associated with thermal injuries (flame, hot liquids, heating pads, clippers and infrared heating lamps). Iatragenic injuries are caused by applying excessive heat to patients which are unable to move away from the heat source. **Caustic burns** produce lesions similar to thermal burns, however, caustic agents (strong alkalis or acids) denature proteins causing coagulation necrosis. Vascular thrombosis may result in further damage of the tissues due to ischemic necrosis. Systemic absorption of toxins through damaged skin must also be considered in overall management. Road injuries can cause friction and hot muffler burns. **Electrical injuries** may cause minor injuries or can be fatal; damage varies according to the current, duration of exposure, the pathway and tissue resistance. Thermal injury is most severe at the point of contact. Deep internal injury may also occur. Most electrical injuries in cats and dogs are due to chewing on electrical cords. Burns in the oral cavity usually occur at the commissures of the mouth, the buccal or lingual mucosa and the tongue. Internal injuries may involve the digestive, respiratory, nervous or musculoskeletal system. Severe non-cardiogenic pulmonary edema (*p. 569*) frequently occurs.

The extent and degree of the burn is determined by the intensity and duration of the heat source or, with caustic injuries, by the volume and spread on the body and duration of contact. The **degree** of burn injury is categorized into superficial (erythema and epidermal injury); superficial, partial-thickness (destruction of the epidermis and upper dermis); deep partial-thickness (destruction of deeper layers of the dermis); and full-thickness (involving all layers including subcutaneous tissue). A partial-thickness injury may progress to full-thickness if vasoconstriction occurs secondary to shock and poor perfusion. Skin releases retained heat slowly allowing thermal injury to continue. Cooling the affected area as soon as possible will reduce the extent of the injury and pain. (*see Management B below p. 685*). Often, the degree of injury may not be known for up to two weeks. Dogs and cats can recover from injury to 50% of total body surface area (TBSA), however this is dependent on the **degree** of burn and associated internal and other external injuries. The more severe the degree of injury, the greater potential for systemic illness and poorer prognosis. The author has seen full recovery of full-thickness involvement of the complete dorsal area from head-to-tail in one dog, and complete hemi-thorax and abdomen, with some limb involvement in another. Extensive lesions to the skin can be expensive to treat, however, and this should be made clear to the owners as this may be the deciding factor on pursuing therapy. As these injuries are extremely painful and early resuscitative treatment is necessary for successful outcome, the decision to pursue treatment or not should be made quickly.

Shock occurs with severe burns. Cardiac output may fall by 25% – 50% within minutes of injury due to hypovolemia; increased systemic vascular resistence reduces oxygen delivery to tissues. Burn toxins, such as myocardial depressant factor reduce cardiac contractility and cardiac output. **Secondary problems** associated with severe or extensive burns are sepsis, disseminated intravascular coagulation, renal failure, hypothermia, hypoalbuminemia, acute pancreatitis, major skin loss, biological tourniquets due to eschar on limbs and thorax requiring extensive surgery, and protracted medical/surgical management.

Smoke inhalation injury can be present without associated skin burns. The injury may be restricted to the larynx and trachea (direct heat injury, laryngeal spasm and edema). With reduced ciliary activity, carbon monoxide and other toxic gases and particulate matter are carried to the lower airways causing direct injury or bronchospasm/constriction. Alveolar macrophages may be killed predisposing the patient to pneumonia, pulmonary edema, atelectasis and respiratory failure. Inhalation of carbon monoxide results in a shift of the oxyhemoglobin dissociation curve to the left impairing oxygen release at the tissue resulting in cellular hypoxia, reduced myocardial function, a predisposition to re-perfusion injury, lipid peroxidation and central nervous system demyelination. Delayed (4 – 5 days) neurologic dysfunction has been reported in this instance. Acute (within hours) neurological injury is caused by cyanide and other toxins released from melting plastics and fabrics.

History/Signalment

While examining the patient presented immediately after the incident, **go to** MANAGEMENT **A – E** (*p. 685*).

- Question the owner regarding the cause of the injury and when it occurred.
- If involved in a house fire, sometimes the skin burns cannot be detected at the time of the fire as the hair and skin may appear normal. However, within 7 – 15 days, an area of skin becomes necrotic (leathery appearance progressing to black). Presentation may be at this late date also.
- Accidental/iatrogenic heat sources (i.e., heat lamps, hot packs, recent hospitalization).
- Free-roaming animals are predisposed to road injury.
- Puppies, more than adult dogs and kittens/cats, tend to chew live electric cords. These animals may be found collapsed, or in a tonic state with the cord in the mouth.
- Lightening strikes or high-tension power transmission lines also cause burns but usually death.
- If the injury is due to an unfamiliar caustic substance ask the owner to bring the container (paint solvents, furniture paint strippers, flea dips and solutions).

Clinical Signs/Physical Examination

Go to MANAGEMENT **A – E below** (*p. 685*) while carrying out primary survey. **Note:** Burn patients are at high risk for infection and sepsis. **Always wash your hands** and wear examination gloves and surgical gown (or other overgarment) when handling the patient, or administering medications. Aseptic technique is absolutely necessary when performing any invasive procedures (even blood collection).

- Quickly assess respiratory pattern and effort. Smoke inhalation, and injuries to the airways, lung parenchyma, and skin over the thorax will interfere with ventilation and cause hypoxemia. Following electric-cord bite, increased breath sounds and crackles may be auscultated varying with the degree of pulmonary edema.
- Mucous membrane colour may be pale due to destroyed red blood cells, cyanotic due to pulmonary parenchymal injury, or red due to inhalation of carbon monoxide.
- Capillary refill time (variable), heart rate is increased, pulse pressure is normal or low with vasoconstriction (pain, fear, shock). If in shock begin fluid therapy immediately (*see p. 606*).
- The body temperature may be increased due to retention of heat after the thermal injury, or decreased due to heat loss from the injured area.
- Examine the head carefully as corneal ulcers (*see p. 524*) may be present; the ears and nose may have a purulent discharge if the injury was >48 hours. The oral cavity may contain mucous with carbon particles suggesting lower airway contamination, the buccal mucosa may be burned or blistered and there may be pharyngeal swelling. Injuries in these areas are considered severe due to possible loss of function and appearance, and potentially associated with smoke inhalation where progression of signs almost always occurs. Electric-cord bite injuries usually involve the commissures of the mouth, the tongue and mucosa of the maxilla. These lesions are well circumscribed and may or may not bleed. Occasionally, erosion to the palatine artery causes hemorrhage.
- Palpate the neck, trunk, limbs and abdomen for areas of pain and texture change to fur and skin. Soft tissue edema may be present due to leakage of plasma proteins into the burn site and translocation of water across microvascular membranes. Extensive inflammation occurs due to release of mediators from burned tissue. Look at the footpads, genitalia, anus and between the fur for injuries. Pluck the hair, if easily epilated then a partial or full-thickness burn may be present, although lack of epilation does not ensure this injury is not present.
- **Superficial burns** are erythematous and dry but don't cause blisters; the patient is hyperesthetic or allodynic when lesions are touched. Areas of **deeper partial-thickness burns** are denuded, blistered, may have an exudate and are very painful. **Deep dermal-full thickness burns** appear pale or dark, with ruptured bullae; there is decreased sensation to light touch but deep sensation is present. **Full-thickness burns** are charred, leathery and do not bleed, hair if present is easily epilated. There is little or no pain with pressure to these lesions. A deeper level of burn would include extension into the subcutaneous, muscle and bone. Most burns are not uniform in depth with areas of full thickness and partial thickness being mixed. Surgery is required at some point to repair most except the superficial burns, but again, the extent of the injury has to be considered. In the author's experience, occasionally, there is no external evidence of dermal injury, only to appear 7 – 15 days later when the skin appears brown and leathery and the hair falls out or is easily epilated; therefore, the patient may present some time after the incident. Also, the wound can extend dramatically beyond what appeared to be normal skin during the ensuing 7 – 15 days.

- Carefully clip the hair around any obvious lesions to evaluate the extent of the injury Calculate the area of burned skin by employing the 'rule of nines'. Each forelimb accounts for 9%; each rear limb, 18%; head and neck 9%; the dorsal (thorax) and ventral (abdomen) halves of the trunk, 18% each, of TBSA. The area of burn may extend during the following 24 – 48 hours. This estimate is used for prognosis, assessing the level of care and fluid requirements. An assessment of a <25% TBSA burn may be considered local, and >25% TBSA burn generalized and associated with systemic affects. However, the severity of burn is not factored into this. In humans, the degree of burn is also considered where a >25% TBSA **deeper partial-thickness** burn is assessed as a severe burn, so would a 10%TBSA **full- thickness** burn. A 20% TBSA burn in children constitutes severe. In addition the areas involved, such as the eyes, ears, face, genitalia and feet constitute a category of severe.
- Palpate the **urinary bladder** and continue to note urine production. Acute renal failure due to hypovolemic shock is common when inadequately resuscitated. Look for possible associated injuries such as fractures, blood loss, neurological injuries etc. (*see Triage p. 4*).
- **Electrical injuries** can be similar to thermal injuries. A thorough examination of the mouth is required. Cardiac arrhythmias may be detected as well as abdominal pain, diarrhea and vomiting due to internal injuries. Dyspnea can be extremely severe in these patients. Neurogenic pulmonary edema may occur secondary to massive catecholamine release with peripheral vasoconstriction and redistribution of blood centrally. Seizures may also occur.
- **Chemical burns** may also be severe (*see J below p. 686 and Toxicological Emergencies p. 630*).
- **Neurological** signs may be present ranging from ataxia to coma (*see Neurological Assessment in Head Trauma p. 698*).

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV** may be decreased with associated blood loss, coagulation necrosis and lysed cells; the red cell loss may not be apparent due to increased plasma loss. The PCV may be markedly increased with plasma loss. Increased viscosity here predisposes to microthrombi and decreased perfusion.
- **TS** may be normal with minor burns, but very low with major burns and plasma loss.
- **ACT** may be decreased, normal or increased depending on degree of injury and time of presentation after the injury. A coagulopathy may occur (e.g., DIC).
- **Stick BUN** as a cursory assessment of renal function and degree of pre-renal fluid loss. 'Hyovolemic shock renal failure' is well recognized due to fluid shifts in major burns.
- Blood glucose may be high due to stress, normal or low if septic from a sub-acute injury.
- **Venous blood gases** (or total CO_2) may identify a non-respiratory acidosis due to low circulation blood volume or hypoxia. An increased $PvCO_2$ associated with increased respiratory effort, indicates injury to pulmonary parenchyma.
- **Arterial blood gases,** to assess degree of hypoxemia due to smoke, cyanide, and carbon monoxide toxicity. CAUTION: cyanide and carbon monoxide are not detected when evaluating PaO_2 and oxygen saturation, as these appear normal; however, impaired oxygen release to the tissues occurs. Where possible measurements of carboxyhemaglobin should be obtained to identify the presence of carbon monoxide.
- **Electrolytes** must be obtained as these can be altered with third space losses (hypernatremia, hyperchloremia), but hyponatremia may exist with anti-diuretic hormone (ADH) response; and hyperkalemia with large areas of tissue injury.
- **ECG** should always be performed as cardiac arrhythmias may be associated with moderate to severe burns and electrical injuries.
- **Systemic blood pressure** monitoring is essential in moderate-to-severe injured patients. In dogs, partial-thickness burns of 20% TBSA resulted in loss of 28% of the plasma volume during the first 6 hours. SBP may be normal even with large fluid losses due to intense vasoconstriction, therefore physical exam must be assessed in light of pressures.
- **Radiographs** as indicated (pulmonary edema, possible fractures) when stable.
- **Culture and sensitivity** of older contaminated wounds.

Extended Laboratory Data Base

- **CBC.** Thermal injury causes morphological changes in erythrocytes which enhances removal from the circulation.
- **Biochemical profile** in moderate-to-severe injury to assess overall health of the patient. ALT can increase due to reduced hepatic blood flow within 30 minutes of burn.
- **Urinalysis** may identify hemoglobin or myoglobin if red cell and/or muscle injury are present.
- Further individual tests required are based on patient's presentation and progress.

MANAGEMENT

A. **Administer oxygen ALWAYS,** via flow-by at the nose and mouth, or mask at 150 – 200 mL/kg/min. Intubate and ventilate if necessary. Avoid traumatizing the perilaryngeal and tracheal tissue. (*see Respiratory Emergencies p. 564 for guidelines*). Oxygen is necessary to counteract carbon monoxide (CO) poisoning. As CO levels can only be measured on specific blood gas monitors, assume this is present in all cases and continue with high oxygen flows for at least 4 hours and beyond if needed (*see Oxygen Supplementation p. 577*). Where CO poisoning is confirmed or highly suspect and the patient has worsening neurological signs despite the administration of oxygen, hemoglobin-based oxygen carrying solutions (HBOCS – *see Fluid Therapy for details p. 364*) (Oxyglobin) administration may improve circulating oxyhemoglobin adequately to reverse the neurological signs associated with CO. In cats 5 mL/kg over 3h (not to exceed 5 mL/h); dogs: 15 mL/kg over 3h while monitoring vital signs. If electrical cord injury with severe pulmonary edema go to C – E. Frequently, respiratory symptoms worsen over a 12–72h period. *See monitoring **P**. below p. 687.*

B. **Cool the burned area** with water (7° – 17°C [45° – 63°F], gauge temperature by degree of discomfort the animal shows (personal experience finds the lower to be less painful!) by immersion, compresses or shower spray for at least 30 minutes. Do not use ice as this will compromise circulation to the area. Monitor temperature q5–7min and avoid hypothermia (<38°C [100.5°F]). Remove **caustic substances** by immersion or shower spray. Lavage eyes with sterile saline. Removal of **hot tar** requires liberal application of an emulsifying agent. Tween-80 (contained in Neosporin ointment, Burroughs-Wellcome) or polysorbate, should be applied during immersion or shower spray. Alternatively, solubilizing with mineral or vegetable oil, and then washing with detergent (e.g., Ivory soap) or dishwashing liquid (not dishwasher) has been recommended. Copious lavage for at least two hours is required for strong acid burns and up to 12 hours for **strong alkali burns!** Neutralizing agents can be useful but should be diluted and applied to the wound as a compress. (specific antidotes should be pursued *see Toxicological Emergencies p. 630*). Surgical excision may be required if prolonged contact has occurred, however *see J below p. 686.*

C. Place a **peripheral catheter** in a non-burned area (strict aseptic technique). Collect blood for above tests. A central catheter may be placed later if required.

D. **Analgesics** are **absolutely necessary** as pain is severe.
1. **Initially,** cat and dog, **oxymorphone or hydromorphone at 0.05 – 0.2 mg/kg** IV, IM q2–4h or **fentanyl 5 – 10 μg/kg** IV, or **morphine or methadone at 0.2 + mg/kg IM** AND
2. If required **ketamine** titrate at 0.5 mg/kg boluses IV (cats and dogs) until a state of relaxation and analgesia is reached, even anesthesia.
3. **General anesthesia** with higher dosages of ketamine or inhalant (*see p. 117*) is necessary for wound debridement.
4. Avoid non-steroidal antiinflammatory analgesics until the patient is stable with normal renal function (*see Analgesics and Sedatives p. 81*).
5. **Butorphanol 0.1 – 0.4 mg/kg IV** or IM q2–4h (cats and dogs) may be effective for mild first degree burns.
6. Consider **epidural morphine** if burn injuries are on the hind limbs or perineum and skin at injection site is not injured (*p. 112*).
7. The effective regimen should be continued throughout hospital stay.
8. Addition of **gabapentin 5 – 20 mg/kg PO q8h** (usually 10 mg/kg to start) is reported to reduce the discomfort and pruritus associated with burn wounds. Do not stop therapy abruptly, wean off.

E. **Moderate to Severe pulmonary edema and dyspnea** due to electric cord bite. In addition to oxygen give **furosemide 2 mg/kg (dog and cat) once.** Do not administer excessive amounts of furosemide as hypovolemia will occur. Usually diuretics do not help with fulminating pulmonary edema as the lesion is leakage of plasma, or plasma and red cells into the interstitium + alveoli secondary to 'stretching' or tearing of endothelium during the period of increased hydrostatic pressure at the time of electrocution. Leak continues for a variable period of time. Intubation and assisted ventilation is often required. It may take 2 – 4 days for resolution of edema while being ventilated. Moderate pulmonary edema may be managed with oxygen delivered via nasal cannula.

F. **Ventricular arrhythmias** are managed with **lidocaine 2 mg/kg (dogs) or 1 – 2 mg/kg (cats) IV,** followed by CRI (*see Ventricular Arrhythmias p. 179*).

G. **Fluids.** Due to variability in extent and severity of burns it is impossible to give absolute guidelines for fluid administration, individual and careful assessment has to guide rate and volume. Crystalloid fluid requirement

(Plasma-Lyte® 148 or A, Normosol® R or lactated Ringer's) can be calculated by assessing the extent of injury and fluid losses of the individual; 2 – 4 mL/kg x % TBSA of burn (dogs) or 1 – 2 mL/kg x % TBSA (cats). [i.e., 10 kg dog with 20% TBSA deep dermal burn might require 3 x 10 x 20 = 600 mL, more severe burn would require 4 mL/kg]. Administer half during the first 8 hours and the remainder during the next 16 hours. This is in addition to maintenance fluid rate (*see Fluid Therapy p. 347*). If in shock, increase the rate initially to 1.5 – 3.0 mL/kg/min (dogs) or 1.0 – 2.0 mL/kg/min (cats). Monitor q5min for improvement in mentation, pulse pressure, capillary refill time and heart rate, and evidence of adverse effects (*see Fluid Therapy p. 347*). Slow the infusion to maintenance when improved or stop if overhydrated (increase in respiratory rate, restlessness, serous nasal discharge, crackles or wheezes develop). **Caution** is required with fluid therapy where pulmonary edema exists. Administer only according the clinical signs and measurements of adequate circulating volume. Urine production (*p. 709*) should be monitored to assist with guiding therapy.

H. **Colloids and hypertonic saline** are only recommended in those patients dying of hypotensive shock. Synthetic colloids may offer transient improvement with 2.5 mL/kg aliquotes to a maximum of 10 mL/kg (cats – no faster than over 15 min) or 5.0 mL/kg aliquots to a maximum of 20 mL/kg (dog); or 5 – 7.5% hypertonic saline 2 mL/kg (cat) or 4 mL/kg (dog) given once at 1 mL/kg/min. **If possible avoid synthetic colloids or plasma** until 6 – 8 hours after injury because vascular leakage with extravasation of colloids, plasma proteins and sodium, and accompanying water will occur prior to this time. Once vascular membranes stabilise, translocation of fluid back into the instravascular space occurs and cardiovascular overload may occur.

I. **Fresh or fresh-frozen plasma** may be required after, or during, fluid resuscitation and prior to 6 hours to maintain serum albumin, antithrombin and antiprotease levels (*see Transfusion Therapy p. 673*). Start with 2 – 3 mL/kg, double this if necessary. Continue at 6 – 10 mL/kg q8h as required. If markedly hypoalbuminemic (<14 g/L) with continual fluid losses, 25% Human Serum Albumin may be helpful (*see Hypoalbuminemia p. 431*).

J. **Wound management** (analgesia/anesthesia *see D1-3 above and Chemical Restraint for Procedures p. 97* prior to performing wound management) After copious lavage (B above), carefully clip around the area(s) involved and examine the extent and depth of the burn. Aseptic technique is mandatory as these wounds are highly susceptible to infection. Where the skin is still intact, even though erythematous and may form an eschar in a few days, maintaining tissue viability by prevention of dessication and infection, is of prime importance. There are a few options for treatment:

1. **Silver sulfadiazine (SS) 1%,** is the water soluble ointment recommended initially in veterinary medicine, but should be avoided in renal or liver failure. **SS modified with addition of cerium nitrate** may be more appropriate with very large wounds as it has greater bacterial and fungal coverage with less resistance developing than SS. Either product is placed liberally over the wound and covered with a sterile occlusive dressing. Once or twice daily changes and lavage are required. This may become very expensive.

2. An alternative, cheaper method is the application of **non-pasteurized honey** (from an apiary source), or **granulated table sugar** (from the supermarket) directly onto the wound; even the most contaminated wounds with particulate matter or infection are candidates. This is the author's preference as both are very effective anti-microbial agents, both enhance lymph flow to the wound, mechanically debride the non-viable tissue, and are non-toxic. Depending on the amount of fluid drawn into the bandage (strike through), bandages may require changing at least twice daily initially. When strike through ceases, once daily changes suffice. For honey dressings, bandage from a new packet is cut into the desired length with sterile scissors and placed into the honey and completely soaked or a small amount of honey is placed onto the wound (if painful, administer ketamine D 2 above). Strips are generously laid onto the wound, a sterile towel is applied and wrapped in place. If sugar is used, apply 2 cm thick, place sterile towels over it and bandage in place. If there are islands of dead tissue, these are removed with the bandage. When the demarcation of larger, elevated, hard, black, leathery eschar is defined, this can easily be removed by cutting the devitalized tissue holding it in place. Frequently, no other debridement is needed as smaller areas of non-viable tissue is removed with the bandage leaving small islands of viable epidermal or dermal cells to function as in-situ grafts. Sugar and honey treatment should continue until a healthy granulation bed is formed. Skin may be closed when this occurs usually in 5 – 7 days (*see Suggested Readings below*).

3. Debridement should wait until the patient is stable and the injured area becomes more defined, this may take a few days. If the animal is presented days after the incident, lavage with 37°C (98°F) tap water, debride grossly devitalized tissue (i.e., can lift it up and it is easily dissected free) and manage with any of the above methods.

K. **Oral wound management** varies with severity of injury; a thorough examination when the patient is stable is required to assess extent of injury. Definitive surgical debridement should be delayed until the extent of the lesion is known; many minor lesions heal by secondary intention. Chlorhexidine (0.2%) mouthwash applied into the mouth is very well tolerated and reduces oral infection and odour. A **protective emollient (Orabase®,** Squibb) or Sucralfate suspension directly applied to the lesion may also be of benefit. Alternatively **topical lidocaine gels** (i.e., Lidodan 2%, viscous lidocaine hydrochloride oral topical solution, or injectable lidocaine mixed with amphogel) may be applied q4h. Analgesia is important for these animals and tube feeding may be necessary (*see V below*).

L. Measure **urine production.** Only place a urinary catheter if sterility on placement and maintenance can be assured, or if placement is necessary due to area of burn injury. During the first 48 hours, it may be difficult to restore normal plasma volume, however attempt to maintain urine production of 0.5 – 1.0 mL/kg/h. After 48h, edema fluid is reabsorbed and urine output increases. If it doesn't increase to at least 1 – 2 mL/kg/h, this indicates inadequate plasma volume and an increase in fluid rate or the administration of synthetic colloids, plasma (or whole blood if PCV low) is necessary.

M. **Serum electrolyte** monitoring is essential. Hyperkalemia may occur initially due to intracellular potassium release from injured cells. Subsequent loss via the urine may occur after 48h where potassium supplementation may be required (*see Hypo/Hyperkalemia p. 394*). Hyponatremia may develop with anti-diuretic hormone release, or sodium loss, and higher sodium-containing fluids may be required to manage this in the short term (*see Fluid Therapy p. 347, Hypo/Hypernatremia p. 381*) .

N. **PCV and TS** should be measured q30min during shock therapy and q1h–q12h depending on values. If PCV <25% and TS <40 g/L, whole blood is required. Red cells are required for oxygen transport to injured tissue. If red cell mass is not adequate, healing is retarded and more costly.

O. **ECG and arterial blood pressure** monitoring should be either continuous or intermittent throughout the first 48h. Cardiac arrhythmias may develop up to 72h post injury. Blood pressure is usually stabilised by 24–48h if the patient is continually improving, unless sepsis due to nosocomial or overwhelming community acquired infection occurs. Hypoalbuminemia with translocation of fluid may also precipitate low arterial pressures.

P. **Respiratory rate and effort** must be monitored hourly. If increased rate and effort is required to maintain blood gases within normal range or the patient is fatigued, positive pressure ventilation is required (*see Respiratory Emergencies p. 555* and *Supplemental Oxygen p. 577*) for criteria required for positive pressure ventilation. Where there is injury to the respiratory tract, sloughing of necrotic tissue into the airways occurs at ~12–72h. Bronchoscopic examination and removal of this material improves respiration significantly. This should be performed whether being mechanically ventilated or not.

    1. **Bronchodilator therapy** may benefit patients with smoke inhalation.
        a. **terbutaline 0.01 mg/kg SC cats and dogs,** repeat in 15 min if there is no relief. Check heart rate first, if high then the drug is absorbed, the medication should not be repeated. A respiratory rate or effort that drops by ≥50% suggests a beneficial effect. Repeat as required q4h providing tachycardia is not present.
        b. **Salbutamol 4 μg/kg IV diluted (cats and dogs)** (criteria as in a. terbutaline). If required repeat in 15 min at 4 – μg/kg.
        c. **aminophylline 6 – 10 mg/kg IV (over 10 mins), IM, SC, PO q8–12h (dogs) or 4 – 8 mg/kg IM, SC, PO q12h** (cats) during the first 18h. Start with the low dose as tachycardia frequently occurs.

Q. **Pentoxyfylline 2 mg/kg followed by 2 mg/kg/h IV CRI for 48–72h** has been shown to reduce airway inflammation and subsequent obstruction by mucous and cellular debris. Also, there is improved hemorheologic and antithrombotic effects which improve microcirculation. Overall, there is reduction of perfusion/ventilation mismatch resulting in improved oxygenation, and decreased inflammation and potential for reduced pneumonia (*see Suggested Reading 5 below*).

R. **Corticosteroid therapy** is CONTRAINDICATED overall, however if pharyngeal or laryngeal edema is evident on presentation or soon after, a single dose of dexamethasone sodium phosphate 0.25 mg/kg may be beneficial.

S. **Prophylactic antibiotics** are contraindicated for both smoke inhalation and burn wounds. Administration at this stage would reduce normal flora and increase the risk of nosocomial infection. If clinical signs of pneumonia or

wound infection develop, culture and sensitivity should be performed and the appropriate antibiotic from the antibiogram selected. As systemic antibiotics rarely reach the infected area due to poor blood supply, topical management is recommended. Antibiotics should only be administered where there is evidence of systemic infection which may occur at 72 hours post-severe burn if absolute sterile technique, or adequate wound care is not performed. Culture blood and urine (*see Sepsis/Septic Shock p. 588*) The dosages of antibiotics may have to be increased in patients with severe burns due to the increased volume of distribution (edema & effusion from wounds) and hypermetabolic state.

T. **Airway humidification** (vaporization) is preferred to nebulization to prevent carriage of bacteria to the lower airways and alveoli. Coupage and exercise, if the patient is ambulatory, is recommended. If infection is suspected, transtracheal wash (*p. 574*) is recommended for definitive identification of bacteria and antibiotic susceptibility.

U. **Gastric Ulcer treatment** where there is evidence of ulceration (*see Gastric Hemorrhage p. 67*).

1. **Famotidine 0.5 – 1.0 mg/kg IV slowly (dog) SC (cat) q12h.**
2. **Sucralfate 0.5 – 1.0 g/dog or 0.25 g/cat q8h** (*see Gastric Hemorrhage/Ulcer Prophylaxis p. 69*).

V. **Nutritional support** (*p. 499*) is necessary. If voluntary intake is not possible or the patient is not interested, partial parenteral nutrition should be considered although enteral nutrition is superior. If long term support is required due to extensive injuries, especially in the mouth, a gastrostomy or esophagostomy feeding tube should be placed (*see appendix to Nutritional Support p. 508*). There is a HIGH caloric requirement in severe burns due to hypermetabolism. Parenteral nutrition (*p. 511*) should contain 50% non-protein calories as lipids. Avoid high glucose as this results in high CO_2 which increases the work of breathing. Vitamin and mineral supplementation is required, especially A, C and zinc. Ensure body weight is at least MAINTAINED by the patient.

W. **After 48 hours,** fluids should be adjusted to account for re-distribution and translocation of edema fluid into the intravascular space, increasing urine output, evaporative losses from the wound, diuresis, etc. Fluid therapy should also be adjusted when nutritional support is instituted. Electrolytes, PCV and TS should be monitored and managed as needed.

X. **Ongoing, wound management** with SS + cerium, includes daily gentle wound debridement. All devitalised tissue should be removed as soon as possible. If honey or sugar treatment is selected, debridement occurs with the treatment. Avoid aggressive manipulation to prevent bacteremia/endotoxemia. Final closure should only be performed on healthy, granulation tissue (*see Suggested Reading 5*). As the wound heals pruritus may occur as it does in human patients. If the animal shows signs of this (i.e., scratching, self-mutilation) administer an antihistamine (e.g., **hydroxyzine 2.0 mg/kg PO q8h.** If the animal is not improved discontinue the antihistamine and administer **gabapentin** D 8 above *p. 685.*

Y. Continual vigilance with regard to aseptic technique, respiratory function, fluid and electrolyte requirements, urine output, organ function, onset of pancreatitis, nutritional support, analgesia, wound management, nursing (tender loving care) are all important in managing these very fragile patients.

PHARMACOLOGY

1) **Silver sulfadiazine** is an antibacterial cream that hastens the production of healthy granulation tissue. It should not be used in patients with liver or renal failure.

2) **Aminophylline** is a bronchodilator by relaxing bronchial smooth muscle. It may also cause diuresis and increase gastric secretion, both of which are undesirable side effects in burn patients. Tachycardia may also occur. Should these side effects occur, discontinue it. Aminophylline blood levels are increased when cimetidine is co-administerd therefore cimetidine should not be used for ulcer prophylaxis.

3) **Terbutaline and Salbutamol** produces bronchodilation by stimulation of the beta2- adrenergic receptors in bronchial smooth muscle. Terbutaline also produces a decrease in airway and pulmonary resistance. Also available as an inhaler. Use with caution in patients with a history of seizures. Hypokalemia may result with excessive use.

4) **Famotidine and Sucralfate.** See Gastric Hemorrhage/Ulcer prophylaxis .

5) **Pentoxifylline** appears to increase deformability of erythrocytes and leukocytes, decrease fibrinogen levls, increase secretion of tissue plasminogen activator, inhibit platelet aggregation and increaseprostacyclin production from endothelial cells. All these effects have improved rheologic and antithrombotic properties.

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NOTES

INTRODUCTION

Lacerations involving the skin and cartilage of the pinna are usually traumatic in nature, most commonly from a dog bite or cat scratch.

DIAGNOSIS

History/Signalment

- Recent trauma, especially from an animal fight, is most typical of the history.

Clinical Signs/Physical Examination

- Bleeding or hemorrhage from the pinna, if recent trauma.
- Laceration may be full- or partial-thickness.
- Examine all regions of the body to identify if there are other areas of trauma.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV** and **TS** to assess severity of blood loss.
- Further laboratory tests are performed as indicated by any co-existing conditions.

MANAGEMENT

A. Pinnal lacerations may bleed substantially. Digital pressure should be applied as needed to control hemorrhage.

B. The wound should be assessed, lavaged and debrided as indicated (*see Wound Management p. 705*).

C. Partial-thickness wounds may be left to heal by second intention.

D. Full-thickness lacerations should be treated by primary or delayed primary closure (*see Wound Management p. 705*):
   1. Polypropylene or nylon suture material (3-0) on a cutting needle is preferable.
   2. Simple interrupted sutures should be placed through the skin and may include the involved cartilage.
   3. Wounds involving a flap of skin should be sutured by apposing the skin at the margins of the wound, as well as sutures placed through both the skin and cartilage in the centre of the flap.

E. Sutures should remain in place for 10 – 14 days.

F. An Elizabethan collar is recommended to reduce the risk of self-inflicted trauma to the pinna.

G. For open wounds or pinnas with a high risk of further trauma, position the pinna over the dorsal aspect of the head and apply a soft-padded bandage to pinna and head.

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INTRODUCTION

It is important to classify head injury into mild, moderate or severe as specific therapeutic interventions are guided by this classification. Prognosis depends on degree of head injury and other injuries. Mild and moderate head injured animals recover well; the severely head injured patient may also recover (*see Neurological Assessment below*). **Dogs and cats have the ability to recover good neurological function even with what appears to be severe injury. Time should be given to fully assess the injuries and treat appropriately.** The physical damage that occurred at the time of the accident cannot be changed. The goal of therapy is to minimize secondary brain insults and increased intracranial pressure (ICP) due to systemic causes.

Hypotension (systolic blood pressure <95 mm Hg), hypoxia (PaO_2 <60 mm Hg), hyperthermia, hypercapnia, hypocapnia, electrolyte imbalances, hyperglycemia, hypoglycemia and acid-base abnormalities are detrimental and impact significantly on outcome. Intracranial hemorrhage, cerebral edema and seizures are more difficult to control but should be anticipated. Maintaining adequate cerebral perfusion pressure (CPP) and oxygen delivery to brain tissue by manipulation of the mean arterial pressure (MAP) have a significant impact on outcome. An increase in MAP to 'drive' cerebral blood flow should be provided (CPP = MAP – ICP) to reduce further brain injury, cell death/swelling/edema and further increases in ICP. Previous recommendations of keeping head injury patients somewhat dehydrated should be discarded. Normovolemia, or slight hypervolemia, should be the goal. Perfusion pressures of <70 mmHg may be associated with poor outcome following head injury. **Maintaining cerebral perfusion is a priority in the management of animals with severe head injury. CPP = 80 mmHg should be the goal.**

Following adequate volume expansion, the use of mannitol is the next most useful therapeutic modality to reduce ICP in **severe** brain injury. Decompressive craniotomy is indicated in expanding hemorrhage. The key to optimizing outcome from head injury is constant monitoring of vital signs and neurological status, recognition of deterioration and rapid therapeutic intervention. This monitoring is imperative because compensation for expanding intracranial tissue does occur and ICP usually remains constant until a critical mass is reached. Various mechanisms exist to try and compensate for the increased ICP, including shunting of CSF to the spinal subarachnoid space, increasing CSF absorption, decreasing CSF production and shunting venous blood out of the skull. It is for this reason, that jugular veins must not be occluded. Obviously, this compensation is finite; an exponential rise in ICP occurs due to increasing edema or hemorrhage and arterial blood flow to the brain decreases. It is important to note the subtle neurological changes that occur as this is approaching. As CPP rises, tentorial herniation of a cerebral hemisphere or herniation of the cerebellum through the foramen magnum may occur. If rapid intervention occurs prior to, or at this time, the animal may still recover. As an increase in ICP tends to occur for 48 hours, it is recommended that this period of time be given to trend and treat the animal to avoid secondary brain insult and assess prognosis. In addition, other life-threatening injuries also have to be considered.

DIAGNOSIS

History/Signalment

- Ask the owner for details of the injury such as blunt injury (i.e., car injury, fall, assault), size and speed of vehicle, determine if the animal was conscious after the accident, if it could walk, was it aware of its surroundings, seemed confused, responded to commands etc. This information will assist with determination of mild, moderate or severe degree of head injury and other potential injuries.
- Similarly ask details of potential penetrating injury (knife, gunshot, impalement).
- Obtain age of the animal, medical history and current medication, last meal etc.
- Discuss prognosis with the owner and potential for referral to a 24-hour care facility.

Clinical Signs/Physical Examination

PRIMARY SURVEY

- Observe the **Airway, Breathing, Circulation** rule of triage (*p. 4*). **Do not place a nasal cannula** as injury to the cribriform plate may exist. **Endotracheal intubation may increase ICP** (*see MANAGEMENT A (1) below p. 694*). **Manipulation of the neck may worsen cervical injury.**
- Observe **respiratory pattern** and localize potential problems into upper or lower (thoracic) airways.

- **Inspect and palpate head & face for**

    - lacerations, scalp swelling (hematomas),
    - skull fractures, note:
        - closed or open, note parenchymal herniation, debris
        - depressed less than or greater than skull thickness
        - fracture-related crepitus
        - facial bone fractures note: sinuses – subcutaneous emphysema, movement of soft tissue associated with respiration. Periorbital fractures may cause severe ocular pain and injury.
    - leakage of CSF or blood into the ears, nose, or externally from a penetrating wound or fracture.

- **Ophthalmological examination** should be carried out as soon as possible as facial swelling and edema may occur rapidly precluding a thorough examination (*see Ophthalmologic Emergencies p. 520*).

    - Pupillary size and responses to light, visual acuity (i.e.,menace response, following a hand), hemorrhage of conjunctiva, ocular chambers or retina, penetrating injury, luxation of lens, proptosis. Ocular injury may prevent neurological assessment via pupillary light reflexes.

- The **rectal temperature** should be taken and the animal warmed or cooled to ~37°C (98.7°F).
- Examine the **spine and limbs** for fractures, prior to moving the animal.
- FOLLOW RULES OF TRIAGE FOR CONCURRENT INJURIES (*see Triage p. 4*).

Laboratory Evaluation/Diagnostic Imaging

Stat
Place peripheral vein catheter to obtain:

- **PCV/TS** to assess degree of blood loss. Concern if PCV <30%.
- **ACT** for baseline as injured brain tissue is a trigger for DIC.
- **Stick glucose** as a baseline, as hyperglycemia contributes to morbidity.
- **Stick BUN** if increased may indicate prior renal insufficiency or poor perfusion.
- **Venous blood gases** to assess metabolic status as an indicator of perfusion. Adjusted base excess <-4 mEq/L, HCO_3^- <16 mEq/L suggests inadequate oxygen delivery due to anemia/poor perfusion/ inadequate oxygenation. A PO_2<65 mmHg on **arterial blood** indicates inadequate oxygenation potentially associated with pulmonary injury.
- **Lactate** levels if >2.5 mmol/L (dogs), >1.5 mmol/L (cats) indicate poor perfusion or increased muscle activity.
- **Electrolytes** as baseline, to detect abnormalities and aid to selecting appropriate fluids.
- Measure **oxygen saturation**; if <95%, oxygen supplementation required.
- **Blood pressure** monitoring is essential to maintain adequate arterial and cerebral perfusion pressures. Systolic blood pressure (SBP) <95 mmHg, MAP <65 mmHg associated with head trauma suggests decreased CPP.
- **ECG** monitoring essential due to potential for head trauma associated cardiac arrhythmias (brain-heart syndrome), or other trauma associated arrhythmias. Should these be present refer to *Supraventricular Tachycardia p. 170 and Ventricular Tachycardia p. 179.*
- **Skull and chest radiographs** once the patient is stabilized. If pulmonary contusions are present, fluid therapy must balance perfusion without causing pulmonary edema. Skull fractures that are open or depressed greater than the thickness of the skull, require surgical intervention.

Extended Laboratory Data Base

- **CBC** as baseline to confirm anemia, and detect any pre-existing abnormalities, and to monitor potential thrombocytopenia, leukocytosis/penia.
- **Biochemical profile** to assess other potential injuries and metabolic disorders (renal, liver, protein, pancreas).
- **Urinalysis** to assess renal concentrating ability.

Management will depend on severity of head injury and accompanying injuries. **SHOULD THIS ANIMAL BE REFERRED TO AN INSTITUION WITH CONTINUOUS CARE?** If so, stabilize and refer as soon as possible. All animals with moderate to severe injury require continuous care. On the other hand, NOT all animals with head injury require aggressive therapy; in fact, it may be deleterious if administered inappropriately. Strict attention to detail is required. However, it is recommended that all patients receive oxygen and have a peripheral IV catheter placed.

A. **Oxygen flow-by at 100 mL/kg/min.** Hoods and other head covers are contraindicated without very high flows to prevent re-breathing of CO_2. Avoid pressure on the neck as it causes an increase in the ICP. Keep the forequarters in a normal to slightly elevated (30°) position. Avoid nasal cannula as injury to cribriform plate may exist. If hypoxemic and continuous oxygen is required, nasal prongs may be considered if nasal meati and planum are desensitized with local anesthetic to prevent sneezing; sneezes increase ICP. Measure oxygen saturation (pulse oximetry or arterial blood gases) and maintain it greater than 95%. If the patient is **unconscious or severely dyspneic and unable to achieve 90%** or greater oxygen saturation on supplemental oxygen, if $PaCO_2$ is >50 mmHg, or if total CO_2 is above normal range, **and** with excessive respiratory effort, or is apneic, mechanical ventilation will be required. **If mechanical ventilation is necessary:**

  1. **PRIOR TO INTUBATION**, give **1.0 mg/kg (dogs and cats) 2% lidocaine IV** to prevent elevation in ICP.
  2. **SHOULD SEDATION BE REQUIRED FOR INTUBATION**, a combination of **hydromorphone 0.05 mg/kg and propofol 0.5 – 2 mg/kg** (slowly administered) **or thiopental 5 – 10 mg/kg** (both may cause hypotension), should be administered, to facilitate intubation. A major concern with the opioids is that vomiting may occur with too much, which increases ICP. Conversely, too little may result in 'traumatic' intubation, both increase ICP. The lowest dose possible to facilitate a non-traumatic intubation is advised. For **long term sedation/ intubation try fentanyl 10 – 30 μg/kg and diazepam 0.25 – 0.5 mg/kg** as an IV bolus and maintain a CRI of **fentanyl 4 – 10 μg/kg and diazepam 0.25 – 0.3 mg/kg/h**. If necessary, add **pentobarbital 1 – 5 mg/kg** or to effect; wait 5 minutes for full effect prior to repeating the dose. This may be repeated as an hourly CRI. If possible monitor $PaCO_2$ or end-tidal CO_2 (~ 40 mmHg). Prior to extubation, **lidocaine 1.0 mg/kg (dogs and cats)** should be repeated IV. If narcotic-induced hypoventilation is of concern, titrate naloxone (0.4 mg/mL) 0.1 mL or 0.25 mL added to 10 mL saline and titrate to effect. **Avoid** hyperventilation hypocapnia ($PaCO_2$ <35mmHg, or $PvCO_2$ <40mmHg) unless profound neurological dysfunction has occurred; 2 – 3 minutes of hyperventilation hypocapnia, while **J below** is underway, may decrease ICP temporarily.

B. Cover **severe lacerations, open skull fractures**, etc. with sterile laparotomy sponge or small surgical towels soaked in sterile saline, while providing oxygen supplementation.

C. Place a **peripheral intravenous catheter** if not yet done. Take blood for the stat laboratory tests listed above. It is recommended that jugular vein catheterization be avoided as occlusion of the jugular veins increases ICP.

D. **FLUID RESUSCITATION AND SUPPORT OF MEAN ARTERIAL PRESSURE**
Head injury alone (unless large scalp wound with evident blood loss) does not cause hypotension; if findings in 1 – 4 below are present, severe blood loss elsewhere is occurring and must be identified. If no visible injuries are present, consider blood loss into a femoral fracture, intra-thoracic or intra-abdominal hemorrhage, or fractured spine with distributive shock (note differential temperature of hind feet [warm] compared to front [cold]). Blood loss with reduced cerebral perfusion will alter mentation. Normovolemia must be attained prior to assuming that neurological deficits are due to head trauma.

  1. If the patient is **HYPOTENSIVE** (MAP 40 – 50 mmHg or SBP <90 mm Hg), rapid volume resuscitation is necessary, with the exclusion (caution with delivery) of geriatric patients, those with cardiac disease, pulmonary contusions, non-compressible hemorrhage and significant hypothermia <36°C (97 °F).
     a. **Body temperature** must be increased to 36°C (97°F) as low blood pressure may be due to low temperatures, especially in cats; high fluid volumes here may be contraindicated. Warm the patient (*p. 295*) while commencing with warm **crystalloid boluses: Plasma-Lyte® 148 or A, Normasol® R or lactated Ringer's (dogs: 20 mL/kg and cats 10 mL/kg).** Repeat 2 – 3 times. Do not warm patient to higher than 36°C (97°F) unless shivering, then warm to 37°C (98.4°F). If hypotension persists, then it is not related to hypothermia but blood loss. **See b – f for further treatment.**
     b. **Blood products** are indicated with PCV <25, TS <50 g/L (5 g/dL) and ongoing resuscitation is required. Alternatively, give **Oxyglobin 2.5 mL/kg bolus (cat and dog), repeat to effect in dogs (max 14 mL/kg cats, 20 mL/kg dogs).** Cannot assess PCV if Oxyglobin administered, rely on acid-base, lactate (<2.5 mmol/L dogs, <1.5 mmol/L cats), hematocrit and improved clinical signs.

- Observe **level of consciousness (LOC).** Assess alertness response vocal stimuli, and response to painful stimuli, or if unresponsive to all stimuli. Animals with massive blood loss, moderate to severe hypothermia or hypoxia may have an altered LOC without head injury. The LOC in head injured animals worsens with hypoxia and reduced perfusion pressure. Once corrected, the LOC improves. If hypoxia/hypovolemia are excluded, the altered LOC is likely due to traumatic central nervous system (CNS) injury.
- **Manipulation of the head and neck must be kept to a minimum**, while a rapid examination of the airway is performed to rule out obstruction due to blood clots or tissue trauma, until cranial and cervical injuries have been identified. Perform rapid assessment for bleeding, or cerebrospinal fluid (CSF) leakage, from the nose or ears (skull fractures), lacerations or abrasions of the head or neck, ocular injuries, and limb movements. Seriously injured animals require immobilization of the entire animal to reduce risk of the torso pivoting on the neck and head, and worsening of an unidentified cervical injury.
- **Auscultation of the thorax** is rapidly conducted to rule out pneumothorax, hemothorax, pericardial effusion and thoracic wall injuries. The presence of jugular distension may be noted in these conditions.
- **Assess perfusion** by mucous membrane colour and capillary refill time; peripheral pulses should be palpated for rate, rhythm and strength.

SECONDARY SURVEY

While secondary survey is being conducted, it may be necessary for you to commence **MANAGEMENT** below. Not all head injured animals require aggressive management.

Oxygen should be administered.

- Avoid manipulation (extension, flexion or rotation) of the cervical region until cervical instability is ruled out. Any animal with pain upon manipulation of the neck, with altered level of consciousness or with multi-system injury must be **considered** to have cervical injury. Absence of neurologic deficits does not exclude injury.
- **Mini neurologic examination** to classify head (brain) injury as mild, moderate or severe. The classification is based on the injured animal's mental status (*see Neurological Assessment p. 698 below* for in-depth aspects of the neurological examination).
    - **Mild head injury** may be associated with mild concussion, a detectable degree of temporary neurologic dysfunction may be observed. In animals, this degree of injury may go unnoticed but is manifested in people as confusion/disorientation. An owner may report this in their pet based on 'odd' behaviour following the accident. Short-term amnesia in people may be experienced with slightly more severe injury; thus, a similar occurrence may happen to animals. This injury is reversible and not associated with major sequelae. However, 3% of humans deteriorate, therefore, close observation by the owner or clinician is required for 24 hours.
    - **Mild to moderate head injury** may be associated with classic cerebral concussion that results in loss of consciousness. **Mild injury** in people is associated with amnesia, the length of which is related to severity of injury. This amnesia is transient and reversible and usually lasts up to 6 hours. Many humans have no residual effects, however, dizziness, nausea, anosmia, may exist and is referred to as a post-concussion syndrome. This may occur in animals. When awake, people are still able to follow simple commands but are confused (in animals, this behaviour may be noted as 'demented'), or somnolent and may have focal neurologic deficits (this also occurs in animals). With **moderate injury** a human could not follow simple commands. An animal may be awake but appear very demented. If the animal presents unconscious but responds to voice, touch or painful stimuli (stupor) it can be considered as having a moderate head injury; whereas those that progress to loss of response (coma), should be managed as **severely-head injured** patients.
    - **Moderate to severe brain injury** is adversely affected by secondary insults. Hypoxia, hypotension and anemia may be fairly common in this group due to severity of injury to other organs and associated blood loss. If hypoxia and hypotension are not corrected, mortality increases. Intra-cranial hemorrhage in dogs is often extensive and parenchymal. A neurological examination should be performed as soon as possible to differentiate brainstem versus cerebral injury. Brainstem injuries carry a poorer prognosis than damage limited to the cerebrum.
    - **Severe head injury.** With severe brain trauma, diffuse neuronal injury resulting in **deep coma,** not due to a mass lesion or ischemic insult, may be present. These animals may exhibit decerebration
    - **See Neurological Assessment** below *p. 698.*

c. **Hypertonic saline (HS)** may exacerbate intracranial and other areas of hemorrhage but overall has been shown to be beneficial for rapid resuscitation and head injury. **See J1 for guidelines based on neurological examination.** The risk to benefit ratio must be considered. For **3% or 5% HS, bolus 2 mL/kg/min (6 – 10 mL/kg max), OR 7% HS administer at 1 mL/kg/min (4 – 8 mL/kg max)** for dogs, **quarter of this for cats,** [respiratory arrest and/or vagoreflex bradycardia may occur, treat with 0.02 mg/kg atropine], followed by

d. If crystalloid alone ineffective, add **colloid boluses** of pentastarch, hetastarch or dextran-70 at **(dogs) 5 mL/kg to effect or maximum to 20 mL/kg,** and **(cats) 2.5 mL/kg to effect or maximum to 10 mL/kg** (no faster than over 15 minutes; given rapidly, it may induce vomiting.

e. Reduce the volumes when blood pressure reaches normal limits. **Assess effect prior to each bolus of fluids or colloid.**

f. Blood pressure, vital signs and mentation should be used to assess completion of resuscitation. *See (2) and (3) below and Fluid therapy p. 351, Hemorrhage p. 623.*

2. If MEAN PRESSURE IS 60 – 80 mmHg or SYSTOLIC PRESSURE 95 – 100 mmHg, **crystalloid boluses (dogs: 5 mL/kg and cats: 2.5 mL/kg) to effect (normal blood pressure).** Pentastarch or hetastarch may be administered if further pressure support is required. Maintain systolic pressure at 120 mmHg and a mean of 80 – 100 mmHg to maintain normal cerebral perfusion pressure. Be **cautious** with MAP >70 mmHg or systolic >110 mmHg in non-compressible hemorrhage (abdomen, thorax). If there is ongoing hemorrhage, preferably whole blood should be given and the source of hemorrhage corrected. While lower than normal MAP and CPP contributes to worsening neurological signs, **caution** is necessary when non-compressible hemorrhage or pulmonary contusions are present and only mild head injury is sustained. Worsening hemorrhage due to increased blood pressure may result in a worse outcome. Treatment decisions must be based on individual patient assessment.

3. If there is NO FURTHER BLOOD LOSS BUT HYPOTENSION PERSISTS AFTER MORE THAN ADEQUATE FLUID/COLLOID RESUSCITATION, and temperature is ≥37°C (98.7°F) try the following:

   a. **dopamine 3 – 10 μg/kg/min** (cats and dogs) starting at the low dose. Renal blood flow may be compromised at higher doses. Stop if tachycardia develops.

   b. Gradually reduce pressor support over several hours or more rapidly if tachycardia or hypertension develops. An underlying cause for this hypotension should be sought as ongoing occult hemorrhage is likely and pressor support would be contraindicated.

4. If EUVOLEMIC AND NOT IN SHOCK (cap refill time <1.5 sec, mucous membrane colour pink, peripheral pulses strong and regular, mean blood pressure 80 – 100 mmHg or systolic blood pressure 120 mmHg and heart rate 80 – 150), maintenance fluid rate should be started initially and the patient monitored for potential ongoing blood loss with associated drop in blood pressure (*Fluid Therapy p. 351*).

5. If systemic HYPERTENSION exists (MAP >100 mmHg, systolic pressure >120 mmHg), assess neurological status. Increasing blood pressure and bradycardia (Cushing's Reflex) in the presence of declining neurological function may indicate an increase in intracranial pressure requiring immediate treatment (*see* **J**). If an increase in ICP is ruled out, give an opioid analgesic (*see M*).

E. Glucocorticosteroids. The administration of glucocorticoids in head trauma, as well as the particular glucocorticoid to use, is controversial. If acute trauma with abnormal neurological findings, we currently suggest **dexamethasone sodium phosphate at 0.25 mg/kg q24h for one or two days.**

F. Glucose-containing fluids are contraindicated in head trauma, unless hypoglycemic (<3.2 mmol/L). If blood glucose is <2.5 mmol/L (45 mg/dL) and contributing to neurological signs, administer 0.125 – 0.25 g/kg dextrose (0.25 – 0.5 mL/kg of 50% dextrose diluted 1:3 with saline) IV and maintain on 2.5% dextrose solution (50 mL of 50% dextrose/L of balanced electrolyte isotonic fluids). If >2.5 – 3.0 mmol/L (45 – 55 mg/dL) maintain on 2.5% dextrose added to balanced electrolyte solution. Do not allow hyperglycemia (>8.7 mmol/L, 120 mg/dL) to develop as this increases morbidity. Monitor blood glucose frequently if administering glucose.

G. Repeat neurological examination frequently to monitor the animal's progress. See NEUROLOGICAL ASSESSMENT *p. 698.* Consider giving hypertonic saline or mannitol if there is worsening of the neurological status (*see* **J**).

H. A thorough **ophthalmological** examination (*including fundoscopy p. 534*) should be performed daily if orbital or periorbital structures have been traumatized (glaucoma, uveitis etc. may be a problem).

I. **Pulse, respiratory and temperature** monitoring is essential as alterations can be an indication (or cause) of neurological deterioration.

1. **Severe bradycardia** with extremely high blood pressure (Cushing's reflex) in **the presence of deteriorating mental status** suggests severe increase in intracranial pressure with impending herniation and requires immediate treatment (*see J below*). Bradycardia and other cardiac arrhythmias can be associated with brainstem lesions (brain-heart syndrome). These are usually transient, and should be differentiated from the Cushing's reflex. If therapy is required for supraventricular (*p. 170*) or ventricular arrhythmias (*p. 179*), see specific protocol.

2. **Alterations in respiratory pattern** may indicate worsening of neurological status (*see NEUROLOGICAL ASSESSMENT J below*) or primary respiratory problems associated with pulmonary contusions or aspiration. Maintain PaO_2 >60 mmHg (saturation >90–95%) and $PaCO_2$ at 35–40 mmHg (not sub-normal as previously recommended). Elevated CO_2 (>50 mmHg) and decreased O_2 (PaO_2 <60 mmHg or saturation <90%; Pv (jugular) O_2 <35 mmHg or <50% saturation) can cause cerebral vasodilation and increased ICP. Low $PaCO_2$ (<30 mmHg) can cause cerebral vasoconstriction, poor cerebral perfusion and hypoxia.

3. **Fever** increases intracranial pressure. Maintain at **37°C** (98.7°F) or cooler (cool to point where shivering is **not** induced). Cool head and neck if necessary with cold towels or ice wrapped in towels and place around the patient. Do not compress the jugular veins. Maintaining low-normal temperature is extremely important in preventing cerebral edema and pre-disposing the patient to tentorial herniation.

4. Vomiting, gagging, coughing and sneezing should be prevented as these cause an increased ICP.

J. **Neurological Deterioration**

Hyperosmolar, Diuretics and Osmotic agents. If these agents are required:

1. **Hypertonic saline 5% or 7% bolus 1 mL/kg/min – no faster (6 – 10 mL/kg max) dogs, quarter of this for cats.** (Caution with pulmonary contusions or fluid overload). Maintain serum sodium levels **<160 mmol/L.** Hypertonic saline is currently favoured over mannitol by some in human medicine. An indication for hypertonic saline administration is a comatose patient, or deteriorating patient who initially has normal, reactive pupils but then develops unilateral pupillary dilation. Other indications are similar to those for (3) mannitol, below. Mannitol may be required if hypertonic saline is not successful, or with extremely rapid deterioration, mannitol may be the drug of choice.

2. **If anemic due to blood loss,** Oxyglobin 2.5 mL/kg boluses (cat and dog) **to a maximum of 14 mL/kg in cats** and to 20 mL/kg in dogs. **(Caution with pulmonary contusions)** may be an alternative to hypertonic saline and packed red blood cells or whole blood. Furosemide 0.25 mg/kg may be indicated if fluid overload exists prior to Oxyglobin administration.

3. **Mannitol 0.25 g/kg IV** – (volumes greater than this are usually not necessary) given over 5 – 10 minutes; but repeat immediately if no improvement. A **clear indication** for mannitol administration in human patients is a **comatose patient** who initially has normal, reactive pupils but then develops unilateral pupillary dilation. Mannitol is **also indicated in comatose patients** with bilaterally dilated and non-reactive pupils who are not hypotensive. Another sign of **impending herniation** is the patient who develops dilated pupils, unilateral or bilateral ventrolateral strabismus, vocalization, opisthotonus with rapidly developing coma. While mannitol may exacerbate hemorrhage, it is the drug of choice in this situation regardless of whether hemorrhage is suspected or not as hemorrhage may not be a cause of this deterioration. Hemorrhage may be a cause for deterioration occurring ≥ 24 hours after the traumatic incident, but edema is also highly likely (a CT scan or MRI is recommended for definitive diagnosis). In **patients without such focal neurologic deficits or clear evidence of neurologic deterioration,** the indications for the acute administration of mannitol are less clear and likely **should be withheld.** Mannitol can be repeated q4h as needed for 3 – 4 times in a 24-hour period, based on the neurological assessment. **Do not** administer by constant rate infusion as previously recommended. Extensive diuresis may occur, **reassess fluid status.** Note the concentration of mannitol on the bottle (% weight by volume = grams/100 mL). MANNITOL IS CONTRAINDICATED IN CONGESTIVE HEART FAILURE, VOLUME OVERLOADED, HYPEROSMOLAR OR ANURIC RENAL FAILURE PATIENTS (see furosemide (2) or lidocaine (3) below)

4. **Lidocaine 2% 1 mg/kg IV** has been used by the author (KM) to halt and reverse clinical neurological signs of **tentorial herniation.** Lidocaine can be used in combination with hypertonic saline or mannitol and is the author's (KM) preference to furosemide, unless fluid overload is the cause for the deterioration.

5. **Furosemide at 0.5 – 2.0 mg/kg** may also be considered in those cases referred to in (3) above; however lidocaine (4) above should be tried first, **unless fluid overload** is the cause for deterioration. CAUTION: extensive diuresis secondary to furosemide may cause hypovolemia/hypotension, which may worsen CPP. Furosemide

combined with mannitol has been recommended previously; however, this combination results in extreme fluid loss through diuresis and is not routinely recommended.

K. **General nursing care.** Place the patient at a graduated incline of 30° from chest to head. Do not raise just the head as this kinks jugular veins. Place a urinary catheter in stuporous/comatose and any other recumbent animal. Monitor urinary output and fluids administered (*see Acute Renal Failure p. 709*). If the patient cannot blink, instill artificial tears in both eyes q4h. Nutritional support should be considered by 24 hours (*see Nutritional Support p. 499*). Avoid gagging or vomiting. *See P below.*

L. **Seizures.** Administer **diazepam 0.5 – 1.0 mg/kg** once. Repeat in 5 minutes if necessary; dogs only (*see Seizures for Dogs p. 462, Cats p. 458*).

M. **Pain** can increase intracranial pressure. For **moderate to severe pain: fentanyl 2 – 4 μg/kg** bolus followed by this dose per hour as a CRI, **oxymorphone or hydromorphone at 0.025 – 0.1 mg/kg,** OR **morphine OR methadone at 0.1 – 0.5 mg/kg. Mild to moderate pain butorphanol 0.2 – 0.4 mg/kg.** CAUTION: As the degree of pain is not known and opioid in excess may cause vomiting and increased ICP, it is best to titrate the opioid slowly to effect. Respiratory depression tends not to be a problem when pain exists, however, should an excessive amount be administered, hypoventilation may occur; this must be prevented. Reverse opioid overdose by titrating 0.1 mL – 0.25 mL Naloxone (0.4 mg/mL) in 10 mL saline and titrate 1 mL/min to effect i.e., reversal of adverse effect only (*see Opioids p. 81*).

N. **Vocalization/thrashing** can cause injury and increase intracranial pressure. **Gabapentin 5 – 25 mg/kg PO q8–12h** may be very useful in reducing or preventing this activity. Start with **10 mg/kg** and increase or decrease depending on the level of sedation, taper off slowly, do not stop abruptly (*see Analgesics and Sedatives p. 81*).

O. **Gastroprotectants.** Caution with oral administration of medication as **vomiting** may cause increased ICP and aspiration. For moderate to severe head injury, consider:
1. **Famotidine** – 0.5 mg/kg IV, IM, SC, PO q12h dogs, not IV in cats **OR**
2. **Omeprazole** at approximately **1 mg/kg q12h in dogs** (20 mg/dog if >20 kg, 10 mg if dog is >5 kg and <20 kg, or 5 mg if <5 kg). **Cats 0.7 mg/kg PO q24h OR**
3. **Pantoprazole 1 mg/kg** to maximum 40 mg q12h.
4. **Ulcer treatment Sucralfate Suspension 1 g/10 mL** – don't use tablets. **Dogs 0.5 – 1 g q8h. Loading dose of 3 – 6 g** if severe concurrent gastrointestinal ulcer noted (hematemesis, melena). **Cats 0.25 – 0.5 g q8h.** To avoid interference with absorption of other oral medications, administer on an empty stomach 2 hours apart from other medication.

P. **Aspiration** pneumonia may occur secondary to vomiting, injury to CN IX causing an accumulation of mucous and inability to swallow, and aspiration of blood from areas of nasal or oral trauma. It is advised to carefully suction the oral cavity. Administer **1 mg/kg lidocaine** IV, 3 – 5 minutes prior to suctioning.

Q. **Skull fractures.** Radiographs, or more appropriately a CT scan or MRI if available, of the head should be taken as soon as the animal is stabilized. Fracture fragments, depressed more than the thickness of the skull, penetrating wounds and open fractures, need surgical intervention. Rapid deterioration due to expanding hematoma requires craniotomy.

R. **DIC. If the ACT** is prolonged, the platelet count is decreasing and the patient is not improving or deteriorating systemically, consider administration of fresh or fresh frozen plasma (*see Transfusion Therapy p. 671*).

S. **Discharge home.** If mild injuries noted, and owners are able to interact with the animal every 2 hours with assessment (*see Table 1 p. 700*) and return to the clinic should any of these signs develop, then the animal can be discharged home. It is better to discharge the patient with strict instructions to the owners to call should there be deterioration, than to leave the animal in a cage in the clinic without supervision.

T. **Polyuria** may develop in 2 – 5 days due to a reduction in antidiuretic hormone (ADH), or by natriuresis due to cerebral mediated salt losses. The latter is a disorder referred to as the cerebral salt wasting syndrome (CSWS). CSWS is associated with hyponatremia. Early quantitation of urine volume and urine sodium concentration is necessary to establish the correct diagnosis. While the decrease in ADH, and CSWS is usually reported to occur with severe head trauma, the author (KM) has witnessed polyuria in several cases with only moderate head injury. It is recommended that urine production always be closely monitored to avoid dehydration and hypovolemia.

NEUROLOGICAL ASSESSMENT

Frequent neurological examination is of utmost importance in order to detect early changes and intervene therapeutically before irreversible damage occurs. It is the rapidity of change that reflects the severity of clinical signs rather than the degree of change. The initial examination aims at localizing the lesion so a prognosis can be given. In most cases, the decision of whether or not to treat can be made at this stage, based on the neurological examination and other injuries present.

The neurological examination of the head injured patient includes the evaluation of the LOC, the pupillary size, symmetry and light reflexes, the presence of the physiological nystagmus and palpebral reflexes, the position of the globes, the posture of the head and body and the respiratory pattern.

1. **Level of consciousness.** In head trauma, the injury is sudden leading to abnormalities that are different from that of slowly progressive diseases such as tumours. The clinical signs are quick to appear and in most cases result in stupor or coma. This is because the reticular formation of the brainstem (Ascending Reticular Activating System or ARAS) does not succeed at arousing the cerebrum which received the force of the blow. Similarly, when the injury is at the base of the skull as in the young (cranial sutures still open), stupor or coma may be the result of direct damage to the ARAS. Typically, with deterioration, the LOC changes from an alert and awake animal to a depressed, then stuporous (nearly unconscious, with diminished response to external stimuli) and finally comatose (unconscious and non- responsive to painful stimuli) animal. Response to a painful stimulus should be assessed in all patients. Often, these patients may be hyperalgesic and sometimes temporarily demented. Frequent neurological assessments will detect the progression from alert to stuporous or stuporous to comatose; detecting the transition allows early therapeutic intervention.

2. **Resting pupillary size, symmetry and pupillary light reflexes.** (The pupillary light reflexes should be evaluated in a darkened room using a bright light, preferably a transilluminator).

   The nuclei of the CN III are situated in the midbrain. The oculomotor nerves are responsible for pupillary constriction. Conversely, the sympathetic fibers are responsible for pupillary dilation and extend from the hypothalamus through the entire length of the brainstem (midbrain, pons, medulla). The midbrain is particularly vulnerable in head injury due to its location directly ventral to the tentorium cerebelli. The latter is a ridge that separates the cerebrum from the cerebellum. The midbrain, origin of the CN III, connects the cerebral hemispheres and thalamus to the pons and medulla oblongata. When there is downward displacement of the cerebral parenchyma under the tentorium cerebelli following head injury, the herniated cerebral parenchyma compresses the midbrain with secondary effects on the pupils.

   a. Cerebral damage results in a dysinhibition of the CN III with pupils that are small, but responsive to light. Good prognosis.

   b. Damage to CN III or its cell bodies results in dilated, unresponsive pupils. Parasympathetic fibres (pupillary constrictors) lie on the surface of CN III. Paralysis of these fibres, by compression of this nerve, results in pupillary dilation due to unopposed sympathetic activity

   All pupillary abnormalities observed are variations of (2a) and (2b) above. Typical observations to note:

   i. Miotic but responsive pupils indicate a cerebral or subcortical lesion which carries a fair to good prognosis.

   ii. If the patient is unresponsive to stimuli and has pinpoint pupils, with or without ptosis and prolapsed third eyelid (Horner syndrome), the brainstem is involved. The prognosis is guarded but therapy should be persude.

   iii. Bilaterally dilated and unresponsive pupils, or pupils fixed in mid position, are indicative of severe midbrain damage (nuclei of CN III) or bilateral CN III involvement. The latter can be observed, especially in the young, with hemorrhage associated with basilar skull fractures. These animals may survive. However, as the cranial nerves are located at the base of the skull (optic, oculomotor, facial and vestibulo-cochlear among others), significant and irreversible damage often ensues. The prognosis is guarded.

   iv. A unilateral, dilated pupil, unresponsive to light is associated with CN III or cell body dysfunction. If not present previously and earlier signs were related to the cerebrum, it is suggestive of tentorial herniation. Prior to herniation, the neurological deficits are contralateral to the affected hemisphere if the lesion is unilateral. Once herniation takes place, the pupil is dilated due to direct effect of the herniated parenchyma (often the occipital lobe) on the ipsilateral midbrain and cell bodies of CN III. A ventral and lateral deviation of the globe (down and out) may follow. Identifying these lesions immediately and treating aggressively (*see* J *above*), may reverse this lesion with potential neurological recovery. The author (KM) has observed this return to function.

    v. A rapid change to pupillary constriction or dilation with change in mentation in a previously awake animal, indicates a rapid rise in ICP and should be treated immediately (*see* J *above*).

    Primary ocular injury may alter the pupillary size and light reflexes, and must be considered in the assessment of the pupils.

3. **Position of the globe(s)** may be altered due to direct trauma (variable), pain (retracted), or compression of CN III. With CN III involvement, initial unilateral pupillary dilation occurs followed by full oculomotor paralysis. A ventral and lateral deviation of the globe (down and out) or an eyeball that appears fixed in the orbit may also be present.

4. **Physiological nystagmus**
   a. The physiological nystagmus evaluates the overall function of the brainstem. For this reflex to occur, the vestibular system (peripheral vestibular apparatus, brainstem vestibular nuclei), nerves III (oculomotor), IV (trochlear) and VI (abducent), the ocular muscles and finally the medial longitudinal fasciculus (MLF) must be intact. Therefore, the absence of physiological nystagmus in a comatose animal indicates a poor to grave prognosis.
   b. Spinal injury must be ruled out prior to moving the head and neck. Nystagmus is induced by moving the head sideways. If the head and neck cannot be moved, or if the nystagmus could not be induced by moving the head, the caloric test is performed. This requires instillation of ice-cold (4°C) or warm (37°C) [98.7°F] water in one ear for three minutes. If the brainstem is intact, a resting horizontal nystagmus will be induced with the fast phase away from the side where the water was instilled. This test should not be performed if the tympanic membrane is ruptured or if a skull fracture has resulted in blood or cerebrospinal fluid leakage from the ear.
   c. Arousable animals with an abnormal nystagmus, resting or positional, rotatory, vertical or horizontal, have vestibular dysfunction. These animals have a favourable prognosis.

5. **Palpebral reflexes.** A blink reflex (closure of the eyelids) is expected upon touching the lateral or medial canthi of the eyes. In this reflex, the afferent pathway is the trigeminal nerve (CN V) whereas the efferent pathway is the facial nerve (CN VII). This is a brainstem reflex as the cell bodies of both nerves are within the medulla of the brainstem. Presence of this reflex indicates integrity of the medulla.

6. **Posture**
   a. **Decerebrate rigidity** is a posture observed in severe brain injury. The posture (rigidity of all four limbs with dorsiflexion of the neck in an unconscious animal) is present transiently and comes and goes upon stimulation of the animal. Its presence indicates dysfunction in the upper motor neuron nuclei of the midbrain. It is suggestive of (1) cerebral involvement that is progressing to the midbrain; (2) progressive lesion of the caudal fossa destroying the midbrain. It usually indicates severe head injury but should not be used as a prognostic tool. Decerebrate rigidity may be present in severe metabolic disorders.
   b. **The adversive syndrome** is observed with unilateral cerebral or thalamic dysfunction. For this syndrome to be present, the patient must be aroused. Upon stimulation, the animal has a tendency to circle or adopt a curved posture (body, head and neck) toward the side of the hemisphere affected. As the animal becomes more aware, the circling progresses from tendency to circle to compulsive circling toward the side of the lesion. The prognosis is usually good as the injury is mostly confined to one hemisphere.
   c. **Decerebellate rigidity** is a posture with opisthotonus, extension of the forelimbs and **flexion** of the hind limbs in a patient that can be aroused. The presence of this posture is indicative of a vermal cerebellar lesion, which frequently progresses to involve the brainstem that lies beneath it. It is observed with injuries to the back of the head. Prognosis is guarded to good depending on severity of the lesion.

7. **Respiratory pattern.** Different patterns may be observed according to the level of the lesion. The most frequent abnormal pattern encountered is the **central neurogenic** hyperventilation associated with midbrain lesion. There is an increased rate and depth of the respirations as if the animal was panting. This pattern can reduce the $PaCO_2$ to extremely low levels. This abnormal respiratory pattern does not carry as bad a prognosis as the following. The **Cheyne Stokes** pattern is a periodic hyperpnea that regularly alternates with apnea. This rarely observed pattern is indicative of a deep bilateral cerebral hemispheric lesion with incipient tentorial herniation. **Apneustic** breathing is an irregular respiratory pattern with periods of apnea, which is associated with brainstem injury. Cheyne Stokes and apneustic respiratory patterns carry a guarded prognosis. Caution must be exercised when interpreting respiratory changes because metabolic (*see Acid-Base p. 406*) and neurogenic causes often are intermingled.

8. **Motor responses.**
   a. Unilateral brainstem (pons, medulla) injury results in ipsilateral hemiparesis.
   b. Unilateral injury cranial to the midbrain, or cerebral injury, results in contralateral proprioceptive deficits.
   c. Unilateral midbrain injury results in variable hemiparesis.

TABLE 1. Head-Injury Discharge Instruction

Your pet does not have a serious head injury, however, new signs and unexpected complications can develop hours, or even days after the injury. The first 24 hours are the most crucial and you, or another reliable person, must stay with your pet at least during this period. If any of the following signs develop, call Tel: and ask for a veterinarian.

1. Drowsiness or increasing difficulty in awakening your pet (awaken every 2 hours during period of sleep)
2. Nausea or vomiting
3. Convulsions or fits
4. Bleeding or watery drainage from the nose or ear
5. Depression/hangdog appearance as though in pain
6. Weakness or difficulty walking properly. Note which side is affected.
7. Strange behaviour or disorientation
8. One pupil (black part of the eye) is much larger than the other; peculiar movements of the eyes
9. Unusual breathing pattern
10. Very slow or very fast pulse rate (optional to perform)
11. Increase swelling at the site of injury

Do not give any other medication than that prescribed. If you are concerned about pain, call the above. Should you have any concerns about your pet, call the above.

PHARMACOLOGY

1) **Hypertonic saline** increases intravascular osmotic pressure, which attracts water from the interstitial and intracellular space. This results in a reduction in extravascular hydrostatic pressure and tissue dehydration. It should not be used in moderate – severely dehydrated patients. Hemorrhage may be exacerbated with administration. The increase in blood pressure produced is rapid but short lived, approximately 20 minutes. Crystalloids should be administered but at half the calculated dose that would be required if hypertonic saline was not administered. Rapid infusion may cause a vagal reflex and bradycardia and respiratory arrest (*see Fluid Therapy p. 347*).

2) **Pentastarch/hetastarch or dextran 70** are colloids which remain in the intravascular space. Pentastarch will increase intravascular volume by 1.5 times the volume administered due to its osmotic Donan effect. Dextrans can increase bleeding tendencies and should be used with caution (*see Fluid Therapy p. 364*).

3) **Dopamine** and **dobutamine** are pressor agents. In this protocol dobutamine and the beta- or alpha-adrenergic effects of dopamine are required to maintain a systemic blood pressure greater than intracranial pressure to ensure adequate cerebral perfusion.

5) **Mannitol** is an osmotic diuretic, which causes rapid removal of both extravascular and intravascular fluid, has a favourable rheological effect (reduces blood viscosity), causes cerebral vascular constriction and is an oxygen radical scavenger. If given too rapidly, may cause vomiting which will increase ICP. It is the treatment of choice for acute cerebral edema resulting in increased ICP.

6) **Furosemide** is a loop diuretic that is used in this protocol for acute cerebral edema resulting in increased intracranial pressure where mannitol is contraindicated and lidocaine ineffective.

7) **Lidocaine** is a local anesthetic which, when used to desensitize the pharynx and larynx for endotracheal intubation, reduces the gag and subsequent increase in ICP. Lidocaine also causes cerebral vasoconstriction and reduced blood flow, and can be used to lower ICP in the emergent setting.

8) **Oxymorphone, hydromorphone, methadone, fentanyl, morphine, and butorphanol** are opioids recommended for head injured patients (*see Analgesics and Sedatives p. 81*).

9) **Thiopental** and **pentobarbital** are barbiturate anesthetics used to facilitate assisted ventilation. Both cause hypotension.

10) **Propofol** dose-dependently, induces sedation and anesthesia. Causes respiratory arrest and hypotension if administered rapidly.

11) **Dexamethasone sodium phosphate** is a glucocorticoid, which is recommended for veterinary head trauma patients based on its purported cerebral protective properties of reducing edema.

12) **Midazolam** and **diazepam** are benzodiazepines which are used as sedatives or for treatment of seizures.

13) **Gabapentin** is an antiepileptic and analgesic agent. It has been suggested that the antiallodynic actions of gabapentin involve a central mechanism of action by binding with the high affinity $\alpha_2\delta$ subunits of voltage dependent calcium channels, blocking calcium currents in cortical neurons and blocking maintenance of spinal cord central sensitization. Gabapentin is excreted by the kidneys; animals with renal insufficiency may require less frequent dosing due to slower elimination. As dosing to effect is the method by which the appropriate dose is selected, once this effect is reached, twice a day rather than three times daily treatment may suffice. Nephrotoxicity is not an issue. The author (KM) has found gabapentin useful in treating animals following head injury, cardiopulmonary arrest or seizures that are extremely restless, disoriented, vocalizing and/or manic. Signs of overdose are reduced activity and excessive sleepiness, progressing to depression. Tapering the dose down is important, as stopping the drug abruptly may lead to rebound pain which may be severe.

SUGGESTED READING

1. Advanced Trauma Life Support for doctors: Chapter 6 Head Trauma. American College of Surgeons Committee on Trauma: Student course Manual 1997.
2. Bayir H, Clark RSB, Kochanek PM. Promising strategies to minimize secondary brain injury after head trauma. Crit Care Med 2003;31(1 Suppl):S112-117.
3. Dewey CW. Emergency management of the head trauma patient.Vet Clin NA: Sm Anim Pract. 2000:30(1):207-225.
4. Donati-Genet PC, Dubuis JM, Girardin E, Rimensberger PC. Acute symptomatic hyponatremia and cerebral salt wasting after head injury: an important clinical entity. J Pediatr Surg. 2001;36(7):1094-7.
5. Kirby R. Brain Injury. In: Tilley LP, Smith FWK, (eds). The 5 Minute Veterinary Consult. Canine and Feline. 3rd ed. Philadelphia: Blackwell Publishing, 2004:168-169.
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NOTES

INTRODUCTION

A wound refers to the gross disruption in the integrity of a tissue, and may be characterized as an abrasion, laceration/incision, avulsion or shearing injury. The classification system of traumatic wounds refers to the likelihood of contamination or infection and may be considered as follows:

- Clean-contaminated: wound was created by a grossly "clean" object (e.g., sharp piece of glass) AND is less than 6 hours old ("Golden Period").
- Contaminated: wound was created by a grossly "dirty" object (e.g., road surface, tooth) and/or is greater than 6 hours old.
- Dirty: wound contains purulent material or necrotic tissue.

For naturally-occurring wounds, the degree of contamination or tissue injury is less easily controlled. In general, a healthy patient should be able to tolerate contamination equal to 10^5 bacterial organisms per gram of tissue, without an infection developing. Factors which decrease the number of organisms needed to produce an infection (the patient's infection threshold) include but are not limited to: compromised immune system, diabetes mellitus, tissue necrosis, foreign debris, implants (suture material, etc.), blood clots, local ischemia, tissue dead space. Wound healing involves the processes of hemostasis, inflammation, repair, epithelialization and contraction. Wound management therefore involves promotion or acceleration of these stages.

Treatment of the wounded patient should first involve systemic stabilization (*see Fluid Therapy p. 347 or Hemorrhage p. 624*), including hemostasis if indicated. The wound should be protected from further contamination, then explored, lavaged, debrided and definitively managed.

DIAGNOSIS

History/Signalment

- Ask owner as to where, when and how the trauma occurred. This will aid in determining management and potential antibiotic selection. For example: road injury, farm injury (barn, manure), dog fight, gunshot.

Clinical Signs/Physical Examination

Recognize the type of wound:
- **Laceration.** Sharp edges, linear or jagged edges. Minimal tissue necrosis or compression.
- **Avulsion.** Tissue which has been pulled free of its natural attachments. Results from tensile forces and tissue damage may be mild to severe.
- **Shearing** results from obliquely directed forces, usually due to high friction such as a road traffic injury. Often causes severe tissue injury of variable depth.
- **Puncture/bite.** Small wound(s), usually from tooth. Characterized by severe compressive forces and trauma to underlying tissue, and often involve disruption of tissue planes and large amounts of dead space. Regarding bite wounds, bacteria are often deposited deep in wound. Dog bites typically create small superficial wounds with extensive crushing and shearing damage to the underlying tissues. As a result, it is essential to fully explore the extent of tissue injury, to determine:
    - if the wound communicates with a body cavity
    - the extent of associated muscle injury
    - the presence of tissue "pockets"
- **Penetrating wounds** using sticks, knives, bullets and others.
- **Pressure necrosis.** Common complication of bandage applied too tightly and immobilized recumbent animals.

Associated Clinical Signs

- Hemorrhage especially if footpads are lacerated.
- Exposed tendons, bone or joint surfaces.
- Dyspnea from thoracic wounds, especially penetrating wounds if pneumothorax, hemothorax, fractured ribs are present.
- Subcutaneous emphysema penetrating wounds from an open pneumothorax or severe avulsion of underlying tissue planes.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV** may be anemic due to blood loss or other illness.
- **TS** may be reduced due to blood loss or other illness.
- Stick **BUN** to assess potential pre-renal, renal or post-renal lesion.

Diagnostic imaging

Thoracic radiographs: For deep or puncture wounds over the thorax or abdomen, radiographs of these body regions should be performed once the patient has been stabilized. Evaluate pleural cavity for pneumothorax (if communicating thoracic wall wound or perforated lungs), pleural effusion (hemorrhage or pyothorax). Evaluate lung parenchyma for atelectasis, consolidation or lung lobe torsion. Evaluate ribs for fractures and vertebral bodies for fracture/subluxation injuries.

Abdominal radiographs: evaluate for free air in the peritoneal cavity (indicating perforated bowel or full-thickness abdominal wall wound) and lack of serosal detail in the retroperitoneal space (indicating uroabdomen, hemoabdomen, bile peritonitis, septic peritonitis).

Extremity radiographs: wounds on the lower extremity have minimal soft tissue coverage. The underlying bones and ligaments may therefore also be injured (especially with shearing or bite wounds). It is important to perform radiographs of a region if there is any suspicion of associated bone or ligament injury. Shearing injuries over the carpal or tarsal joint may also warrant stress radiographic views to detect ligamentous instability; however, this should only be performed once the animal is stable and has sufficient analgesia. Bullets can result in severely comminuted fractures.

MANAGEMENT

A. STABILIZE PATIENT

1. Where appropriate place an **IV catheter** and administer balanced electrolyte fluids (*see p. 351/362*).

2. **Protect wound** from further contamination by applying sterile dressing (gauze sponges).

   If the injury appears to communicate with the thoracic cavity, seal the wound by covering it with a sheet of commercially available medical adhesive film such as Op-Site (clear adhesive polyurethane film) or Ioban (iodine-impregnated adhesive polyurethane film).

3. **Control hemorrhage:** local pressure with soft bandage is preferred; an Eschar bandage or rubber tourniquet may be considered if direct pressure fails to control hemorrhage. An Eschar bandage may be used over the forefoot or hindfoot, and is applied by wrapping elastic bandage (e.g., Vetrap) tightly over the foot, stopping just proximal to the wound. A window is then created in the bandage over the wound, exposing the tissues and allowing identification and ligation of vessels. The Eschar bandage is then promptly removed.

   A tourniquet is used for the purpose of identifying and ligating vessels that continue to hemorrhage despite the application of direct pressure. If any form of tourniquet is used to control hemorrhage of a distal extremity, it should be placed distal to the elbow or stifle joint and its use limited to 20 minutes at a time. Use caution and note that nerve damage or ischemic injury may result from tourniquet application.

B. ANTIBIOTICS

Systemic antibiotics are not routinely used in all wounds. Preferably, topical preparations should be used where possible (*see below*). NB: Clean lacerations should be managed with local irrigation and no systemic antibiotics. With large contaminated wounds, systemic antibiotics may not reach the wound and may contribute to development of resistant organisms.

Criteria for systemic antibiotic administration are:
1) Systemically ill (obtain blood cultures where possible) (*see Septic Shock p. 588*)
2) Open fractures
3) Closed fractures where implants will be used for correction
4) Deep wounds (obtain cultures where possible)

Suggested antimicrobial therapy

    1) Road injuries – cefazolin 20 mg/kg IV q6h OR cephalexin 20 mg/kg PO q8h for 3 – 7 days depending on the wound.

    2) Farm/barnyard injuries – ampicillin 20 mg/kg IV q6h OR ampicillin-clavulanate 10 mg/kg PO q12h.

C. PENETRATING FOREIGN BODIES

1. **Linear Penetrating Foreign Bodies** (e.g. large sticks, arrows, knives). **Remove only under appropriate conditions!** Since these foreign bodies may be plugging a rent in a large blood vessel, their removal without precautions may result in fatal hemorrhage. Due to the potentially numerous soft tissue structures involved (large blood vessels, lung, gastrointestinal tract, vital organs, nerves), the removal of a penetrating foreign body involves careful surgical exposure of the affected body region or cavity and the ability to control hemorrhage or repair vascular damage if necessary. For this reason, it is recommended to stabilize the patient and promptly refer such cases to a specialist for surgical exploration.

2. **Bullets:** These are generally the only indications for surgical removal of a bullet foreign body. Bullets do cause significant tissue injury upon entry and/or exit. Radiographs should be performed of the involved body regions, and the wounds explored and managed as described in this chapter.

   Bullet foreign bodies do not generally cause a problem, and may be left *in situ* UNLESS they are impinging on a nerve or located in a synovial joint.

   Emergency exploration of the abdominal cavity is always indicated if the bullet has penetrated the abdomen. Due to the potential for severe organ injury from the bullet, we recommend stabilizing the patient and referring such cases to a specialist for surgical exploration.

D. WOUND CARE

1. You may need the following items:

   – Water-soluble lubricant (KY jelly)
   – Clippers
   – Sterile gloves
   – Sterile instruments:
   – hemostatic forceps
   – tissue forceps
   – Mayo or metzenbaum scissors
   – Needle drivers & suture scissors
   – Suture material (monofilament) or skin staples
   – 35 mL syringe & 18 ga needle
   – Lavage solution (see below)

2. Administer analgesic/sedative; wound care is often painful.

3. Apply sterile lubricant (KY jelly) to wound surface.

4. Clip hair from surrounding body regions.

   a. **Wound Exploration**

   After preparing the wound as described above, use sterile hemostatic and tissue forceps to carefully probe the extent of the wound:

   i. whether it communicates with a body cavity (chest, abdomen).
   ii. damage to underlying tissue planes and muscles.
   iii. presence of debris or necrotic tissue deep within the wound.

   This is especially important to perform for penetrating or puncture/bite wounds.

Thoracic or Abdominal Cavity Penetration

Small wounds over the thoracic cavity do not necessitate emergency exploratory thoracotomy unless the patient cannot be stabilized. Large penetrating thoracic wounds usually require surgical exploration and closure in order to re-establish negative pressure in the thoracic cavity. Penetrating or crushing (i.e., bite) abdominal wounds warrant emergency exploratory laparotomy to evaluate organ damage, especially bowel perforation or kidney avulsion. Full-thickness abdominal wall wounds may be debrided and the body wall closed from the laparotomy approach, and the superficial (overlying) tissues managed by external bandaging and wound care.

b. Lavage

To reduce discomfort of lavage, warm solution to $\sim 30 - 37°C$. Room temperature lavage solution is uncomfortable to painful.

Use a 35 mL syringe and 18 ga needle in pulsatile fashion; or a hose and shower head (for tap water).

Lavage solutions: 0.9% saline, LRS , 0.05% aqueous chlorhexidine (savlon), 1% betadine, luke warm tap water. Tap water, although hypotonic and non-sterile, is effective for mechanical debridement of grossly contaminated areas (i.e., gravel and dirt) and daily cleansing of wounds treated with honey or sugar. It is best suited for shearing injuries, but should be avoided in wounds with deep pockets since drainage of water from these regions is impaired.

Note: If bone segments or articular surfaces are exposed, the use of sterile saline or lactated Ringers solution is preferred.

c. Debridement

Use scissors or a blade, dry gauze and lavage solution to remove debris and necrotic tissue.

Recognizing nonviable tissue:

i.   Failure to bleed on cut surface or when pricked with a hypodermic needle

ii. Grey or green in colour

iii. Failure to detect arterial flow using Doppler

Note: some thrombosed or edematous tissue may initially appear nonviable and fail to bleed. Therefore … if unsure whether tissue is viable, LEAVE in place and re-evaluate at subsequent bandage changes. Unless it is a clean-contaminated wound with healthy tissue, wet-to-dry bandaging is recommended to ensure complete wound debridement. The application of granulated sugar or unpasteurized honey has also been shown to be very effective in wound debridement. Bandages should be changed daily.

d. Local antibiotic therapy is beneficial for heavily contaminated wounds. Topical therapy using unpasteurized honey or granulated sugar is also excellent for these wounds for both antimicrobial and continuous debridement therapy. Honey impregnated strips of bandages (dip in container of honey) are placed on the wound, or if granulated table sugar is used a 2 cm depth should cover the wound. Both are wrapped with a sterile towel or sandwich bandage to absorb the fluid, followed by an outer bandage layer. Bandage change may be required twice daily if it becomes wet, but at least once daily thereafter. Topical antimicrobials may be of minimal benefit for clean and clean-contaminated wounds, unless applied prophylactically within 3 hours of contamination.

e. Assessment of Closure

i.   Primary Closure: suturing the wound margins in apposition, upon initial evaluation of the wound.

ii. Delayed Primary Closure: surgical closure of the wound following debridement and wet-to-dry bandaging.

iii. Secondary Closure: surgical closure of the wound once granulation tissue is present.

iv. If a wound is contaminated or dirty, primary closure should not be performed. It is best to perform wet-to-dry bandaging until debridement is complete, then reassess and close if indicated. Similarly so if sugar or honey are used for debridement.

E. DRAINS

1. **Indications:** large amount of dead space (from avulsed or undermined tissue planes); contaminated or dirty wound.

   Drain Types
   a. **Open: Passive drainage (Fig. 1)**
      Relies on gravity and capillary action to remove fluid
      Advantages: inexpensive; easy to place and maintain
      Disadvantages: potential for ascending bacterial infection; drainage may be less effective than active drain; not suitable for removal of air
      Examples: Penrose (latex tubing) drain

2. **Placement:** drains should be inserted in the deepest region of dead space and exit from a stab incision that is separate from the wound; passive drains (i.e., Penrose, **Fig. 1**) rely on gravity and should exit from a dependant region; FOR A CLOSED DRAINAGE SYSTEM (**Fig. 2**) use a suture or Chinese Finger Trap to secure drain to skin at exit site.

FIGURE 1.
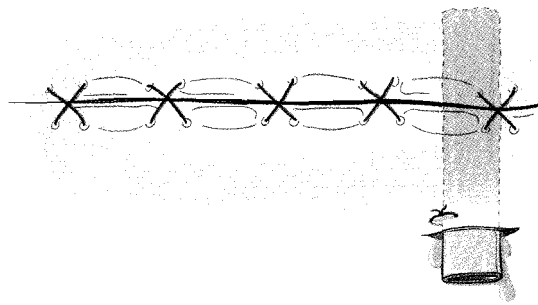
3. **Maintenance:** cover drain with sterile bandage; tie-over bandages (**Fig. 3**) are useful for areas that are difficult to bandage. The presence of drains inherently produces 1 – 2 mL/kg/day of serosanguinous fluid. Remove the drain once the volume has decreased to approximately this level and stabilized (approx 2 – 3 days). The presence of purulent discharge or a sustained high volume of, from a drain may indicate persistent infection and warrants re-exploration of the wound and/or bacterial culture of the drain or its contents.

FIGURE 2.
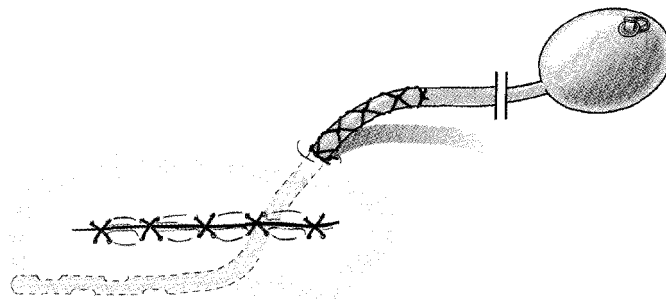
      b. **Closed: Active drainage (Fig. 2)**
Relies on intermittent or continuous negative pressure to remove fluid and/or air
Advantages: lower risk of ascending infection; negative pressure increases effectiveness of suction; indicated for removal of fluid and/or air
Disadvantages: more expensive; more difficult to secure tubing and reservoir to patient.
Examples: Jackson-Pratt drain; continuous-suction unit; tubing-and-Vacutainer

F. BANDAGING

1. Primary (Contact) Layer

Function: placed in direct contact with the wound or incision; may be adherent, non-adherent, occlusive, semi-occlusive or non-occlusive. If debridement of the wound is indicated a wet-to-dry technique using an adherent dressing (i.e., moist or dry gauze) should be used; non-adherent (i.e., Telfa pad, petroleum-impregnated gauze) material is indicated if healthy granulation tissue and migrating epithelium are present.

Materials commonly used: saline-moistened gauze, Telfa pad, petroleum-impregnated gauze, porcine submucosa (BioSIS), hydrocolloids, hydrogels.

Products commonly used for contact layer:

Antimicrobials:
Silver sulfadiazine (Silvadene)
Nitrofurazone (Furacin)
Non-pasteurized honey, granulated sugar, 50% dextrose
0.05% chlorhexidine on sterile gauze

FIGURE 3.

Agents Used to Enhance Wound Healing:
Non-pasteurized honey or granulated sugar
Iamin (Iamin® Hydrating Gel), Procyte Corporation, Kirkland, WA
Acemannan
Porcine submucosa collagen (BioSIS)

Semi-Occlusive Dressings:
Petroleum-impregnated gauze (Adaptic, Johnson & Johnson)
Telfa pad

Occlusive dressings:

2. Secondary Layer

Function: pads and protects the limb, body region, wound, or incision; absorbs wound exudates (serum, blood, purulent material) by capillary action.

Materials commonly used: roll cotton or cast padding; applied layers must be thick enough to collect the fluid; cotton must be applied tightly enough to prevent loosening of bandage.

3. Tertiary (Outer) Layer

Function: secures the primary and secondary layers; offers some water-resistant properties.

Materials commonly used: roll gauze and Vetrap or surgical adhesive tape.
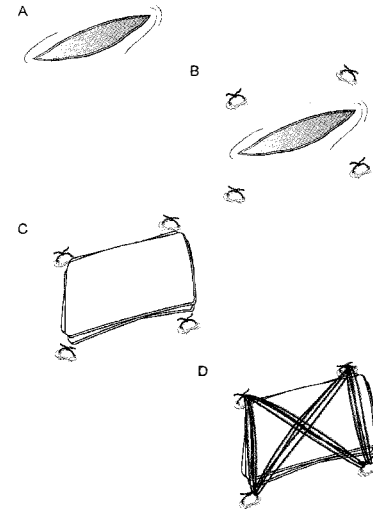
G. BANDAGE CARE

1. Bandage should be changed once to twice daily during debridement stage.

2. Once granulation tissue has formed, NON-adherent dressing is placed, and frequency of bandage changes may be decreased to every 2 – 3 days depending on the amount of exudate produced.

3. Immobilization of the healing area is recommended, to prevent disruption of the new capillary buds.

4. Bandages should remain clean and dry at all times.

5. Owners should seek immediate veterinary attention if they notice a wet or loose bandage, foul smell, swollen digits or body part, or the patient is chewing at the bandaged body part.

H. EMERGENCY CARE OF OPEN FRACTURES

1. **Clean wound** and prevent further contamination. Address wound over fracture site, as described above (lavage with sterile saline solution, debride as needed, wet-to-dry bandaging).

2. **Temporary stabilization** of fracture segments is required until definitive treatment is performed. Stabilize fracture segments using external coaptation if applicable.

3. **Definitive stabilization** of the fracture (internal or external fixation) should be performed once sufficient circulation has been re-established to the adjacent soft tissues. This may require one to three days of wet-to-dry bandaging and soft tissue debridement. If surgical exposure of the fracture segments is performed too soon after the injury, further vascular compromise of the soft tissues may result.

I. ANCILLARY SUPPORT

1. Analgesics (*see p. 81*).

2. Monitor patient's vital signs and organ function where applicable (*see Monitoring p. 12*).

PHARMACOLOGY

1) **Topical antimicrobials: Triple-antibiotic ointment** (bacitracin-neomycin-polymyxin): broad-spectrum of activity; zinc-bacitracin enhanced epithelialzation.

2) **Silver sulfadiazine (Silvadene):** effective against *Pseudomonas* spp; drug of choice for burn wounds; however unpasteurized honey or sugar are also effective.

3) **Nitrofurazone:** superficial broad-spectrum activity.

4) **Gentamicin sulfate:** excellent activity against gram-negative organisms. Honey or granulated sugar both have broad spectrum antimicrobial activity, draw lymph fluid to the wound, enhance macrophage movement to the wound, enhances granulation tissue and provide nourishment to the healing wound.

5) **Modifiers of wound healing: Honey, granulated sugar, 50% dextrose:** superficial antimicrobial activity; decreases edema formation; excellent during debridement phase of wound care.

6) **Acemannan:** activates macrophages.

7) **Tripeptide-copper complex** medication (Iamin-Vet Skin Care Gel®): enhances fibroplasia and rate of wound healing.

8) **Porcine collagen (VET BIOSIS):** encourages ingrowth of adjacent tissue; accelerates granulation tissue production and wound healing.

9) **Lavage solutions: Tap water:** inexpensive and readily available; hypotonic.

10) **Sterile saline:** Isotonic, painless, non-toxic.

11) **Lactated Ringers solution:** Isotonic, painless, non-toxic.

12) **0.05% Chlorhexidine:** antimicrobial properties; delays granulation tissue formation at high concentrations.

13) **1% Betadine solution:** antimicrobial properties; inactivated by organic matter, reduces leukocyte migration.

SUGGESTED READING

1. Hedlund CS. Surgery of the Integumentary System: General Principles and Techniques. In: Fossum TW. Small Animal Surgery, St. Louis, Mosby 2002:134-152.
2. Mathews KA, Binnington AG. Management of wounds using honey. Compendium Cont. Edu for Pract Vet. 2002;24(1):53-60.
3. Mathews KA, Binnington AG. Management of wounds using sugar. Compendium Cont Edu for Pract Vet 2002;24(1):41-50.

INTRODUCTION

Renal failure can be described as acute or chronic, or acute-on-chronic. Renal failure may be anuric (urine production <0.08 mL/kg/h), oliguric (urine production <0.27 mL/kg/h) or polyuric (>2 mL/kg/h). Acute renal failure (ARF) is an abrupt and, severe reduction in renal function. It is most commonly caused by ischemic (e.g., hypotension, hypovolemia) or toxic insults, but may be associated with infectious agents, and may be characterized by anuria, oliguria, or polyuria renal failure or insufficiency describes the failure of the kidney to appropriately perform the function of urine concentration or dilution, or to eliminate the products of metabolism of such a magnitude that it causes azotemia (increased serum urea and creatinine). The inability to concentrate or dilute the urine usually occurs with approximately 66% reduction in renal function whereas recognizable failure to eliminate products of metabolism (azotemia and uremia) occurs at a reduction of 66% to 75+%. While creatinine is not a measure of glomerular filtration rate (GFR), a change from baseline can indicate a change in GFR; an increase in creatinine in this setting is highly indicative of a reduced GFR even if the absolute value is within normal limits. When the creatinine value of a well hydrated animal lies in the upper end of the range of normal, this may suggest more than a 50% reduction in renal function at that time, depending on circumstances of presentation. Several problems can mimic or predispose to ARF, therefore all pre-renal, renal and post-renal causes must be considered. Urinary tract injury should be suspected in all trauma patients until ruled out; there should be a high index of suspicion in patients sustaining abdominal or pelvic injuries (*p. 727*). Refer to Tables 1 – 4 for potential etiologies.

Acute renal failure may occur in any hospitalized patient, therefore, steps should be taken to avoid predisposing animals to ARF by ensuring normal hydration and normovolemia, especially prior to anesthesia. Nephrotoxic drugs (e.g., aminoglycoside antibiotics) should be avoided in situations where the possibility of hypotension, hypovolemia, or any situation in which splanchnic perfusion may be jeopardized (i.e., abdominal surgery, prolonged anesthesia/surgery, geriatrics) may occur. Furosemide is frequently used in oliguric states and will enhance aminoglycoside toxicity. Amphotericin and some non-steroidal anti-inflammatory analgesics may result in renal injury and should be used judiciously. As renal failure can potentially occur in any hospitalized patient, vigilance is mandatory; serum urea and creatinine, or at least a stick BUN, should be performed in all animals upon admission to hospital to screen for possible renal failure or insufficiency. Sepsis, systemic inflammation, and administration of contrast agents, may predispose patients to acute renal failure. Normal urine production is between 0.5 – 2 mL/kg/h for animals receiving fluid therapy, but may be reduced in dehydrated animals. The volume of urine produced must be considered in light of urine specific gravity (Table 5).

The history and physical examination, in combination with the laboratory data will determine whether the causes are pre- or post-renal or primary renal in origin.

DIAGNOSIS

History/Signalment

- The history may reveal a period of polyuria and polydipsia, or an abrupt reduction in urine production (frequently associated with post-renal obstruction).
- A thorough history should be obtained to determine a pre-, renal or post-renal cause (Tables 1 – 4). Include questions with regard to toxin ingestion (*Toxicological Emergencies p. 630*), environmental conditions, previous polyuria/polydipsia, stranguria (*see Urethral Obstruction p. 745*) , hematuria (*p. 731*), recent trauma (*p. 727*), gastrointestinal problems, 'constipation' (straining due to perineal hernia [*Urethral Obstruction p. 745*]), cardiovascular disease, and medications administered.
- When did the patient last urinate This will establish the severity of illness.
- Consider congenital (peri-natal problems), or genetic etiology. The Lhaso apso, Shihtzu, Shetland sheepdog, Golden Retriever, Labrador retrievers, and soft-coated Wheaten Terrier are breeds reported to experience early onset renal failure. Polycystic kidneys in Persian cats.
- Determine if the animal is urinating a "steady stream" vs urinating "little drops at a time"
- If the patient is in hospital, examine the medical record in regards to calculation of urine output (check that people cleaning the cage record if urine was present) and volume of fluids administered. Investigate any precipitating cause, including technical issues with the urinary catheter, if in place.

Clinical Signs/Physical Examination

- Examine the patient carefully for any precipitating events (Tables 1 – 4), urethral obstruction (*p. 745*), retroflexed bladder into perineal hernia (*p. 745*), trauma (*p. 727*), cystitis/urethritis (reflex dyssinergia) (*p. 745*). Renal involvement may be secondary to systemic disease resulting in glomerulonephritis (e.g., polyarthritis, dermatitis, endocarditis, pyometritis, neoplasia).
- In all emergency situations, the volume of urine within the bladder should be assessed upon presentation to the veterinarian by abdominal palpation, abdominal radiographs or ultrasound examination, urinary bladder catheterization or voiding. If bladder size is large and turgid, consider an obstruction (*p. 745*). If the bladder cannot be palpated, consider anuria or a ruptured bladder (*p. 727/745*).
- The clinical signs will vary depending on the etiology.
- Assess hydration status; severe dehydration is a pre-renal cause of anuria/oliguria.
- Bradycardia, hypothermia, pale mucous membranes with prolonged capillary refill time, hyperpnea and halitosis are often evident with prolonged oliguria or anuria and indicate severe metabolic and electrolyte derangements (uremia).
- The kidneys are usually normal in size, or large and painful (e.g., pyelonephritis, acute inflammation or hydronephrosis due to obstruction); rarely, acute on chronic renal failure may occur where the kidneys are smaller than normal. Kidneys affected by lymphoma are diffusely large; other tumours may result in abnormally shaped kidneys as do polycystic kidneys
- If oliguria/anuria develops in hospital and a urinary catheter is in place, insure that it is not kinked, obstructed or displaced.
- Post-renal obstruction (*p. 745*) must be identified and relieved prior to aggressive fluid therapy. If the patient is in shock, cautious titration of bolus fluid therapy is advised (*see Urethral Obstruction p. 746 and Shock p. 606*).

Laboratory Evaluation/Diagnostic Imaging

Stat

All samples should be obtained prior to fluid therapy.
- **PCV/TS** for baseline information. PCV may be below normal in chronic renal failure, increased with polyuric renal failure or other situations of fluid loss resulting in dehydration. TS may be low with inflammatory conditions, including sepsis, protein-losing enteropathy, glomerulonephritis, and protein losing nephropathy,; or liver disease (Table 6).
- **BUN, serum urea, creatinine,** to evaluate severity of renal failure.
- **Electrolytes** are variably altered depending on the condition causing anuria/oliguria (Table 6). (*see Hyper/Hyponatremia p. 381, Hyper/Hypokalemia p. 394, Hyper/Hypophosphatemia p. 390, Hyper/Hypocalcemia p. 373/377*). Potassium, phosphorous, calcium and magnesium may be increased in renal failure (Table 6), and hypercalcemia may be a cause of renal failure (e.g., Vitamin D toxicosis, neoplasia). Hypocalcemia may also be present.
- **Acid-base** evaluation (ABE, pH, HCO_3), total CO_2, are frequently altered with the degree varying with severity of illness (Table 6). Most commonly, non-respiratory acidosis is present (*see Acid-Base p. 406*).
- **Blood glucose** may be decreased with sepsis, or increased with stress in cats and diabetes mellitus.
- **Urine.** See Table 5 for interpretation. Low specific gravity cannot be interpreted where corticosteroids, diuretics or other drugs causing diuresis have been given, or with hyper/hypoadrenocorticism, diabetes mellitus, any condition inhibiting antidiuretic hormone (ADH) release or function (e.g., head trauma, renal diabetes insipidus, *E. coli*, and other infectious causes of cystitis). The urine specific gravity is helpful in localizing the cause of the azotemia. Dehydrated, azotemic patients with urine specific gravity >1.030 in dogs and >1.045 in cats most likely have pre-renal azotemia. However, cats can concentrate beyond this, even with significant reduction in renal function, therefore, concentrated urine in cats may not exclude renal failure. A significant pyuria is present with pyelonephritis and moderate to severe cystitis, unless a low specific gravity and polyuria are present, where the cell count will appear relatively low.
- **Serum osmolality measurement** (Table 7) is warranted if ethylene glycol or salicylate intoxication is suspected. If the difference between calculated (see equation below) and measured osmolality is >10 – 15 mosm/L, an unidentified substance is present and confirms suspect intoxication (e.g., ethylene glycol, aspirin, ethanol or methanol); or may be increased due to uremic toxins if renal failure is moderate to severe, ketoacidosis or lactic acidosis.
- Measure **anion gap** (Table 7). High anion gap acidosis is typical in renal failure (*see Acid-Base Assessment p. 408*).
- **Urine culture** if urine sediment or physical examination suggests possible infection. Escherichia coli (and possibly other bacteria) cystitis/pyelonephritis can cause a profound polyuria resulting in dehydration, without typical signs of cystitis (pollakiuria or stranguria). Patients with diabetes mellitus or hyperadrenocorticism may not be able to mount an adequate immune response, therefore only a low number of WBCs may be seen on the smear. If polyuric and polydipsic, bacteria may not be seen due to the high volume and dilute urine.

- **Abdominocentesis.** Cytology, PCV and TS, creatinine and potassium (*see Urine Leakage p. 727*) of abdominal fluid if present. NOTE: false positive results can be obtained on BUN sticks. Should a positive result be obtained, perform creatinine on the fluid. A negative result on BUN stick is real, indicating the fluid is not urine.
- **Abdominal and pelvic radiographs** to assess bladder size, if cannot be determined on physical examination, or for other reasons as determined by physical examination and differential diagnoses (Tables 1 – 4). ± abdominal ultrasound, ± contrast studies should trauma indicate injury to the urinary system (*see Urine Leakage p. 727*).
- **Central venous blood pressure** monitoring to assess pressure and intravascular volume.
- **Arterial blood pressure** should be measured. Hypotensive/hypovolemic patients will be identified. Non-volume loss ARF can result in hypertension.
- **ECG** monitoring to detect cardiac arrhythmias that may be a cause of renal failure (i.e., primary cardiac disease), or as a result of renal failure (e.g., *Hyperkalemia p. 397*).

Extended Data Base

- Complete serum **biochemical profile** to assess involvement of other organs (e.g., pancreatitis, hepatitis) and for measurements of phosphorous and calcium. which can be increased **primarily causing renal** failure, or may be increased (early and late RF-phosphorous, late RF-calcium) **secondary to acute renal failure.** These may also be low or normal.
- **CBC** may reveal a leukocytosis associated with infection or inflammation (GN); thrombocytopenia, potentially associated with leptospirosis; absence of a stress leukogram, (*Hypoadrenocorticism p. 275*) or leukopenia, due to an overwhelming infection (*Sepsis/Septic Shock p. 588*).
- **Urine electrolytes** (fractional excretion of sodium [FeNa] (Table 7), may help localize the problem.
- **Serology** is advised where leptospirosis is suspected. This is a zoonotic disease and veterinary personnel and family members must be notified of potential infection. Serological testing is suggested where any organisms listed in Table 4 are suspected.
- **Ethylene glycol** test for suspect ethylene glycol toxicity (*p. 656*).
- Specific **diagnostic imaging** procedures will depend on the history, physical findings and hematological/biochemical data. Ultrasonographic imaging is useful in identifying pyelonephritis (dilated renal pelvis), hydronephrosis, neoplasia, and injuries. Pyelocentesis for culture and antibiogram, fine needle aspirates and/or biopsies may be performed.

MANAGEMENT

I. PREVENTION OF RENAL FAILURE

A. **Intravenous administration of contrast media** has the potential to exacerbate renal function. For intravenous urography (IVU) and angiogram, the contrast agent is usually ionic with high osmolality. Computed tomography and myelography also requires a contrast agent. Initially, the renal artery responds to administration of an ionic contrast agent by a transient vasodilation, however this is followed by a prolonged period of vasoconstriction that has a tremendous negative effect on renal perfusion. To prevent potential renal injury:

   1. **Pre-contrast fluid therapy,** at the very least, is advised.

   2. Acetylcysteine, an antioxidant, has been shown to be renoprotective in human patients undergoing contrast studies; **acetylcysteine 150 mg/kg in D5W** administered IV over 30 minutes, followed by 2 doses of **10 mg/kg IV, PO q12h** is recommended.

B. **Inflammatory states.** Acetylcysteine may improve hepatosplanchnic blood flow and improved organ function during sepsis. In treatment or prevention of multiple organ dysfunction in septic patients, the author has used

   1. **Acetylcysteine 150 mg/kg in D5W** administered IV over 30 minutes, followed by **10 mg/kg IV q12h** until 'out of the woods', with no apparent ill-effects.

   2. Wide ranges of doses have been used in human patients.

II. MANAGEMENT OF RENAL FAILURE

The goals of treatment are to correct fluid, electrolyte and acid-base disorders, establish or maintain urine flow and treat the underlying cause of renal failure. Discontinue any potential nephrotoxic drugs.

A. **Weigh** the patient prior to fluid therapy.

B. **Place an IV catheter** (*p. 368/369*), either peripherally for fluid resuscitation; or jugular or very long saphenous (cats into the posterior vena cava) for fluid administration, measurement of CVP and blood sampling.

C. **Electrolyte abnormalities** may be present. Life-threatening hyperkalemia (*p. 397*), may have to be treated simultaneously with fluid therapy. Other abnormalities, such as calcium (*p. 373/377*) and phosphorous (*p. 390*) may also be present, however, if fluid therapy and diuretics are successful in increasing the glomerular filtration rate, these abnormalities will often self correct.

D. If oliguric or anuric, place an indwelling urinary catheter (*p. 720/721*), using sterile procedure, to monitor urine output.

E. **Fluid volume expansion** may overcome some forms of intra-renal vasoconstriction. Initially, a "fluid push" should be given to correct undetectable dehydration or hypovolemia (*see Fluid Therapy p. 351*, or *Hemorrhage p. 625/626*) should hypovolemia/hypotension/hemorrhage be the cause of anuria/oliguria. A **balanced electrolyte solution** (BES) (Plasma-Lyte® 148, lactated Ringer's, Normosol® R) is preferred in most patients, as this improves acidemia, which facilitates potassium translocation into cells should hyperkalemia be present. If ARF is associated with hypercalcemia (e.g., neoplasia or vitamin D_3 rodenticide toxicosis), **0.9% sodium chloride** is preferred to enhance calciuresis. Fluid therapy may improve renal perfusion, initiate diuresis, hasten removal of nephrotoxic substances and prevent (or clear) renal tubular obstruction of cellular debris.

1. As a guide to the volume of fluid required to rehydrate an animal, calculate hydration deficit and multiply by body weight in kilograms (*see Fluid Therapy p. 351*). Where hydration is considered to be normal, it has been recommended that 3 – 5% dehydration be assumed. In anuric or rapidly oliguric animals, regardless of their hydration status, perform the following (note 4 & 5):
2. **20 mL/kg (dogs), 10 mL/kg (cats) over 10 minutes** in anuric (or rapidly oliguric) animals OR
3. **15 mL/kg/h (dogs), 7 – 10 mL/kg/h (cats) over 4 – 6 hours** if more caution is required (e.g., heart disease, geriatric) or patient is oliguric.
4. This fluid challenge is not appropriate if pulmonary or peripheral edema is present (*see F below*).
5. If **cardiac disease** is present, a lower fluid rate with close monitoring of the fluid challenge, preferably using CVP monitoring, is required (*see F* and guidelines for **response** Table 8).
6. If **hypovolemia/hypotension** is not corrected with crystalloid fluids, administer 5 mL/kg (dogs), 2.5 mL/kg (cats) boluses of pentastarch (Pentaspan®, Dupont), or hetastarch (Hespan®, Dupont) IV to MAP ≥ 60 mmHg or maximum of 20 mL/kg (dogs), 10 mL/kg (cats) (a maximum of quarter of this dose in animals with heart disease). If not achieved refer to 7 and G below.
7. If ARF is due to **hypotension in a hypovolemic, hypoproteinemic** (TS <45g/L) or anemic (PCV <25%) patient after appropriate crystalloid, hetastarch or pentastarch administration, consider administration of plasma, 25% human serum albumin or whole blood (anemia) (*see Transfusion Therapy p. 667/673*). Go to G below if desired MAP is not achieved.
8. **Administer a diuretic** (*H below*) if euvolemic/hypervolemic and the fluid challenge is not successful in producing urine.

F. Monitoring fluid administration. Volume expansion may result in hypervolemia and overhydration in any patient. Intolerance of the fluid rate, or overhydration must be avoided (Table 9).

1. **Auscultate the lungs** prior to, and during the infusion; any changes are *late* indicators of fluid overload and the infusion should be lowered or stopped.
2. **Weigh the patient** after the initial re-hydration phase and q8h thereafter; any acute changes are due to fluid gains or losses, and the fluid rate should be adjusted accordingly. An acute change of 0.1 kilogram body weight can be translated to an equivalent 100 mL of fluid.
3. **Monitoring CVP** is recommended in any patient, but does not guarantee against overhydration (Guidelines for **response** Table 8).
4. **Monitor systemic blood pressure** to assess fluid response to hypotension and to detect hypertension (*see L below if hypertensive*).

5. **Measuring 'ins and outs'.** When increased urine flow is established, calculate a fluid rate that will maintain urine output at a minimum of 2 mL/kg/h, if there is renal tubular injury (loss of concentrating ability) (*see N below*). It is important to measure fluids 'in' and urine 'out' in order to ensure adequate fluid administration without overhydrating the patient.

6. If **urine cannot be collected** for measurement, place a towel or diaper under the patient and weigh it <u>before</u> <u>and after</u> the patient urinates, the difference is approximately equal to urine produced.

7. If the patient can walk or stand, catch the urine in a basin and measure it.

G. If **hypotension persists** after more than adequate fluid, colloid and blood resuscitation, consider:

1. **Dopamine.** 'Renal dose' dopamine has been shown not to improve renal function. However, should hypotension, in the face of adequate volume, be a potential cause of oliguria/anuria, pressor support is indicated. In this setting, dopamine as a pressor may be of benefit (*see Dopamine Infusion Chart p. 233 and Pharmacology section*). Administer in incremental doses of 1 – 2 μg/kg/min to achieve adequate mean arterial pressure (60>80 mmHg) occasionally 5 – 8 μg/kg/min may be required before an effect is seen. As hypotension improves, heart rate should decrease. If an increase in heart rate is noted after dopamine administration, decrease rate until the baseline heartrate, or lower is reached. High dosages may worsen renal perfusion.

2. **Dobutamine** at incremental doses of 2 μg/kg/min may improve systemic BP in septic patients.

3. **Norepinephrine 0.05 μg/kg/min** increasing to effect over several minutes to a **maximum of to 0.3 μg/kg/min** can be administered if dopamine or dobutamine fail (*see Norepinephrine Infusion p. 253/254*).

4. **Prednisolone sodium succinate or methylprednisolone 1 mg/kg** if **Hypoadrenocorticism** (*p. 275*) suspected. Repeat at 0.25 mg/kg q12h. Adrenal insufficiency may be primary or secondary, or may develop post-trauma or surgery, and during sepsis and other critical illness.

5. Once the patient is normotensive and euvolemic, with urine production <1.0 mL/kg/h, administer a diuretic.

H. **Diuretic therapy** may be of value but the phase of oliguria/anuria during which diuretic therapy is instituted can influence the effect of diuretics on renal function. **Prophylactic diuretic therapy,** administered during the fluid phase (E above) in the euvolemic patient may be advantageous rather than waiting for the effects of the fluid challenge to be observed. The decision as to which diuretic to use first i.e., mannitol vs furosemide, is based on clinician preference and the patient's condition.

1. **Furosemide**

   a. **Bolus 2 – 4 mg/kg (dog), 2 mg/kg (cat).** This should result in diuresis within 30 minutes. For acute anuria secondary to hypotension persisting after more than adequate fluid replacement, dopamine should be started with furosemide administration (*see G above*). If no beneficial effect is seen, repeat furosemide once more in 30 – 60 minutes. If anuria persists, there is no point continuing with furosemide. ENSURE ADEQUATE FLUID THERAPY.

   b. **CRI 0.2 – 1 mg/kg/h** if urine is produced initially and subsequently decreases to below 2 mL/kg/h. Duration of furosemide CRI is patient dependent but often required for at least four hours to maintain diuresis.

2. **Mannitol.** Consider mannitol if the patient is acutely anuric secondary to renal ischemia (due to prior hypotension/hypovolemia), and thereby causing acute tubular necrosis; and the bolus fluid challenge is not successful in producing urine in the face of euvolemia and normal blood pressure, (either prior to or subsequent to the furosemide bolus). Mannitol is primarily used to induce or maintain diuresis.

   a. SHOULD **NOT BE** ADMINISTERED TO overhydrated, dehydrated, hyperosmolar (diabetes mellitus, early ethylene glycol intoxication, hypernatremia), hemorrhaging patients, or patients with pulmonary or interstitial edema, capillary leak or vasculitis, or heart failure.

   b. **Initially,** give **0.25 – 0.5 g/kg IV** slow push over 5 – 10 minutes.

   c. **Note concentration** of the mannitol solution on the bottle as it can vary.

   d. To **maintain diuresis,** repeat in 30 – 40 minutes.

   e. A **total mannitol dose** should not exceed 1.5 g/kg.

   f. **Do not** repeat mannitol if there is no improvement in urine flow (1 – 3 mL/kg/min) within 60 minutes after the initial bolus.

3. **Hypertonic dextrose:** 20% (20 g/100 mL) dextrose in water, has been used as an osmotic diuretic.

    a. Give 2 – 10 mL/min for 10 – 15 min, followed by 1 – 5 mL/min, for a total daily dosage of 22 – 66 mL/kg as an osmotic diuretic.

    b. **Alternatively,** 0.5 – 1.0 g/kg (1 – 2 mL/kg of 50% solution) of dextrose can be infused over 15 – 20 min.

    c. Monitor any urine produced for glucose. **Glucosuria** indicates saturation of renal tubular transport and at this stage urine output should approach 1 – 4 mL/min if glucose has been effective.

    d. This treatment can be repeated two to three times daily if effective.

    e. If adequate urine volume is not produced, do not continue with dextrose diuresis.

I. **Diltiazem.** Currently, at the OVC we are using diltiazem as a treatment for ARF due to leptospirosis, combined with fluids (above) and early furosemide therapy (*see Pharmacology*). Our current protocol is established as soon as possible, especially if anuric or oliguric.

    1. **Diltiazem 0.3 – 0.5 mg/kg slow push (10 min)** followed by **3 – 5 μg/kg/min CRI** for as long as it takes to lower the creatinine to normal values (may take 48 – 72 hours), assuming the dog was normal before the event. Incremental increase to high end of the range is suggested while monitoring systolic blood pressure and heart rate. A lowering of ~15 mmHg systolic BP is expected. It is recommended, to continue treatment to normal serum creatinine values in all animals, but this may not be necessary as the effects of diltiazem may persist beyond the time of discontinuation. Monitor blood pressure and heart rate throughout the course of treatment. Reduce dose if heart rate or BP drop below normal, which may occur in very small breeds. Furosemide may be used in conjunction with diltiazem (*using separate IV lines as they are incompatible*); however, furosemide may be discontinued once a brisk diuresis commences.

    2. **Diltiazem as above,** is also used in hypertensive patients to reduce BP.

    3. **Diltiazem in cats** may be of value but our experience here is limited.

J. **Peritoneal (*p. 723*) or hemodialysis** is required should urine flow not be established.

K. **Antibiotic therapy.**

    1. If urinalysis indicates presence of infection, **pyelonephritis** may be the cause of RF. Antibiotic therapy should be based on culture and antibiogram. Commonly isolated bacteria include gram negative rods: *E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis* and gram positive cocci: *Staphylococcus aureus, Streptococcus spp.* While antibiogram results are pending, administer

        a. **amoxicillin/clavulanic acid 10 mg/kg PO q12h,** OR

        b. **ampicillin-sulbactam (Unasyn®) 20 mg/kg IV q8h,** OR

        c. **cefazolin 20 mg/kg IV q6h(dogs), q8h (cats)** OR **cephalexin 30 mg/kg PO q12h.**

        d. If pseudomonas suspected, no gram positive cocci seen on gram stain, and previous antibiotic not effective, **enrofloxacin 5 – 10 mg/kg IV (slowly), PO q24h** OR

        e. **ticarcillin 33 – 50 mg/kg IV q6h (cats & dogs)**

    2. If **leptospirosis** suspected, administer **ampicillin 20 mg/kg IV q6h.**

L. **Monitoring to assess fluid requirements.** Once urine flow has been established, careful monitoring of urine production, by continuous urine output where possible, or measuring all voided samples, is essential to avoid dehydration or overhydration.

    1. Weighing the animal several times a day will assist in estimating fluid losses and gains. Should the animal's weight decline despite fluid therapy, it is assumed that ongoing losses such as high urine output, vomiting, diarrhea, excessive salivation, fever or are in excess of fluid administration. Assume a weight loss of 0.1 – 0.3 kg BW/1000 kcal energy requirement/day in an anorexic animal (*see p. 502*) which is not associated with fluid losses.

    2. After urine flow has been established, regardless of the underlying problem, ongoing fluid requirements are calculated as follows:

        a. divide the day into six 4-hour intervals, four 6-hour intervals or three 8-hour intervals, depending on severity of illness and availability of staff.

        b. Determine urine produced during each time interval and add the estimated insensible loss for that period.

        c. Determine ongoing losses in vomitus, diarrhea and saliva over this same interval.

        d. Determine insensible loss, 20 mL/kg/day and for each degree Celcius above 38.5 add 10% of normal daily maintenance fluid requirement (if normal daily requirements are 1 L and temperature is 40.5°C then 200 mL should be added). Divide this amount by 6, 4 or 3 depending on intervals selected above. This total volume of fluid is to be delivered over the next time period.

e. Urine output will depend on the underlying problem. The goal is to maintain at least 2 mL/kg/h. However, if there is renal tubular injury or other causes for loss of concentrating ability, urine output can be extremely high (25 – 40 mL/kg/h!). Hence, the importance of urinary output measurement and adequate fluid replacement.

3. **Once rehydration is complete,** the type of fluid administered will depend on **serum electrolytes.**

   a. The damaged kidney may not be able to excrete a high sodium load and hypernatremia may develop, therefore, a lower sodium containing fluid such as 0.45% sodium chloride or Plasma-Lyte® A or 148, Lactated Ringer's or Normasol® R diluted 1:1 with sterile saline (*see Fluid Therapy p. 362/363*) may be required.

   b. With diuresis, hypokalemia may occur and potassium supplementation will be necessary (*see Hypokalemia p. 395*). Cats with hypokalemia may paradoxically develop a more severe potassium loss with intravenous fluid therapy.

   c. Furosemide diuretic therapy results in hyponatremia, hypochloremia, hypokalemia and alkalosis; therefore, fluid adjustments may be required (*p. 386–389/394–396/410*).

M. **Urinary catheter** care. Placement of triple antibiotic ointment at the junction of the catheter and the vulva or prepuce may reduce bladder infection. Tincture of chlorhexidine is used to clean the outside of the catheter from prepuce or vulva (don't touch the tissue with tincture!) toward the urine collection bag q8h. Should the prepuce or vulva become soiled they are cleaned with chlorhexidine soap, rinsed with warm water and dried. Systemic antibiotics are avoided unless required to treat an existing infection. The urine is cultured after 72 hours, or sooner, if indicated.

N. **Continual patient monitoring** (*see Table 10*). As various problems associated with the inability to void can exist, which are unrelated to renal function, the urinary bladder may have to be catheterized, palpated or imaged to assess whether urine is being produced over time. Injury to the urinary system may interfere with urine output.

O. **Fluids** should be gradually discontinued when hydration and urine production are restored and fluids 'in' and urine 'out' are matched, the serum urea and creatinine are normal (or stabilized) and the patient is able to eat and drink. Taper fluids by 25 – 50%/day, depending on the duration of therapy. If more rapid reduction is indicated, decrease by 5%/h. Should severe polyuria continue and the patient is unable to maintain adequate oral fluid intake, consider placement of an esophagostomy or gastrostomy tube where oral fluids can be administered by the owner at home. This has been very successful in both cats and dogs in our institution. Normal serum creatinine has been maintained in a dog with renal tubular failure secondary to trauma, for over three years, by supplementation of fluids via a gastrostomy tube.

TABLE 1. Renal Failure due to Primary Renal Causes

Ischemia	**Immune-mediated (many etiologies)**
Severe pre-renal causes (see Fig. 2)	Glomerulonephritis
Renal vascular thrombosis	Interstitial nephritis
Renal parenchymal injury	Systemic lupus glomerulonephritis
Nephroliths	
	Neoplastic
Toxic	Lymphoma
Polymyxin B	Hemangiosarcoma
Cephaloridine	Polycystic
Amphotericin B	Hypercalcemia (paraneoplastic)
Aminoglycoside antibiotics	
Sulfonamides	**Miscellaneous**
Tetracyclines	Myoglobin
Thiacetarsamine	Hemaglobin
Methoxyflurane	Red cell stroma
Carbon tetrachloride	
Non-steroidal anti-inflammatory drugs	
Heavy metals	
Ethylene glycol	
Compost ingestion	
Vit D_3 Rodenticide toxicity (hypercalcemia)	
Lillies	
Grapes and raisins	

TABLE 2. Renal Failure due to Pre-renal Causes

Inadequate intravascular volume due to fluid translocation or loss

Vomiting	Diarrhea	
Third space losses	Thermal burns	Neoplasia
Heatstroke	Blood loss	
Hypoadrenocorticism	Hypoalbuminemia	
Vasculitis	Pancreatitis	
Diabetes mellitus	Overzealous diuretic use	
Diabetes insipidus (central or renal – e.g., endotoxin)		

Increased renal and systemic vascular resistance
Various causes of increased circulating catecholamines
Renal sympathetic nervous stimulation (e.g., unilateral nephrectomy affecting contralateral renal function)
Angiotensin II
Hypothermia

Inadequate intravascular volume due to vasodilation

Anaphylaxis	Inhalational anesthetics
Sepsis	Heatstroke
Vasodilator therapy	ACE inhibitors

Inadequate cardiac output

Congestive heart failure	Cardiac tamponade
Arrhythmias	Positive pressure ventilation
Post-cardiac arrest	Selective anesthetic protocols
Restrictive pericardial or cardiac disease	
Hyperviscosity	
Polycythemia	
Hyperproteinemia/hyper(gamma)globulinemia	

Miscellaneous (reduced urine volume, high specific gravity, but not necessarily azotemic)
Antidiuretic hormone (ADH) secretion due to
-hypotension or hypovolemia
-lung pathology (ADH activity)
-ventilator patients ($\uparrow$ intra-thoracic pressure)
-opioids (resulting in ADH activity ADH mimetic)

TABLE 3. Renal Failure due to Post-renal Causes

Trauma

Ruptured bladder	Herniated bladder
Ruptured/avulsed ureters (both)	Ruptured/avulsed urethra
Post-traumatic scarring, ureters or urethra	Bladder or urethral hematoma (i.e., post biopsy or trauma)
Iatrogenic ligation of both ureters or urethra	

Obstruction

Uroliths	Granulomatous urethritis
Neoplasia (extra-or intraluminal,intramural)	Prostatic disease
'Stump' pyometra	Reflex dyssinergia
Urethral inflammation	Herniated, retroflexed bladder
Problems with indwelling urinary catheter	Urethral hematoma

Neurological
Spinal injury/disease

TABLE 4. Renal Failure due to Infectious Causes

Leptospirosis (several serovars)
Ehrlichiosis (*p. 307*)
Borelliosis (*p. 307*)
Dirofilariasis (*p. 185*)
Babesiosis (*p. 307*)
Leishmaniasis
Pyelonephritis (several bacteria, most commonly *E. coli, Klebsiella, Staph aureus*)
Pyometritis (*p. 756*)

TABLE 5. Differentiation of Pre-renal/Post-renal Azotemia/Parenchymal Acute Renal Failure based on Urine Analysis

Laboratory test	Pre-renal Azotemia	Parenchymal Acute Renal Failure	Post-renal Azotemia
Urine specific gravity	>1.035 dogs >1.045 cats	1.008 – 1.029 dogs 1.008 – 1.034 cats	Variable
Urine to plasma osmolality	>5:1		
Urinary Na^+ concentration	<20 mEq/L	> 40 mEq/L	
Fractional excretion of Na^+	<1%	>1%	
Urine creatinine:Plasma creatinine	>20:1	<10:1	
Urine protein:Urine creat	<2.0	1 to > 13	<2.0
Urine glucose	absent	variably present	absent
Urine sediment[@]:			
Proteinuria	absent/trace	present	
Granular casts	absent	present	
Renal epithelial cells	absent	present	
Red blood cells>5/hpf	embolic exercise Coagulopathy	glomerular injury glomerulonephritis transplant rejection	absent to many
Red blood cell ghosts	cardiac/emboli	renal tubular injury	absent to many
White blood cells >5/hpf	absent	present	absent/present
Cellular debris	absent	present	absent/present
Neoplastic cells	absent	Renal neoplasia	bladder/urethral neoplasia
Urine colour			
Dark red/brown	myoglobin hemaglobin		
Red	blood	blood	blood

[@] All or individual components of the urine sediment may be present depending on severity, the time from onset of renal injury to presentation and etiology.

TABLE 6. Differentiation of Pre-, Post- and Intrinisic Renal Failure – Serum Electrolytes and Blood Gases

Laboratory test	Pre-renal Azotemia	Parenchymal Acute Renal failure	Post-renal Azotemia
Packed cell volume	≥ normal*	normal*	≥ normal*
Total solids	≥ normal*	Normal*	≥ normal*
Serum potassium	Normal High (hypoadrenocorticsm) Low (loop diuretic)	Normal or High	Normal or high
Serum sodium	Normal High Low#	Normal Low ±#	Normal
Metabolic acidosis	Present	Present	Present
Anion gap	Increased	Increased	Increased

* Assuming blood loss or anemia of systemic illness, including chronic renal failure, is not present.
#ADH release due to ineffective circulating volume or opioid administration.

TABLE 7. Formulas

Anion gap

$(Na^+ + K^+ + UC^+) - (HCO_3^- + Cl^- + UA^-) = 15 - 25$. Total CO_2 can be used instead of HCO_3^-

Fractional Excretion of Sodium (FE_{NA}) **(spot check)** (Caution: Units for urine and serum creatinine must be the same. Occasionally, the lab reports urine creatinine in mmol/L not mmol/L. Serum creatinine is reported in mmol/L)

$[(U_{sodium}/P_{sodium}) \times (P_{creatinine}/U_{creatinine})] \times 100 < 1\%$ = pre-renal, >2% acute tubular necrosis

A combination of pre-renal plus tubular necrosis may result in <2% FE_{NA}

Urine Protein:Creatinine ratio (spot check) (U = Urine)
U protein (mg/dL)/U creatinine (mg/dL) OR
International System Units [U protein (g/L)/Urine creat (umol/L)] x 8.84

Calculation of effective serum osmolality (mOsm/kg)

System International (SI) Units: [1.86 $(2Na^+ + K^+)$] + glucose], all units mmol/L
Traditional units: $2[Na^+]$ + [glucose (mg/dL)]/18
Consider hyperosmolar if >320 mmol/L in dog (normal 290 – 310) or >330 mmol/L in the cat (290 – 330)

Average daily maintenance fluid requirements for ill animals with normal renal function
= 1.2 (70 x Body Weight in kg$^{•75}$). See *Fluid Therapy* for *Table p. 366.*

TABLE 8. Interpretation of CVP values in response to a rapid infusion of 20 mL/kg crystalloid or 5 mL/kg colloid in a patient. NOTE: This volume may not be tolerated. The first four signs listed in Table 9 have been noted by the author at this rate.

Response to Infusion	Interpretation of Response
2 – 4 cm H_2O increase from baseline returning to baseline in 15 min.	Euvolemia and normal cardiac function.
An increase in CVP maintained >4 cmH_2O above baseline.	Increased venous blood volume, reduced cardiac compliance, or both.
A slow (15 min) return to baseline.	Normal blood volume.
A prolonged (>30 min) return to baseline.	Increased blood volume relative to cardiac performance. to cardiac performance.
Minimal to no increase in CVP.	Markedly reduced intravascular volume. Requires further resuscitation.
An increase in CVP with rapid (<5 min) return to baseline.	Reduced intravascular volume and accommodation of fluid within the intravascular space and subsequent reduction in vascular tone. Requires further resuscitation.
Raise CVP by 2 – 4 cmH_2O within first few minutes of bolus therapy. If falls rapidly to baseline, repeat bolus therapy until CVP 5 – 10 cm H_2O (3 – 7 mmHg) requiring 10 – 15 min to fall. At this point, blood volume and venous return are optimal relative to cardiac performance.	Further resuscitation is required.
Greater than this may predispose to pulmonary edema. Continual resuscitation will lilely not improve cardiac output.	CVP ~ 7 – 9 cm H_2O (10 – 12 mmHg) with normal intra-pleural and intra-abdominal pressures fluid.

TABLE 9. Potential Clinical Signs Associated with Volume Overload and Overhydration

- shivering
- nausea (swallowing and licking lips)
- vomiting (may be early or late)
- restlessness
- polyuria (patient dependent)
- serous nasal discharge
- tachypnea (early or late)
- cough (late)
- chemosis (late)
- dyspnea (late)
- diarrhea (late)
- ascites (late)
- exophthalmous (late)
- depressed mentation (late)
- tachycardia (followed by bradycardia, when severely overloaded)
- subcutaneous edema (especially hock joint and intermandibular space) (late)
- pulmonary crackles and edema (late)
- excessive weight gain

TABLE 10. Daily Monitoring to Assess Efficacy of Therapy, and to Prevent, Identify, and Treat, any Abnormalities should they Arise

- Serum creatinine or urea or both (daily).
- PCV/TS if noted to be low or high initially, until stable.
- Urine volume measurement every 18 hours plus urine specific gravity.
- Urine sediment (every 48 hours if acute tubular necrosis).
- Weight gain or loss (every 8 – 24 hours to assess fluid loss/gain).
- Serum electrolytes, specifically potassium (q4–24h with hypo- or hyperkalemia until corrected).
- Venous blood gases, or total CO_2, (q6–24h to assess metabolic status until corrected).
- Calculate anion gap (with electrolyte and blood gas or total CO_2 measurements) and assess in light of albumin level (*p. 409/410*).

PHARMACOLOGY

1) **Furosemide** is a loop diuretic thatinitially causes vasodilation of afferent arterioles resulting in increased renal blood flow (RBF), urine flow and possibly GFR. Later, there can be a reflex vasoconstriction with reduced perfusion and GFR and reduced urine output. Furosemide therapy, in conjunction with dopamine, is recommended in this circumstance. Furosemide also inhibits chloride reabsorption in the thick ascending limb of the loop of Henle after secretion into the proximal tubule (there must be a "drop" of urine produced for furosemide to have an effect); sodium then follows chloride in the tubular fluid resulting in diuresis. The decreased sodium transport offers a protective effect in that the work required of the injured cells to reabsorb sodium is reduced.

2) **Dopamine** is a catecholamine with dopaminergic, beta-adrenergic and alpha-adrenergic effects that are dose dependent. In this protocol, dopamine is used for the beta-adrenergic effects where an increase in cardiac output may improve renal perfusion.. The 'renal effects' of dopamine are in question for humans. The effects of dopamine with respect to an improvement in GFR in both cats and dogs still has to be proven. Caution must be used with excessive dosing ($>8\ \mu g/kg/min$) as the alpha effects may occur here causing afferent arteriolar vasoconstriction and reduced RBF.

3) **Mannitol** is an osmotic diuretic, which promotes tubular urine flow by increasing GFR and reducing sodium reabsorption in the proximal tubules. Additional effects, in the situation where hypoxia results in tubular cell injury, death and exfoliation into the tubular lumen, is to reduce cellular edema and actively "flush" the debris through the tubules; both prevent obstruction. It is also an oxygen radical scavenger, which reduces re-perfusion injury.

4) **Hypertonic dextrose** may be as effective as mannitol, easily detected in the urine and offers a few calories. However, the salutary effects of this solution on renal function and urinary flow rate have not been rigorously compared with those of other diuretics. Other diuretics appear to be more potent.

5) **Diltiazem,** a calcium channel blocking agent. Has been shown to be protective in the transplanted kidney. The effects of diltiazem on the transplanted kidney are hypothesized to be due to the anti-endothelin effects, prevention of apoptosis and reduced workload of renal tubular cells. Endothelin is a potent vasoconstrictor and increases in ARF. Diltiazem is an endothelin antagonist. In addition, diltiazem has a direct effect on reducing renal vascular tone. Following a hypoxic event, the 'health' of renal tubular epithelium is jeopardized; diltiazem prevents calcium cytosolic and mitochondrial calcium accumulation and inhibition of Ca-dependent and calmoldulin-regulated enzyme activity, thus reducing the generation of reactive oxygen metabolites and other radicals resulting in tubular epithelial cell death.

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PLACEMENT OF A URETHRAL OR PRE-PUBIC CYSTOTOMY URINARY CATHETER

A. PLACEMENT OF A URETHRAL URINARY CATHETER

INDICATIONS

1. Intermittent or continuous catheterization for bladder decompression.
2. Recumbent patients to avoid soiling
3. Urine collection/sampling
4. Measuring urine output

DOGS

Male
Materials
Sterile gloves
Sterile pediatric feeding tube or other male urinary catheter
Sterile lubricant jelly.
Needle and suture material
Sterile closed collection system. (IV tubing and fluid bag, or commercial system).

Technique

Pre-measure catheter length from urethral opening, along ventral abdomen caudally around ischial arch to the pubis (approximately to the trigone of the bladder). This is important as an excessive amount of catheter within the lumen could result in curling and knotting of the catheter in the bladder. The prepuce and tip of the penis is cleaned with chlorhexidine soap and rinsed off. The prepuce is pulled back exposing the penis. The catheter with sterile lubricant is placed into the urethral opening and advanced to the pre-measured point. If urine does not appear, then aspirate with a syringe. If urine is aspirated, advance the catheter 1" or 2" further into the bladder (depends on the size of dog) and secure the catheter in place with a friction knot. If urine is not present, pass the catheter further and aspirate. Pass 1" or 2" after urine appears.

Female
Materials
Sterile 2% lidocaine gel in cartridge (Astra)
Sterile gloves ideal, alternatively, wash hands three times with chlorhexidine soap and rinsed.
8-12Fr Foley urinary catheter (depending on size dog) is ideal; red rubber feeding tube, less ideal
Sterile closed collection system (IV tubing and fluid bag or commercial system)

Technique

Clip long hair contacting the vulva. Wash vulva with lanolin hibitane soap and rinse. Place sterile lidocaine gel cartridge into vaginal vault and place 4mg/kg lidocaine into vagina; hold vulva closed for 5 minutes (some gel will spill out). Lubricate Foley tip with this gel but leave the catheter in the inner plastic bag. The stylet must be to the tip of the catheter and not protrude through the lateral opening to avoid traumatizing the urethra. If right handed, place the ubricated left index finger gently into the vagina while 'searching' for the urethral papilla (often feels like a mucosal fold or slight bump) just beyond the pelvic brim (occasionally can be further). Keep left index finger over this area while passing the catheter with the right hand (slowly pulling back the plastic cover), under the index finger of the left hand. The tip of the catheter will then enter the urethral opening. Pass catheter until urine is flowing or until confident it is in the urinary bladder. Ascertain placement by 'feeling' the catheter disappear into the urethra and not continuing into the vagina. Remove the stylet while holding the catheter in place. Inflate the Foley balloon with sterile saline at 1mL less volume than suggested for size of catheter. The catheter must remain in the urethra. If the dog is uncomfortable, check placement as occasionally the catheter may be in the urethra.

CATS
Male
Materials
Sterile gloves
Open-ended 'tomcat' catheter, or preferred, a 3 ½ Fr or 5 Fr Feeding tube
Sterile lubricant jelly
Needle and suture material
Sterile closed collection system. (IV tubing and fluid bag or commercial system).

Technique

Clean prepuce as for the dog. Lubricate the catheter with sterile lubricant and pass gently to avoid damaging the urethra while holding the prepuce and extending the penis dorso-caudally (make as straight a urethra as possible). Check for presence of urine from the catheter to confirm presence in the bladder prior to securing. 'Butterfly' the tape around the catheter as close to the penis as possible. Suture each 'wing' to the perineal skin to prevent the catheter from pulling out.

Female
Materials
Sterile 2% lidocaine gel in cartridge (Astra)
Sterile gloves
3 ½ Fr or 5 Fr Feeding tube.

Technique

Prepare as for the female dog. The catheter is placed blindly into the vaginal vault, keeping the catheter on the ventral aspect of the vagina. Usually, the catheter enters the urethral orifice quite easily. Pass another 2 cm after urine flows through the catheter. The catheter must be securely sutured to the perineal area using the 'butterfly' technique.

B. PLACEMENT OF A URINARY CATHETER VIA PRE-PUBIC CYSTOTOMY

INDICATIONS

In the short-term, for emergency decompression of the bladder due to urethral obstruction , trauma to the urinary tract, and any other situation where the bladder cannot be emptied naturally. Pre-pubic cystotomy is preferred to multiple cystocenteses while preparing for corrective surgery. For long-term urinary diversion techniques.

Materials
8 Fr Foley urinary catheter (preferred for short-term), or a de Pezzer mushroom-tip catheter
absorbable suture material

Methods
It is preferrable to have a (1) lateralized, rather than (2) linea alba, pexy of the bladder to the abdominal wall to avoid incision into the bladder should future laparotomy be required. However the technique selected is based on personal preference and the situation at hand.

1. A 2 – 3 cm incision **lateral** to the midline is made through the abdominal wall midway between the umbilicus and pubis (cranial to the flank fold). The bladder is minimally exteriorized and stabilized using two retention sutures with needle remaining on both; a purse-string suture (using absorbable suture) is placed either full-thickness through the bladder wall, or through the serosa and muscular layers (depending on the condition of the bladder wall) of the ventro-lateral apical region of the bladder, or healthy portion of bladder. A stab incision is made within the purse-string suture and the Foley catheter is introduced. The balloon is inflated with sterile saline and the purse-string suture is carefully tightened snugly (avoid tying too tightly or suture line necrosis may occur). The retention sutures are passed through the abdominal wall and tied. The incision is closed routinely. The catheter is connected to a closed collection system.

2. A 2 – 3 cm **midline** incision is made through skin and abdominal wall, midway between the umbilicus and pubis in cats and female dogs. The incision through the skin is made lateral to the prepuce in male dogs and continued through the abdominal wall to the bladder, or the prepuce is retracted laterally and incision made through the linea alba. The remaining procedure is as described in (1 above), except the retention sutures are placed through the linea alba. The midline incision is closed routinely. The catheter is connected to a closed collection system.

3. The bladder incision must be closed surgically if the catheter is removed prior to 14 days; otherwise, the catheter must remain in place for at least 14 days to facilitate adhesion. When removed, the stoma is allowed to granulate closed. Petroleum jelly should be placed around the site to prevent urine scalding

All animals
To reduce the chance of urinary tract infection, a continuous, closed, sterile urine collection system should be used. Swab the exterior of the catheter, from prepuce or vulva, along its length with alcohol or tincture of chlorhexidine q8h. Do not touch the penis, prepuce, or vulva with this stuff!

NOTES

INTRODUCTION

The process of dialysis requires a semipermeable membrane (in this instance the peritoneum) to separate blood from a solution (dialysate). As many substances can diffuse across a semipermeable membrane from an area of high concentration to one of low concentration, the dialysate placed into the abdomen will influence the diffusion of water or solutes from the blood, across the peritoneum into the fluid placed into the abdomen. The abdominal fluid is then removed with the dialyzed solute or water.

INDICATIONS

The major indication for dialysis is oliguria or anuria after all medical attempts at diuresis have failed and when there is potential for reversal of the underlying renal disease, or an improvement in the uremic state such that the patient can be maintained without continuing dialysis. Presurgical dialysis in management of uremia due to various urological problems (e.g., uroabdomen, urinary obstruction) may be indicated in some patients.

Other rare conditions that may benefit from peritoneal dialysis (lavage) are hypothermia or hyperthermia where an increase or decrease in body temperature has failed standard therapy, or severe fluid overload (e.g., congestive heart failure with acute renal failure). Peritoneal lavage in severe pancreatitis may rarely be of benefit. Barbiturate, ethylene glycol, methanol, amphetamine, aminoglycoside intoxication may require peritoneal dialysis for substance removal. Peritoneal dialysis may be warranted in severe hyperkalemia/metabolic acidosis and hypercalcemic crises.

CONTRAINDICATIONS

Peritoneal dialysis is contraindicated in patients with recent abdominal surgery, bowel distension, abdominal distension, obesity, severe catabolic states with marked hypoalbuminemia and intra-abdominal conditions that affect more than half of the peritoneal surface and limit dialysate exchange (e.g., abdominal wall trauma and peritoneal infections or adhesions).

TECHNIQUE

A. **Select the dialysate.** Commercial dialysate (e.g., Dianeal•, Baxter) contains sodium (132 mEq/L), chloride 96 mEq/L), calcium (3.5 mEq/L), magnesium (0.5 mEq/L) and lactate (40 mEq/L) with dextrose at 0% (272 mOsm/L), 1.5% (360 mOsm/L), 2.5% (411 mOsm/L) or 4.5% (522 mOsml/L).

Homemade dialysate using lactated Ringer's, OR **0.45% saline,** OR **0.9% saline** may be substituted depending on the goal of dialysis therapy (hypo- or hypernatremic states). The osmolality should closely approximate the patient's unless hyper- or hypoosmolar solutions are indicated. The **high dextrose (4.5%)** solution is usually selected for fluid removal in over-hydrated patients, this is then reduced to **2.5%** and otherwise maintained on a 1.5% dextrose solution which is adequate for removal of most solutes. **Do not use** Plasma-Lyte® A or 148, or Normosol® as these fluids are **very** painful .

B. **Preparation of the dialysate.**
Strict aseptic technique is required to avoid contamination and the risk of peritonitis. Sterile gloves and mask should be worn. Preparation should be conducted ideally under a fume hood; however, a clean area such as the surgical suite will suffice.

All supplies should be placed on a sterile tabletop and all injection ports should be cleaned with alcohol. Tincture of chlorhexidene or povidone-iodine soaked sponges should be placed over all connections.

Do not use multidose vials for injection. If you do, start with a new one and alcohol the injection port prior to use, each time.

Dextrose 50%: 30 mL added to each liter = **1.5%; 50 mL** added = **2.5%,** or **90 mL** added = **4.5%.** The amount of dextrose to add will depend on the fluid status of the patient. If severely edematous the **4.5% solution** is recommended to remove the excessive fluid, or where hyperosmolar syndrome (*p. 279*) is present. Ensure the patient is euvolemic even though it may be edematous. Addition of insulin to the dialysate may be required if the patient is hyperglycemic. A **2.5% solution** is recommended in all well-hydrated (not overload) patients initially as a greater volume of fluid is removed than the 1.5% solution. 1.5% is then used as the maintenance solution when fluid balance is achieved.

Magnesium, calcium and potassium can be added to the dialysate as required based on the patient's serum levels. The amount of calcium in LRS is usually satisfactory, but more may be added if required. Potassium, 4 mEq/L should be added to the saline solutions (unless hyperkalemic) to prevent hypokalemia.

Sodium bicarbonate 30 – 45 mEq/L should be added to **saline solutions** to provide a source of alkali if patients are not alkalemic.

Calcium-free commercial dialysate is not available, therefore patients that are hypercalcemic may benefit from a homemade 0.9% or 0.45% (depending on serum sodium) saline solution with glucose added. However, the calcium concentration is less than serum in this instance and should not be a problem.

Heparin, 500 units/L should be added to all dialysate solutions to decrease clot formation and outflow obstruction. Reduce to 250 units/L if ACT increases.

Antibiotics are not routinely added.

The spike of the intravenous tubing with a roller clamp in line is placed aseptically into the dialysate bag. Extension tubing may be necessary if extra length is required.

Wrap the dialysate with a circulating water pad or some other device that will warm, and **maintain, the fluids (38° C [101°F]).**

C. Patient preparation.

1. Strict aseptic technique is imperative. Place a urinary catheter. Ensure that the urinary bladder is empty to avoid iatrogenic injury during catheter insertion into the abdomen.

2. **Prepare dialysate catheter.**
    a. **Purchased.** As directed.
    b. **Homemade** using a 7 Fr, 20 cm central venous catheter utilizing a guide wire can be placed using a modified Seldinger technique (e.g., MILA Long term, or Arrow single or double lumen), has been used short-term by the author. Employing aseptic technique, make fenestrations with a scalpel blade, alternating holes (less than one-half the circumference) around the catheter for ~12 cm. The fenestrated portion of the catheter must remain within the abdomen, therefore, leave adequate length without fenestrations. Add an extension set with 3-way stopcock.
    c. **Homemade** using a 12 or 16 Fr Argyle Trocar Thoracic catheter with a **few** additional holes may also be used. Care must be taken to avoid 'rough' edges where the holes are made. Follow above directions.
    d. **Jackson-Pratt suction drain.** Remove the 'vacuum' bulb and attach 3-way a stopcock.

3. Administer **hydromorphone or oxymorphone 0.025 – 0.05 mg/kg IV, fentanyl 3 – 5 mg/kg IV, or morphine 0.2 mg/kg IM, SC.** Clip widely, **surgically prepare** and drape the mid-caudal abdomen. **Move the skin slightly caudally or medially** to create a tunnel for the catheter prior to placing lidocaine. Place **1 – 3 mL 1% lidocaine** into the skin, subcutaneous tissues and abdominal wall , 1 – 2 cm caudal to the umbilicus on the midline. Hold skin in place. (Note: If skin retraction is difficult, ignore). Insert 14 or 16 gauge over-the-needle catheter through the incision and infuse 10 mL/kg of warm dialysate into the abdomen prior to dialysis catheter placement. This will elevate the abdominal wall away from the organs. Place two stay sutures at each end of the proposed incision; elevate the abdominal wall area of the incision, remove the catheter, keep the skin retracted and go to 4 or 6 below.

4. If a purchased dialysis catheter, or the 12 Fr Trocar Thoracic catheter is used , make a 2 – 3 mm incision (where the IV catheter was) with a scalpel blade through the skin, SC tissue and abdominal wall slightly lateral to the linea alba to 'tightly' accommodate the catheter. Where a Jackson-Pratt suction drain is used, make the incision no bigger than the size of the tubing.

5. Insert **peritoneal dialysis catheter** of choice with stylet/ trocar, through the incision with firm, but controlled effort, into the abdomen, (using a twisting motion) towards the right side (away from spleen) of the pelvic inlet. If difficult to pass apply sterile saline around the outside of the catheter. Once into the abdomen, retract stylet/trocar into the catheter before advancing catheter. Advance the catheter towards the pelvic inlet making sure all the holes are within the abdomen before stylet is removed. Previously instilled dialysate should flow into the catheter. Where the Jackson-Pratt suction drain is used, place the tip of the drain between the tips of a large hemostat and insert through the incision into the abdomen. The hemostat remains in place while the drain is passed into the abdomen with the hand. The fenestrated portion of the drain must be within the abdomen. Release the skin. Secure with a pursestring suture through the skin. Use a 'Chinese finger-trap' to secure the catheter to the abdomen. Place an appropriate adapter and attach a 3-way stopcock. Connect a sterile IV line.

6. If the **central venous catheter** selected, the skin should be pulled cranially or medially as above. The needle is placed through a 2 mm incision through skin and subcutaneous tissue, between the two stay sutures, landmarks as above. A distinct "pop" is usually felt after advancing the needle through the linea alba into the peritoneal cavity. The guide wire is passed through needle just to enter the abdomen. The guide wire is lubricated with sterile saline and the catheter is passed over the guide wire into the right lower quadrants of the abdomen for the full extent of the catheter. The skin can then be released. Secure the catheter to the abdomen by suturing the wings of the catheter to the abdomen. Attach a sterile IV fluid delivery set to each luer-lock on the double-lumen catheter; one is used for infusion, the other for collection; or a 3-way stopcock onto a single-lumen catheter.

7. Apply sterile dressing, cover with surgical adhesive drape, and bandage to the catheter site.

8. The single-lumen collection system can be managed in two ways depending on the volume of the dialysate bag and the volume to be infused with each dwell time.
   a. If you have a small patient and the dialysate volume in the bag will suffice for several dwells, attach a sterile intravenous line with in-line roller clamp and a sterile collection bag onto the 3-way stopcock or Y adapter. Roll up the collection bag and leave next to the patient and keep warm, ~40°C. Ensure that disconnection will not occur. If it does, use chlorhexidene or povidone-iodine to clean the catheter. Aspirate the contents of the catheter using a sterile syringe. Avoid flushing into the abdomen. Replace the 3-way stopcock, Y adapter or extension tubing that may have become contaminated.
   b. If you have a larger patient and the dialysate volume in the bag will be used for each dwell, this can also be used as the collection bag and a second (collection) bag will not be required.

9. After attachment of the infusion line (and collection bag) to the dialysis catheter, wrap each connection with tincture of chlorhexidine or povidone-iodine soaked sterile gauze.

D. Dialysis

1. Select a 1.5% dextrose peritoneal dialysate solution if fluid balance is normal or below normal, 2.5% if well-hydrated or 4.5% if edematous or hyperosmolar. Do not confuse leakage of dialysate into subcutaneous tissue with edema. The dialysate should be warmed to body temperature prior to infusion.

2. Initially, infuse 10 mL/kg warm (39.5°C/102.5°F) dialysate over 15 min into the peritoneal space by gravity flow. Close the stopcock or the Y adapter to the patient. Allow infused dialysate to remain in contact with peritoneal surfaces for 30 minutes (dwell time). Record amount infused. If this volume is well tolerated, there is no effect on respiratory function, the abdomen is not too distended and there is no leakage around the insertion site, the volume may be gradually increased to 20 or 30 mL/kg after 12 hours.

3. If all the dialysate in the bag is used, close the roller clamp; lower the bag, to below the patient. If dialysate remains in the infusion bag, open the stopcock to allow flow from the dialysate to the collection bag (close to the patient) and flush a few milliliters of dialysate into the collection bag (to flush any possible contaminants into the bag prior to opening the stopcock from the patient to the bag) then lower the designated collection bag to below the patient and open the roller clamp. Open the roller to allow slow drainage by gravity over 15 min. Drain as much fluid out as possible. Record amount recovered and discard.

4. Repeat D1 – 3 every 1/2 hour initially. As the patient improves and stabilizes, the procedure can be extended to 1–4h. Increase frequency if creatinine does not improve.

5. Records must be kept of all infusion volumes and dialysate recovered.
   a. Volumes recovered may be **less than infused** due to:
      i. absorption if the patient is dehydrated. Once hydration is corrected, volumes should equalize.
      ii. absorption due to relatively low osmolality of the dialysate. Increase osmolality of dialysate.
      iii. obstruction of the catheter fenestrations because of omental entrapment, clots or fibrin adhesions. Flush the catheter using strict aseptic technique, gently re-position the patient.
   b. Volumes recovered **may increase** due to ultrafiltration if the patient was edematous, or the 4.5% dextrose solution is dehydrating the patient.

E. The patient should be weighed at least twice daily, between infusions, to assess possible fluid overload or too much loss. Central venous pressure measurements may also detect excessive intravascular volume (*see Acute Renal Failure p. 712/718*).

F. Monitor the patient's PCV, TS to assess hydration daily; temperature at least twice daily and white blood cell (WBC) count and differential for indication of infection every 2 days; serum electrolytes, blood gases, creatinine, osmolality; urine output and urine for protein, casts, cells, glucose and bacteria, and dialysate for WBCs and bacteria, daily. Cytology and culture and susceptibility testing should be done on the dialysate if it appears cloudy or hemorrhagic. Follow an antimicrobial regimen as below, pending culture and susceptibility results.

G. Monitor ACT daily as occasionally this is prolonged further than baseline due to the heparinized dialysate.

H. Administer empirical systemic antibiotics ONLY where indicated (e.g., ampicillin in patients with Leptospirosis and acute renal failure or patients with clinical signs of peritonitis such as fever, pain) and while waiting for culture and sensitivity results. **Cefoxitin 20 mg/kg** has broad-spectrum coverage. Drug dosages may require adjustment during dialysis. Cefoxitin, for example, is minimally dialysed therefore, in anuric renal failure patients, it should only be administered q24h; with renal insufficiency q12h and with normal renal function, q6 – 8h. If infection is identified, base therapy on culture and sensitivity results and research the dosing regimen.

I. Monitor the dialysis catheter site daily for leaks or infection. The bandage should be checked regularly and changed daily or sooner if it becomes moist in order to avoid tunnel exit infection.

PHARMACOLOGY

1) **Cefoxitin** is a second-generation cephalosporin with moderate Gram positive, very good Gram negative and good anaerobic coverage. It is not active against *Pseudomonas spp*.

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NOTES

INTRODUCTION

Uroabdomen refers to the accumulation of urine in the abdominal cavity. The urine may be leaking from the kidneys, ureters, urinary bladder or urethra. Uroabdomen is usually associated with blunt trauma, but injuries or obstruction to any part of the urinary tract may also result from nephroliths, abscesses, neoplasia, perineal, inguinal or abdominal hernias, and iatrogenic injuries. Traumatic uroabdomen is usually secondary to a ruptured bladder or ureteral avulsion. A urethral tear is most commonly iatrogenic, resulting from urethral catheterization, but may also occur following trauma or urethral calculi. Nephroliths, may obstruct urine flow from the pelvis of the kidney, causing hydronephrosis with possible traumatic injury and rupture. If the nephrolith is associated with an infectious agent, which they frequently are, abscessation and rupture may occur, resulting in peritonitis. Dehiscence of urinary tract surgical site, or disruption of blood supply, are rare complications of urinary tract surgery. Neoplasia of the urinary tract may result in erosion and leakage. Depending on the localization of the urethral tear, urine may leak into the abdomen, the perineal (perineal urethra or rarely, urethral avulsion), or dorsal lumbar subcutaneous tissue (dorsal tear in the proximal urethra). If leakage is not detected early, urine may dissect through the subcutaneous tissue down the hind limbs or along the dorsum as far cranial as the scapulae!

Urinary tract injury should be suspected in all trauma patients until ruled out; the incidence of urinary tract injury associated with pelvic trauma can be as high as 40%. In a study of hospitalized animals only 40% of the diagnoses of ruptured bladder were made within 12 hours after trauma, and 22.7% were not diagnosed until necropsy. Diagnosis and localization of urinary tract injury is based on history, physical findings and the emergency minimum data base, continual examination, and diagnostic imaging. Diagnostic imaging should be performed in all highly suspect cases of urinary tract trauma.

DIAGNOSIS

History

A thorough history should be obtained, to ascertain the likely source of urine leakage. It is important to determine whether the patient has a history of any of the following:
- Trauma (blunt or penetrating).
- Urethral catheterization or attempts at catheterization.
- Abdominal (including urinary tract) surgery.
- History of cystic/urethral calculi.
- The presence and onset of the following clinical signs:
    - Stranguria
    - Hematuria
    - Pollakiuria
    - Vomiting
    - Lethargy
    - Abdominal distention

Clinical Signs/Physical Examination
- Lethargy, which may be due to dehydration, uremia, or hyperkalemia.
- Vomiting, which may occur with uremia and hyperkalemia.
- Dehydration and hypovolemia may result in hypotension.
- Tachycardia may be due to pain, dehydration, hypotension, and early stage of hyperkalemia (*see Hyperkalemia p. 396*).
- Cardiac arrythmias, such as bradycardia or idioventricular rhythm may occur if serum potassium is above 7.0 mEq/L. Ventricular (*see p.* 179) or supraventricular (*see p. 170*) arrhythmias may also be present.
- Areas of tenderness and bladder size.
- Abdominal distension, bruising of abdominal wall and/or cellulitis of prepuce, perineum, vulva, inguinal region, hind limbs or dorsal lumbar/thoracic region will be noted with urine leakage in these sites following blunt trauma.
- Penetrating abdominal or inguinal wounds such as bites, gunshot, or sticks may result in urinary tract injury and urine leakage.

- Purple discolouration of skin + fluctuation may indicate the presence of subcutaneous hemorrhage or urine.
- Prepucial or vulvar bleeding.
- Rectal examination performed very carefully, may identify sharp or penetrating bone segments resulting from a pelvic fracture.

Repeated physical examination should be performed to detect early signs of intra-abdominal injury.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **Serum Electrolytes** as potassium may be elevated – mild to severe.
- **Blood Gases** as hypovolemia and uremia may result in acidosis.
- **Lactate** may be elevated due to hypovolemia and poor peripheral perfusion.
- **PCV/TS** may be elevated if dehydrated; may be decreased if trauma was associated with hemorrhage.
- **BUN, Urea, Creatinine** may have mild to severe elevations: mainly postrenal azotemia, but may have both prerenal (dehydration) and renal (trauma, ischemia) components.
- **ECG** as hyperkalemia (>7.0 mEq/L) causes flattened or absent P-waves, prolonged P-Q intervals, and spiked T-waves. Bradycardia, idioventricular arrhythmia or atrial standstill may result.
- **Blood pressure** may be low depending on traumatic blood loss, third space losses due to peritonitis or normal if the animal is presented early without associated fluid/blood losses.
- **Abdominocentesis** is indicated if abdominal effusion is suspected.

    - With the patient standing or in lateral recumbency, clip and surgically prepare the ventral abdominal wall from the level of the umbilicus to the pubis. Insert 20 gauge hypodermic needle immediately posterior to the umbilicus. Collect free flowing fluid into sterile red-top and EDTA tubes. Submit fluid in red-top tubes for creatinine and potassium evaluation. If no fluid is obtained on free flow, gently aspirate with a syringe. If no fluid is collected, mentally divide the prepped area into four quadrants: right cranial, left cranial, right caudal, left caudal. Insert four 20 gauge hypodermic needles, one in each of the four quadrants, approximately 2 cm from midline. Be cautious to avoid penetrating the spleen, located in the left cranial abdomen. Collect any effusion as above.
    - Compare [effusion creatinine]:[serum creatinine]
       effusion:serum creatinine ratio >2:1 indicates urine
    - Compare [effusion potassium]:[serum potassium]
       effusion:serum potassium >1.4:1 indicates urine.

Imaging
- Once the patient has been stabilized (**A below**), routine thoracic and abdominal radiographs should be obtained:
- **Thoracic Radiographs** to evaluate for traumatic pneumothorax, fractured ribs, and thoracic effusion.
- **Abdominal Radiographs** to evaluate for defect in abdominal wall (traumatic hernia), lack of serosal detail (peritoneal effusion), lack of detail in retroperitoneal space (hemorrhage or urine leakage), presence and size of urinary bladder silhouette.
- **Pelvic Radiographs** as urethral tears may result from the sharp bone segments of pelvic fractures; the pelvis is therefore important to evaluate in any patient with a history of trauma and uroabdomen or cellulitis as described above.
- **Contrast Radiography is required for location of defect** (*see Suggested Reading 1 for details*): (kidneys, ureters, urinary bladder, urethra) and is performed, once the patient has been stabilized with repletion of intravascular volume. For renal or ureteral tears, excretory urography (intravenous urography [IVU] or pyelography [IVP]) is the preferred diagnostic test. This should be performed prior to a cystourethrogram in the event that both tests need be considered. Note that the intravenous contrast medium may cause nephrotoxicity or hypotension, and should be used with caution in patients with severe azotemia. Instituting diuresis or administration of acetylcysteine prior to study may confer renoprotection. Potential regimens suggested are:
    1) acetylcysteine 8 – 10 mg/kg PO q12h prior to and the day of study
    2) acetylcysteine 150 mg/kg IV over 30 minutes followed by 10 mg/kg q12h

In the case of a rupture involving the lower urinary tract (urinary bladder or urethra), a contrast cystourethrogram should be performed. Urethral catheters may pass easily into the bladder and urethral injury may not be suspected, therefore a urethrogram is also recommended.

MANAGEMENT

A. **Fluid Resuscitation** is most important to correct hypovolemia, prerenal azotemia and acidosis, and to increase renal perfusion and lower serum potassium and lactate. For smaller animals place a burette in line to avoid fluid overdose.

1. **If hyperkalemic:** commence fluid therapy with Plasma-Lyte•-148, Normasol•, lactated Ringers at appropriate rate for fluid or blood loss (*see Hyperkalemia p. 397–399 and Fluid Therapy p. 351*).
2. **If hemorrhage:** (*see Hemorrhage p. 625*).
3. **If hypovolemic and normokalemic:** (*see Fluid Therapy p. 351*).

B. **Hyperkalemia** should be addressed immediately. If immediate (within minutes) protection of the mycardium is required due to life-threatening hyperkalemia, administer 50 – 100 mg/kg (0.5 – 1.0 mL/kg) of 10% calcium gluconate IV over 2 – 5 min with continuous ECG evaluation. This lasts approximately 20 min. While administering calcium gluconate obtain **0.2 units regular insulin/kg IV and 2 g (4 mL of 50% diluted to half) dextrose/unit insulin IV administer as a slow push, and make a 2.5% dextrose solution** (add 50 mL of 50% dextrose solution/L fluids). This should be separate from resuscitation fluids (*see Hyperkalemia p. 398*).

C. **Arrythmias:** usually respond to fluid therapy and resolution of hyperkalemia. If severe bradycardia or atrial standstill occurs *see Bradycardia p. 168, Ventricular Tachycardia p. 179, or Supraventricular Tachycardia p. 170*, may be due to hyperkalemia, trauma or other etiology (i.e., reperfusion injury). **Do not** treat ventricular arrhythmias due to hyperkalemia with lidocaine, treat the hyperkalemia (*p. 397–399*).

D. **Urine drainage** must be established either via urethral catheterization or a urinary diversion technique, to prevent further accumulation and absorption of urine. This is performed on a short-term basis, to stabilize the patient prior to general anesthesia and surgery.

1. For small tears in the urinary bladder or urethra, an indwelling urinary catheter or cystostomy tube may be used. Catheters should remain in place for 7 – 10 days while the tear heals. The urinary catheter should be carefully placed in the urethra to prevent iatrogenic damage to the urethra or urinary bladder. Monitor for adequate urine flow (0.5 – 2.0 mg/kg/h). If urine flow decreases, it may be due to an improper position of the catheter or tube, blockage or kinking of the catheter, or poor urine production.
2. If urethral catheterization is not possible, and urine leakage originates from a kidney, ureter or the bladder, urine drainage should be established directly from the abdominal cavity.
   a. Penrose drains are **not recommended** as they will occlude by fibrin and omentum within 6 – 12 hours.
   b. A closed-suction drain (e.g., Jackson Pratt with multiple fenestrations and a 'grenade' reservoir) may be placed through the ventral abdominal wall to provide drainage of urine.
   c. A dialysis catheter or Foley catheter may also be placed into the abdominal cavity
3. **Tube cystotomy** should be placed if urine leakage originates from the pelvic and distal urethra, or if a catheter cannot be passed. Placement of a cystotomy catheter is preferred to multiple cystotomies while stabilizing the patient for definitive surgical correction.

   Methods: Make a small incision, the size of the 8 Fr Foley catheter, lateral to the midline midway between the umbilicus and pubis. Tunnel the 8 Fr Foley urinary catheter through the lateral incision, subcutaneously to the midline. On the midline make a 2 – 3 cm incision through skin and abdominal wall, midway between the umbilicus and pubis. The bladder is exteriorized through the midline incision and stabilized using two retention sutures (leave the needle on); a pursestring suture is placed through the serosa and muscular layers of the ventral apical region of the bladder. A stab incision is made within the pursestring suture and the Foley catheter is introduced. The balloon is inflated with sterile saline and the pursestring suture is carefully tightened snugly (avoid tying too tightly or suture line necrosis may occur). Each retention suture is passed through the linea alba and tied as a simple interupted suture. The midline incision is closed routinely. The catheter is connected to a closed collection system. NOTE: While the lateral incision and tunnelling of the catheter is ideal, due to potential discomfort if local anesthesia at the site is inadequate, direct entry into the abdomen is recommended.

E. SURGICAL MANAGEMENT

Surgery is indicated for leakage from the kidneys or ureters for large bladder tears, or for complete circumferential (360°) urethral tears. Small bladder tears or small linear urethral tears may be managed by maintaining an indwelling urinary catheter or cystostomy tube for 7 – 10 days.

Traumatic ruptures of the renal parenchyma or renal pelvis, or avulsion of the ureter from the renal pelvis are usually treated with unilateral nephrectomy. Ureteral tears or avulsion from the bladder may be repaired primarily, but ureteral stricture formation is a possible post-operative complication.

Surgical procedures of the upper urinary tract are technically challenging and should be performed by a specialist.

Large bladder ruptures should be managed with surgical exploration once the patient is stable. Partial cystectomy of the affected region of bladder wall and primary closure of the margins is the treatment of choice for large traumatic bladder ruptures. When performing surgery on the urinary bladder, care must be taken to ensure viability and patency of the ureters. If a traumatic cause of bladder rupture has not been determined, the excised tissue should be submitted for histopathological evaluation to rule out a neoplastic-induced bladder wall rupture.

Large urethral tears or complete urethral avulsion is indication for surgical exploration and anastomosis. As with upper urinary tract surgery, these surgical procedures are technically challenging and should be performed by a specialist.

F. POSTOPERATIVE CARE

Following surgical repair of a ruptured bladder, it is NOT recommended to leave an indwelling urinary catheter, due to the risk of ascending urinary tract infection and urethral trauma.

The patient's mentation and urine output should be monitored. Hematuria and stranguria may be noted for 2 – 3 days, due to the cystitis.

The urinary tract mucosa heals very rapidly (<21 days), and the prognosis for an uncomplicated bladder rupture is good.

PHARMACOLOGY

1) **Acetylcysteine** has vasodilatory properties, is an antioxidant and prevents direct oxidative injury to cells. It has good cellular penetration. Contrast agents cause renal injury by producing a prolonged period of vasoconstriction (initial transient renal vasodilation), which reduces renal perfusion. There is also a reduction in antioxidant activity and a direct toxic effect on tubular epithelium due to increased lipid peroxidation and reactive oxygen species.

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NOTES

INTRODUCTION

Hematuria is defined as the presence of whole blood in urine. The owner usually presents their pet to the veterinarian because they have observed red or brown urine. Urine normally contains fibrinolysins to prevent the formation of blood clots, which could obstruct the ureters or urethra. The presence of blood clots in the urine indicates hemorrhage severe enough to overwhelm this protective mechanism. In addition, in some animals, significant hematuria may be diagnosed after microscopic evaluation of urine that looks grossly clear. In these instances, the client may report that the red urine is intermittent, or resolved when microscopic hematuria persists. Hematuria should be differentiated from other causes of red urine, such as hemoglobinuria or the ingested plant pigments (e.g., beets) or injected dyes (e.g., phenolphthalein, phenazopyridine).

Systemic causes of bleeding should be considered when other sites of bleeding are noted, or if other causes of urinary tract bleeding are ruled out. Ischemia can also result in hemorrhage. Infarction of the kidney secondary to disseminated intravascular coagulation of any cause (e.g., heat stroke *p. 417*), or secondary to septic emboli as in bacterial endocarditis, is the most commonly described cause of ischemia. Organ specific hematuria can result from neoplasia, urolithiasis, infection, parasitism (*Dioctophyma renal, Capillaria plica*), or drugs (e.g., cyclophosphamide). Chronic passive congestion of the kidneys from any cause has also been associated with mild hematuria.

The most common cause of hematuria in cats is variably known as feline urologic syndrome, idiopathic hematuria of the lower urinary tract, or interstitial cystitis. In dogs "benign essential hematuria" is defined as renal bleeding in which no pathologic process can be identified.

Hematuria is rarely life-threatening except in instances of massive bleeding leading to hemorrhagic shock or when large blood clots in the bladder obstruct urine outflow.

DIAGNOSIS

History/Signalment

In Welsh corgis, hematuria is the most common clinical finding in telangiectasia of the kidneys. Geriatric animals may be more prone to neoplastic disorders. Neoplasia can affect kidneys, ureters, bladder, urethra, or prostate gland and hematuria may be the primary problem noted.

Two clinical questions need to be answered: where is the blood from and what is the cause?

An accurate observation of when blood occurs in the urine stream can be extremely helpful in localization (Fig. 1). Question the owner as to when blood is most frequently observed:

- If the blood is consistently noted at the beginning of urination or independent of urination, then the most likely source is the urethra, the prostate gland in males, or the reproductive tract in females. Primary urethral diseases are fairly uncommon except for neoplasia in the old dog and urethral urolithiasis in males.
- If the blood is consistently at the end of urination, the bladder is the most likely origin.
- If the blood is throughout urination, the origin may be kidney(s), ureter(s), bladder, or prostate gland.
- If dysuria is an accompanying sign, the lower urinary tract and prostate gland are the most likely. An exception to this is that passage of large blood clots of renal origin may cause dysuria.
- If blood is associated with strenuous exercise, then it may be transient.

Question the owner as to whether the animal has any other sites of bleeding, suggesting a coagulopathy.

A free roaming dog may ingest a rodenticide with subsequent coagulopathy, or have experienced a traumatic event. Any urinary tract organ can be traumatized resulting in bleeding, particularly with blunt abdominal trauma. However, animals with urologic injury do not always have hematuria.

Recent treatment with cyclophosphamide may cause hematuria (*see Oncological Emergencies p. 443/447–448*).

Clinical Signs/Physical Examination

- The kidneys should be checked for size, shape, consistency, and symmetry.
- The bladder should be carefully palpated for wall thickness and the presence of calculi (*see Urethral Obstruction p. 745*).
- The prostate gland should be palpated rectally in male dogs (*see Prostatic Disease p. 742*). In cystic prostatic hyperplasia, increased prostatic vascularity may result in prostatic bleeding into the urethra.
- The prepuce should be examined for bleeding in males (*p. 736/740*) and the vagina in females (*p. 759*).
- The animal should be examined for other sites of bleeding (*see Toxicological Emergencies p. 638, Thrombocytopenia p. 451, Hemorrhage p. 619*). Clipping the hair of the abdomen and perineum allows thorough visual examination of the skin.
- A painful lumbar mass or bruise suggests possible renal trauma.
- Urine extravasation from a damaged urethra may cause perineal, scrotal, or preputial discoloration and swelling. If urine extravasation continues, necrosis and sloughing of the skin can occur (*see Urine Leakage p. 727–728*).

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV, TS** should be performed to note severity of blood loss. Note colour of plasma; if free hemoglobin is present it will color the plasma pink.
- **ACT, PT/PTT** should be performed where possible to rule out a coagulopathy.
- **BUN, Serum creatinine** must be performed to further localize the lesion; increased values suggest a renal origin, or a post-renal problem such as obstruction (*p. 745*) or rupture (*p. 728*).
- **Urinalysis.** If urinalysis cannot be conducted immediately, urine should be refrigerated until examined, preferably within a few hours. Cystocentesis, catheterization, and manual expression can result in **iatrogenic trauma** and mild hemorrhage. To avoid this, urinalysis is first performed on a voided urine sample and then on a cystocentesis sample. If blood is present in a voided, but not a cystocentesis sample, diseases of the distal urethra, prepuce or prostate in the male, or vagina and uterus in the female, are potential sites. If blood is present in urine from both the voiding and cystocentesis samples, the origin must be kidney(s), ureter(s), bladder, or proximal urethra. Blood from the prostate may appear in both voiding and cystocentesis samples because of reflux of hemorrhagic prostatic fluid into the bladder or leakage into the urethra. A complete urinalysis should always be performed. The presence of RBC casts indicates renal bleeding, but they are uncommonly seen and their absence does not exclude a renal origin. Complete urinalysis will determine whether inflammation exists (pyuria), and whether it is associated with infection (bacteruria) or parasitism (parasite eggs). A marked proteinuria is suggestive of glomerular disease.
- If the **occult blood reaction** is positive, but **RBCs are not present** in the urine, there are three major possibilities:

  - Hemoglobinuria with or without hemoglobinemia. If the plasma is hemolyzed, hemoglobinuria is caused by hemoglobinemia. When intravascular hemolysis releases hemoglobin, circulating haptoglobin rapidly binds the hemoglobin. The hemoglobin-haptoglobin complex is too large to be filtered through the glomerulus and is cleared by the reticuloendothelial system. However, if the haptoglobin binding system becomes saturated, free hemoglobin will be present in the plasma and is filtered by the glomerulus, resulting in hemoglobinuria.
  - If there is no evidence for hemoglobinemia, hemoglobinuria may be secondary to the complete lysis of red blood cells in urine. Red blood cells may lyse in dilute or aged urine, thus it is important that urine be examined soon after collection. In a voided sample, contamination with blood from an external source, such as dissolution of flea dirt, may be the source of the hemoglobin in the urine.
  - Myoglobinuria will also result in a positive occult blood reaction with no red blood cells in the urine sediment. Myoglobin is relatively small and is rapidly cleared through glomeruli without altering plasma color. Myoglobin gives more of a brown than red color to urine, but blood in urine is also often brown. With myoglobinuria, there should be clinical evidence of active muscle disease or injury. An **ammonium sulphate precipitation test** can be used to distinguish hemoglobinuria from myoglobinuria.
- Both the occult blood reaction and the urine sediment examination for red blood cells are negative for ingested or injected dyes.
- **Urine culture** is necessary to identify an infectious cause.
- In a **semen** sample from a dog with hematuria, hemorrhage suggests prostatic (*p. 742*), testicular, or epididymal origin (*p. 739*). The prostate is directly connected to the urinary tract, thus worsening hemorrhage after prostatic massage helps identify the prostate as the source of the hematuria.
- **Survey radiographs** of the abdomen may reveal enlargement and increased density of the retroperitoneal space following disruption of kidneys or ureters or may reveal radiopaque uroliths.

Extended Laboratory Data Base

- **CBC.** Leukocytosis is more common with acute inflammatory diseases or abscessation of the kidneys and prostate gland, than with bladder diseases or chronic inflammation anywhere in the urinary tract. Thrombocytopenia may cause hematuria.
- Platelet function (bleeding time), PT/PTT, thrombin time, Von Willebrand's Disease, and fibrinolysis (fibrin degradation products, fibrinogen) may need to be performed to confirm a coagulopathy as a cause of hematuria.
- **Imaging.** The type of imaging study is based on the most probable site of origin as determined by history and physical examination (Fig. 1).
    - **Ultrasonographic examination** can detect abnormalities in shape, size, and texture of any of the urinary organs and prostate and is useful for identifying radiopaque and radioluscent uroliths. Should 'masses' be identified within the bladder, a biopsy should be obtained as polyploid cystitis may be mistaken for neoplasia based on gross appearance; imaging results should be differentiated by histologic examination. For increased echogenicty, suggestive of inflammation, within the kidney, a renal biopsy should be obtained as autoimmune glomerular diseases have also been associated with hematuria.
    - **Excretory urography.** The excretory urogram is useful in detecting ureteral injury, ureteroliths, and neoplasia of the kidney and ureters. In a traumatized animal, the animal should be rehydrated and normotensive before excretory urography because radiographic contrast material can produce hypotension and bradycardia.
    - If **urethral damage** is suspected, a **retrograde urethrogram** is performed prior to cystogram if this is also being considered. If the urethral injury is confirmed, an excretory urogram is done instead of a retrograde cystogram, to avoid catheterizing the injured urethra.
    - **Bladder tears** are best delineated by positive **contrast cystography. Bladder masses** can be delineated with a **double-contrast cystogram.**
    - **Cystoscopy and urethroscopy** are particularly useful for identifying urethral and bladder masses and uroliths.
    - **Renal scintigraphy** is recommended to evaluate the renal function of the opposite kidney if the clinician is considering nephrectomy because of severe renal bleeding (i.e., causing severe anemia).

MANAGEMENT

The key to managing hematuria is to identify the location and predisposing cause. Treatment plans for all possible causes of hematuria are beyond the scope of this chapter, however, the following should be noted:

A. Hematuria after a **traumatic event** is not an indication for immediate surgery. Shock (*p. 606*), respiratory distress (*p. 563*), and severe hemorrhage (*p. 625*) are managed first. The animal should be kept quiet in a cage, and its vital signs, clinical status, and hematocrit serially monitored (*p. 17/621*) until the urine grossly clears of blood. If the hematuria persists, further diagnostic tests are needed. Of course, deterioration of clinical status or hematocrit necessitates re-evaluation.

B. In dogs with **idiopathic renal bleeding,** blood clots may form in the bladder and if large enough can cause dysuria and even obstruction. If a ventral cystotomy is required to remove the blood clots, the ureteral openings should be examined closely to determine which kidney is bleeding. A biopsy of the affected kidney is submitted for light and electron microscopic and immunofluorescent examination to try to identify a cause of the bleeding. Nephrectomy is not performed unless the opposite kidney is healthy and the bleeding is intractable.

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FIGURE 1. Lesion Localization for Hematuria.

Ultrasonography
Kidney & Bladder

Negative → Positive
Treat
accordingly

CYSTOGRAPHY

Positive → **CYSTOSCOPY EXPLORATORY BIOPSY**

Negative → Excretory Urography

Cystic calculi → **CYSTOGRAPHY**

Bladder neoplasia → **CYSTOSCOPY EXPLORATORY BIOPSY**

Polypoid cystitis → Medical Management

Positive

Negative → Clotting profiles

Negative

Positive → Coagulopathy → Medical Management see Hemorrhage (*p. 625–629*) Rodenticide toxicity (*p. 650*)

EXPLORATORY

Positive

Negative → **URETERAL CATHETERIZATION to identify lesion or R or L kidney as source of hemorrhage**

Cysts   Calculi   Renal neoplasia

BIOPSY

Positive

Negative → Hematuria of non-traumatic origin

Calculi   Parasites   Vascular abnormalities

Renal scintigraphy

NEPHROTOMY and/or PARTIAL OR TOTAL NEPHRECTOMY or NEPHROURETECTOMY

INTRODUCTION

Conditions of the male urogenital tract requiring emergency assistance may be congenital or acquired in origin. Acquired conditions may be associated with sexual behaviour, including coitus, or are more often traumatic in origin. As urinary outflow obstruction is a common finding in acquired injuries, it is necessary to conduct a thorough physical examination, including observation when urinating, as it is crucial that the animal maintains the ability to urinate.

Canine Diseases	Feline Diseases
Paraphimosis	Paraphimosis
Phimosis	Phimosis
Priapism	Priapism
Orchitis/epididymitis	Orchitis/epididymitis
Testicular torsion (scrotal and abdominal)	Urethral obstruction (*p. 745*)
Penile trauma	
Fractured os penis	
Penile/Preputial mass	
Preputial hemorrhage	
Urethral prolapse	
Prolonged Tie	
Prostatic diseases (*see chapter*)	
Bladder neoplasia (*p. 731*)	
Hematuria (*p. 731*)	
Urethral obstruction	

GENERAL APPROACH

DIAGNOSIS

- **Characteristic** features are preputial discharge, masses protruding from the prepuce, or swollen scrotum.
- **Determine origin** of discharge or mass with **cytology** (of mass, discharge, urine, and semen, if possible).
- **Imaging:Radiographs** of caudal abdomen including penis, transabdominal **ultrasound** of caudal abdomen and testes, and fine needle aspirate(s) as indicated for each problem.
- If not paraphimosis or priapism, **extrude the penis** from the prepuce, including the bulbus glandis in dogs, and examine penile (preferably while erect if bleeding is the problem) and preputial mucosa.

A. Many of these problems are very painful; analgesics must be administered. Opioids are the analgesics of choice. Hydromorphone 0.02 – 0.05 mg/kg IM, IV q3–4h, fentanyl 2 – 4 μg/kg q20–30 min, or morphine or methadone at 0.2 – 0.3 mg/kg. If surgery is required and there are no contraindications for non-steroidal anti-inflammatory analgesics, post-operative meloxicam 0.2 mg/kg (dogs & cats), or carprofen 0.4 mg/kg (dogs) may be administered with the opioid or alone (*see Analgesics p. 81*).

PARAPHIMOSIS

Clinical Signs/Physical Examination

- Penis is completely or partially extruded from the prepuce and not easily replaced.
- More common in dogs, especially following copulation or masturbation, penis often only partially entrapped in a partially inverted prepuce.
- Seen commonly in toy and small breed dogs, often in neutered ones.
- Penis is **NOT** erect but may be very large and edematous.
- May be painful or not.
- Penile spines on toms indicate the presence of testis(es) and may factor into finding the cause.
- Urination may still be possible, however this is dependent on the degree of mucosal deterioration and trauma.
- The dog may be oblivious to the problem, or constantly licking or chewing the penis. The behaviour is usually dependent on the degree of injury (desiccation, excoriation and ischemia), which is generally associated with the duration of paraphimosis.
- Careful palpation is required to rule out fracture of the os penis.
- Neurological examination should be performed if there is no history of sexual arousal. Encephalitis and intervertebral disk disease have been associated with paraphimosis.
- Check preputial opening for injury or scarring, etc., as a reason for the inability to retract the penis.

MANAGEMENT

A. Focus on returning the penis into the prepuce. Gently clean off any debris. Place the animal in a position where the penis is not dependent (i.e., supported in lateral or dorsal position), generously apply water-soluble lubricant (K-Y Jelly). If the edema is minimal this may be all that is required to gently massage the penis into the prepuce. Should the edema and swelling be marked to severe, a chilled hyperosmotic solution (50% dextrose), or granulated table sugar should be very generously placed on the penis. The sugar is rinsed off when wet and replaced if necessary. When the penis is observed to approach normal size, generously apply K-Y Jelly prior to attempting placement into the prepuce.

B. Usually the prepuce has rolled in on itself; pulling the caudal aspect of the prepuce caudally will expose the preputial opening. While maintaining slight caudal tension, the now exposed preputial opening can be held and pulled over the well-lubricated penis while caudal retraction is slowly released with the cranial movement of the prepuce until the penis is covered.

C. Address cause:
  1. If the preputial opening is small, enlarge surgically (*see Suggested Reading 4*).
  2. If there is excessive trauma to penis, strangulated with ischemic necrosis, or a large mass is present, amputation of the penis +/- prepuce, castration and perineal urethrostomy is required. Due to the complexity of this procedure a surgical specialist should be consulted.

D. If this is a recurrence of the paraphimosis, consider tacking penis to prepuce or suturing the preputial opening (*see Suggested Reading 4*).

PHIMOSIS

Clinical Signs/Physical Examination

- More common in young cats. In dogs often not noticed until breeding event.
- Usually the preputial orifice is too small or long hair has trapped the penis in the prepuce.
- Urine may be dribbling, or total obstruction may be noted.
- Purulent material may be present due to the collection of secretions, urine and bacteria.
- Acquired phimosis may occur following trauma or local infection at any age.

A. Remove and trim hair if this is the cause.

B. If in very young animal with pin-sized preputial opening, must enlarge, but just enough for a good flow of urine (*see Suggested Reading 4*). Castrate.

C. Surgically enlarge preputial opening for animals intended for breeding only if acquired, not congenital (*see Suggested Reading 4*).

D. Flush prepuce with warm saline. Avoid soaps as they lead to desiccation and irritation.

E. Insert water soluble lubricants within the prepuce.

PRIAPISM

DIAGNOSIS

Clinical Signs/Physical Examination

- Penis is completely exposed and erect.
- Because venous drainage has been compromised, blood stagnates and ischemic necrosis eventually ensues.
- The animal is extremely painful. "Low-flow " priapism only type described in veterinary medicine.
- It is difficult, or impossible, to urinate.
- Differentiate from hematoma due to trauma, a bleeding disorder with hemorrhage, and edema as in paraphimosis above.
- Examine the patient for other injuries that may suggest trauma as a cause.
- Neurological disease such as that caused by distemper could be a cause.
- Thromboemboli from neoplasia of the bladder or local masses affecting venous drainage
- Consider malicious strangulation of the penis.

Laboratory Evaluation/Diagnostic Imaging

- CBC, biochemical profile, urinalysis and culture, and coagulation profile to rule out causes for clinical signs and abnormal physical findings.
- Transabdominal ultrasound and radiography looking for caudal abdominal masses. The cause in dogs is generally a condition elsewhere that is affecting the penis so extensive diagnostic work is usually necessary.

MANAGEMENT

A. If less than 24 hours, immediate attention may prevent loss of reproductive ability, depending on the cause. **Pain medication** as in **General Approach A** above. Apply protective lubricants and try to replace into prepuce and maintain there until the cause is addressed (*see paraphimosis above*). Lubrication, massage and "slinging the penis" will help prevent further dependent blood and fluid accumulation.

B. If greater than 24 hours, pain medication as above is needed. **Ravage** is indicated and possibly diagnostic. Ravage requires incision of the tunica albuginea over the bulbus glandis and also possibly further down the shaft (pars longa glandis) followed by flushing heparinized saline through the incision while massaging the penis. The goal is to massage out as much viscous blood and thrombi as possible. Short incisions at either end of the penis may be required, but start with the bulbus glandis. Collect samples for cytology to check for malignant cells. Continue flushing and massaging until fresh-looking blood appears. Some authors suggest injection of phenylephrine directly into the shaft whereas others recommend anticholinergics such as terbutaline. None of these have been investigated, but may help in those cases less than 24 hours old where maintenance of breeding ability is desired. None of the dogs described in the literature has returned to breeding, but the return of the ability to urinate is a good start.

C. **Penile amputation** with perineal urethrostomy is frequently required. All the feline cases reported in the literature were treated surgically.

ORCHITIS/EPIDIDYMITIS

DIAGNOSIS

Clinical Signs/Physical Examination

- May occur at any age, but often in the juvenile or geriatric dog.
- Swollen painful scrotum, often with systemic signs of sepsis.
- May not even be detected by the owner at all and found on routine physical exam.
- Examine scrotum for traumatic causes, or scrotal dermatitis permitting transcutaneous transmission of organisms through the scrotum as opposed to ascending infection from the penis or prostate, or via blood borne pathogens.
- In cats FIP is frequently the underlying cause.
- Examine prostate as a possible source of ascending infection.

Laboratory Evaluation/Diagnostic Imaging

- CBC, biochemical profile, urinalysis and urine culture to identify the above etiologies.
- Semen collection (if possible) and culture to localize source.
- *Brucella canis* titre or DNA test.
- Ultrasonographic examination is very helpful in differentiating among orchitis, epididymitis, torsion, abscess, tumour, and fluid around the testes.
- Prostatic ultrasonography may identify this as a source of ascending infection.

MANAGEMENT

A. Castration is recommended if fertility is not an issue.

B. Systemic broad-spectrum antibiotics capable of passing the blood testis barrier, e.g., potentiated sulfas, fluoroquinolones, doxycycline are recommended while awaiting definitive culture and sensitivity results.

C. If *Streptococcal* spp. may be a cause, avoid fluoroquinolones as this may predispose to streptococcal fasciitis.

D. Analgesics are required. Opioids are the analgesics of choice.
  1. **Hydromorphone 0.02 – 0.05 mg/kg IM,** IV q3–4h, OR
  2. **Fentanyl 2 – 4 μg/kg q20–30 min,** OR
  3. **Morphine or methadone at 0.2 – 0.3 mg/kg,**
  4. **Post-operative,** meloxicam 0.2 mg/kg (dogs & cats), or carprofen 0.4 mg/kg (dogs) may be administered with the opioid or alone (*see Analgesics p. 81*).

TESTICULAR TORSION

DIAGNOSIS

Clinical Signs/Physical Examination

- Sudden onset swelling, and pain of scrotum, testis, spermatic cord
- Differentiate from orchitis/epididymitis – the spermatic cord is usually enlarged with torsion and only occasionally with epididymitis or abscess. Ultrasound (see above) can be used for diagnosis and for aspirate of appropriate samples, for example, fluid around the testis(es).
- More common in abdominal testes, especially with tumour. Presentation is typical of an acute abdomen (*p. 21*).

Laboratory Evaluation/Diagnostic Imaging

- Ultrasonographic examination, see above for orchitis/epididymitis
- CBC, biochemical profile, urinalysis and urine culture to help rule out orchitis/epididymitis

PENILE TRAUMA/FRACTURED OS PENIS

DIAGNOSIS

Clinical Signs/Physical Examination

- History of trauma. Always examine the penis as frequently injury is detected after problems arise.
- Visual inspection may identify the injury.
- Palpation of preputial contents may reveal crepitus or definite abnormality.
- Expose entire penis if possible and thoroughly examine it.
- The dog may not be able to urinate, pass a urinary catheter if possible.
- Assess viability of penile tissue.

Laboratory Evaluation/Diagnostic Imaging

- Radiography is required to assess the os penis (and other injuries associated with the traumatic event) (*see Urethral Obstruction p. 746*).
- If the urinary catheter is difficult to pass, contrast urography is suggested to identify the degree of obstruction.

MANAGEMENT

Depends on severity.

A. No obstruction (hematoma), or displacement of the fracture

1. Observe for normal urination
2. No primary stabilization of the os penis is required.
3. Support penis within prepuce if had been exposed and keep the prepuce/penile surface well lubricated.

B. Mild to moderate obstruction or displacement

1. Urinary catheter placement for up to 10 days.
2. See A 3 above.
3. No further treatment usually required.

C. Significant displacement

1. Small finger plate to maintain reduction of the fracture
2. See A 3 above if indicated.
3. Pre-scrotal urethrostomy necessary if there is a comminuted fracture with obstruction of the urethra.

URETHRAL PROLAPSE

DIAGNOSIS

Clinical Signs/Physical Examination

- Often presented for hematuria or hemorrhagic preputial discharge.
- Visual inspection, but some only apparent during erection.
- Much more common in brachycephalics, especially English Bulldogs.

MANAGEMENT

A. Conservative treatment of questionable utility – avoid erections if that is when condition occurs – castration, avoidance of intact bitches, behavioural modification, consider antiandrogen therapy.

B. If occurs regardless of erection, remove prolapsed portion surgically (*see Suggested Reading 5*), and Elizabethan collar with sexual rest until healed; castrate if fertility not an issue or if regarded as a genetic condition.

PENILE/PREPUTIAL MASS

DIAGNOSIS

Clinical Signs/Physical Examination
- Often presented for hematuria or hemorrhagic preputial discharge, however, may interfere with urination or cause a local bacterial infection.
- Transmissible venereal tumour (TVT) most common tumour, but in northern latitudes it is only seen in dogs that travel to the South.
- TVT is also found in the nose and mouth.
- Benign tumours include hemangioma, papilloma and histiocytoma.
- Malignant tumours include squamous cell carcinoma, chondrosarcoma, mast cell tumour, hemangiosarcoma, melanoma, and several other tumours possible.

MANAGEMENT

A. Treatment is dependent on the particular tumour diagnosed.

B. Vincristine is recommended for TVT.

PROLONGED TIE

DIAGNOSIS

Clinical Signs/Physical Examination
- History of tie lasting longer than one hour.
- Both animals are usually uncomfortable.

MANAGEMENT

A. Sedation/analgesia for the bitch with butorphanol 0.2 – 0.4 mg/kg IM, IV, or hydromorphone 0.02 – 0.05 mg/kg, or fentanyl 2 – 4 μg/kg, depending on the severity of pain. The male can be treated similarly, but avoid use of phenothiazines as they may contribute to problem.

B. If insufficient sedation/analgesia, titrate boluses of propofol 1 mg/kg IV, or 0.10 mL/kg ketamine:diazepam mixture of 1 mL ketamine (100 mg/mL), diazepam (5 mg/mL) in the bitch to a point of relaxation permitting the penis to withdraw.

C. Treat both with butorphanol or hydromorphone as in A. above and local application of 2% lidocaine gel to the penis, and the vagina of the female. The amount of lidocaine should not exceed the dose administered systemically. Lidocaine will be absorbed through the inflamed mucosa.

D. Apply lubricant (e.g., K-Y Jelly) and treat for paraphimosis above if necessary. Assess viability of penile mucosa and monitor.

PHARMACOLOGY

1) **Vincristine** for TVT may be used alone or in combination with other chemotherapeutic agents, but by itself causes resolution in >90% cases within 2 to 7 weeks when given either 0.025 mg/kg or 0.6 mg/m² intravenously once weekly until 2 weeks following resolution. Side effects are vomiting and transient leukopenia.

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INTRODUCTION

Prostatic disease should be considered as a possible cause of many acute and chronic conditions in sexually intact male dogs, especially large breed dogs over five years old. Depending on the cause for seeking veterinary attention, the dog may appear gravely ill or otherwise absolutely healthy. The main prostatic diseases are benign prostatic hypertrophy/hyperplasia (BPH), chronic bacterial prostatitis, acute bacterial prostatitis, prostatic cysts (intra-and extra-parenchymal), prostatic abscess, and primary or secondary tumours. Dogs that were neutered peri- or prepubertally are rarely afflicted with any prostatic disease other than tumours, transitional cell carcinoma or prostatic adenocarcinoma, or occasionally metastatic tumours.

DIAGNOSIS

History/Signalment

A thorough history is necessary. If the dog is castrated, determine whether it was performed recently or prepubertally. Determine duration of the clinical problem. Many older intact dogs, especially stud dogs, have had repeated hematuric incidents. Depending on the presenting signs, refer to chapters on urinary obstruction (*p. 745*) or sepsis (*p. 588*), if indicated. BPH does NOT cause urinary tract obstruction in dogs but all other prostatic diseases may do so.

Some terrier breeds, such as Scottish Terriers have been given the reputation of having a normally large prostate; however, this is not the case. Consider any dog with an enlarged prostate accompanied with clinical signs and physical examination as described here, to be pathological.

Clinical Signs/Physical Examination

Dogs present with a variety of signs referable to the prostate, including: acute abdomen, sepsis, pollakiuria, dysuria, stranguria, tenesmus, constipation, hind end weakness or lamenes, pain, hematuria, pyuria, hemorrhagic or purulent preputial discharge, or chronic weight loss. Roughly 80% of intact dogs over five-years-old have BPH (a large, symmetric, freely moveable nonpainful prostate). BPH often exists prior to other prostatic diseases, except tumours or paraprostatic cysts.

- **Palpation** of the prostate and pelvis *per rectum* is an essential part of the physical exam. Those dogs neutered when young should have barely perceptible pelvic prostates. In intact dogs, most enlarged prostates will be in the abdominal, not pelvic cavity. Many dogs resent rectal manipulation, so one must differentiate discomfort due to this procedure from a painful prostate. Due to the abdominal location, one should use simultaneous rectal and abdominal palpation. In large dogs this still only permits evaluation of the caudodorsal aspect. In normal prostates the lobes are smooth and symmetric, a raphe is palpable, and the consistency is homogenous. The prostate and associated urethra are locally mobile, and palpation does not elicit pain. If the prostate is large or fails one or more of these tests, this does not mean that it is the cause of the clinical signs. It does indicate that further tests should be performed. One should always check carefully for a perineal hernia if tenesmus has been evident.
- Occasionally testicular tumours produce **estrogens** that can cause squamous metaplasia of the prostate. Prostatic fluid cannot escape the gland, thereby resulting in multiple intraprostatic areas of fluid accumulation of various sizes. Estrogens also cause **enlargement of nipples** and/or gynecomastia (often bilaterally symmetrical flank alopecia and hyperpigmentation of the axillae and inguinae), so be sure to examine for evidence of such feminization, especially if the owners are reluctant to castrate the dog.

Laboratory Evaluation/Diagnostic Imaging

- **CBC** may reveal anemia associated with chronic infectious prostatitis or abscess, or tumour. Neutrophilia presents with acute, perhaps chronic, prostatitis or abscess, or tumour.
- **Abdominal Radiography** reveals enlarged prostate, perhaps peritonitis or local inflammation in acute prostatitis or abscess, or tumour, as well as enlarged or calcified lumbar lymph nodes. It is necessary to rule out other causes of acute abdomen.
- **Transabdominal Ultrasound Scanning** is often diagnostic. Cysts and abscesses appear hypoechoic, but echogenic areas may be blood clots or purulent material. Cyst fluid is usually anechoic. Areas of hyperechogenicity are seen with calcification in tumours, and occasionally chronic bacterial disease.

- **Urinalysis,** particularly if collected by cystocentesis, may yield the organism and/or cytological specimen necessary for diagnosis since prostates produce fluid continually, which normally enters the urinary bladder or the ejaculate. Red blood cells are almost always seen with any prostatic disease and neutrophils possibly with all but BPH. Engulfed bacteria are seen with both abscess and acute bacterial prostatitis, but rarely with chronic.
- **Prostatic fluid cytology** differentiates between bladder and prostatic disease. Prostatic fluid is obtained by collecting the third fraction of the dog's ejaculate, which is fluid produced by the prostate (may be impossible to do in a septic, aggressive or painful animal), by ultrasound-guided prostatic aspiration or biopsy (may not be readily available), or by prostatic massage (makes differentiation of bladder or prostate difficult). Cytology may reveal hemorrhage, inflammation, infection and/or neoplasia. In dogs with prostatic neoplasia, there is often inflammation, usually with bacterial infection. **Preputial cytology** is indicated where an estrogen-secreting testicular tumour is suspected. Normally the preputial epithelium has small round cells with about a 1:1 nuclear:cytoplasmic ratio and many neutrophils, but estrogens will change this to a stratified squamous epithelium, reminiscent of estrous vaginal smears. The penis, however, is covered by stratified squamous epithelium so care must be taken not to gather cells from the penile surface, just the prepuce.
- **Prostatic fluid bacterial culture** should be performed despite immediate initiation of a broad spectrum antibiotic. Acute or chronic prostatitis most commonly reveals *E. coli* or other Gram-negative rods, but Staphylococcus, Streptococcus/Enterococcus and rarely, anaerobic bacteria, fungi (systemic mycoses) and Mycoplasma have been reported. If dogs have been on antibiotics before the diagnosis is made, bacteria may be difficult to find in the prostatic fluid. Prostatic fluid is usually mildly acidic (pH 6.0 – 6.8) except in *Proteus* infections.
- **Serum biochemistry** is variable, but may show postrenal azotemia, hyperkalemia and/or metabolic acidosis with obstructive disease. Other parameters are variable depending on severity and chronicity. There are rarely changes in chronic bacterial prostatitis.

MANAGEMENT

ACUTE

If the diseased prostate has caused sepsis (*p. 588*), or obstruction of the urinary (*p. 745*) or caudal digestive tract (*Constipation p. 51*), refer to those chapters for immediate treatment.

A. **Antibiotics** should be given for 2 – 6 weeks (longer if dog remains intact), chosen according to the bacteria's sensitivity with consideration for requirements for high lipid solubility, low protein binding, and basic pKa. These would include trimethoprim/sulpha, enrofloxacin, and chloramphenicol. Enrofloxacin is contraindicated in streptococcal infection, therefore bacterial identification is mandatory. Empirical therapy gram -ve, enrofloxacin **5 mg/kg q12h** or trimethoprim sulfadiazine **15 mg/kg q12h** (Gram +ve also). Chloramphenicol **50 mg/kg** IV, SC, PO q8h is recommended for gram -ve, +ve and anaerobes.

B. **Castration** will cure the most common prostatic diseases (BPH, chronic and acute bacterial prostatitis). This almost immediately alleviates clinical signs. Castration should be considered as a component of definitive therapy (as removing the underlying cause of any other emergent surgical problem) and therefore, performed as soon as possible with consideration and support of cardiovascular status. Palpation *per rectum* should show a 50% decrease in prostate size within three weeks, or even sooner.

C. **Castration** and surgical or ultrasound-guided **drainage** are usually necessary in dogs with prostatic abscesses. A 6 week course of antibiotic therapy is necessary. These patients must be monitored after surgery for urinary obstruction as another abscess may form, or it may recur. Urinary incontinence is a common post-operative sequela. Castration without surgical drainage may alleviate the obstruction, but recurring clinical signs are likely.

D. Large paraprostatic cysts should be **drained** surgically and the dog should be **castrated.** These cysts may have occurred due to Müllerian duct remnants, following estrogen therapy for BPH, or due to an estrogen secreting testicular tumour. These should not be mistaken for the intraparenchymal cysts seen in many cases of BPH or chronic bacterial prostatitis where castration is usually curative and surgery (other than castration) unnecessary.

E. Adenocarcinoma and transitional cell tumours of the prostate are not cured nor prevented by castration. However, the lack of clinical improvement noted after castration of dogs afflicted by neoplasia may aid in diagnosis of these less common prostatic conditions. Both inflammation and infection are often seen with these tumours along with a history of chronic cystitis. These are rarely presented for only hematuria or pyuria, but more commonly for

obstruction of the urinary tract or tenesmus or hind end locomotion problems. Adenocarcinoma frequently metastasizes to the iliac lymph nodes, vertebral bodies and lungs, also pelvic bones, long bones and scapula, ribs and digits. Once diagnosed the disease usually progresses, requiring euthanasia within two months.

F. **Radiation therapy,** delivered as intraoperative orthovoltage, seems promising to increase life expectancy in dogs with adenocarcinoma if no metastases are found.

G. For transitional cell carcinoma, **piroxicam 0.3 mg/kg/day** has been recommended.

H. Treatment of BPH, chronic and acute prostatic disease and prostatic cysts in stud dogs may be approached slightly differently. If owners are reluctant to castrate, **5α-reductase inhibitors** and/or non-steroidal **antiandrogens** may be used.

1. **Finasteride 5 mg once daily** orally for the rest of his breeding career until castration can be performed, OR
2. **Flutamide, 2.5 – 5.0 mg/kg PO once daily,** OR
3. **Megestrol acetate 0.55 mg/kg daily.**
4. All three drugs must be given daily since, once discontinued, prostate growth rebounds very quickly. A common situation is to treat until the prostatic fluid is no longer affecting semen quality, the semen is cryopreserved, and the dog castrated. If no improvement in semen quality is noted after three to four months of treatment, the dog should likely be castrated anyway.

PHARMACOLOGY

1) **Finasteride** (Proscar®, Merck Frosst Canada, Inc.) is approved for use in treatment of human BPH and has a variable response in alleviation of clinical signs of BPH and bacterial prostatitis in dogs. Finasteride is a human Type II 5α-reductase inhibitor that starves the prostate of dihydrotestosterone (DHT), the active metabolite of testosterone. Thus, the stud dog can continue to produce testosterone and sperm while the prostate will shrink by about 30% in volume. Testosterone is converted to DHT by the 5α-reductase enzyme and DHT is the active metabolite responsible for prostatic fluid production and secretion. Decreasing DHT only and leaving testosterone elevated differs from castration, so effects on the prostate take longer. Thus, finasteride is not recommended in gravely ill animals that need the rapid shrinkage of the prostate achieved only by castration. The dosage is 5 to 10 mg orally per day per dog. It is packaged in 30 tablet boxes. There are minimal to no side effects on health or fertility. Warnings regarding the potential for sexual differentiation problems in babies are on the label for people, but this is highly unlikely to affect puppies unless the bitch is inadvertently given the tablet. Owners of possibly pregnant females should be cautious if the tablets need to be broken.

2) **Flutamide** (Euflex®) is a nonsteroidal antiandrogen. It is used in men in a manner similar to use of finasteride, and has been shown to be effective at prostate shrinkage without affecting libido or semen quality. It is an androgen receptor inhibitor so the production of testosterone is not affected, similarly to finasteride. Owners of possibly pregnant females should be cautious if the tablets need to be broken.

3) **Megestrol acetate** (Ovaban®) is a progestagen approved for suppression of estrus in bitches, but is not labeled for dogs. It has been shown to be an effective cheap 5α-reductase inhibitor in dogs without affecting semen quality in the short term, but is not approved for this purpose. Long term (>1 month) studies need to be done to evaluate health risks and semen parameters. It has been used with some success in prostate shrinkage at 0.55mg/kg orally daily.

SUGGESTED READING

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INTRODUCTION

Urethral obstruction may be either anatomic (i.e., urolithiasis, neoplasia, post-surgical/trauma), most common, or functional (i.e., reflex dyssynergia due to inflammation associated with interstitial or bacterial cystitis). It occurs much more often in males than in females. The clinical condition of a dog or cat with urethral obstruction will depend on the duration and severity (partial or total) of the obstruction. Post-renal azotemia develops within 48 hours and uremia rapidly develops beyond this time. If presented within 24 hours of obstruction, systemic signs are usually not present. This protocol will deal with the symptomatic management of urethral obstruction in the cat or dog.

Causes of Obstruction

Uroliths
Neoplasia (extra-or intraluminal intramural)
'Stump' pyometra
Urethral inflammation
Problems with indwelling urinary catheter

Granulomatous urethritis
Prostatic disease
Reflex dyssinergia
Herniated, retroflexed bladder
Urethral hematoma

DIAGNOSIS

History

- Obtain a history on recent behaviour (straining or urinating in inappropriate places), volume and frequency of urine voided (note the last time urinated), hematuria, polakiuria, stranguria, or recent cystitis.
- Dalmations are prone to urethral obstruction.
- Owners may misinterpret straining for constipation.
- Cats frequently vocalize (howl) when attempting to urinate.
- Question the owner regarding diet in both cats and dogs. High protein diet may predispose to cystic calculi.
- The age and history of the patient may suggest neoplasia vs. calculi, porto-systemic shunt and ammonium biurate uroliths, while recent cystitis/urethritis may indicate reflex dyssynergia.
- With respect to cats, question the owner regarding any potential stressors, which may precipitate interstitial cystitis. Interstitial cystitis may result in reflex dyssynergia and inability to pass urine.

Clinical Signs/Physical Examination

- Clinical signs will vary, but a common feature is straining to urinate.
- With total urethral obstruction, no urine is voided; however, an occasional drop of urine may be seen to drip from the penis or vulva.
- An animal may appear normal systemically, or signs may vary from depression, vomiting and anorexia to shock or coma.
- Critically ill animals may have muscle tetany or muscle stiffness if hypocalcemic. These clinical signs may be masked if severe acidosis is also present.
- Abdominal palpation should be performed carefully to avoid causing more pain and rupturing a very tense urinary bladder. The kidneys may be enlarged with obstruction and hydronephrosis.
- Pain is elicited on palpation of the abdomen.
- If a bladder cannot be palpated in a very depressed to comatose animal, where the history suggests urethral obstruction was present, suspect a ruptured bladder, or bladder herniation into perineal hernia.
- Bradycardia, hypothermia, pale mucous membranes with prolonged capillary refill time, hyperpnea, and halitosis are evident with prolonged obstruction.
- In cats with uroliths, the tip of the penis may be dark red/purple and may be swollen.
- In dogs with uroliths, the penis may be discoloured and the urolith may be palpated anywhere from the ischial arch to the os penis. Urethral catheterization is required to locate an obstruction within the os penis or female urethra.
- If uroliths have been ruled out, perform a rectal examination of the prostate and bladder trigone in the male dog; in the female dog perform a vaginal examination for vaginal/urethral masses and a rectal examination for evaluation of the bladder trigone. Transitional cell carcinoma is a common neoplastic disorder of the bladder and urethra.

Laboratory Evaluation/Diagnostic Imaging

Stat

- **PCV/TS** should be obtained for baseline information, as abnormalities may be present. Stick BUN, urea or **creatinine** (preferred), (this should suffice in the bright and alert animal) to establish baseline values and the degree of renal compromise.
- **Electrolytes (especially potassium),** and **venous blood gases (or total CO$_2$)** should be performed in the more severely ill patient as hyperkalemia and acidosis frequently occur, and will establish the severity of metabolic disturbance and aid in selecting appropriate therapy. Ionized calcium measurement is recommended, as this may be very low in the more critically affected animals and will predispose to cardiac arrhythmias.
- **ECG** assessment in the depressed patient as hypovolemia, hyperkalemia, and acidosis predispose to cardiac arrhythmias. Hyperkalemia frequently results in sinus bradycardia (*p. 164*) progressing to ventricular tachycardia (*p. 179*); however, initially, sinus tachycardia may be seen.
- **Systemic blood pressure** should be measured as hypotension is a concern in critically ill animals.
- Carefully aspirate a perineal 'bulge' as this may be a herniated bladder with urine present.

Extended Data Base

- CBC and biochemical profile, urinalysis with culture (*see below*) and cytology, **in all but the bright and alert animal** with obstructive uropathy. In moderately to severely ill animals, many changes in the CBC and biochemical profile, as well as urine, may be detected requiring therapy.
- Survey abdominal radiographs, to include the kidneys, ureters, bladder, perineum, ventral abdomen, and penis in males (follow the urethra) to identify radiopaque uroliths (oxalates, struvite, calcium phosphate) anywhere within the urinary system. Calculi that may be less clearly outlined are the matrix, mixed, cystine, ammonium urates and uric acid uroliths. The radioluscent urolith ammonium biurate will not be visualized unless this was a nidus for formation of any of the previously mentioned (*see Tables 1 & 2 for frequency of occurrence of uroliths*).
- Where a straightforward diagnosis of obstructive uropathy due to uroliths is not apparent, ultrasonographic and/or contrast urography is required. Evaluation of the upper and lower urinary tract may be required in selected patients (*see Contrast Urography in Urine Leakage p. 728*).
- In all patients where urolithiasis is identified, analysis of the urolith is advised for future therapy and prevention.

MANAGEMENT

A. **Oxygen** by mask, flowby, hood or nasal prongs if poor perfusion.

B. **Venous access,** and obtain blood for emergency laboratory evaluation.

C. **Fluids.** [If animal alert this is not necessary therefore go to (G) below]. **CAUTION WITH FULL BLADDER.** Commence fluid therapy but perform cystocentesis as soon as possible if urethral obstruction cannot be relieved.

   1. **Isotonic crystalloid solution** (Plasma-Lyte® 148 or A, Normasol® R or lactated Ringer's solution are beneficial as they are alkalinizing; the potassium in them is insignificant.
   2. **Estimate degree of dehydration** (5% if signs are mild, 8% if moderate and 12% if severe or shock). Calculate fluid requirement: % dehydration x BW (kg) = L (i.e., 5% dehydration: 5/100 x 3 kg = 0.15 L = 150 mL). Maintenance fluid rate is in addition.
   3. **Guidelines for fluid administration:**
      a. For shock /poor perfusion administer 5 mL/kg bolus fluids (C1 above) until improved.
      b. May require a 2.5 mL/kg bolus pentastarch/ hetastarch if non-responsive.
      c. Rehydrate over 12 hours.
   4. Fluid administration will depend on the individual patient based on continual assessment of vital signs, azotemia, urine production, mentation and hydration (*see Acute Renal Failure p. 709, Fluid Therapy p. 349*).
   5. Weigh the animal twice daily to assess rehydration/ overhydration. Monitor PCV/TS as needed. Auscultate chest q4h.
   6. Fluid rate above maintenance will probably be necessary due to post-obstructive diuresis. Fluids (ins) and urine (outs) must be monitored carefully to avoid medullary washout and dehydration (*see Acute Renal Failure p. 712/713 or Fluid Therapy p. 347*).

D. ECG monitoring is recommended if the animal has arrhythmias, hyperkalemia or acidemia. If bradyarrhythmia (note lack of P waves, tall spiked T waves, prolonged QT interval, wide QRS) or ventricular arrhythmias (*p. 179*) with poor perfusion consider hyperkalemia (*p. 396*).

E. Treat acidosis if associated with bradyarrhythmia and/or HCO_3^- <12 mmol/L after appropriate fluid resuscitation (acidosis usually corrects after alkalinizing fluids, improved perfusion and establishment of diuresis). Calculate bicarbonate requirement at $[(HCO_3^-$ normal i.e., 20) $- (HCO_3^-$ actual)] x 0.3 x BW kg. Give one-half of this (in the burette) over 30 minutes. Monitor ECG. Hopefully, treating the acidosis will treat the hyperkalemia. If metabolic acidosis is not improved following bolus fluid therapy, continue with sodium bicarbonate (the aim is not to correct to normal, but to bring pH out of the critical zone, which is pH <7.2, HCO_3^- <12). Monitor blood gases q2 – 6h as needed.

F. If **life-threatening hyperkalemia:**

1. **Potassium is >8 mEq/L with severe cardiac arrhythmia: Do not use anti-arrhythmic drugs prior to lowering the potassium** (*see Hypokalemia/Hyperkalemia for details on management p. 397*).
2. Treating the acidemia (*see E above*) will also decrease the serum potassium. If hypocalcemia present, clinical signs may appear with alkalinization.
3. Treat this life-threatening hyperkalemia (*p. 397*) prior to relieving obstruction (*H below*).
4. Once obstruction is relieved and acidemia resolved, K^+ will drop to below normal levels and supplementation may be required.
5. Monitor electrolytes q2–4h initially as needed.

G. **Analgesia/Sedation.** If patient depressed, sedation is not necessary; however, pain may still be perceived, therefore administer an analgesic. **For pain**, cats and dogs:

1. Apply topical **sterile 2% lidocaine 0.25 mL** in the urethral orifice of cats. In cats, avoid flushing urethra with lidocaine in saline unless CAREFULLY monitored, as it may become absorbed and can be toxic. In dogs increase dose appropriate for size of dog. In dogs and cats, do not exceed 2 – 4 mg/kg.
2. **Butorphanol 0.1 mg/kg**; or incremental doses of **oxymorphone, or hydromorphone 0.01 mg/kg IV** (requirement depending on mentation and response to manipulation) **combined with diazepam or midazolam 0.2 – 0.5 mg/kg IV, or 0.01–0.03 mg/kg acepromazine** if required for greater effect.
3. **Cats:** if further restraint required and renal function normal, mix **1 mL ketamine (100 mg/mL) with 2 mL diazepam (5 mg/mL) and give .05 – 0.1 mL/kg IV** – more or less to effect. **Propofol 2 – 4 mg/kg**, or **isoflurane** anesthesia are also effective, and are preferred in cats with renal compromise. Use the lowest possible dose sufficient to facilitate painless urethral catheterization.
4. **Dogs:** as above for cats (G.3). Occasionally, it will not be possible to relieve obstruction without general anesthesia, and often the relaxation with this facilitates unblocking the urethra in both males and females. Ketamine is metabolized by the liver in dogs.

H. **Relieving obstruction.**

1. If the bladder needs to be relieved immediately due to the patient's critical condition perform **cystocentesis** prior to relieving obstruction. Use a 22 gauge over-the-needle catheter, remove the needle and attach an extension with 3-way stopcock. Aspirate carefully, do not move the catheter as it might tear the bladder. Remove as much urine as possible to empty the bladder and avoid urine leakage into the abdomen, or perineum if perineal hernia. This will reduce pressure and facilitate urethral flushing, or replacement into the abdomen. Proceed to unobstruct the urethra. **For perineal hernia go to 8 below.**
2. **Urinary catheter** placement in all animals requires sterile technique (*see Acute Renal Failure p. 770*). Pre-measure all urinary catheters prior to placement to avoid excessive amount entering bladder which may 'circle' and knot. Clean prepuce/penis, or vulva, and surrounding hair (clip long hair if necessary in dogs) with chlorhexidine soap and rinse off. Use sterile lubricant gel to **lubricate the urethral catheter**, and wear sterile gloves. If the catheter passes easily consider interstitial or bacterial cystitis, a tumour, or other inflammatory causes. *See 3c below for fixation of the urinary catheter in cats and 6 below for dogs.*
3. **Male Cats:** GENTLY massage penis between thumb and forefinger initially to remove any distal 'plug'.
   a. If obstruction not immediately relieved, try urohydropulsion using an open-ended 'tomcat' catheter, an ophthalmic lacrimal duct flush cannula, olive-tip catheter or a 22 or 20 gauge over-the-needle catheter (needle removed). The catheter should be passed gently to avoid damaging the edematous urethra. For **hydropulsion** fill a 12 mL syringe with sterile saline, add a little sterile lubricant jelly to the saline (shake into an emulsion) to lubricate the urethra during hydropulsion. Other options include adding **lidocaine**

1 mg/kg, or using a smaller syringe (i.e., 3 mL) for added pressure. Hold the prepuce, extend the penis dorso-caudally (make as straight a urethra as possible) and flush penile urethra while advancing the catheter. Pre-rectal compression of the urethra with concurrent hydropulsion may assist with relieving obstruction.

    b. Do not compress the bladder until the urethra is unblocked (save urine for sediment analysis, cytology if neoplasm, or culture and sensitivity if bacterial cystitis suspected).

    c. Place a 3 1/2 Fr feeding tube/catheter (preferred to 'tomcat' catheter especially in large cats) into the bladder. Fix the catheter by fashioning a 'butterfly' tape around the catheter and suturing the proximal edge of the 'wings' to the perineum. The fixation must be close to the prepuce otherwise the catheter will slide out of the penis. Flush the bladder gently with warm sterile saline until the urine is clear. Connect to a closed collection system.

    d. Female cats will appreciate a small application of **sterile 2% lidocaine gel** (Astra) in the vaginal vault to reduce the discomfort of passing the urinary catheter.

    e. If obstruction cannot be relieved quickly (possible neoplasm) then cystocentesis is recommended, as above (H1). Attempt catheterization again. If not possible then consider pre-pubic percutaneous placement of a Foley catheter for bladder decompression (*see Urine Leakage p. 729*), or perform emergency perineal urethrostomy.

4. **Dogs:** as in cats above with regards to cystocentesis.

    a. Administer an **analgesic** (see G above) if not already administered. Sedations with acepromazine should not be administered in hypovolemic/hypotensive animals. Relaxation is very important for this procedure as this facilitates passage of the catheter.

    b. In **female dogs,** sterile 2% lidocaine gel in a cartridge (Astra) placed into the vaginal vault will desensitize the area somewhat and facilitate passing of a urinary catheter. Visualization of the urethral papilla using a sterile vaginoscope, or digital palpation with downward pressure on the papilla and passing the catheter under the digit, usually facilitates passage of the catheter into the urethra.

    c. For **hydropulsion,** select the appropriate size urinary catheter, and use as short a catheter as possible to reach the bladder (reduces resistance for hydropulsion). This catheter can be replaced after unobstructed. Hold the prepuce closed in males during hydropulsion. Rectal palpation and pressure on the urethra proximal to obstruction during hydropulsion of the urethra may facilitate dislodgement of the obstruction. Continue hydropulsion with sterile saline. If unsuccessful use a 1:1 sterile aqueous lubricating jelly (muco lubricating jelly) and sterile saline in flush starting with a 12 mL syringe; may need a 35 mL syringe. Do not use if tears or deep abrasions are suspected in the urethra or bladder. Flush bladder to remove jelly until the urine is clear. Empty bladder and connect urinary catheter to a closed collecting system.

5. If unsuccessful, anesthetize, as total relaxation may facilitate relief of the obstruction. If **unable to relieve the obstruction,** a temporary pre-pubic, percutaneous Foley catheter placed into the bladder for temporary decompression (*see Urine Leakage p. 729*), or emergency urethrostomy should be performed.

6. Once the catheter is successfully placed into the bladder, secure to the prepuce using a simple suture continued with a 'finger trap' technique on the urinary cathete. Connect to a urinary collection system (purchased urinary collection bag) or sterile IV line and fluid bag. See end of this chapter for catheter maintenance. It is necessary to leave the urinary catheter in place for 24+ hours depending on the case.

7. A cystotomy is required to remove the uroliths retropulsed into the bladder.

8. If urinary bladder is **herniated into a perineal hernia,** empty bladder via cystocentesis, attempt to 'push' bladder into abdomen, success is dependent on size of hernia. Pass a urinary catheter and connect to collecting system to maintain an empty bladder. If bladder is replaced into abdomen, surgical correction of perineal hernia should be arranged with a surgeon (this surgical procedure can be very difficult and should not be performed by the inexperienced) as soon as the patient is stable. Proceed to laparotomy, and reduction of the bladder into the abdomen with pexy if replacement cannot otherwise be achieved. Reduction must be performed as soon as possible to prevent permanent neurological dysfunction.

I. Following reief of the obstruction, monitor urine output hourly initially and adjust fluid therapy accordingly.

1. Ideally, a minimum urine output of 2 mL/kg/h should be achieved.

2. If post-obstructive diuresis occurs and urine production is greater than 2 mL/kg/h, increase fluid rate to keep up with urine output initially. Slowly reduce fluids, assess specific gravity and stick BUN (*see Acute Renal Failure p. 714/715*). Allow access to fresh water if the animal is able to drink.

3. If urine volume decreases or ceases consider obstructed catheter or collection system. Check line patency (and not kinked), flush urinary catheter with sterile saline, palpate bladder.

4. If system is OK, flush bladder with warm saline and assess distension.

    a. If bladder does not distend consider ruptured bladder and perform contrast cystography (*p. 728*).

    b. If bladder atonic, check q2h and gently express.

    c. If cannot relieve obstruction, advise urethrostomy.

    d. Re-assess hydration status. The following should only be performed if urethra confirmed to be patent.

        i. If **normovolemic or still dehydrated**, give an IV bolus of fluids 10 – 15 mL/kg (dog), 5 – 10 mL/kg (cat).

        ii. If **hydrated and normovolemic, and anuric for ~1 hour** give **furosemide 1 – 2 mg/kg** or a slow push of **mannitol 0.25 – 0.5 g/kg.**

        iii. If **over-hydrated**, give **furosemide 1 – 2 mg/kg IV.**

        iv. S*ee Acute Renal Failure p. 711* for further guidance.

J. Monitor TPR until satisfied that all is well.

K. Remove urethral catheter after 24 – 48 hours. Culture urine (NOT catheter tip) at this time to assess if infected from the procedure.

L. Observe urination for 24 hours to ensure urination is normal.

    1. If unable to urinate consider re-obstruction, bladder atony, urethral damage, urethral spasm or reflex dyssynergia due to inflammation.

    2. **Phenoxybenzamine 5 mg/cat or 5 – 15 mg/dog** q12–24h for 5 – 7 days has been used for reflex dyssynergia; the beneficial effects may not be noticed for several days. [Note: In Canada phenoxybenzamine is only available on an Emergency Drug Release certificate from the Bureau of Veterinary Drugs, Ottawa].

    3. **Meloxicam 0.1 mg/kg IV, SC or PO q24h for 2 days** (cats and dogs), **carprofen 2 mg/kg once** (cats) and 2 days (dogs), non-steroidal anti-inflammatory analgesic (renal function must be normal). If urea/creatinine minimally increases and patient is receiving IV fluids a single dose of NSAIA may be administered. This may reduce inflammation and discomfort. OR

    4. **Prednisone or prednisolone sodium succinate, 1 mg/kg** once or twice (24 hours apart) has been used for treatment of urethritis, however this may not be of any value and could predispose to urinary tract infection.

    5. If the bladder can be manually expressed, but the patient is unable to void, atony of the bladder due to over distension during obstruction, or urethral spasm may have occurred.

    6. **Bethanechol 1.25 – 5.0 mg PO q8h** in combination with phenoxybenzamine (as above) should be considered for bladder atony. Do not use if there is any suspicion of obstruction.

    7. **For urethral spasm,**

        a. **Midazolam 1 – 2 mg/cat q12h OR**

        b. **Diazepam 1 – 2 mg/cat q12h**

        c. For no more than 2 days. May help but effects are variable. Potential side effects are over-sedation, weakness, excitement, or idiosyncratic hepatic necrosis (diazepam).

    8. **Bacterial Cystitis/urethritis.** If inability to void is due to bacterial inflammation causing reflex dyssinergia, treat with the appropriate antibiotic (culture), phenoxybenzamine and **meloxicam: Cats 0.1 mg/kg q24h x 2 days then 0.1 mg/CAT q48h; Dogs 0.1 mg/kg q24h for 2 – 3 days,** if renal function is normal.

L. **Serum potassium** should be measured if profound diuresis occurs. Hypokalemia (*p. 394*) may occur.

M. If anorectic after 12 hours, (possible causes ruled out) consider nutritional support. Place nasoesophageal catheter and commence with CRI of Renal/Clinicare (50:50 with electrolyte solution for first 12 hours). Calculate nutritional requirements and deliver as outlined (*see Nutritional Support p. 499*).

PHARMACOLOGY

1) **Bethanecol** is a parasympathomimetic, which facilitates detrusor muscle contractionin the presence of bladder atony (MUST CONFIRM URETHRAL OBSTRUCTION IS NOT PRESENT). Parasympathetic innervation predominates during the voiding phase of micturition. The urethra **must be patent** (or **reflex dyssynergia must not be suspected**) or bladder rupture can occur. A response should be observed within a few hours. If vomiting or diarrhea occurs, the dose should be reduced.

2) **Phenoxybenzamine** is an alpha adrenergic antagonist blocking alpha receptors in the trigone and urethra, which form a functional internal urethral sphincter when contracted. Hypotension may occur in sensitive individuals or overdose. Do not use in cats with cardiomyopathy. Onset of action may take up to several days.

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TABLE 1. Urolith Composition and Sex of Top 6 Canine Breed Submissions

BREED	SEX[a]	# STONES	UROLITH COMPOSITION							
			Calcium Oxalate		Struvite		Urates		Calcium Phosphate	
			#	%	#	%	#	%	#	%
Miniature schnauzer	M	966	866	89.6	33	3.4	25	2.6	8	0.83
	F	1415	668	47.2	586	41.4	13	0.92	18	1.27
Shih tzu	M	607	422	69.5	84	13.8	34	5.60	26	4.28
	F	1591	217	13.6	1155	72.6	17	1.07	38	2.39
Bichon frise	M	609	538	88.3	30	4.9	2	0.33	16	2.63
	F	1368	253	18.5	952	69.6	1	0.07	32	.234
Lhasa apso	M	530	460	86.8	16	3.0	8	1.51	18	3.40
	F	508	172	33.9	252	49.6	3	0.59	20	3.94
Dalmatian	M	553	2	0.36	5	0.90	545	98.6	0	0
	F	20	0	0	5	25.0	11	55.0	0	0
Yorkshire terrier	M	343	281	81.9	22	6.4	20	5.83	7	2.04
	F	170	49	28.8	101	59.4	2	1.18	3	1.76
Totals		8680	3928		3241		681		186	

[a] M = castrated male, F = spayed female

Houston DM, Moore AEP, Favrin MG, Hoff B. Canine urolithiasis: A look at over 16,000 urolith submissions to the Canadian Veterinary Urolith Centre from February 1998 to April 2003. Can Vet J 2004; 45:225-230.

TABLE 2. Urolith Composition and Sex of Top 5 Feline Breed Submissions (excluding urethral plugs)

BREED	SEX[a]	# STONES[b]	UROLITH COMPOSITION							
			Calcium Oxalate		Struvite		Urates		Calcium Phosphate	
			#	%	#	%	#	%	#	%
Domestic Shorthair	M	1682	933	55.5	624	37.1	60	3.6	22	1.3
	F	1644	691	42.0	864	52.6	49	3.0	11	0.07
Domestic Longhair	M	426	217	50.9	176	41.3	13	3.1	6	1.2
	F	416	132	31.7	265	63.7	6	1.4	5	1.2
Himalayan	M	169182	136	80.5	30	17.8	0	0	1	0.6
	F	112	65	58.9	46	41.1	1	0.1	0	0
Persian	M	103	77	74.8	20	19.4	4	3.9	1	0.1
	F	76	40	52.6	33	43.4	0	0	1	1.3
Siamese	M	61	44	72.1	8	13.1	9	14.8	0	0
	F	41	20	48.8	12	29.3	6	14.6	0	0
Totals		4730	2355	49.8	2078	43.9	148	3.1	47	2355

[a] M = male, F = female; [b] Includes cystine (5), silica (4), mixed and compound uroliths (93)

Published with permission: Houston DM, Moore AEP, Favrin MG, Hoff B. Feline urethral plugs and bladder uroliths: A review of 5484 submissions 1998-2003. Can Vet J 2003; 44:974-977.

INTRODUCTION

Animals presented for obstetrical assistance may be stable or require immediate emergency intervention. Animals may be in shock due to sepsis, acute blood loss and/or dehydration. Delivery of puppies or kittens may require medical or surgical assistance. The decision to proceed to a cesarean section (C-section) depends on the presenting condition of the animal, and the owners' wishes concerning the life/health of the bitch or queen versus that of the puppies or kittens already born or still in utero.

DIAGNOSIS

History

Once a partially delivered fetus is dealt with, examine the animal more thoroughly while taking a history. Many obstetrical decisions are based on history.

The likelihood of requiring a C-section is increased in the following situations:

- Brachycephalic breeds and Corgis.
- Small terrier breeds and Dachshunds.
- Nervous miniature or toy breeds.
- Giant breeds with one or two pup litters.
- Certain breeds of cats (i.e., Manx) at risk for fetomaternal disproportion/fetal monsters.
- Large litters with several puppies born and a pause for more than 3 hours.
- Previous parturition resulting in a C-section.
- Pelvic injury of the dam.
- Any illness during pregnancy, especially any requiring medications other than antibiotics.

A recent history with any of the following requires a C-section:

- A dam in extreme distress (i.e., excessive urination, crying, biting her perineum).
- Vaginal discharge indicative of uterine content (red, black, green, brown) for more than 3 – 6 hours with no fetuses born.
- Malodorous vaginal discharge with no fetal births.
- More than 12 – 18 hours since the first fetus was born.
- Rectal temperature decreased more than 24 hours prior and no puppy born yet to whelp a single fetus.
- More than 70 days since last breeding, and confirmed pregnant.
- More than 60 days since the first diestrus vaginal cytology smear (bitches), and confirmed pregnant.
- A dam that had stillborn offspring previously, or had primary or secondary uterine inertia, and the owner prefers a C-section to ensure viability of these fetuses.
- A bitch whose serum progesterone dropped to <6 nmol/L (<2 ng/mL) more than 24 hours prior.
- A systemically ill dam.

Clinical Signs/Physical Examination

Immediate attention is required for the bitch or queen with a fetus lodged within the vagina and protruding from the vulva (*see Management below*).

In general, determine from the history and physical examination whether the animal is in labour and at which stage.

- **Stage I:** If no puppies or kittens have been born and no contractions have been noted, or she may not be in labour at all (consider that she may not even be pregnant). A black, dark green, brown or hemorrhagic vaginal discharge indicates that the cervix is open/opening and that fetuses should be delivered soon. Perform a digital vaginal examination to identify fetuses lodged in the vagina.
- **Stage II:** If the fetus(es) has already been born, or there is active abdominal straining.
- **Stage III:** If all puppies, but not all placentas, have been passed.

Medical or surgical intervention is required when:

- Strong abdominal contractions for more than 30 minutes result in no fetus at the vulva.
- Straining hard for more than 15 minutes with a fetus at the vulva or partially exposed.
- More than 3 hours have elapsed since the last fetus was born.

Laboratory Evaluation/Diagnostic Imaging

- **Abdominal radiographs** are essential with respect to identifying the number of fetuses *in utero,* possible fetal monsters, excessively large fetuses, if fetuses are dead ('C' shape), or free abdominal fluid (peritonitis or uterine rupture). Two views are essential to identify uterine torsion, transverse presentation, and for determination of alive/dead status of the fetuses. Mummified fetuses can be difficult to view.
- **Transabdominal ultrasonographic** examination can determine fetal viability (normal HR >160) and stress (sustained <140) but is often not useful for assessing fetal numbers. In protracted dystocias, the presence of gas in the vagina and uterus or emphysematous fetuses makes recognition of remaining fetuses more difficult with ultrasonographic examination than with radiography.
- **PCV and TS,** especially if hemorrhage is noted, but should be performed routinely as anemia and hypoproteinemia may occur. If dehydrated, the converse may be true.
- **Stick BUN (or urea or creatinine)** is advised when pre-renal azotemia may be present.
- **Blood Glucose** to rule out hypoglycemia.
- **Serum calcium** measurements are essential to rule out hypocalcemia.
- Other tests will depend on the individual's past medical history and physical examination.

MANAGEMENT

The patient evaluation will determine whether medical or surgical treatment is required. **Emergency management** such as oxygen, or fluid therapy (*see Fluid Therapy p. 349*) must be considered where appropriate.

Fetus lodged in the vagina –

1. Lubricate the puppy or kitten and birth canal. Inserting a catheter into the vagina to deliver the sterile lubricating jelly around the wedged fetus may help.
2. Gently twisting the fetus from side to side will facilitate further lubrication of the fetus.
3. Work with the mother's abdominal contractions to deliver the puppy or kitten. NOTE: legs and mandibles should not be pulled too vigorously as they may luxate. If possible, use spoons or sponge forceps to grasp a larger body part.

SURGICAL TREATMENT

If the criteria for performing a C-section are present (see above) then this procedure should be performed immediately to avoid fetal death. Waiting can result in fetal death and a C-section to remove only dead fetuses. If the owner demands that the fetuses be delivered alive, one may be forced to perform a C-section as soon as Stage I labour is evident.

A. *See Chemical Restraint for Specific Emergencies p. 109* for appropriate analgesia/anesthesia techniques.

B. With the animal in dorsal recumbency, a ventral midline incision is made from the umbilicus to pubis. The abdomen is packed and draped with sterile towels. The uterus is exteriorized. A longitudinal incision is made in the body of the uterus and each fetus is 'milked' down the horn towards the incision. The fetus is exteriorized with or without its amnion intact. An attempt is made to gradually pull the placenta off the uterine wall. If excessive hemorrhage occurs the placenta is left attached. The umbilicus is clamped (and severed distally if the placenta could not be easily removed) and the fetus, clamp and placenta handed to an assistant with a warm towel for drying and revival of the fetus.

C. After all the fetuses have been delivered, any remaining placentas can be teased out or may remain if still strongly attached.

D. **Assess endometrial hemorrhage.** Administer **5 IU oxytocin into the myometrium or intravenously,** regardless of assessment. While the hysterotomy incision is being sutured, further monitor the degree of uterine hemorrhage. A blood transfusion may be required.

E. **Ovariohysterectomy** may be performed after the oxytocin if one pays careful attention to hypovolemia. The ovaries and uterus are not required for lactation but their removal is equivalent to a large volume of blood loss.

F. **Colostrum** is vital to neonates, and they should be encouraged to suckle as the dam is waking from anesthesia. Washing any disinfectant off the milk bars will further encourage suckling.

G. **Oxytocin 1 – 5 IU SC** 5 minutes prior to putting neonates onto the nipples will increase milk let down. Oxytocin may be continued SC every 2 – 3 hours during the first day, 5 minutes prior to suckling, to facilitate milk letdown, maternal bonding, and prevent uterine hemorrhage.

H. **Neonates' perineum** should be wiped with a warm wet cloth to encourage urination and defecation if the dam is still too groggy to perform these tasks. Manual stimulation of urination and defecation should be continued after each feeding until the dam is obviously accomplishing this herself.

MEDICAL TREATMENT

A. Oxytocin

1. Should **ONLY** be considered in the healthy dam with a failure to progress during whelping, if the cervix is open and there is no evidence of fetomaternal disproportion, malpresentation, fetal monster or obstruction (for instance, uterine torsion).
2. The wisdom of "inducing" the first fetus of a large litter using oxytocin in an open-cervix, term bitch, is questionable, as is delivering the entire litter with oxytocin if more than four fetuses are present, and in general is not recommended.
3. Overdose may precipitate intense labour, uterine rupture, fetal injury or death.
4. Water intoxication may occur if large doses are infused. Intoxication may be manifested by listlessness, depression, seizures, coma and death. **Severe intoxication may be treated with 0.25 g/kg mannitol or 0.1 – 0.2 mL/kg bolus of 50% dextrose with or without furosemide.**

B. In dogs, **'feathering'** the dorsal vaginal wall to encourage endogenous oxytocin release may be attempted. If this fails, administer **oxytocin 0.5 – 1 IU IV, IM or SC ± calcium gluconate** (*see E below*). **Higher doses** of oxytocin frequently cited in the literature are **not** recommended as uterine spasm, rather than organized contractions from cranial to caudal horn, occurs. A second dose may be given in 30 minutes if necessary. If no fetus advances after this, a **C-section** is indicated after re-examination of the dam (*see Surgery above*).

C. If the initial oxytocin injection results in a live fetus, and labour ceases again, another injection of **oxytocin** is indicated **± calcium gluconate** (*E below*). **Caution** is advised with oxytocin use, as this has been associated with the birth of dead fetuses. Premature placental separation is the potential etiology therefore, a **C-section** should be considered rather than administering more than two doses of oxytocin (*see Surgery above*).

D. **Queens** often present after having one or more kittens born, but have stopped queening for several hours. If no abnormalities are found on radiography, queens can be given **oxytocin 0.5 – 1 IU SC or IM** and placed in a quiet, warm, secluded cage. Repeat oxytocin, after 30 minutes **± calcium gluconate** (*E below*). If no kittens are born, a **C-section** should be performed (*see C above*).

E. Calcium gluconate 10% solution 0.1 – 0.15 mL/kg:

1. **If serum calcium levels are known to be decreased, administer slowly.**
2. Animals showing signs of hypocalcemic tetany (*see Hypocalcemia p. 377*) should be given **calcium gluconate 10% IV slowly, 0.1 – 0.15 mL/kg, to effect.** Careful cardiac monitoring for bradycardia or other arrhythmias is necessary. The infusion should stop if this occurs.
3. If serum calcium levels are not known, **10 – 15 mL calcium gluconate 1% SC** (mix 1 mL 10% solution with 9 mL sodium chloride) may be administered. Do **NOT** use calcium chloride.

F. Hypoglycemia (*see p. 280*) and hyperthermia may also be present.

G. Hypocalcemic tetany (restlessness, muscle twitching/spasms, **hyperthermia,** panting, a general change in behaviour occurring prior to seizures) usually occurs 2 – 3 weeks *post partum*. If the puppies or kittens are old enough (usually 3 weeks or more), they should be weaned.

H. Seizure activity, due to hypocalcemic cerebral edema, rarely occurs, and is treated with:

    1. **Diazepam 0.5 mg/kg IV, or to effect.** Once neurological signs have dissipated, administer

    2. **calcium gluconate 10% 1 – 3 mL (100 – 300 mg) in queens and 3 – 5 mL (300 – 500 mg) in bitches.** Subcutaneous 1% calcium gluconate is given q8h until the dam is stable.

    3. As soon as possible, administer **oral calcium supplementation with calcium carbonate, 10 – 30 mg/kg (Tums® has 500 mg calcium carbonate or 200 mg elemental calcium so one Tums® tablet per 5 – 10 kg)** and continued q8h throughout lactation.

CARE OF THE NEONATE

Neonatal resuscitation may be required during vaginal or Cesarean delivery. Puppies and kittens may arrive already breathing, squeaking and wriggling, or totally limp.

A. Regardless, the neonate should be **dried thoroughly.** Rapid rubbing with warm towels serves to remove water and stimulate the neonate.

B. **Maintenance of body temperature** is critical to the process. If the surface of the neonate feels cool to the touch, warming should be a priority.

C. **The umbilicus** should be examined for any hemorrhage and ligated 1 cm from the ventral body wall. Care is taken to avoid undue tension on the umbilicus.

D. **Often heartbeats are too weak** to palpate, but certainly a palpable heartbeat requires continual attempts at resuscitation.

E. **If opiates** have been administered to the dam, a drop of naloxone (0.4 mg/mL) under the tongue or injected into the umbilicus will reverse fetal depression.

F. **Doxapram** may be used similarly if rapid rubbing and drying do not result in strong attempts at breathing. However, doxopram has not shown to be of benefit.

G. **Examine the upper airways and oral cavity** removing all fluid by gentle suction or careful "swinging" of the neonate. If swinging is attempted, the neonate must be held in the palm of the hand and on the distal forearm with the neck and head prevented from movement, usually with a towel and a firm hold with the opposite hand. Once secure, the neonate is swung rapidly downward to permit centrifugal force to remove fluid. This is repeated until no further fluid is noted on the floor or at the nares and no 'wet' sounds are noted during respiration.

H. **Supplemental oxygen** should be available for any neonate taking more than a few minutes to cry and breathe strongly.

I. **A warm (37°C, [98.6°F])** draft-free environment is essential for neonates breathing well on their own.

J. **Should resuscitation fail** and the puppies or kittens are cold, they should be warmed to at least 37°C (98°F) with continued assistance. A general rule is that puppies and kittens are not declared dead until they are both warm and dead. Heartbeats are difficult to discern in hypothermic neonates.

K. **Use of the Jen Chung acupuncture point** (at the base of the nares in the nasal philtrum) sometimes aids respiratory effort. A 25 gauge-needle is inserted until bone is contacted and then rotated.

PHARMACOLOGY

1) **Oxytocin 20 IU/mL** is used to continue parturition. Time to effect is 5 minutes after SC injection, and within seconds when placed intrauterine. Effects last for 20 – 30 minutes. Oxytocin may be used in stressed or maiden mothers to facilitate milk letdown.

2) **Calcium gluconate 10%** solution is a calcium supplement used to treat emergent hypocalcemia.

3) **Doxapram** is a respiratory stimulant. Cough, dyspnea or laryngospasm may occur. Overdose may cause tremour, excessive salivation, lacrimation, occasional vomiting, diarrhea or stiffness of extremities. Hyperventilation, arrhythmias or urinary retention may also occur with overdose. Its use has not been proven to be of benefit and currently, is unavailable.

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NOTES

INTRODUCTION

Pyometra refers to the accumulation of inflammatory cells, bacteria, and secretions within the uterus. Bitches are much more likely than queens to be presented for pyometra. Although the pathogenesis is similar in both species, the queen is at decreased risk due to being an induced ovulator. Both usually suffer from this condition within two to eight weeks (most four to six weeks) after a heat and, in the queen, usually, but not necessarily after being bred. Almost every clinically relevant pyometra is due to the influence of progesterone on the uterus.

DIAGNOSIS

History/Signalment

- Recent heat (and breeding in the queen) should increase your suspicions of pyometra.
- Animals are most often presented because the owners have noted a vaginal discharge (open pyometra) or
- The dog or cat may have no visible discharge (closed pyometra), but the owners may report the following:
  - lethargy
  - polyuria/polydipsia
  - anorexia
  - lameness
  - enlarging abdomen
- Occasionally the bitch has actually been a bit sluggish for several weeks and the owners attributed this to pregnancy rather than disease.

Clinical Signs/Physical Examination

- Lethargy, depression, and dehydration are common in closed pyometra but may be present with open pyometra.
- Vaginal discharges are rare in the queen so the observation of a mucopurulent discharge with or without evidence of blood (red or brown) is highly suggestive of pyometra. The bitch, however, often has a vaginal discharge during pregnancy, and especially with vaginitis, so it is vital to decide whether the condition is pyometra or vaginitis.
- Vaginitis is rarely life-threatening whereas pyometra may cause death. Vaginitis occasionally may cause a hemorrhagic discharge, whereas the classic pyometra discharge in the bitch is likened to tomato soup.
- Abdominal palpation frequently elicits pain (occasionally severe enough to confuse with spinal pain). A distended tubular organ in mid- and caudal abdomen is noted.

Laboratory Evaluation/Diagnostic Imaging

Stat
- **PCV & TS** may be elevated if dehydrated.
- **CBC** is recommended to identify inflammatory leukogram. A **neutrophilia** ± left shift, due to endotoxemia, may be present. Frequently mild anemia is noted.
- **Stick BUN, urea and creatinine** may be elevated if dehydrated, often noted if the patient is polyuric/polydipsic.
- **Urinalysis.** Urinary tract infection is present in approximately 30% of dogs with pyometra. It is prudent to perform a cystocentesis with culture and sensitivity of the urine. The cystocentesis should only be performed at the time of surgery (not percutaneously), to avoid puncturing the distended uterus. **White blood cells** may be present in urine sediment if urinary tract infection is present. **Proteinuria** may be present in urinary tract infections and/or with glomerulitis. **Bacteria** may be present in urine sediment in urinary tract infections. **Low urine specific gravity** may be due to endotoxemia, urinary tract infection, and/or fluid therapy.
- **Culture of vaginal discharge/uterus (at ovariohysterectomy).** The most common organism involved in pyometra in both species is *E. coli* although other Gram negative rods have been found, and occasionally cocci or anaerobes.
- **Biochemical Profile.** Alkaline Phosphatase may be elevated in patients with pyometra. Depending on the age of the patient and extent of illness, various abnormalities may be present.
- **Abdominal radiographs and/or ultrasonographic** examination will identify a distended tubular soft tissue structure in mid- and caudal abdomen. The urinary bladder may be large due to polyuria/polydypsia. Ultrasound is preferred when trying to differentiate a distended uterus with fetuses versus purulent debris.

Animals with pyometra are in danger of septic peritonitis and endotoxemia with associated septic shock, thereby requiring stabilization prior to ovariohysterectomy (*see B below*). More often, the bitch does not appear to be gravely ill and the owners may request medical treatment in an effort to preserve the bitch as breeding stock.

A. Medical Management

1. Medical treatment may successfully treat a bitch with closed pyometra, especially if she is not noticeably systemically ill. Owners that routinely have a bitch scanned ultrasonographically for pregnancy may find a closed pyometra before becoming clinically ill. This may open and drain similarly to an open pyometra. Frequently, however, animals are ill which prompts presentation to the veterinarian. A toxic bitch with closed pyometra may not respond to medical management prior to becoming seriously ill and would therefore require ovariohysterectomy (*see B below*).

2. Medical therapy should only be undertaken if the owners accept that the bitch must be bred at her next heat. Medical treatment is only considered for a breeding bitch without systemic disease as there is a high likelihood that pyometra will recur after subsequent heats. An attempt at medical treatment should be reserved for the bitch with a reasonable expectation of successful pregnancy afterward; i.e., not a five-year-old bitch that has been bred unsuccessfully four times and now has pyometra, nor one that has heats more frequently than every three months or less. A young bitch that previously received estrogen therapy after a mismating appears to be an excellent candidate for medical therapy.

3. No specific pharmaceutical treatments are currently licensed for use in bitches or queens. The purpose of medical treatment is: i) to contract the myometrium to permit drainage of the purulent debris; and ii) to halt progesterone production by the corpora lutea. In **pseudopregnancy** the latter is extremely important. Progesterone production is easier to reduce/stop when therapy is initiated at the later stage of pseudopregnancy or diestrus; i.e., after 30 days in bitches and 40 days in queens, as the corpora lutea were undergoing luteolysis on their own. In very late pseudopregnancy it may appear that antibiotics alone will make the patient feel better; however progesterone levels are decreasing at this time with luteolysis and may be the reason for improvement. If incomplete luteolysis occurs, the patient may improve only to relapse a week or so following initial treatment.

4. **Prostaglandin F$_2\alpha$ (PGF$_2\alpha$)** will aid luteolysis and cause myometrial contractions requiring a minimum of five and up to 14 (or more) injections for luteolysis to occur despite the dosage used. The dose of PGF$_2\alpha$ is titrated to the individual.

    a. **Side effects** start within 5 minutes of subcutaneous administration and last 45 minutes to one hour because the hormone is rapidly metabolized. They may include restlessness, panting, pacing, salivation, vomiting (do not administer oral medication or feed the patient for at least two hours after PGF$_2\alpha$ injection), diarrhea, frequent urination or assumption of the whelping/queening posture, including straining. Queens may vocalize as in labour. The amount of discharge can be copious. Prevention of self-grooming of the perineum is advised.

    b. The **natural PGF$_2\alpha$, dinoprost tromethamine (Lutalyse®)** is preferred and the dosage following is ONLY for this product. Start with **0.01 – 0.025 mg/kg SC q8–12h.** If only mild side effects are noted this can be increased with each administration gradually up to **0.1 (bitches) – 0.25 (queens) mg/kg.** If an individual shows excessive side effects stay at that dose or go lower, but not below 0.01 mg/kg. Large and giant breed dogs generally require less mg/kg than toy breeds or cats. **Lutalyse is a 5 mg/mL liquid so may have to be diluted with saline for queens and small bitches.**

5. **Supportive therapy** with IV fluids (*see Fluid Therapy, p. 349*), antibiotics (*D below*) and analgesics (*see Assessment and Control of Pain, p. 117*).

B. Surgical Treatment

Surgical treatment with ovariohysterectomy is the most common treatment for pyometra. This is recommended for systemically ill bitches with open pyometra and all bitches with closed pyometra.

1. The patient must be stabilized with IV fluid therapy (*see Fluid Therapy p. 349*), prior to being anesthetized for surgery (*see Analgesia Anesthesia p. 114*). A routine midline laparotomy approach is performed; the surgeon must be prepared to extend the surgical incision from the xyphoid to the pubis in order to adequately expose and exteriorize the uterus.

2. An ovariohysterectomy is performed, being cautious to avoid rupturing the large friable uterus. Due to the infected nature of the uterine contents, pack off the abdomen with moist laparotomy sponges or small sterile towels and place Carmalt forceps across the uterine body prior to transecting the uterine stump. This will minimize the amount of spillage from the lumen of the uterine body. We do NOT recommend a Parker-Kerr over-sew of the uterine stump, as this may create a pocket of purulent material and result in stump abscessation.
3. Prior to abdominal closure, the uterine stump and, if indicated, the abdominal cavity should be thoroughly suctioned and lavaged several times with warm physiological saline.

C. **Analgesics** are required for approximately 3 days. Opioids (*see Assessment and Management of Pain, p. 117*) are required perioperatively but a non-steroidal anti-inflammatory analgesic may be administered once hydration status and renal function has returned to normal and there are no other contraindications.

D. **Antibiotic therapy.** The most common organism resulting in pyometra is *E. coli* spp, followed by *Staphylococcus* spp, and *Streptococcus* spp. When surgical or medical intervention is performed a 1st generation cephalosporin or amoxicillin-clavulinic acid should be administered and continued for 14 – 21 days. Intravenous administration is recommended peri-operatively. Bacterial culture and sensitivity of uterine contents is indicated if the patient has been on antibiotic therapy prior to the surgery as the organism may be resistant to the chosen antibiotic. Include anaerobic cultures for completeness. Antibiotic therapy is essential as bacteremia may occur with involvement of other organs (i.e., vegetative endocarditis).

PHARMACOLOGY

1) **Lutalyse®** Dinoprost tromethamine 5 mg/mL, a natural prostaglandin $F_2\alpha$ ($PGF_2\alpha$). Produces luteolysis (eventually) and myometrial contractions (immediately).

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NOTES

INTRODUCTION

Masses protruding from the vulva, or a frank hemorrhagic discharge from the vulva may be presented as an emergency. Large masses located immediately within the vulvar labia may present as sudden remarkable enlargement of the perineum. Many vaginal and uterine neoplasms will bleed under estrogenic influence, that is, during heat. The normal serohemorrhagic vulvar discharge seen during heat in bitches is only red blood cells originating in the uterus, not whole blood. Thus, finding clots of blood in the discharge should immediately alert one to a problem. Hemorrhagic vulvar discharge is not seen during normal heat in queens. In both queens and bitches, vaginal cytology is a fast, accurate and simple estrogen assay, much superior to a blood sample. Uterine masses are usually only detected prior to routine ovariohysterectomy if they bleed and then only if the cervix is open. Vaginal masses may interfere with defecation and/or urination so one should consider vaginal tumours in animals with stranguria, dysuria, dyschezia or tenesmus. The most common masses are vaginal hyperplasia (particularly in brachycephalic breeds), leiomyomas, fibropapillomas (vaginal polyps), fibroleiomyomas, fibromas. Less than a third of vaginal tumours are malignant. These include leiomyosarcomas, transitional cell carcinomas (TCC) and, depending on geographic location, transmissible venereal tumours (TVT). TCC seldom, if ever, protrude through the vulvar labia whereas the others commonly do so. Foreign bodies can be located in the vestibule, clitoral fossa or vagina. These may be self-inflicted or iatrogenic. Clitoral hypertrophy with an os clitoris is usually seen in 4 to 8 month old dogs thought to be female that actually have a testis(es). The age is notable as that is when testosterone production causes ossification of the os. Animals with os clitoris are usually presented for hemorrhage, hematuria, irritation or the appearance of a large red mass that may not protrude continually. Queens rarely present for vulvar masses or hemorrhage unless associated with parturition or as a congenital anomaly.

DIAGNOSIS

History/Signalment

The history is often one of sudden onset. Many vaginal tumours respond to increased estrogens so the amount of bleeding often increases over time with increasing production of estrogens during proestrus. A vaginal hyperplasia will enlarge similarly in response to increasing estrogens and this is often seen during the pubertal heat (8 – 14 months old) in brachycephalic breeds. "Hyperplasia" is a misnomer as these are really caused by excessive edema, not excessive growth. Uterine prolapse is a rare peripartum disease. When acute, the animal is usually stable, but becomes progressively shocky so treatment must be addressed immediately. Ovarian remnant syndrome should be considered in bitches and queens presenting with vaginal discharges as vaginitis is rare in queens, and hemorrhagic vaginitis is rare in both queens and bitches. Regardless of type, uterine, vaginal and vestibular tumours are usually found in older patients, compared to vaginal hyperplasia or circumferential "vaginal prolapse" which is usually first noted during puberty. Transmissible venereal tumours (TVT) do not occur in northern latitudes but are more common as one travels south (*see p. 741*).

Clinical Signs/Physical Examination

- In young bitches with masses, consider **vaginal hyperplasia. Palpation** of the vestibule/vagina using the index finger will find that a hyperplasia arises from the floor of the caudal vagina, just cranial to the urethral opening. Lifting up the mass will permit identification of the **urethral opening** directly underneath.
- Circumferential protrusions (**vaginal prolapses**) also occur during proestrus/estrus and are doughnut shaped involving the caudal vagina. Elevating the mass dorsally will identify the **urethral opening,** which may exterior to the labia. Elevating a clitoral hypertrophy/os clitoris will not reveal the urethra but rather the corrugated appearance of the clitoral fossa. The urethral opening is dorsal to the clitoris. Occasionally this is actually a small penis and a urethral opening is at the distal end of the protuberance. Careful palpation of the vestibule, vagina and clitoral fossa may also identify foreign bodies. **Palpation *per rectum*** is sometimes useful in determining the length of a vaginal mass, especially in small dogs and spayed animals where a finger is too large to enter the vagina.
- **Vaginal and vestibular tumours** may arise from anywhere inside the labia, are often multiple, or are attached so far cranially one cannot palpate their origin(s). Some masses will have a pedicle. Occasionally a vaginal hyperplasia may appear as though it has a pedicle. If so, this would originate as described above. TCC's are usually extremely hard, gritty, irregular and multiple and are located around and within the urethral opening. TVT are often multiple, irregularly shaped and seen in bitches traveling in southern areas with other dogs that roam freely.

- **Uterine prolapse** is a rare condition that usually occurs during or just after parturition. The everted uterus is identified easily when both horns prolapse and is a bit more of a challenge when only one horn has prolapsed as that will look more like a doughnut-shaped mass, similar to vaginal prolapse, but occurring at parturition, not heat. In bilateral prolapse, a finger cannot go around the mass, it has to turn the mass back inside itself to progress through the vagina/cervix. Most post partum bitches and queens have easily palpable vaginas (look at the size of a kitten or puppy). Uterine prolapse occurs in any age and any parity in bitches and queens.
- **Urination** often will be slow and difficult.
- The degree of desiccation, excoriation, swelling and loss of mucosal covering of these protrusions should be assessed as prolonged exposure is associated with a greater risk of trauma from the environment and/or the bitch or queen. With uterine prolapse systemic signs increase to severe shock over several hours compared to vaginal masses and prolapse which may go on for weeks with little systemic change.
- Depending on the degree of blood loss, signs of hypovolemic shock are possible (*see Hemorrhage p. 623*).

Laboratory Evaluation/Diagnostic Imaging

- **Vaginal cytology** is prepared by inserting a moistened cotton-tipped swab **above the mass** in a vaginal hyperplasia or **into the "doughnut hole"** in a vaginal prolapse. This will reveal cells indicative of proestrus or estrus, but often with excessive debris. If the history spans weeks, the heat may be over but circumferential masses often continue to protrude where hyperplasia usually recedes back into the labia at the end of heat (baseline estrogen). Pubertal heats, however, can go on for months. If the history is one of urination difficulty and no external mass is noted, vaginal cytology may show cells characteristic of neoplasia, such as transitional cell carcinoma where the tumour has spread through the urethral opening into the vestibule. Other vaginal tumours (except TVT) rarely exfoliate, but cytology can rule out estrogen influence and give some idea of the degree of inflammation. Pyometra may present as frank hemorrhagic vaginal discharge and cytology is quite helpful (*see Pyometra p. 756*). It is useful for the surgeon to know whether the bitch is still under the influence of estrogens prior to surgery as tissues will bleed more easily during heat. Foreign bodies and vaginal tumours often cause a mild to marked vaginitis. Single horn uterine prolapse may be identified using an **impression smear** of the prolapsed tissue and identification of characteristic endometrial cells (basally located nucleus in a columnar cell) or trophoblast cells (large foamy cells often with dark staining irregularly shaped multiple nuclei).
- **Culture and sensitivity** of a vaginal swab is needed for any masses requiring surgery or after removal of a foreign body, particularly if the foreign body was self-inflicted from scooting on the vulva due to chronic irritation.
- **CBC** may reveal a neutrophilia with a left shift in pyometra or, in a long-standing, now infected, mass of the vagina or uterus or those leading to chronic cystitis. Hemorrhagic shock may occur in uterine prolapse. Anemia can occur if blood loss is severe with other masses. Most often no changes are noted. In cases of prolonged heat-like conditions thrombocytopenia and aplastic anemia may be seen if an estrogen-secreting ovarian tumour is present.
- **Urinalysis** should be done with any of these conditions as normal urination habits are often compromised and a secondary cystitis may also be present.
- **Serum biochemistry** may show evidence of renal injury (TCC or any vaginal mass interfering with urination).
- **Transabdominal ultrasound and ultrasound of any protruding mass not yet identified** will show if the mass(es) have metastasized; to what degree the bladder is involved; whether there is fluid trapped in the cranial vagina or within the uterus or vagina; and permits aspiration of specific areas of the mass. This may also show that what was thought to be a normal heat or an ovarian remnant, may be an ovarian tumour.
- **Abdominal and thoracic radiographs** are indicated where a mass is possibly a tumour.
- **Fine needle aspiration** of the mass(es).
- **Biopsy,** fine needle or surgical, of the mass(es) will permit a diagnosis, a prognosis and an appropriate therapy.

MANAGEMENT

Hemorrhage

A. If surgery is contemplated, stabilization depending on the degree of blood loss, is necessary. Uterine prolapses often bleed internally as the uterine arteries are compromised. In long-standing cases with minor blood loss, putting off surgery until infection is under control is advisable, especially in vaginal prolapses.

B. If the animal is in heat, estrogen can be a problem due to its effects on vasculature. Consider monitoring until out of heat if blood loss is not severe. If waiting is not an option, have blood products ready as needed. Ovariohysterectomy will instantly decrease estrogen, but runs the risk of further surgical hemorrhage. The removal of an ovarian remnant itself is not usually associated with increased bleeding. However, before abdominal surgery, the presence of an ovarian remnant should be confirmed (*see above*). These should be removed to prevent another bleeding episode at the next heat.

Mass

A. If uterine prolapse is suspected, one must act quickly as the patient's condition will deteriorate. Lavage, application of sugar to decrease swelling and attempts at replacement are fine, but stabilization (*see Hemorrhage p. 619*) is necessary prior to ovariohysterectomy or at least celiotomy to ensure the horns are properly reverted and to assess the integrity of vessels in the broad ligaments. Occasionally one must amputate the uterus outside the labia. This requires ligation of the uterine arteries, but coeliotomy is still recommended to ensure proper reversion and control of hemorrhage. Surgical amputation of a uterine or vaginal prolapse or removal of vaginal masses requires identification and catheterization of the urethra and may require an episiotomy (*Suggested Reading 4*).

B. An Elizabethan collar is often required as these masses can be irritating to the bitch or queen.

C. With any protruding mass, use of boy's/men's briefs (tail goes through the "fly" opening) or special panties for bitches in heat (Bitches Britches® or Seasonals®) with a panty liner covered in water soluble lubricant and/or an antibiotic cream will decrease trauma and self-mutilation. These have to be removed to permit urination/defection or if the bitch will eat them when not closely monitored or wearing a collar, but are usually all that is necessary to get a vaginal hyperplasia through a heat intact. Bedding should be considered if these masses are not covered as shavings, straw and gravel will adhere to them and cause further trauma. These can also be used to permit stabilization of the patient prior to surgery without further damage to the mass.

D. With protruding masses, hair and debris enters the vagina causing a 'foreign material' vaginitis even after the mass is removed. Vaginoscopy or flushing with saline may help locate and remove foreign material

E. In cases of prolonged pubertal heats or when a vaginal hyperplasia/prolapse occurs very early in a heat, an attempt to speed up the conversion of estrogens to progesterone may be wise. Surgery is easier when estrogens are baseline, and most hyperplasias will shrink back into the labia once estrogens decline. One may use either a progestogen (megestrol acetate) or try to luteinize the follicles with gonadotrophin releasing hormone (GnRH) or human chorionic gonadotrophin (hCG).

PHARMACOLOGY

1) GnRH (Cystorelin®, Factrel®, Fertagyl®) 2 to 4 μg/kg q12h twice. Can be used safely several times, however, it does not always decrease the length of heat.

2) hCG (Chorulon®) 20 IU/kg IM q12h twice. Can be used several times, does not always decrease length of heat.

3) Megestrol acetate (Ovaban® or Ovarid®) 2.2 mg/kg q24h PO for at least five days. See 1) and 2).

SUGGESTED READING

1. Hedlund CS. Surgery of the Reproductive and Genital Systems. In: Fossum TWF, Small Animal Surgery. Philadelphia: Mosby-Year Book, Inc., 1997:531-552.
2. Johnston SD, Root Kustritz MVand Olson PNS. Disorders of the Canine Vagina, Vestibule and Vulva. In: Canine and Feline Theriogenology. Philadelphia: WB Saunders, 2001:225-242.
3. Johnston SD, Root Kustritz MVand Olson PNS. Periparturient Disorders in the Bitch. In: Canine and Feline Theriogenology. Philadelphia: WB Saunders, 2001:129-145.
4. Nelson RW and Couto CG, Eds. Disorders of the Vagina and Uterus. In: Small Animal Internal Medicine 2nd Edition. St. Louis, MO: Mosby, 1998:863-873.

NOTES

Test	*Système International d'Unites (SI Units) Approximate Reference Intervals Feline	Canine	Measure Units	Traditional Units Approximate Reference Intervals Feline	Canine	Measure Units	Conversion Factor
Calcium	2.22–2.78	2.50–3.00	mmol/L	7.5–10.8	7.5–11.3	mg/dL	0.2495
Phosphorus	0.80–2.29	0.90–1.85	mmol/L	3.0–7.0	2.1–6.3	mg/dL	0.3229
Magnesium	0.80–1.10	0.7–1.0	mmol/L	1.8–2.4	1.8–2.4	mg/dL	0.4114
Sodium	147–157	140–154	mmol/L	147–157	140–154	mEq/L	1.00
Potassium	3.6–5.2	3.8–5.4	mmol/L	3.6–5.2	3.8–5.4	mEq/L	1.00
Chloride	114–123	104–119	mmol/L	114–123	104–119	mEq/L	1.00
Carbon Dioxide	13–25	16–27	mmol/L	13–25	16–27	mEq/L	1.00
Anion Gap	13–27	13–24	mmol/L	13–27	13–24	mEq/L	1.00
Total Protein	60–84	55–74	g/L	6.0–8.4	5.5–7.4	g/dL	10.00
Albumin	25–44	26–43	g/L	2.5–4.4	2.6–4.3	g/dL	10.00
Globulin	27–48	21–42	g/L	2.7–4.8	2.1–4.2	g/dL	10.00
A:G Ratio	0.7–1.4	0.7–1.8		0.7–1.4	0.7–1.8		–
Urea	6.0–12.0	3.5–9.0	mmol/L	–	–		–
Creatinine	50–190	20–150	mmol/L	0.8–2.3	0.4–1.8	mg/dL	88.40
BUN	–	–		15–34	7–27	mg/dL	–
Cortisol	30–390	30–300		–	–		27–59
Glucose	4.4–7.7	3.3–7.3	mmol/L	70–150	60–125	mg/dL	0.05551
Cholesterol	2.00–12.00	3.6–10.20	mmol/L	82–218	112–328	mg/dL	0.0258
Triglycerides	0.22–1.01	0.2–1.3	mmol/L	20–90	20–150	mg/dL	0.0113
Bile Acids:							
Fasting	0.0–5.0	0.0–5.0	mmol/L				2.45
Postprandial	<15	<25	mmol/L				
Random	<15	<25	mmol/L				
Total Bilirubin	0–3	0–4	µmol/L	0.0–0.4	0.0–0.4	mg/dL	17.10
Conjugated Bilirubin	0–1	0–1	µmol/L	–	–		–
Free Bilirubin	0–3	0–3	µmol/L	–	–		–
Alkaline Phosphatase	16–113	22–143	U/L	16–113	22–143	U/L	1.00
S–Alk Phos	–	0–84	U/L	–	–		–
Gamma–GT	0–6	0–7	U/L	–	–		–
ALT	31–105	19–107	U/L	31–105	19–107	U/L	1.00
Resting Ammonia	–	20–80	µmol/L	–	–		–
CK	62–440	40–255	U/L	64–440	40–255	U/L	0.5871
Amylase	500–1500	300–1000	U/L	500–1500	300–1000	U/L	1.00
Lipase	10–100	60–800	U/L	10–100	60–800	U/L	1.00
Na:K Ratio	28–41	27–40		28–41	27–40		–
Osmolality	296–315	276–306	mmol/L	296–315	276–306	mmol/L	1.00
Total Iron	–	14–32	µmol/L	–	–	µmol/L	0.1791
Total Iron Binding Capacity	–	65–85	µmol/L	–	–	µmol/L	–

*To convert SI Units into traditional units divide the SI unit value by the conversion factor. To obtain SI unit value multiply the traditional unit by the conversion factor.

Reference intervals vary with individual laboratories.

WEIGHT

1 gram (g) = 1,000,000 (μg or mcg)

1 gram (g) = 1,000,000,000,000 (pg)

1 gram (g) = 1000 (mg)

1 kilogram (kg) = 1000 grams (g)

1 kilogram (kg) = 2.2 (lb)

1 micrograms/gram (mcg/g) = 1 parts per million (ppm)

1 milligram (mg) = 1000 micrograms (μg or mcg)

1 milligram/kilogram (mg/kg) = 1 parts per million (ppm)

VOLUME

1 cup (c) = 240 milliliters (mL) = 8 fluid ounce

15 drops = 1 milliliter (mL)

1 gallon (gal) = 3.79 liters (L) = 4 quarts

1 liter (L) = 1000 milliliters (mL)

1 ounce (fl oz) = 30 milliliters (mL)

1 pint (pt) = 0.47 liters (L) = 2 cups

1 quart (qt) = 0.95 liters (L) = 2 pints

1 tablespoon (tbs) = 15 milliliters (mL)

1 teaspoon (tsp) = 5 milliliters (mL)

TEMPERATURE

Celsius to Fahrenheit (°C X 1.8) + 32 = °F

Fahrenheit to Celsius (°F – 32) X 0.555 = °C

Kilograms to Body Surface Area (m²)
Calculation of surface area for cats and dogs: $\frac{(\text{weight in kg})^{2/3}}{10}$

kg	m²	kg	m²	kg	m²
0.5	0.06	14	0.58	28	0.92
1	0.10	15	0.60	29	0.94
2	0.15	16	0.63	30	0.96
3	0.20	17	0.66	35	1.07
4	0.25	18	0.69	40	1.17
5	0.29	19	0.71	45	1.26
6	0.33	20	0.74	50	1.36
7	0.36	21	0.76	55	1.47
8	0.40	22	0.78	60	1.55
9	0.43	23	0.81	65	1.64
10	0.46	24	0.83	70	1.72
11	0.49	25	0.85	75	1.80
12	0.52	26	0.88	80	1.88
13	0.55	27	0.90	85	1.96

ADH	Anti-diuretic hormone		IM	Intramuscular
ACT	Activated clotting time		IMHA	Immune-mediated hemolytic anemia
ALT	Alanine aminotransferase		ITP	Idiopathic thrombocytopenia
ALP	Alkaline phosphatase		MAP	Mean arterial pressure
BAL	Bronchoalveolar lavage		MM	Mucous membranes
BER	Basal energy requirement		NPO	Nothing per os
BEE	Basal energy expenditure		NSAIA	Non-steroidal anti-inflammatory analgesics
BES	Balanced electrolyte solution		NSAID	Non-steroidal anti-inflammatory drugs
BP	Blood pressure		$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
BUN	Blood urea nitrogen		$PvCO_2$	Partial pressure of carbon dioxide in venous blood
BW	Body weight		PaO_2	Partial pressure of oxygen in arterial blood
CBC	Complete blood count		PvO_2	Partial pressure of oxygen in venous blood
CK	Creatine kinase		PIVKA	Protein-induced vitamin K antagonism
CHF	Congestive heart failure		PCV	Packed cell volume
CO_2	Carbon dioxide		PO	Per os
CRI	Constant rate infusion		PPN	Partial parenteral nutrition
CRT	Capillary refill time		PRN	As required
CRTZ	Chemoreceptor trigger zone		PT	Prothrombin time
O_2	Oxygen		PTT	Activated partial thromboplastin time
DDAVP	1-deamino-8-D-arginase vasopressin		RBC	Red blood cell
DCM	Dilated cardiomyopathy		RER	Resting energy requirement
DIC	Disseminated intravascular coagulation		SC	Subcutaneous
DKA	Diabetic ketoacidosis		SBP	Systemic blood pressure
ECG	Electrocardiogram		SPO_2	Saturation of oxygen assessed by pulse oximetry
ELISA	Enzyme-linked immunosorbent assay		SVT	Supra-ventricular tachycardia
$ETCO_2$	End-tidal carbon dioxide		VT	Ventricular tachycardia
FFP	Fresh frozen plasma		TS	Total solids (plasma sample)
FeLV	Feline leukemia virus		TP	Total protein (serum sample)
FIV	Feline immunodeficiency virus		TPN	Total parenteral nutrition
GGT	Gamma glutamyltransferase		fT4	Free thyroxine
GD	Gastric dilation		TT4	Total thyroxine
GDV	Gastric dilation/volvulus		TSH	Thyroid stimulating hormone
HCM	Hypertrophic cardiomyopathy		TTW	Transtracheal wash
IER	Illness energy requirement		VPC	Ventricular premature contraction
IV	Intravenous		WBC	White blood count

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Karol graduated from the Ontario Veterinary College in 1980, receiving her Doctor of Veterinary Science degree in Small Animal Surgery in 1986 (OVC) and became a Diplomate of the American College of Emergency & Critical Care in 1993.

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The evolution of the Emergency and Critical Care Manual has been a labour of love for Karol and is a result of her long dedication to teaching students, and assisting practitioners in expanding their knowledge in this area.

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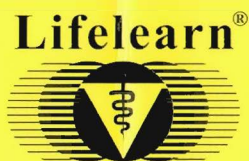
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