

The Association of Exotic Mammal Veterinarians
Presents



Exotic Companion Mammal Emergency Medicine and Critical Care

&

Applied Clinical Topics in Exotic Companion Mammal Medicine



SATURDAY, AUGUST 8TH, 2009

MILWAUKEE, WISCONSIN



Wetlab Hosted by Marla Lichtenberger, DVM, DACVECC of

24 HOUR ANIMAL ER Milwaukee Emergency
Center for Animals
And Specialty Services

ASSOCIATION OF EXOTIC MAMMAL VETERINARIANS 2009 CONFERENCE PROCEEDINGS

SATURDAY, AUGUST 8TH 2009

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Table of Contents

SATURDAY MORNING LECTURE AND WETLAB NOTES:

EXOTIC COMPANION MAMMAL EMERGENCY MEDICINE AND CRITICAL CARE

Exotic Companion Mammal Emergency Medicine and Critical Care.....	1
Exotic Companion Mammal Emergency Techniques.....	16

SATURDAY AFTERNOON LECTURE SERIES:

APPLIED CLINICAL TOPICS IN EXOTIC COMPANION MAMMAL MEDICINE AND SURGERY

The Gastrointestinal System: Exotic Companion Mammals.....	25
The Respiratory System: Exotic Companion Mammals.....	41
Ferret Neoplasia.....	50
Essential Exotic Companion Mammal Surgeries.....	57

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Exotic Companion Mammal Emergency Medicine and Critical Care

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Vascular Access

Intravenous (IV) catheterization is relatively easy in the ferret, rabbit, and larger guinea pig. Sites most commonly utilized include the cephalic vein in ferrets, the cephalic, lateral saphenous, and auricular veins in rabbits and the cephalic and lateral saphenous veins in guinea pigs. Intravenous catheterization is increasingly difficult in smaller patients; however, vascular access is feasible with intraosseous (IO) access, via the tibia or humerus. The authors prefer the use of standard hypodermic needles (27 to 22 g), which are placed, secured with tape and fitted with a standard catheter infusion cap. Confirmation of correct placement can be assumed by stability of the catheter and failure to accumulate fluids in soft tissues, but absolute confirmation requires radiographs of the catheter *in situ* in two views. Fluid infusion is accomplished via intermittent administration with a small volume syringe (1-3 ml), as larger syringes produce excessive pressure. It is often difficult to use an infusion pump in conjunction with a small IO catheter. Small needles used as catheters occasionally occlude with bone or blood clots, which can be removed using very fine sterilized cerclage wire as a stylette.

Sedation and local analgesia enhance the success of IV and IO catheterization, and are discussed in more detail in a later section. Agents and dosages selected depend on overall patient condition. The site is prepared for catheterization, and local lidocaine gel applied. After 5 minutes, the skin is rolled away from the catheterization site and infused with lidocaine (Table 1), then allowed to slide back into place. It is important to wait 10 minutes to allow the local to take effect.

Fluid Therapy

Resuscitation from hypovolemic shock can be safely accomplished with a combination of crystalloids, colloids and rewarming procedures. In the hypovolemic small mammal, a bolus infusion of isotonic crystalloids is administered at 10 to 15 ml/kg. Hetastarch (HES) is administered at 5 ml/kg IV over 5 to 10 minutes. The blood pressure is checked, and once it is above 40 mmHg systolic, only maintenance crystalloids are given, while the patient is aggressively warmed. The warming should be done within 1 to 2 hours with warm water bottles, forced air heating blankets and warming the IV fluids. Once the animal's rectal temperature has risen to 98°F, the blood pressure is rechecked and if the patient is hypotensive then crystalloid (10 ml/kg) with HES at 5 ml/kg increments can be repeated over 15 minutes until the systolic blood pressure rises above 90 mmHg. The rectal temperature must be maintained as needed by a warm incubator and warmed fluids. When the systolic blood pressure is >90 mmHg, the rehydration phase of fluid resuscitation begins.

If endpoint parameters (normal blood pressure, heart rate, mucous membrane color, and capillary refill time (CRT)) are still not obtained, the animal is evaluated and treated for causes of nonresponsive shock (i.e., excessive vasodilation or vasoconstriction, hypoglycemia, electrolyte imbalances, acid-base disorder, cardiac dysfunction, hypoxemia). If cardiac function is normal, and glucose, acid-base, and electrolyte abnormalities have been corrected, treatment for nonresponsive shock is continued. Oxyglobin® has not been approved for use in the cat, ferret, rabbit or small mammal, but has been used successfully in small volume boluses. Administer 2 ml/kg boluses over 10 to 15 minutes until normal heart rate and blood pressure (systolic blood pressure greater than 90

mmHg) are obtained. This is followed by a continuous rate infusion of Oxyglobin® at 0.2 to 0.4 ml/kg/hr. When Oxyglobin® is not available for treatment of refractory hypotension, the authors have used 7.5% hypertonic saline at 3 ml/kg bolus with HES at 3 ml/kg given slowly over 10 minutes. Vasopressors such as dopamine or norepinephrine can be used to treat refractory hypotension, however, when using the above protocol the authors have never had to use these drugs in small mammals.

Fluids for Rehydration

Dehydration deficits are assessed when perfusion parameters are normal. Replacement of dehydration deficits is done with the use of isotonic crystalloids. If losses occurred rapidly, replacement is accomplished over 4 to 6 hours, and added to maintenance fluids. Maintenance fluids rates are estimated at 3 to 4 ml/kg/hr in small mammals.

Fluids for Diuresis in the Renal Failure Patient

Treatment of acute renal failure involves fluid therapy divided into three parts: (1) correction of perfusion, (2) correction of dehydration deficits, and (3) diuresis to correct azotemia, electrolyte and acid base status. Correction of the primary cause needs to be addressed (i.e. urolithiasis, removal of offending drug or treatment for *E. cuniculi* in rabbits). Once the animal is normotensive and rehydrated, record the volume of urine produced every 4 hours. This is the polyuric or diuresis phase of acute renal failure. Measurement of urine volume can be accomplished by continuous urinary bladder catheterization or by placing pre-weighed diapers under the vulva or penis. The volume of urine voided on the diaper can be estimated by assuming 1 ml equals 1 gram. The volume of fluid to be administered in each 4-hour period is the sum of calculated maintenance requirements (3 to 4 ml/kg/hr) and urine volume for the previous interval. Even weighing the patient twice a day can provide insight into the effectiveness of fluid therapy; if the patient loses weight, replacement fluid therapy may be ineffective. Ongoing losses (e.g., diarrhea) also must be estimated and added to the volume of fluids administered; it is safe to assume that most patients with acute renal failure (ARF) become 3% to 5% dehydrated each day as a result of ongoing losses. Therefore, increase the final calculated volume of fluids administered by 3% to 5%.

In many instances, once the polyuric phase of ARF occurs, such large volumes of urine are produced, that only aggressive fluid administration will meet fluid requirements. The urine production may be as high as 5 to 10 ml/kg/hr, which is added to maintenance fluid requirements and ongoing losses (i.e., 5 to 10 times maintenance requirements may be required during the diuresis phase). Rule-of-thumb replacement using 2 to 2.5 times maintenance fluids for diuresis is outdated and ineffective, and may lead to dehydration and ineffective urine production.

Fluids should be gradually discontinued when hydration and urine production are restored (fluids in and urine out are matched), and serum urea and creatinine are normal (stabilized) and the patient is eating and drinking. Taper the fluids by 50%/day. Tapering of fluids will prevent medullary washout.

Monitoring of Perfusion Parameters

During the resuscitation period of hypovolemic shock in small mammals, perfusion parameters that ideally are closely monitored include: 1) blood pressure and heart rate, 2) lactate, 3) temperature, and 4) prothrombin (PT) and partial thromboplastin time (PTT).

Blood Pressure and Heart Rate Monitoring

The indirect blood pressure monitor is most commonly used in veterinary medicine. The indirect method of blood pressure monitoring is extremely useful in determining if a patient is hypotensive, normotensive, or hypertensive. In general, the mean arterial pressure (MAP) should be kept above 60 mmHg and systolic pressure above 90 mmHg to ensure adequate organ perfusion in the conscious and anesthetized patient. Advantages of this Doppler method include relatively low cost, portability, and higher accuracy in small and hypotensive animals compared with other indirect methods (i.e., oscillometric blood pressure monitors). Disadvantages include inability to determine

diastolic pressure, and thus MAP. Although there are several indirect or noninvasive methods available (i.e., oscillometric and Doppler), it is sometimes impossible to obtain a reading on exotic patients. Traditionally, oscillometric blood pressure monitors have been unreliable in the cat and small mammals. The Doppler method is more versatile than the oscillometric method, and is the method used by the authors for all exotic patients. The ultrasonic Doppler flow detector (Parks Medical Electronics Inc., Aloha, OR) uses ultrasonic waves to detect and make audible blood flow in an artery distal to the blood pressure cuff.

The patient is placed in lateral or sternal recumbency. A pneumatic cuff is placed above the carpus, tarsus, or on the tail in a ferret. In the rabbit and other small mammals, the cuff is placed above the elbow. The rear leg can be used for blood pressure recording but is less sensitive than the front leg in the authors' experience. The front limb was more reliable than the rear limb for blood pressure measurements in a study in rabbits. The cuff size should be ideally about 40% of the diameter of the tarsus, carpus, humerus or the base of the tail. Unfortunately, the smallest cuff available is a no. 1 cuff, which is often too large for many smaller patients. A study in ferrets has shown that this larger cuff will give falsely lower indirect systolic blood pressures when compared to direct systolic blood pressures; the indirect systolic blood pressure was about 28-30 mmHg less than the direct arterial blood pressure recordings. The clinician must keep this in mind when recording indirect systolic blood pressures in exotic companion mammals. The divergence between direct and indirect blood pressure monitoring has been seen in other species (i.e., rabbit, dog and cat) to various degrees, and has been attributed to difficulty in correctly determining the appropriate cuff size, variability in cuff sensitivity, and variation in arterial wave forms between anatomical sites. This difference in direct versus indirect Doppler blood pressure in other small mammals and rodents is likely similar to that found in the ferret (e.g., falsely lower blood pressures due to large cuff size).

The hair is shaved on the ventral carpus, tarsus or tail in the ferret and medial midshaft of the radius-ulna area in other small mammals. The transducer probe crystal is placed on the shaved area (radial artery on front leg or digital branch of the tibial artery on rear leg) in a bed of ultrasonic gel and taped or held in place. The cuff bladder is inflated to suprasystemic pressure until the Doppler signal is extinguished. The first sound heard as the cuff is deflated denotes the systolic pressure.

In the authors' experience the manual method using a sphygmomanometer and a Doppler flow probe requires practice, but is extremely useful in exotic companion mammals. In some cases, initial readings are used as a baseline for comparison, especially to detect changes in trends of blood pressure while treating hypovolemic shock or as a monitoring device during procedures or surgery. Years of experience using this method has shown that the normal indirect systolic blood pressures in most exotic companion mammals are between 80 and 120 mmHg.

Lactate Monitoring

Blood lactate concentrations are considered by some to be accurate indicators of inadequate tissue perfusion. Lactate concentrations have been shown to be a superior index of hypoxia when compared with oxygen delivery (DO_2), oxygen consumption (VO_2), the oxygen extraction ratio, and cardiac index (the cardiac output per minute per square meter of body surface area) in clinical studies of critically ill humans.

Lactate monitoring in the critical ill patient is important especially in patients presenting in shock. Lactate values are elevated in domestic animals (i.e., greater than 2.5 mmol/L) when perfusion parameters are poor and usually return to normal when fluids are given to correct perfusion parameters to normal (i.e., heart rate, blood pressure, temperature, CRT). Lactate is used as another critical care monitoring device along with heart rate, blood pressure and temperature to help the clinician correct perfusion deficits.

Normal rabbit lactic acid values have been determined on three different testing devices (Nova Biomedical, Waltham, MA; Idexx Veterinary Chemistry Analyzer, Westbrook, MA; Point of Care Portable Lactate, Arkray, Kyoto, Japan). Twenty blood samples were analyzed and are in publication at this time. Blood lactate values were 7.0 (± 2.6) mmol/L for the Nova, 7.3 (± 2.9) mmol/L for the Idexx and 6.6 (± 3.7) mmol/L for the Point of Care Portable

Lactate Analyzer. There was no statistical difference comparing the Nova with the Point of Care equipment. There was a significant ($p = 0.004$) difference between the results of the Nova compared with the Idexx test.

The conclusions made were that normal mean and ranges of lactate values in rabbits is higher than for most other domestic animals. Values as high as 23 mmol/L have been seen in rabbits with gastric stasis, and may be related to production of D-lactate in the stomach (GA Zello, personal communication). Although there was a statistically significant difference between the Idexx and Nova analyzer results, the differences are most likely clinically insignificant. The Point of Care Analyzer has the advantage of providing immediate results. Future studies are being done with analyzing D-lactate and L-lactate from normal and ill rabbits. Future studies will be conducted to determine change in lactate in response to treatment and as a prognostic indicator.

Temperature Monitoring

Hypothermia is commonly recorded in the exotic companion mammal presenting for hypovolemic shock. The patient must be warmed aggressively using core body temperature warming and external warming methods. Temperatures must be monitored. The most common method of monitoring temperature is with the use of a rectal thermometer. Recently, use of tympanic temperatures have been explored in human and veterinary medicine. Their reliability has been recently questioned.

Temperature monitoring in critically ill small mammal patients provides important data to guide delivery of care. Measurement of core body temperature requires the placement of an esophageal probe. The alternatives are noninvasive use of rectal thermometers, which may be difficult in the conscious patient. Newer methods using infrared thermometry methods have been developed and tested in human patients. The author (Lichtenberger) is currently investigating the use of infrared thermometry in small mammals.

Use of Prothrombin and Partial Thromboplastin Time

Incidence of coagulopathies is not commonly reported in ferrets, although the number of cases of rodenticide may be similar to that seen in dogs and cats. To the authors' knowledge, no studies have reported point-of-care analyzer (PCCA) result for PT and PTT in ferrets. Twelve young healthy ferrets from the Abbott research facility were included in a study. The mean PT/PTT values (\pm std dev) were obtained from each of the two tests. The PT for Antech was 12 ± 1.5 sec and for the SCA2000 it was 20 ± 1 . The PTT for Antech was 18 ± 2 and for the SCA2000 it was 52 ± 19 . There was a good correlation between the PT results from the 2 different testing methods. There was not a good correlation between the PTT results from the 2 different testing methods. The SCA2000 PTT results are also longer in dogs (71 to 102) and cats (70 to 120) and may be more similar to the activated coagulation test (ACT) [personal communication, Urs Gieger, 2004]. To the authors' knowledge, no studies have been done in ferrets to determine normal ACT times. The ACT of ferrets may be similar to the PTT measurements in this study and future studies are warranted in determining ACT measurements in ferrets.

Anesthesia of Exotic Companion Mammals

General anesthesia involves risk, even under the best circumstances. Studies of peri-anesthetic mortality suggest a death rate of 0.1% to 0.2% in dogs and cats. One study reported death rate of 1.39% and 3.80% in rabbits and guinea pigs, 6 to 10 times the death rate of dogs and cats. Most rabbits in this study were not intubated, or were anesthetized with inhalant agents only, or both. The advent of safer inhalant agents was a boon to exotic animal medicine. However, inhalant agents are naturally hypotensive, and untoward effects are dose dependant. The use of inhalant agents as sole anesthetics necessitates higher doses; thus incurs higher risk. No other branch of veterinary medicine uses inhalants as sole agents for anesthesia for what are considered obvious risks. Therefore,

exotic mammal practitioners should consider methods to reduce risk, which include careful patient screening, pre-anesthetic blood work, efficient monitoring, and the use of pre-anesthetic agents and analgesics to reduce the effective amounts of anesthetic agents. Another option to consider is the use of sedation as an alternative to complete anesthesia whenever possible. Recent work with injectable combinations such as ketamine and medetomidine have increased the array of potential agents for use in exotic companion mammals. Much recent attention has been given to the use of medetomidine. While some practitioners find a full injectable protocol useful for procedures where use of inhalant agents is difficult (surgeries of the head or mouth where intubation is difficult to impossible), medetomidine often demonstrates a more profound negative impact on the cardiovascular and respiratory system in many species including the rabbit. Therefore, use in animals without intubation and cardiovascular support, and in ill or debilitated animals should be avoided.

Sedation in Exotic Companion Mammals

Overall, sedation is considered a safer procedure than general anesthesia, and is often adequate for procedures such as phlebotomy, placement of a catheter, diagnostic imaging, and minor wound care where discomfort is expected to be minimal. The addition of local analgesia can reduce any discomfort associated with procedures. A specific example is the use of sedatives, plus a topical anesthetic to facilitate intravenous catheterization. Common agents for sedation include midazolam combined with an opioid, with the addition of ketamine if required (Table 1). Sedation becomes even more important in those patients for which anesthesia presents moderate to significant risk, in particular the ill or critical patient.

Anesthetic/Analgesic Drugs Used in Exotic Companion Mammals

A number of anesthetic and analgesic drugs can be used in the critical exotic companion mammal patient. All doses used by the authors are given in Table 1.

Opioids

Ferrets, rabbits and other small mammals were suspected to have “respiratory depression” after administration of opioid drugs when they were indeed resting very quietly without pain. When used appropriately, opioids can be administered to small mammals and are safe and effective for alleviating pain. Opioids in general have a very wide margin of safety and excellent analgesic properties. In veterinary medicine, the most commonly used opioids are fentanyl, hydromorphone, morphine, buprenorphine and butorphanol. Some animals may respond better to one opioid over another depending on individual variability, breed, species, and source of pain. Opioids act centrally to limit the input of nociceptive information to the central nervous system (CNS), which will reduce central hypersensitivity. Opioids are commonly used in the critically ill patient as they have rapid onset of action and are safe, reversible, and potent analgesics. There are four classes of opioids: pure agonists, partial agonists, agonist-antagonists and antagonists. Their use as a constant rate infusion (CRI) will be discussed in a later section below.

Comments on Individual Opioids

Buprenorphine

Buprenorphine is a mixed agonist/antagonist. Pharmacokinetic and pharmacodynamic data have suggested that 2 to 4 hour dosing intervals may be required for buprenorphine administration in most species of mammals.

Buprenorphine is a slow onset, long acting opiate in mammals that possesses a unique and complex pharmacological profile. Buprenorphine may exhibit a plateau or “ceiling” analgesic effect. In rats, once buprenorphine reached its maximal effect, administration of additional drug produced either detrimental effects or no additional analgesia, although the higher dose may prolong the duration of analgesia. This “ceiling effect” of dosing has also been demonstrated in mice. Analgesic effects at the same dosage can also be variable amongst different strains of rodents. Gastrointestinal side effects are the most commonly reported adverse effect with

buprenorphine, so lower doses are recommended when treating GI stasis. One adverse effect of buprenorphine administration recently been reported in rats is the ingestion of certain types of bedding, especially sawdust or wood chips. This “pica behavior” was not demonstrated when the rats were on a paper pellet-type bedding and it is recommended that rats be housed on other materials after administration of this drug. Buprenorphine is most commonly administered subcutaneously (SC), intramuscularly (IM) or IV. The opioid buprenorphine has the disadvantage of being difficult to reverse (using naloxone) because the drug is difficult to displace at the receptor. Buprenorphine was used as a reversal of mu receptor opioid respiratory depression while maintaining postoperative analgesia for 420 minutes in rabbits. Buprenorphine can be effective when given orally to cats, as long as the pH of their saliva is >7. Studies have shown that oral buprenorphine is effective in dogs too. The author (Lichtenberger) has tested pH of the saliva in rabbits, mice, rats, and chinchillas. Their pH is consistently >8 and buprenorphine may be effective if given orally in these species at the same dose used in cats. The pH of the saliva varies in guinea pigs between 6 and 9. Therefore, oral buprenorphine may not be as effective in this species.

Tramadol

Tramadol (opioid-type drug) is another drug that can be used orally for pain control. No studies have been done on use of this drug in exotic companion mammals. Tramadol binds to opiate receptors and also inhibits reuptake of norepinephrine and serotonin. The agent thus activates two endogenous, antinociceptive mechanisms in the spinal cord and the brain stem. The doses which are currently being used by the authors, as suggested in Table 1, have been extrapolated from human medicine.

Fentanyl

The dose of fentanyl used by the authors is much lower than previously reported for use in small mammals. The authors do see a much greater depressive effect in small mammals when using the high dose ranges of fentanyl. The authors have not seen fentanyl-induced ileus or other gastrointestinal side effects in small mammals when using the lower end of the dose given in Table 1, combined with ketamine.

Use of Opioid Reversal Agents

Naloxone is a mu and kappa antagonist. Naloxone can reverse sedation, respiratory depression and bradycardia, but the reversal of sedation and analgesia can cause pain, excitement, delirium and hyperalgesia. Low-dose naloxone (0.004 mg/kg titrated slowly IV) can be used to reverse CNS depression without affecting analgesia. The duration of naloxone is short. Another option for reversal of other opioids is butorphanol, which will reverse mu CNS depression without antagonizing kappa analgesia effects. Butorphanol should be administered at 0.4 mg/kg IV to reverse only the sedative and respiratory side effects.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal Anti-inflammatory Drugs (NSAIDs) are another option for alleviation of pain. As in other species, there are concerns about preoperative use of NSAIDs in small mammals. The main concerns relate to inhibition of prostaglandin synthesis, which may lead to gastrointestinal erosion, impaired renal function, and bleeding. The limited ability for glucuronide conjugation in ferrets can prolong the duration of action of some NSAIDs, but with appropriate changes in dose and dosing intervals they can be used safely. The advantages of this category of drugs are long duration of action and non-control drug status. In young small mammals with no evidence of renal disease, this group of drugs is a good choice.

NSAIDs should not be used in animals with preexisting renal disease, hypovolemia, or bleeding disorders or if severe surgical hemorrhage is anticipated. The authors do not recommend that NSAIDs be used as a preanesthetic drug in the critically ill patient. The drug can be used postoperatively in the stable, normovolemic exotic companion mammal when they begin eating. Renal values should always be checked before using NSAIDs.

Alpha-2 agonists

Alpha-2 agonists such as dexmedetomidine and medetomidine (Dexdomitor and Domitor, Pfizer Animal Health, Exton, PA) possess analgesic, sedation, and muscle-relaxant properties. The higher dosages (30 µg/kg) are usually reserved for healthy animals because of the cardiopulmonary depression that accompanies their use. One study in healthy rabbits found that the combination of medetomidine and ketamine provided the best sedation, while medetomidine-fentanyl-midazolam had the least cardiovascular effects. Xylazine-ketamine demonstrated the greatest negative cardiovascular side effects.

Microdose medetomidine (1 to 3 µg/kg) minimally affects blood pressure in animals with normal cardiac output, and provides good analgesia, sedation and muscle relaxation when used with a tranquilizer and opioid. Medetomidine requires only a slight alpha2-adrenoceptor availability to decrease noradrenaline turnover and very low doses of medetomidine result in sympatholysis. Therefore, patients who require a high level of sympathetic tone to maintain blood pressure will not tolerate medetomidine (i.e., animals in shock and in compensated heart failure). In conscious dogs intravenous medetomidine at 1.25 µg/kg increased blood pressure by 15% and decreased heart rate by 26% and cardiac output by 35%. In postoperative patients, sympathetic tone was not entirely abolished by medetomidine. Only the unwanted increases in heart rate and blood pressure were attenuated. Medetomidine has no effect on cortisol levels. Alpha-2 agonists are commonly used in human medicine to decrease the stress response. Use in small mammals for the inhibition of the stress response may be warranted. The authors recommend microdose medetomidine for exotic companion mammals, but cautions against use of this drug in any animal with a compromised cardiovascular system.

Low Dose Ketamine

Ketamine (Vetaket[®], Lloyd Laboratories, Shenandoah, IA), is commonly used for induction of anesthesia in small mammals. Reports in human and veterinary medicine indicate variable patient response following ketamine administration which is related to the status of the cardiovascular system at the time of ketamine administration. Ketamine used for induction is well tolerated in the stable patient. Patients that exhibit significant preexisting stress or a patient with hypertrophic cardiomyopathy have an increased risk of cardiovascular destabilization following ketamine administration. Ketamine increases sympathetic tone causing an increase in heart rate, myocardial contractility, and total peripheral vascular resistance. The authors feel that high dose ketamine used for induction of anesthesia in a stressed exotic companion mammal (especially the rabbit) may cause an increased risk of destabilization.

Ketamine may be effective at preventing, or at least lessening, wind-up pain at sub-anesthetic doses. When used with inhalant anesthesia and opioids, there is a reported opioid-sparing and inhalant anesthetic-sparing effects noted. The interesting perspective about ketamine is that very small amounts used via a CRI route combined with an opioid induces an analgesic effect. Microdose ketamine does not cause an increase in sympathetic tone and is frequently used with opioids by the authors for analgesia given as CRI.

Etomidate

Etomidate (Amidate[®], BenVenue Laboratories, Inc, Bedford, OH) is an imidazole derivative that undergoes rapid redistribution and hepatic metabolism, resulting in rapid recovery following a single bolus. Etomidate induces minimal cardiovascular depression and has a wide margin of safety. It can cause temporary apnea and respiratory depression, which is dose dependent. The drug is given to effect, using the lower-end of the dose (1 to 2 mg/kg IV). Patients should be intubated, or at least provide an oxygen mask. Etomidate is frequently used by the authors in high-risk patients. Lichtenberger prefers it for induction of anesthesia for minor procedures and surgery in exotic companion mammals. Etomidate must be used with midazolam to prevent myoclonic twitching. Administer midazolam first to aid in sedation for IV administration of etomidate. The recommended combination is midazolam 0.25 to 0.5 mg/kg IV or IM, followed by etomidate 1.0 mg/kg IV.

Local Anesthetics

Use of local anesthetics for catheterization, sample collection, incisional line blocks, wound infiltration, nerve ring blocks, and epidural anesthesia is extremely useful and highly recommended by the authors. The addition of local analgesia reduces isoflurane mean alveolar concentration (MAC) in humans and traditional pet anesthetic patients, and has been observed by the authors and others to have the same benefit in exotic companion mammal patients as well. Advantages of local anesthetics are their low cost and non-controlled drug status. A complete sensory block prevents nerve transmission, making use of these agents attractive for practical preemptive techniques. Local anesthetics can be infiltrated into the surgical skin site, or discrete nerve blocks can be preformed. The addition of an opioid to the mixture of local anesthetics for local blocks potentially lengthens the median duration of analgesia; in one study the addition of an opioid to a lidocaine/bupivacaine mixture prolonged analgesia 10 hours longer with morphine, and 9 hours longer with buprenorphine. The authors' experience with use in exotic companion mammals concurs with this study. In another study, a buprenorphine-local anesthetic axillary perivascular brachial plexus block provided postoperative analgesia lasting 3 times longer than local anesthetic block alone and twice as long as buprenorphine given by IM injection plus local anesthetic-only block. This supports the concept of peripherally mediated opioid analgesia by buprenorphine. This study was performed in humans with the buprenorphine at 0.3 mg mixed with the lidocaine/bupivacaine as given above. Use of local anesthesia for catheterization was described in a previous section. For incisional line blocks before surgery, use a 25 gauge, 1/4 –inch needle to infiltrate the subcutaneous tissue and skin. The calculated dose of the drugs should not exceed the doses listed in Table 1. Local analgesic protocols (e.g., ring blocks, incisional blocks) are commonly combined with other drugs (i.e., opioids, CRI's) for multimodal analgesia.

Epidural analgesia has been utilized by the authors and many others in ferrets, rabbits, and larger guinea pigs. The technique is identical to that in traditional companion mammals, with the injection site between the last lumbar and first sacral vertebrae in most instances. Drugs used for epidural analgesia include morphine, lidocaine and bupivacaine (Table 1). Epidural placement requires anesthesia, and the use of very small spinal needles or simple injection needles (27 to 25 g).

Dental blocks can be used to provide regional anesthesia for rabbits and other small mammals, and have been used by the authors (personal communication, Dr Dale Kressin): 1) infraorbital nerve block, 2) mental nerve block, 3) maxillary nerve block, and 4) mandibular nerve block. The total dose of the mixture is drawn up into a syringe and 1/4th of the total dose (Table 1) is given into each of 4 sites. Use a 25 to 27 g needle with a 1 cc syringe.

The authors perform castration with IM preoperative injection of an opioid with midazolam (0.25 mg/kg IM), followed by general anesthesia. A testicular block is prepared by mixing 1 mg/kg each lidocaine and bupivacaine with buprenorphine 0.003 mg/kg body weight and diluted with saline to final desired volume (depending on size of injected site). Use a 25 g, 5/8 inch needle for guinea pigs or rabbits and a 27 g, 5/8 inch needle for smaller patients. Place the needle through the testicle starting from the caudal pole aiming for the spermatic cord. It is desirable for the needle to exit the testicle proximally, to provide adequate analgesia for the spermatic cord. Aspirate before injection. Inject, expressing firm back pressure, while withdrawing the needle. Expect to use about 1/3 of the total drug volume per testicle leaving the organ firmly turgid. Repeat for the other testicle and the remaining drug can be used to place a dermal incisional block. This will provide analgesia for 22 hours (personal communication, Stein, 2006).

Constant Rate Infusions (CRIs)

Constant rate infusion of anesthetic and analgesics has several advantages over bolus delivery. Drugs can be titrated to effect, resulting in a reduction of the total amount of drug used, fewer side effects, less “rollercoaster” analgesia, fewer hemodynamic effects and improved cost-effectiveness. CRI also provides an overall inhalant anesthetic sparing effect, which avoids the hypotensive effects of higher concentrations of inhalants. One disadvantage to CRI is a slow rise in drug plasma concentration to therapeutic levels, which is why a loading dose of the drug is frequently given prior to starting constant rate infusion. CRI is ideally administered with a syringe pump capable of delivering very small volumes of drugs. The authors commonly use combinations such as

butorphanol-ketamine, hydromorphone-ketamine or fentanyl-ketamine for CRI (Table 1). Lower doses should be considered for rabbits with gastric stasis.

Monitoring Equipment During Anesthesia

Use of Low Flow Oxygen

In a small exotic companion mammal weighing less than 1 kg, a non-rebreathing or pediatric circle system is preferred. Oxygen flow rates used for traditional small animal patients are suitable for most exotic companion mammals: 50 to 100 ml/kg/min when using a rebreathing system and 200 to 300 when using a non-rebreathing system (Bain, Ayres T-piece). For some vaporizers, the lower limit of oxygen flow rate required to maintain vaporizer accuracy is about 200 ml/min. This should be the lower limit regardless of patient size. Current recommendations for ventilatory support include 2 to 6 breaths per minute using tidal volumes ranging from 10 to 15 ml/kg, with a peak airway pressure less than 10 cm H₂O.

Pulse Oximetry

Many things can interfere with the ability of a pulse oximeter to obtain an accurate saturation reading, including decreased peripheral perfusion (whether from poor overall systemic circulation, peripheral vasoconstriction, or hypothermia), movement, bright ambient lighting, anemia, or dark skin pigmentation.

It is important to recognize that pulse oximetry and the arterial partial pressure of oxygen (PaO₂) are related to one another via the oxyhemoglobin curve. A pulse oximeter reading of 98 to 100% may be associated with a PaO₂ of 100 to 600 (or higher) mmHg. A normal PaO₂ on 100% oxygen should be approximately 500 mmHg. A PaO₂ of 100 mmHg on 100% oxygen reflects a major pulmonary problem. Unless an arterial blood gas is obtained during anesthesia, the anesthetist could be misled that a patient with a hemoglobin saturation of 98% has great pulmonary function. In this patient, detrimental consequences could occur if the patient is recovered on room air. Alternatively, a pulse oximeter reading of 90% correlates to a PaO₂ of 60 mmHg, which indicates moderate hypoxemia. This value would indicate severe pulmonary dysfunction if the patient were on 100% oxygen. However, pulse oximeters are much more sensitive in detecting desaturation than is the naked eye. Most animals will not become cyanotic (have observably bluish mucous membranes) until saturation is less than 70%, but the pulse oximeter will indicate any decrease in saturation, allowing earlier detection of oxygenation and/or circulation problems.

Capnometry/Capnography

Capnometry and capnography are the measurement and graphic display, respectively, of the amount of carbon dioxide (CO₂) in exhaled gas. "End-tidal" CO₂ (ETCO₂) refers to the amount of CO₂ measured at the end of exhalation, when presumably the gas being sampled is that which originated from the alveoli. The amount of CO₂ in end-tidal or alveolar gas theoretically is nearly the same as the amount of CO₂ in blood perfusing the alveoli, which allows ETCO₂ to be used as an estimate of arterial carbon dioxide partial pressure (PaCO₂). Since the equilibrium between arterial and alveolar CO₂ is not quite perfect, normal ETCO₂ is usually 2 to 5 mm Hg less than the normal PaCO₂, which is 35 to 45 mm Hg in conscious small mammals.

When using capnography in exotic companion mammals, a side stream capnograph should be utilized and the dead space associated with the endotracheal tube minimized. The capnograph can be connected to the breathing circuit through an 18-gauge needle inserted into the lumen of the endotracheal tube adapter. The needle should not obstruct the lumen of the endotracheal tube.

Monitoring of ETCO₂ gives an assessment of ventilation, which is often depressed during anesthesia and recumbency. Increases in ETCO₂ above 45 mmHg may indicate respiratory inadequacy, which could be caused by excessive anesthetic depth (depression of brain respiratory center), or the limitations of positioning. The patient should be ventilated to restore a more normal ETCO₂. This means that the rebreathing bag should be squeezed to deliver an inspiratory pressure of 15 to 20 cmH₂O. Never deliver an inspiratory pressure greater than 20 mmHg to

small mammals; ideally use a tidal volume of 15 ml/kg. The cause of the increase in ETCO_2 is investigated and patient position adjusted to ensure the ability to fully expand the lungs, or anesthetic depth lowered.

ETCO_2 measurement has another benefit, in that detection of CO_2 in exhaled gas occurs only when the patient's trachea is properly intubated and there is blood circulating through the alveoli. Thus, failure to detect ETCO_2 in a patient should be cause for alarm. It may indicate esophageal intubation, disconnection or obstruction of the breathing circuit, acute pulmonary thromboembolism, or circulatory arrest.

As with the pulse oximeter, the reliability of the ETCO_2 reading can be evaluated by observing the graphic display of exhaled CO_2 . The normal capnogram has a fairly steep "up" slope (corresponding to the beginning of exhalation), a flat plateau (when end-tidal or alveolar gas is exhaled and the maximum CO_2 is detected), and a steep "down" slope (inspiration). Therefore a capnogram without a plateau is not a reliable indicator of true end-tidal CO_2 .

Typing it all Together in the Critically Ill Surgical Patient

The following example outlines a protocol for the critically ill surgical patient. While specific examples are given, other drug combinations can be considered. Fluid resuscitation for correction of perfusion deficits is initiated as described above. Ideally the patient is rehydrated over 6 to 8 hours. Lower dose sedative-analgesics (i.e., opioid and midazolam) can be administered as required for pain during resuscitation.

One half hour prior to surgery, administer a preoperative loading dose of fentanyl IV along with ketamine microdose (1 to 2 mg/kg IV). Prepare a CRI of fentanyl and ketamine. The CRI can be mixed with saline in a syringe and piggy-backed with a Y connector to the crystalloids and/or colloids being administered during surgery. Alternatively, CRI can be mixed directly with fluids. The disadvantage of combining surgical fluids plus the CRI is the inability to increase rate of either independently (see Hypotension during Surgery, below). Surgical administration rate of crystalloids is 10 mg/kg/hr, and colloids at 0.8 mg/kg/hr.

- **Induction**
 - The animal is induced with etomidate and midazolam IV and intubated if possible.
- **Maintenance Anesthesia**
 - The patient is maintained on isoflurane or sevoflurane at the lowest possible concentration (1 and 2 %, respectively).
- **Analgesia**
 - Administer morphine with or without bupivacaine as an epidural. A lidocaine and bupivacaine incisional block is used. Analgesia is also provided by CRI.

Hypotension During Surgery

If hypotension occurs during the surgery, the inhalant anesthesia is reduced first, while the CRI is increased. The animal should also be treated for hypovolemia if there is blood loss or fluid deficits are suspected until the blood pressure is normal. Checking a blood glucose, PCV/TP and blood gas analysis intraoperatively is recommended. Monitoring devices such as the pulse oximeter, end tidal CO_2 , temperature, ECG rhythm and rate are checked for abnormalities.

Table 1: Anesthetic and Analgesic Drug Dosages for Exotic Companion Mammals

Drug	Pre-op dose for rabbit/ferret	Induction dose for ferret/rabbit	CRI dose/Post-op for rabbit/ferret
A. Tranquillizers			
1. Diazepam	0.5 mg/kg IV		
2. Midazolam	0.25 to 0.5 mg/kg IM/IV		
B. Opioids			
1. Butorphanol	0.2 to 0.8 mg/kg SQ, IM or IV		0.1 to 0.2 mg/kg loading dose, then 0.1 to 0.2 mg/kg/hr
2. Fentanyl	5 to 10 µg/kg IV		Intraop: 5 to 20 µg/kg/hr w/ ketamine CRI Postop: 2.5 to 5 µg/kg/hr w/ ketamine CRI
3. Hydromorphone	0.05 to 0.1 mg/kg IV		0.05 mg/kg IV loading dose, then 0.05 to 0.1 mg/kg/hr
4. Tramadol			Post-op: 10 mg/kg PO q 24 hr
5. Buprenorphine	0.04 to 0.06 mg/kg IM, IV		
C. NMDA antagonists			
1. Ketamine		4 to 10 mg/kg IV	Intraop: 0.1 mg/kg IV loading dose, then 0.3-0.4 mg/kg/hr w/ fentanyl CRI Postop: 0.3 to 0.4 mg/kg/hr w/fentanyl CRI
D. Propofol			
		4 to 6 mg/kg IV	
E. Etomidate			
		1 to 2 mg/kg IV w/ benzodiazepine	
F. Alpha-2 agonists			
1. Medetomidine	1 to 2 µg/kg IM, IV		1 to 2 µg/kg q 4 to 6 hr IV
G. NSAIDs			
1. Carprofen			4 mg/kg PO q24hr
2. Ketoprofen			Postop: 1 to 2 mg/kg q24hr
3. Meloxicam			0.2 mg/kg (first dose) SQ, IV, PO and then 0.1 mg/kg q24hr (rabbit 0.3 mg/kg q24hr)
H. Local anesthetics			
1. Lidocaine			Local infiltration Intraop: 1 mg/kg at incision site or ring block
2. Bupivacaine			Local infiltration Intraop/postop: 1 mg/kg at incision site or ring block
I. Epidurals			
1. Morphine preservative -free		0.1 mg/kg epidural w/ or w/o bupivacaine preop	
2. Bupivacaine 0.125%		0.1 mg/kg epidural w/ or w/o morphine	
3. Lidocaine 1.5%		0.4 mg/kg epidural	

Nutrition

Anorexia is a common nonspecific sign of stress in all exotic companion mammals but especially rabbits and guinea pigs. Stress may be due to dental pain, systemic disease, gastrointestinal stasis or even “anxiety.” Any period of anorexia lasting more than 1 to 2 days is a potential emergency. Anorexic rabbits become dehydrated which slows gastrointestinal motility and eventually leads to hypovolemia and hepatic lipidosis. Rabbits are herbivores and hindgut fermenters. Their digestive system is driven by the presence of fiber in the diet, which allows efficient digestion of the nonfiber portion of food. High-fiber diets stimulate cecocolic motility, and have a low level of carbohydrate and thus decrease the risk of enterotoxemia caused by carbohydrate overload of the hindgut. Frequently, a reduction in the amount of fiber in the diet, an increase in carbohydrate consumption, and disruption of gastroenteric motility lead to alterations in the cecal pH and disruption of the complex bacterial flora of the hindgut. The spore-forming anaerobes, consisting mostly of *Clostridium* spp., and coliform species as *Escherichia coli* increase and the population of normal organisms decrease. This will lead to enterotoxemia, sepsis and death. Prolonged anorexia is harmful in other species as well.

The authors always believe in the old adage “if the gut works, use it” for all animals. Early enteral feeding decreases pain, helps with motility of the gastrointestinal tract, and decreases bacterial translocation. Exotic companion mammals should be assist-fed a diet that closely matches normal diet. For example, feed the rabbit and guinea pig a convalescent diet high in fiber (eg. Oxbow Herbivore Critical Care, Oxbow Animal Health, Murdoch, NE; Emerald Herbivore, Lafeber Company, Cornell, IL). Ferrets can be fed soft diets designed for convalescing dogs and cats or diets designed for nutritional support of ferrets (eg. Oxbow Carnivore Care, Oxbow Animal Health; Emerald Carnivore, Lafeber Company). In some cases, a nasogastric (NG) or esophagostomy tube may be less stressful in the critical patient than force-feeding with a syringe. Oxbow Critical Care Fine Grind has been formulated to provide adequate nutrition and pass through a nasogastric tube in the rabbit. The powdered diet has 28% fiber concentration. When a rabbit presents with anorexia for greater than 24 hours and is dehydrated or poorly perfused, the authors often use an NG tube as part of the treatment plan to deliver nutrition and rehydrate the stomach contents. A 3.5- to 8-Fr Argyle® tube (Kendall Co., Mansfield, MA) is used, and the length necessary to reach the stomach is determined by measuring from the tip of the nose to the last rib. The argyle tube is a softer material than a red rubber tube. A stylet should not be used, since the esophagus of the rabbit can be perforated with any additional force. Placement of a nasogastric tube is facilitated by sedation. A local anesthetic (2% lidocaine gel) is placed into the rabbit’s nostril. The rabbit must be properly restrained while protecting its back, and the head is ventrally flexed but with the neck straight (to avoid compression of the trachea) by an assistant. The tube is passed ventrally and medially into the ventral nasal meatus. The end of the tube is advanced until it reaches the stomach. Verification of placement is determined with a radiograph and/or aspiration of gastric contents. Feed the amount according to manufacturer’s packaging instructions. Placement of an NG tube is possible in larger guinea pigs, but is not practical in the ferret or smaller exotic companion mammals. In these cases, an esophagostomy tube can be placed when assist-feeding is unsuccessful.

Regardless of the level of enteral support selected, food should be available at all times for voluntary consumption. If possible, provide patients with their customary diet including familiar brand and food dish. Rabbits should be offered fresh grass, and timothy or alfalfa hay. When indicated, fresh greens, such as dandelion greens, broccoli flowers and stem, cilantro, dark leaf lettuce, watercress, Brussels sprouts, celery leaves, cabbage, and endive may entice a rabbit to eat.

Promotility Drugs

Prokinetics may be of benefit to promote motility of the stomach and intestines of rabbits. The use of metoclopramide as a motility agent, either SQ or as a CRI is anecdotal. Cisapride is available through compounding pharmaceutical agencies. Oral cisapride in rabbits is absorbed rapidly from the gastrointestinal tract, with a plasma half-life similar to that in dogs. Other data show that cisapride may modify the contractile responses of the isolated rabbit intestine to ranitidine, with a potentiating effect up to a certain concentration; therefore, co-administration

of the two drugs may lead to enhanced motility. Dosages are cisapride at 0.5 mg/kg PO q8hr or via NG tube and ranitidine at 0.5 mg/kg IV q24hr. These drugs are not used when obstruction is suspected.

Venipuncture

Collection of blood for diagnostic testing can be challenging in exotic companion mammals, especially in smaller species. Modern technologies allow acquisition of useful information from very small samples, but samples still must be of high quality and meet minimum volume requirements. The challenge of blood collection is compounded in critically ill, hypovolemic and/or hypothermic patients. In many cases, initial therapy must precede sample collection.

Volume of sample is limited by patient size. A common guideline is to collect no more than 10% of blood volume. Total blood volumes vary from species to species but can generally be assumed to be 6 to 8% of body weight. Clinical judgment may necessitate adjustments to recommended volume limits. Sample collection in exotic companion mammals requires practice. Collection site depends on species, patient condition and practitioner preference. The following guidelines are offered based on the authors' personal preference and experience, and others may advocate other sites or techniques. The "correct" technique is that which results in consistently good results with optimal patient safety. For individuals where manual restraint for sample collection is difficult and risky, or patient struggling is excessive, sedation and/or anesthesia should be considered. The risk of sedation and anesthesia must be balanced against the risk of foregoing diagnostic blood testing. Methods include simple sedation and anesthesia with injectable and/or inhalant agents. The authors have found administration of IV or IM midazolam at 0.25 mg/kg combined with an opioid (example: butorphanol at 0.4 mg/kg IV or IM), plus the use of local anesthesia extremely useful to reduce stress for simple procedures such as sample collection and catheterization in exotic companion mammals. It should be noted that collection from the vena cava in patients other than the ferret requires sedation or anesthesia to prevent patient injury.

Collection Sites

Sample site is based on clinical experience and practitioner preference. The greatest limiting factors in regard to site selection are patient size and ability to safely restrain. Exotic practitioners have utilized the vena cava as a safe and effective method of sample collection for many years. Careful understanding of the anatomical relationship of the vessel, the heart and external landmarks greatly reduces risk. In the ferret, the vena cava is exceptionally long due to relative caudal placement of the heart in the thoracic cavity. The cava is surrounded and protected by fat, and is accessible just below the notch of the sternal manubrium. Correct needle placement is very shallow, and poses no risk to inadvertent penetration of the heart. The cava is shorter in other species, and the distance between accessible vessel and the heart is progressively smaller as patient size decreases. Use of small, short needles (1/2 and 5/8th inch 25 to 27 g) reduces risk. In all but very small guinea pigs, these needles will prevent inadvertent puncture of the heart. In other smaller species, however, risk of cardiac penetration is greater, and the practitioner must avoid advancing the needle into the thoracic cavity. While not ideal and absolutely to be avoided, it should be noted that in most cases, inadvertent cardiac puncture is not associated with severe complications or death in the still, anesthetized patient. It should be stressed that sedation, and often general anesthesia, are absolutely required for collection from the vena cava. A possible exception is venipuncture of calm, well-restrained ferrets.

The general procedure for vena cava puncture in exotic companion mammals is as follows:

- Isolate the center of the cranial sternum and manubrium
- Insert a 25 to 27 g needle to the right or left of the manubrium at a slight angle aiming for the opposing hip
- Advance the needle while applying negative pressure, redirecting slightly until a flash of blood is detected. The vessel is very close to the surface under the cranial sternum, and it is not necessary to advance the needle very far
- Blood should flow readily after detecting the flash. Failure to flow often means the needle was advanced into and through the vessel, or the bevel is obstructed by the vessel wall. Pull out, rotate and/or redirect slightly until blood flow improves.

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EXOTIC COMPANION MAMMAL EMERGENCY TECHNIQUES

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Handling and Restraint

Most practitioners seeing exotic mammals are familiar with safe handling and restraint techniques.

Sedation and Pre-anesthesia

A full discussion of sedation and anesthesia is beyond the focus of this laboratory. However, in many cases, it is extremely beneficial to provide sedation in order to facilitate safe handling of the critical care patient. The authors prefer a combination of midazolam and an opioid such buprenorphine or butorphanol for this purpose. These drugs are generally safe in less stable patients, and reduction of stress and discomfort can enhance survival. In less stable patients, low doses of these drugs can facilitate placement of an intravenous (IV) or intraosseous (IO) catheter, phlebotomy and diagnostic imaging. The authors have noted that many mammals in respiratory distress relax and breathe easier and with less effort with administration midazolam due to an anti-anxiety effect.

- **Midazolam:** 0.25 to 0.50 mg/kg IM or IV
- **Butorphanol:** 0.2 to 0.4 mg/kg IM or IV
- **Buprenorphine:** 0.04 to 0.06 mg/kg IM or IV

Phlebotomy

Sites for collection of blood in exotic companion mammals are well described. Phlebotomy in less stable patients, especially small patients can be challenging. The authors have found the cranial vena cava to be an important site for these patients. It should be kept in mind phlebotomy should ideally be delayed in the unstable patient. Preferred sites for blood collection in various species are described below:

1. Ferrets

Ferrets are wrapped tightly in a blanket up to their front legs. Ferrets are held in dorsal recumbency with the forelimbs pulled caudally over the thorax and the head extended. Needle penetration is performed in the notch between the first rib and manubrium of the sternum. A 25- gauge needle attached to a syringe, is held at a 45-degree angle with relation to the skin, and directed toward the contralateral hip. The needle is inserted to the hub and the plunger is pulled back as the needle is slowly removed.

2. Guinea Pigs, Chinchillas, and Sugar Gliders

Cranial vena cava venipuncture under anesthesia is also possible in many rodents. The potential risks of this technique include hemorrhage into the thoracic cavity and/or pericardial sac and penetration of the heart. To minimize these potential complications, use of a 25 to 27 gauge hypodermic needle and a ½ to 1 ml syringe is recommended. The angle of the needle and syringe are slightly different than that used for cranial vena cava venipuncture in other mammals. In guinea pigs, chinchillas and sugar gliders (all three have underdeveloped clavicle), a 25-gauge, 5/8 inch length needle is inserted cranial to the manubrium and first rib.

3. Rabbits

Although several sites are available for venipuncture (i.e., ear vein, jugular vein, cephalic vein, and lateral saphenous), the authors prefer the lateral saphenous. Vessels in the ears are easily visualized but collapse and have an increased risk of thrombosis and sloughing in small rabbits. Jugular venipuncture may be difficult in obese rabbits and those with large dewlaps. The cephalic vein is maintained for catheter placement. The saphenous vein is most commonly used for collection of blood. The rabbit can be restrained in lateral recumbency and the rear leg is held off above the hock. A 25 gauge needle and 1 cc syringe are used to withdraw the blood sample.

Intravenous (IV) Catheterization

Catheterization of ferrets is relatively easy and straightforward, and accomplished with standard 24 to 25 g catheters. Intravenous catheters of either 24 to 26 gauge can be placed in most small rabbits, and 22-gauge catheters can be easily placed in rabbits over 3 kg. The cephalic or saphenous veins are well suited for indwelling catheters.

Intraosseous (IO) Catherization

This technique is ideal in smaller patients, or when IV catheterization attempts have failed. The proximal tibia (at the tibial crest) and femur (at the greater trochanter) are the most commonly utilized sites. With the exception of extremely large exotic mammals, most can be placed with 18 to 25 gauge hypodermic needles. Use of spinal needles has also been described. The catheter is taped into place and fitted with an injection cap. Larger (greater than 22 g) catheters can be used with an infusion pump, but small catheters require slow, gentle intermittent bolus infusion. Excessive pressure produces discomfort and catheter failure. Occlusion of the catheter is a common complication, but can be resolved with the use of fine sterile cerclage wire cut into sizes and lengths to fit commonly used needles.

Indirect Blood Pressure Monitoring

The indirect blood pressure monitor is most commonly used in veterinary medicine. The indirect method of blood pressure monitoring (whether using Doppler or oscillometric method) is clinically useful in determining if a patient is hypotensive, normotensive, or hypertensive. In general, the mean arterial pressure (MAP) should be kept above 60 mmHg and systolic pressure above 90 mmHg to ensure adequate organ perfusion in the conscious and anesthetized patient. Although there are several indirect or noninvasive methods (i.e., oscillometric and Doppler) available, it is sometimes impossible to obtain a reading on exotic patients. Traditionally, oscillometric blood pressure monitors have been unreliable in the cat and small mammals. The Doppler method is more versatile than the oscillometric method, and is the method of choice used by the authors for all exotic patients. Advantages of the Doppler method include relatively low cost, portability, and a better reliability in small and hypotensive animals compared with other indirect methods (i.e., oscillometric blood pressure monitors). Disadvantages include inability to determine diastolic pressure, and thus MAP. The ultrasonic Doppler flow probe (Parks Medical

Electronics Inc., Aloha, OR) uses ultrasonic waves to detect and make audible blood flow in an artery distal to the blood pressure cuff.

Materials for Doppler Blood Pressure Monitoring

Materials for Doppler Blood Pressure Monitoring include the following:

- Classic Cuff (Critikon®, General Electric Health care, Mexico)
- Sphygmomanometer (Propper Manufacturing Company, Long Island City, NY, USA)
- Ultrasource Transmission Gel (Graham-field, Inc., Bayshore, NY, USA)
- Doppler Blood pressure Monitor [Parks Medical (Parks Medical Electronics, Inc., Aloha, Oregon, USA) or Minidop (Jorgensen Laboratories, Inc., Burlington, WI, USA)]

Procedure for Blood Pressure Monitoring

The ferret, rabbit, or small mammal is placed in lateral or sternal recumbency. A pneumatic cuff is placed above the carpus, tarsus, or on the tail in a ferret. In the rabbit and other small mammals, the cuff is placed above the elbow. The rear leg can be used for blood pressure recording but is less sensitive than the front leg in the authors' experience. The front limb was more reliable than the rear limb for blood pressure measurements in a study in rabbits. The cuff size should be ideally about 40% of the circumference of the tarsus, carpus, humerus or the base of the tail. Unfortunately, the smallest cuff available is a no. 1 cuff or an infant size cuff, which is usually too large for many smaller exotic companion mammals. A study in ferrets has shown that this larger cuff will give falsely lower indirect systolic blood pressures when compared to direct systolic blood pressures. The indirect systolic blood pressure was about 28 to 30 mmHg less than the direct arterial blood pressure recordings in that study. The clinician must keep this in mind when recording indirect systolic blood pressures in mammals. The discrepancy between direct and indirect blood pressure monitoring has been seen in other species (i.e., rabbit, dog and cat) to various degrees, and has been attributed to difficulty in correctly determining the appropriate cuff size, variability in cuff sensitivity, and variation in arterial wave forms between anatomical sites. We suspect that this difference in direct versus indirect Doppler blood pressure in other small mammals and rodents is similar to that found in the ferret (e.g., falsely lower blood pressures due to large cuff size).

For using Doppler method to measure blood pressure, the hair is shaved on the ventral carpus, tarsus or tail in the ferret and in the medial midshaft of the radius-ulnar area in other small mammals. The transducer probe crystal is placed on the shaved area (radial artery on front leg or digital branch of the tibial artery on rear leg) in a bed of ultrasonic gel and taped or held in place. The cuff bladder is inflated to a pressure that exceeding systolic blood pressure. At this time, the Doppler signal of blood flow is diminished and then the blood pressure cuff is deflated gradually. The first sound heard as the cuff is deflated denotes the systolic pressure.

The Doppler method using a sphygmomanometer and a Doppler flow probe is easy to use in small mammals, but requires practice. Normal systolic blood pressure in small mammals ranges from 80 to 120 mmHg. While the Doppler method may not always give accurate measurements when compared to direct methods in exotic companion mammals and birds, its primary use is likely as a trend monitor, especially evaluation and monitoring of the surgery patient or while treating hypovolemic shock.

Electrocardiogram (ECG)

An electrocardiogram (ECG) is useful to detect and diagnose cardiac arrhythmias, but one should remember that electrical activity does not ensure mechanical (pumping) activity. The ECG can actually remain relatively normal in birds and small mammals with severe cardiopulmonary compromise or even cardiac arrest from anesthetic overdose. An ECG machine has little value as a monitor of anesthetic depth.

One of the first signs of deterioration in the anesthetized patient or first indications of an anesthetic overdose may be bradycardia and ST segment depression. Diagnosis of cardiac disease in all species involves a thorough examination utilizing an ECG, blood pressure assessment, radiographs and echocardiographic exam.

Recording the ECG

The most common lead used for determining these abnormalities is the lead II ECG. In emergencies, critical care monitoring and monitoring of the surgical patient, the lead II ECG recording is primarily used to determine presence of arrhythmia or in conjunction with other diagnostic tests to determine presence of cardiac disease. The lead II ECG recording should be used to determine rate, rhythm and conduction abnormalities. For ECG recordings in the conscious animal use of atraumatic alligator clips are recommended. Sternal recumbency is commonly used to record the ECG and there are minimal changes in measurements when compared to the ECG performed in right lateral recumbency. The recording speed of 100 to 200 mm/sec is recommended (due to the fast heart rate in smaller exotic companion mammals and birds) and the machine is standardized at 1 cm= 1 mV. There are ECG machines commercially available that record at 100 to 200 mm/sec (Vetspecs, Inc., Canton, GA; and Vetronics, Bioanalytical Systems, Inc., West Lafayette, In)

Intubation Techniques for Inhalation Anesthesia

1. Ferrets

Endotracheal intubation in the ferret is performed through visualization of the glottis, similar to that in cats and dogs.

2. Rabbits

a. **Endoscope guided.** A semi-flexible fiberoptic endoscope (Focuscope, MDS Inc., Brandon, FL) is inserted into the adaptor end of a 2.0 to 2.5 mm internal diameter (ID) uncuffed endotracheal (ET) tube, and the tip of the scope is positioned to within 1 to 2 mm of the beveled end of the tube. The semi-flexible endoscope has a portable handheld light source. The endoscope and ET tube are advanced over the base of the tongue until the tip of the epiglottis is visible through the soft palate. The tip of the scope is advanced in a dorso-caudal direction, lifting the soft palate and thus allowing the epiglottis to fall forward. The tube is advanced into the laryngeal opening and the ET tube is advanced over the scope into the trachea. The endoscope is removed.

b. **Blind intubation** is performed by positioning the rabbit sternally and hyperextending the head and neck dorsally. The 2.0 to 3.0 mm uncuffed endotracheal tube is advanced into the mouth and the adaptor end placed close to the operator's ear in order to detect the sound of airflow from the trachea. The tip of the tube is placed closest to the epiglottis (indicated by the loudest sound of air) and the epiglottis bumped gently to cause it to fall forward and open. At this point the tube generally falls into place and is taped securely. One of the authors (Lennox) has employed this sole technique for nearly 10 years with great success and without major complication. Anecdotal reports of epiglottal and airway trauma warrant extreme care. At no time should force be applied when implementing this technique.

c. **Nasotracheal intubation.** Some practitioners prefer this technique when working in the mouth of the rabbit to avoid the ET tube. The rabbit is held with extreme extension of the neck so that the neck and head are

perpendicular to the table. An 8 French (small rabbits <1 kg) or ET tube (2 mm ET tube for a 2 Kg rabbit, 3 mm tube for a 3 Kg rabbit) is passed medially and ventrally into the nose. The ventral meatus is entered while the ET tube is passed into the larynx and trachea. Use minimal force when entering the larynx. A butterfly tape is placed around the ET tube at the entrance into the nose. The tape can be sutured to the nose.

3. Smaller Exotic Companion Mammals

Some smaller mammals may be intubated using the same techniques described above for rabbits, in particular guinea pigs with the endoscope-guided technique. Laboratory intubation kits designed for intubation of animals as small as rats are available, but are expensive and require significant practice. When intubation is not possible, most small exotic companion mammals are anesthetized and maintained with inhalant anesthesia using a mask.

Tracheostomy

If an endotracheal tube cannot be placed, a temporary tracheostomy can be performed. A 2 to 3 cm skin incision is made on the ventral midline parallel to the trachea, just caudal to the larynx. The subcutaneous fat and fascia are bluntly dissected which will minimize the risk of cutting through blood vessels imbedded in the fat that can bleed excessively. Blunt dissection is continued through the paired strap muscles to isolate the trachea. A transverse incision is made between the tracheal rings which should not exceed 50% of the circumference of the trachea. Stay sutures are placed in the trachea cranial and caudal to the tracheostomy site. An uncuffed ET tube is inserted into the trachea and secured in place.

Thoracocentesis

When pneumothorax is suspected, a 22 gauge needle or butterfly is placed through the skin and into the thoracic cavity (dorsal and caudal) into the 8th to 9th intercostal space. The needle is then turned toward the body wall to avoid laceration of the lung. When hydrothorax is suspected, a 22 gauge needle or butterfly is placed through the skin and into the thoracic cavity (ventral and cranial) into the 2nd to 4th intercostal space.

Local Anesthetic Blocks

Local anesthesia can be an important part of balanced anesthesia in the critical exotic mammal patient. The use of multi-modal anesthetic protocols allows reduction of other general pre-anesthetic and anesthetic agents, increasing patient safety. Another advantage of local anesthetic is low drug cost and non-controlled status of these agents. Local anesthetic agents can be employed successfully in exotic companion mammals. The two most commonly used agents are lidocaine (Lidocaine HCl oral Topical Soln, USP 2%, Hi-Tech Pharmacal Co., Inc, Amityville, NY) and bupivacaine (Bupivacaine HCl, 0.5%, Abbott Laboratories, North Chicago, IL). The addition of an opioid to the mixture of local anesthetics for local block potentially lengthens the median duration of analgesia. The addition of morphine to the lidocaine/bupivacaine mixture prolonged analgesia 10 hours longer than without the morphine, and 9 hours longer with buprenorphine. Specific uses include incisional line blocks, wound infiltration, nerve ring blocks, epidural and topical anesthesia. The calculated dose of the drugs should not exceed the doses listed in Table 1, Section 1 (page 11).

Epidural Anesthesia

Epidural anesthesia is performed regularly in ferrets and rabbit, and can potentially be utilized in other similarly-sized mammals as well. Epidural drugs achieve pain relief with less to no systemic effects as compared with drugs administered intramuscularly or intravenously. This factor is important in small mammals when the administered drug has negative side effects, such as cardiac and respiratory depression. Epidural drugs may decrease recovery

time, which is always an advantage when working with ferrets and rabbits. The improvement in recovery time occurs because of the decreased percentage of gas anesthesia needed when used in conjunction with an epidural anesthetic.

Drugs used for epidural anesthesia include lidocaine, bupivacaine and morphine. In most small mammals, after epidural injection of lidocaine, analgesia develops within 10 to 15 minutes and lasts 60 to 90 minutes. Bupivacaine can provide up to 6 to 8 hours of surgical analgesia. Ferrets have been treated with lidocaine 1.5% at 0.4 ml/kg. Morphine (Morphine Sulfate inj, USP, Baxter Healthcare, Cherry Hill, NJ) at 0.22 mg/kg administered into the epidural space provides prolonged postoperative analgesia for up to 24 hours.

Intratesticular Block

The authors recommend that castration in small mammals can be performed with an IM preoperative injection of butorphanol or buprenorphine (0.02 mg/kg) with midazolam (0.25 mg/kg) IM. Mix 0.1 mg/100 g body weight bupivacaine (0.5%) and 0.1 mg/100 g body weight of lidocaine (2%) with buprenorphine 0.0003 mg/100 g body weight. This can be diluted in saline to have a final volume of 1 ml.

Use a 25-g, 5/8 inch needle for guinea pigs or rabbits and a 27-g, 5/8 inch needle for a mouse or gerbil. Place the needle through the testicle starting from the caudal pole aiming for the spermatic cord. It is desirable, for the needle to exit the testicle proximally as it is the spermatic cord that will be ligated. Aspirate before injection. Inject, expressing firm backpressure, while withdrawing the needle. Expect to use about 1/3 of the drug volume per testicle leaving the organ firmly turgid. Repeat for the other testicle and the remaining drug can be used to place a dermal incisional block. This will provide analgesia for 22 hours (personal communication, Stein, 2006).

Cardiopulmonary-Cerebral Resuscitation (CPCR)

Anesthesia-related arrests represent one of the more treatable causes of arrest in veterinary patients. Doxapram is given as a respiratory stimulant with respiratory arrest. In the authors' experience most small mammals become bradycardic prior to respiratory arrest while under inhalant anesthesia. The inhalant anesthesia should be turned off and the animal intubated. Begin ventilating with 100% oxygen. Most exotic companion mammals, other than the ferret, and with practice the rabbit, are difficult to intubate. Therefore, the author recommends the following in emergency situations where intubation is not possible or cannot be accomplished quickly:

1. Consider forced high-flow oxygen ventilation using a tight fitting mask over the nose and mouth. Positive-pressure ventilation should be provided using 100% oxygen at a rate of 20 to 30 breaths per minute. The disadvantage of this technique is accumulation of gastric air and bloating which can limit movement of the diaphragm.
2. Emergency Tracheotomy. This procedure is similar to that described in dogs and cats and is described previously.

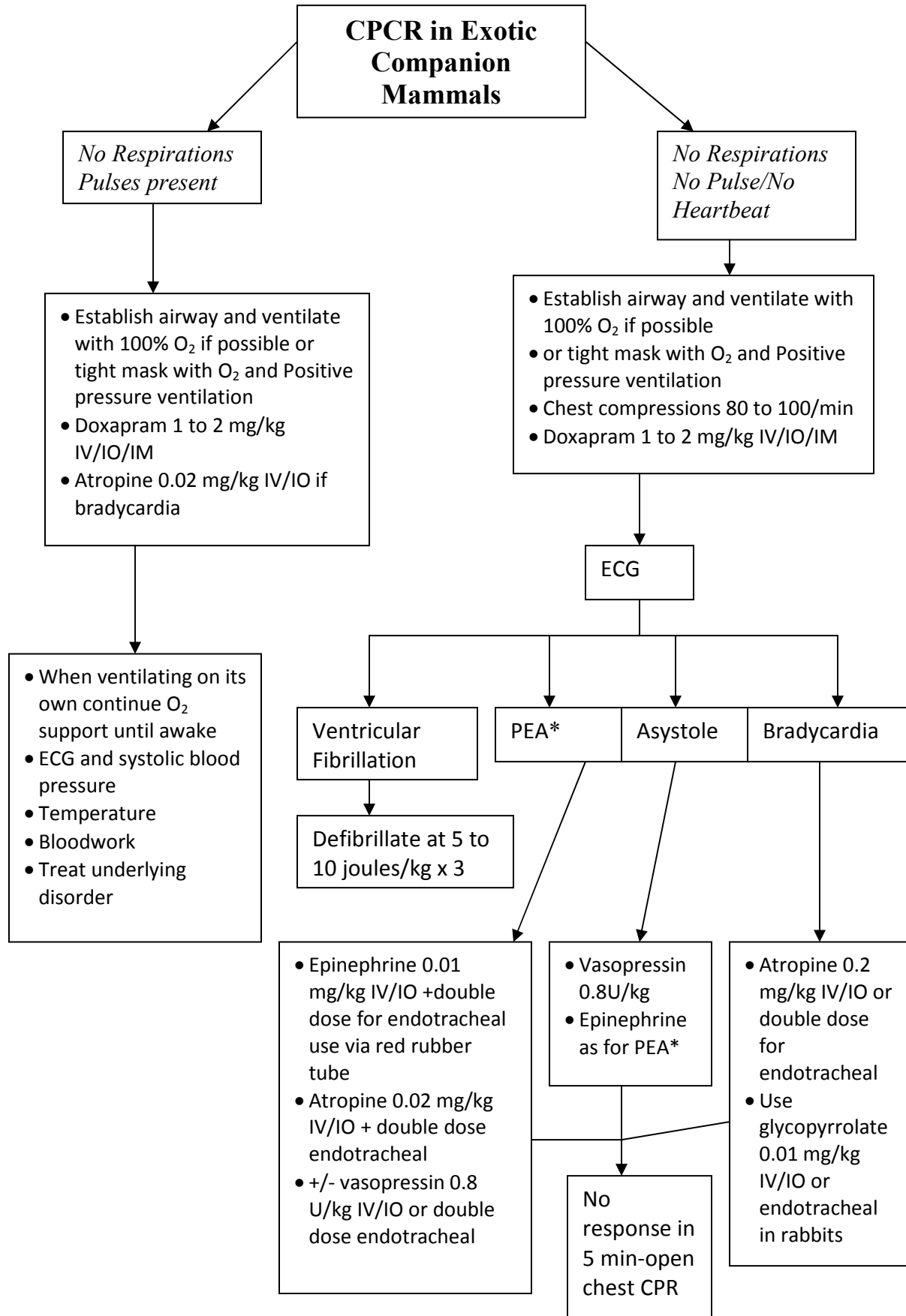
Cardiac arrest involves cessation of effective circulation, and is recognized by the loss of consciousness and collapse (Figure 1). A palpable pulse is not felt, the mucous membranes are pale or cyanotic, and respirations commonly cease (i.e., cardiopulmonary arrest). Immediate basic life support principles (i.e., ABC's) should be initiated. The animal is intubated and ventilated with 100% oxygen. The chest compressions of 80 to 100 times per minute directly compress the myocardium which leads to increased cardiac output. It is important that both hands be placed on each side of the chest with compressions done at the widest portion of the chest. The duration of the compression should take up half of the total compression-release cycle.

The team should continually assess their efforts at cardiopulmonary-cerebral resuscitation (CPCR). Check to see if the efforts are generating a palpable pulse. If no pulse is felt, increase the force of chest compressions and assess the electrocardiogram. Different cardiac arrhythmias may require specific treatments. During cardiac arrest and

resuscitation, progressive ischemia and acidosis are present. Epinephrine has routinely been the vasopressor of choice for ventricular fibrillation, asystole and pulseless electrical activity (PEA), however epinephrine and other catecholamines lose much of their effectiveness as vasopressors when the patient is hypoxic and acidotic. Successful resuscitation depends on adequate coronary artery perfusion. Coronary perfusion pressure above 15 mmHg is thought to be a predictor of return of spontaneous circulation.

Vasopressin is under investigation for possible consideration for asystole, PEA, and ventricular fibrillation. Vasopressin given first during the acidotic state and then epinephrine is added soon after. This may improve rates of restoration of spontaneous circulation and survival. Vasopressin is inexpensive. The use of vasopressin in the treatment of shock states and for CPR should be considered in the veterinary patient. The authors have used the drug in small animals CPR during asystole in a case of cardiac arrest in a rabbit. There was an immediate return of a heart beat and blood pressure. The rabbit did eventually die from other chronic disease processes. The author recommends that the clinician consider administering vasopressin during asystole in small mammals and birds. Consider vasopressin use during CPR with other rhythms (ventricular fibrillation, PEA) refractory to epinephrine, defibrillation and atropine.

Figure 1. Cardiopulmonary-Cerebral Resuscitation in Exotic Companion Mammals Flowchart



* PEA – Pulseless Electrical Activity

Nasogastric Tube Placement

Nasogastric tubes are important for rabbits that have been anorexic for over 24 hours, and proven difficult to assist-feed. Another indication is those patients with conditions of the jaw preventing normal food consumption, for example, mandibulectomy. The nasogastric tube allows delivery of calories and fluids, and helps rehydrate desiccated stomach contents. The authors prefer Argyle 5 to 8 Fr soft flexible pediatric feeding tubes. The length necessary to reach the stomach is determined by measuring from the nose to the last rib. A stylette should not be used, since the esophagus of the rabbit can be perforated with any additional force. A local anesthetic (2% lidocaine gel) is placed into the rabbit's nostril. The rabbit must be properly restrained while protecting its back, and the head is ventrally flexed but with the neck straight (to avoid compression of the trachea) by an assistant. The tube is passed ventrally and medially into the ventral nasal meatus. The end of the tube is advanced until it reaches the stomach. Verification of placement is determined with a radiograph and/or aspiration of gastric contents. The tube is secured with tape and sutured to the skin at the nostrils and between the ears. The Oxbow Hay Company (Oxbow Critical Care Fine Grind, Oxbow Hay Company, Murdoch, NE) and the Lafeber Company (Emerald Herbivore, Lafeber Company, Cornell, IL) have produced hay-based products that have been shown to pass through standard 5 to 8 Fr nasogastric tubes. Most rabbits with uncomplicated gastric stasis will start to eat and produce slightly soft stools after 12 to 36 hours. The tube can remain in place until the rabbit eats on its own and starts to produce stool. Complications that have been observed are nasal discharge from tube irritation. The tube should be removed and antibiotics included in the treatment protocol.

Honey/Sugar Bandage

Contaminated wounds, especially large wounds such as major degloving injuries or burns are very difficult to treat and can be expensive. Initially grossly contaminated wounds are lavaged with body temperature tap water, with a spray nozzle over grating to allow drainage. The wound is patted dry with sterile towels. Resection of necrotic tissue or debridement is performed using sterile technique. However, where viability of tissue is questionable, do not remove. The debridement action of sugar or honey will remove questionable areas but allow viable tissue to thrive. Granulated sugar or unpasteurized honey is poured over the wound to an excess of >1 cm thick. The wound must be filled as the osmolarity within the wound must remain high in order for bacterial killing to occur. Sterile absorbent towels or sterile lap sponges are used as the primary bandage layer. A secondary bandage layer is used to hold this absorbent bandage in place. This is covered with an adhesive layer. Initially, the bandage may need to be changed once to twice a day and then alternate days. The wound is clean usually after 2 to 4 days. Once a healthy granulation bed has formed, infection is eliminated and all pockets have closed, sugar is no longer needed. The wounds can be closed where adequate skin is available. Alternatively, the wound is covered with an antibiotic ointment, using a non-adherent primary layer to encourage epithelialization and secondary healing. Granulation tissue will cover the surface but may take from weeks to months. Honey has antibacterial properties and antioxidant properties. Honey is preferred over sugar because it also helps causes bandage material to adhere to the wound.

References

References available upon request.

The Gastrointestinal System: Exotic Companion Mammals

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Section One: Rabbits and Rodents

Rabbits

Although dental health and thorough examination of the teeth should always be included in the physical examination of a rabbit presented with suspected digestive system disease, this discussion will concentrate on the gastrointestinal system. Nutrition plays an important role in the functioning of the rabbit digestive system and will be discussed as it pertains to the gastrointestinal anatomy, physiology, and major disease syndromes.

Rabbits are true non-ruminant herbivores. Their digestive reservoir permits and increases the efficiency of utilization of fibrous diets. They have a large stomach and well-developed cecum relative to other non-ruminant herbivores such as the horse.

Anatomy and Physiology

Stomach

The stomach of the rabbit holds approximately 15% of the volume of the entire gastrointestinal tract.¹ It is thin-walled, J-shaped and lies to the left of the midline.² The well-developed cardiac sphincter is lined with non-glandular stratified squamous epithelium and prevents vomiting. The fundus contains parietal cells that secrete acid and intrinsic factor as well as chief cells that secrete pepsinogen. The pylorus has a well-developed, muscled sphincter.² The adult rabbit stomach has a pH of 1 to 2. The rabbit feeds frequently – up to 30 times per day of 2 to 8 grams of food over 4 to 6 minute periods. The stomach normally will contain a mixture of food, hair, and fluid even after 24 hours of fasting.² The stomach pH of rabbits up until the time of weaning falls into the range of 5.0 to 6.5. Bacteria is kept in check during the first three weeks of life by the production of milk oil containing octanoic and decanoic fatty acids produced by the enzymatic reaction of the suckling rabbit's own digestive enzymes on the doe's milk.² Young rabbits acquire gut flora by consumption of the doe's cecotrophs beginning at two weeks of age. Milk oil production ceases at 4 to 6 weeks of age. By this time, some ingested organisms have colonized the cecum and hindgut fermentation can begin as the kit weans.² Gastric transit time is approximately 3 to 6 hours.¹ The bulk in the stomach effects intestinal passage of digesta. The high voluntary feed intake (VFI) is at least four times higher *pro rata* than a 250 kg steer. It is also associated with a low gut retention time of 17.1 hours in the rabbit compared with 68.8 hours in the bovine. High VFI together with re-utilization of gut content by reingestion of cecal material supports the rabbit's high nutrient requirement per unit of body weight and improves feed utilization for the rabbit.³ The bovine's main volatile fatty acid (VFA) produced by rumen fermentation is propionic acid while the rabbit's main VFA is acetic acid with cecal fermentation. The primary microflora of the rabbit is *Bacteroides* spp. while *Lactobacillus* spp. is the primary microflora of the bovid.²

Small Intestine

The small intestine is approximately 12% of the gastrointestinal volume in the rabbit.² The bile duct enters into the proximal duodenum. The right lobe of the pancreas is situated in the mesoduodenum of the duodenal loop. The left lobe lies between the stomach and transverse colon. There is a single pancreatic duct that opens at the

junction of the transverse and ascending loops of the duodenum. The duct drains both pancreatic lobes. Technically this is the accessory pancreatic duct as the main pancreatic duct connection to the duodenum disappears during embryonic development.¹ The jejunum is the longest section of small bowel and appears convoluted. Aggregates of lymphoid tissue (Peyer's patches) are present in the lamina propria with increasing prominence distally. The distal end of the ileum has a spherical thick-walled enlargement known as the sacculus rotundus. This marks the junction between the ileum, cecum and colon. The sacculus rotundus is often called the "cecal tonsil" because of its lymphoid tissue and macrophage composition. This organ is unique to rabbits. An ileocolic valve controls movement of ingesta from the ileum into the sacculus and prevents reverse movement of ingesta back up into the ileum. The ileocolic valve opens into the ampulla coli at the junction of the ileum, colon and cecum. There is a weak ileocecal valve that allows chyme to pass into the cecum.²

Gastrointestinal smooth muscle is stimulated by motilin, a polypeptide hormone that is secreted by enterochromaffin cells of the duodenum and jejunum. Motilin is released in response to fat while carbohydrates inhibit release. Motilin activity is not present in the cecum, but is present and stimulates smooth muscle in the colon and rectum.¹ The stomach and small intestine in the rabbit function similarly to other monogastric animals.¹ Cecotroph digestion and some fermentation takes place during the 6 to 8 hours they remain in the gastric fundus. Cecotrophs contain microorganisms and products of microbial fermentation including amino acids, volatile fatty acids and vitamins. A gelatinous mucous coating protects them from some of the stomach acid. As the cecotrophs pass through the colon, lysozyme is incorporated. The lysozyme has bacteriolytic activity that degrades microbial proteins for absorption in the small intestine. Bacteria within the cecotroph produce amylase that converts glucose to carbon dioxide and lactic acid. These products along with amino acids and vitamins are absorbed primarily in the small intestine. Digestion in the stomach begins with hydrochloric acid and pepsin and continues into the proximal small intestine. Amylase from the pancreas is added, although amylase is also present from saliva and cecotrophs. The pancreas also contributes proteolytic enzymes and chymotrypsin through the accessory duct as well as most likely through small ducts connecting directly to the duodenum. Bicarbonate is secreted by the proximal duodenum to neutralize the acidity of ingesta leaving the stomach. The bicarbonate is absorbed in the jejunum. Transit time through the jejunum is 10 to 20 minutes and 30 to 60 minutes through the ileum.¹

Hindgut

The hindgut consists of the cecum and colon. The cecum of the rabbit is large and may contain 40% of intestinal content. It has ten times the capacity of the stomach.² The cecum is thin-walled and coiled in three gyral folds. It ends in a blind-ended tube called the *vermiform appendix*. This appendix contains lymphoid tissue and secretes bicarbonate that buffers the cecal acids, and water to form the cecal paste. In addition to *Bacteroides* spp., there may also be ciliated protozoa, yeasts, and small numbers of *Escherichia coli* and *Clostridia* spp. in the cecal flora.² The fermentation process in the cecum results in volatile fatty acids that are absorbed across the cecal epithelium. Cecal contents have an alkaline pH in the morning and an acid pH in the mid afternoon, termed a "transfaunation" as types of microorganisms fluctuate. In addition to acetate, the predominant VFA, butyrate and propionate are also produced.² The ascending colon is divided into four sections.¹ The *ampulla coli* opens into the first section, approximately 10 cm long and having three longitudinal flat bands of muscular tissue (taeniae) that separate rows of haustra or sacculations.¹ The mucosa of this section has small protrusions approximately 0.5 mm in diameter that are termed 'warzen' or warts. These are unique to lagomorphs and greatly increase the surface area of the colon for absorption. The warts may also aid in mechanical separation of ingesta.¹ The taeniae are innervated with autonomic fibers from the myenteric plexus.¹ The second section of colon has a single taenia and fewer, smaller haustra.¹ There are segmental and haustral contractions that mechanically separates the ingesta into indigestible particles and liquid contents. As the large pellets pass down the middle of the lumen, water is reabsorbed and they are excreted as hard dry pellets. The third section is the *fusus coli*. It is a muscular area about 4 cm long, highly innervated and vascular. Its mucosal surface has prominent longitudinal folds and goblet cells. It opens into the fourth section of ascending colony that is indistinguishable histologically from the transverse and descending colon.¹ The distal colon (sections distal to the *fusus coli*) ends at the rectum. Its mucosa has short crypts with abundant goblet cells. It is thin-walled and usually contains hard fecal pellets.¹

Cecotrophy, not Coprophagy

Cecotrophs are formed in the proximal colon and cecum. Rabbits begin consuming them between 2 and 3 weeks of age as they begin to eat solid food. Fiber material greater than 0.5 mm does not enter the cecum but transits to be formed and passed as hard fecal pellets. The smaller particles and fluid remain in the cecum or are returned to the cecum via antiperistalsis to form high nutrient particles that become coated with mucus as they pass through the colon. They are usually passed 8 hours or so after feeding, which coincides usually to nighttime. This mechanism requires high fiber diets to function properly. Low fiber diets increase cecal retention time and promote hypomotility of the entire gut, which further reduces the cecotrophs produced. Fiber in the diet should be indigestible and at least 15%.² A low protein diet increases a rabbit's cecotroph ingestion. A high protein diet and low in fiber reduces consumption.² In crude fiber terms, diets that are less than 150 grams per kilogram of feed will almost always result in digestive upset while diets with greater than 200 grams/kg crude fiber result in increased incidence of cecal impaction and mucoid enteritis. A diet devoid of fiber has a coefficient of apparent digestibility of organic matter of 0.90. This declines in a linear fashion to 0.40 when the diet contains 350 grams crude fiber per kilogram of feed. Increased crude fiber of the diet increases the crude fiber of the cecal contents. This decreases the protein content. Compounded, pelleted diets require the addition of hay in order to supply a complete diet. In general, the recommendation that hay be supplied on a free-choice basis as a rule of good husbandry of the pet rabbit should be emphasized.³

High carbohydrate diets cause several problems. Excessive glucose allows *Clostridium spiroforme* and *E.coli* to colonize.² Excess VFAs produced drop the cecal pH, which inhibits normal flora and allows pathogens to proliferate and colonize. Gas and toxins can be produced by pathogenic bacteria, and motility and nutrient production and absorption are interrupted. Fats such as full-fat soybeans and oil seeds can be used as a source of energy without causing cecal hyperfermentation.² However, feeding of vegetable fats and seeds decrease the fiber content of the diet, and lead to motility and functional depression.

It is interesting to note that rabbits have a gall bladder and secrete about seven times the amount of bile as a dog of similar weight. They secrete mainly biliverdin rather than bilirubin. Rabbits have low levels of bilirubin reductase.²

Rabbits should be fed in a quiet place, preferably early in the morning and in the evening. Rabbits do not like dusty food. A rabbit will selectively take concentrates if the palatability of roughage is variable. This may result in diarrhea from consumption of too much protein relative to hay. A well-fed rabbit masticates its food extensively whereas when the rabbit is hungry, it doesn't chew to any great extent. The mastication of the fiber is necessary for dental health and normal tooth wear.

Diet Recommendations

The recommended maintenance diet for a mature rabbit consists of unlimited grass hay. Timothy/oat or grass hay based pellets should be limited if the rabbit is hypercalcemic, older or obese. Alfalfa-based pellets should be provided to underweight, normocalcemic rabbits at 5 to 6 lbs /2.5 to 3 kg of body weight. Alfalfa-based foods may also be given to pregnant and lactating females. Fresh foods can be 1 to 2 cups of chopped vegetables (preferably a mix): beet greens, broccoli, carrot and carrot tops, collard greens, mustard greens, parsley, pea pods (flat edible kind), romaine lettuce, watercress, wheat grass. Other acceptable vegetables, but less vitamin A content: alfalfa, basil, bok choy, Brussel sprouts, celery, cilantro, clover, dandelion greens & flowers (not sprayed), endive, escarole/kale, green peppers, mint, peppermint leaves, raddichio, radish tops, radish & clover sprouts, raspberry/blackberry leaves, spinach. Table 1 lists calcium contents of some common rabbit foods. For treats and only if the rabbit is not overweight and the owner is insistent on some sort of "sweet treat" - fruits high in fiber at 1 to 2 tbsp/3kg body weight daily: apple, melon, peach, plum, strawberry, blueberry, papaya, pineapple, raspberry. Practitioners should provide actual quantity recommendations to the owner based on the rabbit's weight in the office call. It may be better to give a smaller quantity value as owners usually over-indulge their rabbit. Remember that rabbits evolved eating grass and herbs, not rich grains, alfalfa, and fruits. Supplementation with vitamins and other treats is not necessary.

Alfalfa based pellets are fed as a larger portion of the diet to does in kindle starting approximately 10 days prior to delivery, as well as to growing, young rabbits up to 10 weeks of age, then the amount of pellets is scaled down to the adult amount. After weaning of the kits, the amount of pellets for the doe is decreased until a non-breeding level of appetite is established. Hypercalcemia and obesity are two very commonly observed diseases with dietary etiologies.

Table 1: Mean calcium and phosphorus contents of feedstuffs used for pet rabbits

Food	Calcium (g/100 g dry matter)	Phosphorus (g/100 g dry matter)	Dry Matter (%)
Alfalfa Hay	1.35	0.27	90
Apple	0.06	0.06	21
Barley	0.07	0.39	89
Cabbage	0.64	0.35	12
Clover (fresh) red	1.80	0.40	20
Clover (fresh) white	1.40	0.51	19
Grass	0.54	0.30	20
Corn	0.01	0.32	87
Oats	0.03	0.03	90
Peas	0.12	0.41	89
Wheat	0.07	0.39	89

Gastrointestinal Illness

Rabbits that are presented with or without malocclusion but with a painful abdomen, anorexia, diarrhea or lack of stool need treatment prior to correction of the oral problems. Immediate administration of analgesics and fluids often results in the rabbit beginning to eat and the gastrointestinal tract beginning to move. Table 2 can be used as a guideline for diagnosing and treating gastrointestinal disease. A detailed history and physical examination, including auscultation of the abdomen, may allow the practitioner to evaluate the stage of gastrointestinal distress in the rabbit.

Radiographs are useful to determine ileus. Contrast series may be utilized to determine an impaction, although barium introduced into the cecum is problematic for function. The author prefers to utilize endoscopy and/or ultrasound, or an iodine-based contrast agent rather than a barium series. Most trichobezoars will move once hydration is corrected and sufficient roughage is available. Use of motility enhancers may be tried if no impaction is present. Once pain is alleviated and hydration corrected, the rabbit may begin to walk around and nibble hay, which will encourage gastrointestinal motility. While not proven, probiotics are often administered *per os* or intrarectally. Remember that these are usually primarily *Lactobacillus* spp. which are not the primary microflora of the rabbit. Vitamin B complex may be given to stimulate appetite. As hepatic lipidosis may be present and playing a role in anorexia, it is advantageous to get some food into the anorexic rabbit as soon as possible. If the rabbit does not immediately start eating hay, a hand feeding diet (eg. Emerald Herbivore, Lafeber Company, Cornell II; or Critical Care, Oxbow Pet Products, Murdock, NE) should be given. This commercial formulation can be mixed with apple juice or flavored electrolyte solution and given orally. Many rabbits can be hand fed using either formula.

Rarely is surgery necessary to relieve an impaction, but if a necrotic or ischemic section of the gut is suspected, surgery may be necessary to resect the bowel. Prognosis is guarded primarily because of endotoxins produced by *Clostridium* sp. present in most herbivore gastrointestinal tracts. The anesthesia further decreases gastrointestinal motility, again setting up the microflora to be altered and toxins produced. It may be necessary to install an intraosseous (IO) or intravenous (IV) catheter to administer antibiotics and fluids perioperatively and post-operatively for several days in these cases. Restoration of gut microbial flora and motility post-surgery are priorities. Antibiotic choices in these cases are a balancing act, as an antibiotic with a primary gram negative

spectrum with efficacy against anaerobes should be used. Antimicrobials that primarily have a gram positive spectrum or that do not kill anaerobes are not recommended.

Table 2. Guidelines for Evaluating Rabbit Gastrointestinal Disease ^{4,5}

Parameter	Level 1 - Outpatient	Level 2 - Watch Closely	Level 3 - Hospitalize
Appetite	Will eat greens & treats, indifferent to pellets, reluctant with hay	Refusing most greens and treat foods	Refusing everything
Activity & Attitude	Normal, frisky; hiding, just not acting right	Depressed, not moving much, not grooming	Reluctant/refuses to move, dull, head down; unresponsive
Pain (abdominal) (note: teeth grinding can occur at any level)	Does not tense abdomen on palpation, but acts slightly uncomfortable. NSAID may be adequate	Tenses on abdominal palpation, shifts stance, reacts by movement or biting: moderate pain: NSAID may eliminate	“Bunny brick” – abdomen is so tense it’s hard, rabbit sits with feet tucked underneath, reluctant to move. Opiate and NSAID recommended: severe pain
Stool	Normal or slightly abnormal consistency: soft-formed, very small & dry. Less quantity	Scant to none: small misshapen. May have had no stool X 24 hr	Fluid diarrhea; mucoid diarrhea; or no stool in several days. Perineum may be stained
Palpation	Normal; fluidy but non-painful; may palpate material in gut, stomach	Painful abdomen, may be hard, gassy, tensing makes it difficult to palpate	Gastric tympany; cecal tympany; mass effect; generalized painful abdomen
Cardiovascular	Mucous membranes pink, ears warm	Mucous membranes usually still pink, usually ears still warm	Pale mucous membranes; ears cool, poor peripheral blood pressure
Gut Sounds	Normal or hyperactive	Decreased or none	No gut sounds
Urine	Volume & color normal; may have brown tinge	May be decreased volume, increased odor; may have brown tinge. Still alkaline	Decreased volume, increased odor, acidic, clear urine.
Body Temperature	101 to 104°F	<101°F or >104°F	<100 °F or >105
Hydration	Normal or slight dehydration	Mild dehydration	Usually marked dehydration
Treatment	Diet corrections: hay, hay, and more hay! Fluids PRN SQ.; Vitamin B inj. NSAID. Encourage exercise.	Analgesics; fluids SC and supportive care including high fiber assist-feeding with probiotics. Motility enhancer, antimicrobials, Vitamin B complex injection. Encourage to walk	IV fluids to start, SC to follow. Analgesics (opiate and NSAID), antimicrobials, motility enhancer if no obstruction. Assist-feeding or gavage, probiotics. Supportive care (warmth, quiet).

The Guinea Pig Gastrointestinal System

Cavies are strict herbivores and are cecotrophic. Dental disease with resulting malocclusions are common and beyond the scope of this presentation. A full dental examination should be included if any gastrointestinal disorder is encountered.

Stomach

Cavies are monogastric with completely glandular stomachs. The lesser curvature of the stomach is small and forms an angle with the esophagus termed “the angular notch.”² The small intestine lies in the right side of the abdomen and is approximately 125 cm in length in an adult. The small intestine is without distinguishing sections and lymphoid tissue (Peyer’s patches) in the lamina propria are found throughout. The large intestine begins at the ileocecal valve.

Hindgut

The cecum is the largest part of the digestive tract, usually containing up to 65% of the gastrointestinal contents. It is large, thin-walled, and fills most of the left ventral abdomen.² It measures approximately 15 to 20 cm in length.² It has three white muscular longitudinal bands: the dorsal, ventral and medial *teniae coli*. The saccular outpouchings between the bands are haustra. The colon appears dark green and is approximately 70 cm long. It functionally is divided into the shorter proximal section (20 cm) and the distal, longer section (50 cm). The proximal colon has mucosal folds on the mesenteric side that forms a longitudinal furrow. The furrow aids in separating high protein and smaller particles from the poorer quality material that will pass out of the colon as dry fecal pellets. Antiperistalsis transports the bacteria and higher protein particles back to the cecum for further fermentation.²

Physiology

Gastric emptying time is approximately two hours with a total gastrointestinal transit time averaging 20 hours (dry fecal pellets). Cecotrophy may be performed 150 to 200 times daily. Young cavies initially populate their intestinal tract by eating the sow’s cecotrophs and pellets. Gut flora is primarily gram-positive bacteria with anaerobic *Lactobacillus* sp.. Coliforms, yeasts, and clostridia may be present in small numbers.⁶ Cavies are more efficient than rabbits at digesting fiber. Satiety is determined by the distension of the gastrointestinal tract. Increasing fiber does not increase appetite. A crude protein level of 18 to 20% is needed for growth and lactation. A crude fiber level in the diet should be 10 to 16%.⁶

Gastrointestinal Disorders

Two conditions involving the gastrointestinal system are seen frequently, and both may be linked. The first is anorexia. The clinician needs to determine if the anorexia is primary (refusal to eat a new brand of pellets), with subsequent malocclusions, and hindgut dysbiosis (change in microflora) and motility, or if the anorexia is secondary to a hindgut disorder or dental disease. Diarrhea is the second most common condition. It needs to be determined if it subsequent to other disease or if it is a primary disease of the gut. Changes in diet, stress, illness, anesthesia, or reproduction may alter gut motility and/or gut microflora, resulting in diarrhea. Clostridial infections secondary to antibiotic therapy that did not control anaerobes is frequently the cause. Antibiotic administration has been linked to disruption of normal gut flora. A generality is that broad-spectrum antibiotics administered subcutaneously or intramuscularly are less likely to cause problems. Chloramphenicol, enrofloxacin (fluoroquinolones), and trimethoprim/sulfonamides have rarely caused dysbiosis. In some large colonies, coccidia may cause diarrhea particularly in young guinea pigs.⁷ Fecal/rectal cultures, gram stains, and parasite evaluation along with history and complete physical examination including the teeth may be needed to determine the etiology. Diarrhea associated with an overgrowth of *Candida albicans* has been seen in cavies on prolonged antibiotic treatment.⁷

Treatment may involve analgesics and NSAIDs, probiotics, motility enhancers, antimicrobials, additional vitamin C, and almost always, fluid therapy. Assisted feeding with Emerald Herbivore (Lafeber) or Critical Care (Oxbow) greatly increases the likelihood of recovery, but as caviae do not tolerate a lot of handling and injections while ill, the prognosis is always guarded!

Chinchilla Gastrointestinal System

Chinchillas share many similarities with guinea pigs, however are generally hardier and tolerate handling and treatment better than caviae. Dental disease is not uncommon, but discussion is beyond the scope of this presentation. The gastrointestinal tract is long, 11.5 feet for the small and large intestine combined in an adult.⁸ The cecum is large and coiled. The colon is sacculated. The cecum of the chinchilla holds approximately 23% of the dry matter content of the large intestine, significantly lower than the rabbit and the guinea pig.⁸ Cecotrophy is similar to the guinea pig except that cecotrophs may be passed in the day as chinchillas feed mostly at night. Fecal excretion is primarily at night. Transit time of ingesta through the gastrointestinal tract is approximately 12 to 15 hours. Chinchilla nutritional needs have not been studied as extensively as the needs of rabbits and other rodents. It currently is recommended that chinchillas receive grasses and hays, and pellets containing 16 to 20% protein, 2 to 5% fat, and 15 to 35% bulk fiber.⁸ A pellets-only diet is not sufficient for roughage and predisposes the chinchilla to enteritis. One to two tablespoons of pellets per day, with ad lib good-quality grass hay, and 1 to 2 teaspoons of fresh leafy vegetables seems to be adequate for dental and gastrointestinal health for non-breeding chinchillas.

Gastrointestinal Disease

Esophageal choke has been described in chinchillas that are fed raisins, fruits, and nuts, or those consuming their bedding or post-parturient females that consume the placentas. Bloat or gastric tympany has been associated with overeating of clover and sudden food changes, particularly those rich in carbohydrates. Bloat can be alleviated with decompression of the stomach, either by passing a stomach tube or trocharization through the abdominal wall. Fluid therapy and analgesics should be administered. Gastric trichobezoars have been seen in chinchillas that are chewing their fur. Trichobezoars will usually resolve with medical treatment similar to that used in rabbits: fluids, analgesics, motility enhancers, and roughage.⁹ Constipation seems to be more of a clinical problem than diarrhea. The usual cause is a diet consisting primarily of pellets without sufficient roughage or fiber provided by hay.⁹ Fluid therapy along with small amounts of fresh foods such as apples, carrots, or leaf lettuce, along with the owner discontinuing any treat foods such as raisins, seeds, and grains usually corrects the problem. In some, a laxative or a motility enhancer may be needed until the diet is corrected. Diarrhea frequently is the result of too much fresh vegetable intake. Infectious diarrheas are accompanied by a chinchilla that presents depressed, dehydrated, and staining of the perianal area. Rectal prolapse is seen in stressed young chinchillas, and may also be a sequellae of diarrhea. The prolapse can be reduced as in other animals, but etiology should be determined. Intestinal torsion, intussusception and impaction of the cecum and/or colon have been diagnosed in chinchillas. Animals present severely depressed and with a painful and usually distended abdomen. Surgery may be required, and the prognosis is guarded.⁹

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Section Two: Ferrets, Hedgehogs, Sugar Gliders, and Small Pet Marsupials

The Ferret

Several of our common small mammal companion pets have a “carnivore” type of gastrointestinal tract although the actual diet may consist largely of insects rather than meat. The gastrointestinal tract of the domestic ferret, *Mustela putorius furo*, has been studied extensively as a model for several human gastrointestinal tract diseases. These include spontaneous gastric and duodenal ulcers, gastro-esophageal reflux, gastric carcinoma and lymphoma, malfunctioning acid mucosubstances, and *Helicobacter mustelae* infection.

The GI tract transit time in the ferret is very short and ranges from 148 to 219 minutes when fed a meat-based diet. The digestive system is under vagal and sacral innervation. The tract is spontaneously active even under anesthesia. Motility can be moderated with atropine. The stomach spontaneously produces acids and proteolytic enzymes. Histamine, pentagastrin and vagal stimulation provoke more secretions.¹

Gut closure for antibody absorption occurs in kits between 28 and 42 days of age. Ferrets can absorb beta carotene and convert it to retinoic acid. Carbohydrases and proteolytic enzyme activity occurs distally in the jejunum rather than more proximally in the duodenum.¹

The Stomach

The ferret has a simple stomach, similar in shape to that of the dog and the human. The vasculature of the stomach is prominent. In addition, there is a prominent lymph node lying in its lesser curvature. The stomach is innervated by parasympathetic fibers from the vagus nerve and sympathetic fibers via the celiacomesenteric plexus. The stomach has considerable storage capacity (100 ml of milk in 10 minutes in an adult). Eighty percent of the meal is stored in the proximal portion of the stomach.¹

The lower esophageal sphincter (LES) and the mechanisms of gastro-esophageal reflux in the ferret have been used as an animal model for a similar problem in humans.^{2,3} It appears that transient LES relaxation occurs to result in the reflux and is unassociated with swallowing in the ferret just as in the human.⁴ Gastric infusions of glucose, lipid and gas are all effective in provoking gastro-esophageal reflux in the ferret. Lipid and glucose also stimulate acid secretion.⁴ The fundus of the stomach and the LES are co-innervated by vagal preganglionic motor neurons as these sections work in tandem: the LES must relax to accommodate food during ingestion or preceding emesis.

The antrum of the stomach provides mixing and propulsion of contents for gastric emptying and is innervated by neurons responding to differing neurotransmitters.^{5,6,7,8,9} The ferret is used as an emetic model to test anti-emetics. Serotonin successfully blocks cisplatin emesis (10 mg/kg).¹⁰ An anti-emetic pursued in the ferret model has been delta⁹-tetrahydrocannabinol (Δ^9 -THC), the cannabinoid that is anti-emetic in humans. Ferrets have the Cannabinoid¹ receptor in the dorsal motor vagal nucleus, with cell bodies in the area postrema, nucleus tractus solitarius and nodose ganglion. This receptor mediates the anti-emetic action of cannabinoids.^{11,12} Δ^9 -THC was

found to cause gastro-esophageal reflux due to the relaxation of the lower esophageal sphincter. This effect may have implications in the treatment of gastro-esophageal reflux and other upper gastrointestinal disorders.¹²

The ferret stomach also secretes acid in response to histamine, pentagastrin and calcium. There is a low concentration of free histamine in the stomach. The ferret lacks the histamine-forming enzyme (L-histidine decarboxylase) in the stomach although histamine-destroying activity is present. Histamine also stimulates secretion of proteolytic enzymes. Histamine H₂ receptor antagonists abolish acid secretion responses to exogenous histamine or exogenous stimulation with pentagastrin. Atropine only reduces acid secretion by 30%.¹

Gastrin is secreted in the gastric antrum and duodenum. Hypoglycemia induced by insulin produces a sustained stimulation of acid secretion.¹ This is particularly relevant to ferrets with insulinomas: therapy needs to include medications that decrease acid secretion.

The Intestine

The ferret intestine consists of three components, as in mammals. Villi and goblet cells are present in all regions. The duodenum is the proximal segment of the intestine. The duodenum is innervated by vagal preganglionic parasympathetic neurons originating in the dorsal motor nucleus of the vagal nerve in the brainstem.¹³ The major duodenal papilla contains the common opening for the bile and pancreatic ducts. This is located about 3 cm from the pylorus. The minor papilla may be absent. Brunner's glands are present in the submucosa of duodenum proximal to bile duct. The glands produce only neutral mucosubstances as in humans.¹

The jejunal and ileal segments cannot be distinguished and may be referred to as the "jejunoileum" that ends at the ascending colon. The small intestine is innervated by the vagus nerve and the sympathetic trunks arise from the celiac and cranial mesenteric plexus.¹

Motility is affected by the hormones secretin, PZ-CCK (pancreozymin-cholecystokinin), an unidentified vasoconstrictor, vasoactive intestinal polypeptide (VIP), and substance P. VIP inhibits jejunal motor activity due to vagal stimulation while substance P excites activity. Both increase water secretion by jejunal epithelium. The muscular layer has a higher concentration of these hormones than the epithelium. Jejunal motility mediated by hormones is not blocked by atropine. 5-hydroxytryptamine (5-HT₃) and synthetic serotonin receptor agonists induce large contractions and defecation. The basal colonic motility pattern was not changed, and the large contractions can be blocked with a receptor antagonist. The implications of this model are for testing pharmaceuticals for constipation without undesired changes in gut motility patterns.¹⁴ Cervical (mechanical) vagus stimulation will affect motility. This has significant implications for the clinician who during intubation may manipulate the neck and thorax and inadvertently stimulate the vagus nerve and intestinal motility at the beginning of surgery.

The large intestine is composed of the colon and rectum. There is no cecum and no ileocolic junction. The junction is inferred by the presence of the anastomoses of the jejunal artery with the ileocolic artery. The colon consists of the ascending, transverse and descending colon, with the largest being the descending. The colon is innervated by autonomic fibers from the vagus, cranial and caudal mesenteric plexus.¹

There are tubular glands and goblet cells in the colon. These secrete sulfated mucosubstances. The motility of the colon resembles that of a dog ileum. Motility is vagus-dependent and mediated by cholinergic and noncholinergic fibers. Sacral innervation is excitatory. Retroperistalsis begins in the colon which may be the genesis of vomiting in the ferret.¹

Exocrine Pancreas and Biliary System

The exocrine pancreas and biliary system are also under vagal stimulation. There is a trophic relationship with capillary connections between the islets and the exocrine pancreatic tissue. A bile salt-dependent lipase is

produced. The adult jill mammary tissue is high in this enzyme. Ferret milk has activity 10 to 20 times higher than human milk. If lipase elevations are present in the blood, consider pancreatic inflammation or disease.¹

The gallbladder contracts in response to cholecystokinin. Cholecystokinin is found throughout the gastrointestinal tract. This contraction inhibits gastric emptying and stimulates small intestine and colonic motility. The contractile response directly affects smooth muscles and/or neurons, which furthers intestinal motility.¹

Diseases of the Gastrointestinal Tract

Ferrets are used as animal models for emesis as they have a low tolerance for many chemicals and the vagal reflex is strong, with a simple stomach for propulsion. They are also used as models of *Helicobacter* gastritis, gastric carcinoma, pyloric and intestinal ulceration, inflammatory bowel disease, colitis, and gastrointestinal neoplasia. As *Helicobacter mustelae* is endemic in most of the commercially-produced pet ferrets, the ferret is set up for gastrointestinal disease from this etiologic agent alone. In addition, ferrets are prone to stress-induced gastrointestinal ulcers with hemorrhage and hypermotility. All of the above conditions may result in varying degrees of diarrhea: acute, chronic or intermittent; with or without visible hemorrhage, and with or without secondary bacterial or viral involvement. Table 1 lists gastrointestinal diseases of ferrets. Table 2 lists treatments published for *H. mustelae*. Table 3 lists adjunctive therapies for gastroenteritis. A detailed history is needed to determine a course of action. This includes volume, color, consistency, frequency and duration the clients have seen diarrhea. The source of the ferret including breeder may play a significant role in the priority of etiologies. Other information should include how long the ferret has been in the household, other ferrets and pets present as well as human family members – are any symptomatic with diarrhea? The type of litter used and sanitation program may be of importance. Diet including treats fed, toys available, and incidental environmental information (such as access to showers or sinks) should be recorded. Ferrets are notorious for licking soaps, chewing on stuffing dug out of furniture, shoes and shoe liners, and even perfume or shampoo bottles. Correlation with activity should also be figured into the evaluation. For example, does it occur around the clock or is it only after intense playtime? Does it only occur after the vacuum cleaner is run near the ferret's cage? Tenesmus or vocalization, or accompanying borborygmus or flatulence should be recorded. Teeth grinding may indicate pain, and anorexia may be a sequella to the pain. A full dental examination should also be done as severe dental disease may be part of the clinical presentation.

A physical examination of the ferret should be thorough and include auscultation of the abdomen and examination of the anal area. A fecal examination should include flotation and direct smear of fresh material, as well as staining to look at bacterial levels and presence of blood cells. A rectal culture and cytology may be indicated. Bloodwork should include lipase which has been shown to be elevated in many cases of inflammatory bowel disease. Anemia is not an uncommon finding and may indicate gastrointestinal hemorrhage. Fecal occult blood can be tested – however the ferret should be placed on a diet that does not contain meat for at least 24 to 36 hours prior to testing as normal ferret foods contain meat and blood products that result in positive test results. Radiographs including a contrast study are frequently useful. Ultrasonography can be used to look at motility of the stomach including the pyloric area. Ultrasonography of the abdomen may also find other pathologic conditions. Endoscopy is useful for examination of the stomach, pylorus and colon. Endoscopy can also be used abdominally. Biopsies can be taken endoscopically or via laparotomy. A PCR test for gastric *Helicobacter mustelae* is available from Research Associates Laboratory (R.A.L., Inc., Dallas, TX, www.vetdna.com). The author uses a sterile length of infusion set tubing measured for the particular ferret. Using a sterile hemostat, the culturette swab can be inserted into the tubing and pushed in until it is firmly seated. The tube is then passed into the sedated ferret's stomach and the stomach manually massaged around the culturette.^{15,16,17,18}

Inflammatory bowel disease (usually lymphoplasmic) probably has multiple causes and may have an underlying genetic component, particularly considering its progression to neoplasia in many ferrets. Food allergies have yet to be explored, other than a few clinical trials using alternate proteins found in feline diets. The grain carbohydrates used in commercial food formulations may be a problem: allergy testing as done in dogs and cats should be pursued. Immunomodulating medications such as prednisone (prednisone USP, Roxane Laboratories, Columbus,

OH), azathioprine (Imuran, GlaxoSmithKline, Research Triangle Park, NC), and metronidazole (metronidazole USP, Watson Laboratories, Inc., Corona, CA) have been used based on therapies for other species. Budesonide at 0.5 mg/kg PO q12h (Entocort EC, Prometheus Laboratories Inc., San Diego, CA) along with supplemental vitamin B₁₂ is also useful for chronic inflammatory bowel disease. Table 3 lists dosages.

Table 1. Etiologies of gastrointestinal disease. Diarrhea is most common clinical sign in ferrets.^{15,16,17,18}

Disease	Diagnosis	Treatment	Age Grouping
Bacterial: primary or secondary 1. <i>Helicobacter mustelae</i> 2. <i>Lawsoni/Desulfovibrio</i> 3. <i>Campylobacter jejuni</i>	Culture and Sensitivity 1. Helicobacter PCR, histopathology 2. Biopsy and Histopathology 3. Culture difficult, human labs	Appropriate antimicrobial therapy, adjunctive	Any. #2 – usually younger
Bacterial: uncommon 1. Mycobacteriosis	Histopathology PCR	? Zoonotic risks?	> 2 years
Viral: 1. Ferret Enteric Coronavirus (FECV) 2. Rotavirus 3. Canine Distemper Virus	Coronavirus isolation PCR PCR PCR	Supportive care	#1. Any, usually following stressful event, ferret gathering #2. baby, weanlings #3. Ferrets who did not complete their baby series of vax
Parasitic: 1. Coccidiosis 2. Giardiasis	Fecal floatation, direct smear	Anti-coccidial drugs	Usually < 1 year
Inflammatory Bowel Disease	Histopathology	Some suggest anti-inflammatory drugs; caution in ferrets with possible <i>Helicobacter</i>	Usually > 2 years, history of intermittent diarrhea
Gastrointestinal Neoplasia	Histopathology	Surgical excision Chemotherapy	Usually > 3 years
Foreign Body Ingestion	PE, radiographs, exploratory surgery	Surgery	Usually < 2 years
Stress: medical or psychological	History Detection of underlying medical condition	Correction of underlying medical disorder or psychological stress	Any
Idiopathic Megaesophagus	Radiology	Unrewarding	Any

Table 2: Treatment Regimens for *Helicobacter mustelae* Based on Clinical Trials^{17,18}

Effective Combinations	Unsuccessful Medications
Amoxicillin (30 mg/kg PO q8h X 21 to 28d; Metronidazole (20 mg/kg PO q8h X 21 to 28d; Bismuth subsalicylate (7.5 mg/kg PO q8h X 21 to 28d)	Amoxicillin alone. May not be effective at q12hr even in combinations Metronidazole alone. May not be effective with Amoxicillin if given at q12h intervals Chloramphenicol alone Enrofloxacin alone
Enrofloxacin (8.5 mg/kg/day PO divided q12h) X 14d; Bismuth subcitrate* (12 mg/kg PO divided q12h) X 14d	Tetracycline Bismuth subsalicylate alone Omeprazole and Amoxicillin
Clarithromycin (12.5 mg/kg PO q12h X 14d Ranitidine bismuth citrate*(24 mg/kg PO q12h X 14d)	Omeprazole alone
Clarithromycin (12.5 mg/kg PO q8h X 14d; Ranitidine bismuth citrate* (24 mg/kg PO q8h X 14d) This is also a published dosage	

* not commercially available in the US, can be compounded

Amoxicillin	Amoxil, GlaxoSmithKline, Research Triangle Park, NC
Metronidazole	USP, Watson Laboratories, Inc., Corona, CA
Bismuth subsalicylate	Pepto-Bismol, Proctor & Gamble, Cincinnati, OH
Enrofloxacin	Baytril, Bayer, West Haven, CT
Clarithromycin	Biaxin, Abbott Laboratories, Abbott Park, IL
Omeprazole	Prilosec, AstraZeneca Pharmaceuticals LP, Wilmington, DE

Table 3 Medications Used as Adjunctive Therapy of Gastroenteritis^{17,18}

Drug	Dosage	Comments
Azathioprine	0.9 mg/kg PO q24 to 72h	Used in IBD if other treatment ineffective. Immunosuppressive
Budesonide	0.5 mg/kg PO q12h	Used in IBD, immunomodulator. Pharmacy must pack into #4 or smaller capsules for administration.
Famotidine	0.25 to 0.5 mg/kg PO, IM, IV q24h	Histamine antagonist; available over the counter; decreases gastric acid; provides pain relief. Oral OTC can be crushed, mixed with flavor gel, palatable
Metronidazole	50 mg/kg PO q24h	IBD, some immunosuppressive effects
Omeprazole	0.7 mg/kg PO q 24h	Protein pump inhibitor, short term usage only
Prednisone	1-2.5 mg/kg PO q24h	Anti-inflammatory. Used in eosinophilic gastroenteritis, IBD, palliative in LSA
Ranitidine USP	24 mg/kg PO q8h X 14d	Histamine inhibitor; decreases gastric acid; provides pain relief. Tablet form available over the counter, must be compounded as human formulation unpalatable
Sucralfate	25 mg/kg PO q8h	Coats esophageal and gastric mucosa, local effect only. Suspension palatable

Azathioprine	Imuran, GlaxoSmithKline, Research Triangle Park, NC
Budesonide	Entocort EC, Prometheus Laboratories Inc., San Diego, CA (division of AstraZeneca)
Famotidine	Famotidine tablets USP, Zenith Goldline Pharmaceuticals, Inc., Miami, FL
Metronidazole	Metronidazole USP, Watson Laboratories, Inc., Corona, CA
Omeprazole	Prilosec, AstraZeneca Pharmaceuticals LP, Wilmington, DE
Prednisone	Prednisone USP, Roxane Laboratories, Columbus, OH
Ranitidine	USP: Ranitidine Tablet USP, Perrigo Co, Allegan, MI
Sucralfate	Carafate Aventis Pharmaceuticals, Inc., Kansas City, MO

Although *H.mustelae* is found in most adult ferrets, it is not always implicated in clinical gastritis or ulcers. It does play a role as an opportunist, and exacerbates ulceration of the stomach and intestines. It appears to play a role in the development of gastric neoplasia, and may play a role in inflammatory bowel disease and colitis. As *H.mustelae* is a model for human *H.pylori* infection, further improvements in clinical implications, diagnosis and treatment will be forthcoming.

In summary, the ferret gastrointestinal tract is designed to be excitatory, have rapid motility and be highly secretory. Exogenous stressors, chemical and neurologic stimulations further increase motility and secretion. During any hypoglycemic episode the clinician needs to be aware of the pancreatic and gastric physiology and treat the nausea and secretions in addition to the hypoglycemia. It may also be prudent to administer medication to inhibit acid secretions prior to surgeries and in any stressed, ill ferrets.

The Hedgehog

African pygmy hedgehogs (*Atelerix albiventris*) are classified as insectivores, but most are omnivorous/carnivorous and opportunistic, including consumption of carrion. The gastrointestinal system of the hedgehog is similar to most carnivore gastrointestinal tracts. It has a simple stomach, smooth non-complex colon. It does not have a cecum and has a poorly defined ileo-colonic junction. Gut transit time in one study was reported as 12 to 16 hours.¹⁹

Disease etiologies and clinical manifestations of disease are similar to those of other carnivores. Treatment with oral medications may be more difficult in those that are not used to having the owner manipulate its head and mouth. *Salmonella* serotype Tilene has been identified from pet hedgehogs in the United States. Table 4 lists diseases, diagnoses, and therapies of gastrointestinal disease in pet hedgehogs. A complete workup with hematology, serum chemistries, imaging, and fecal parasite examination are recommended for any hedgehog presenting with gastrointestinal disease. Diagnostics listed in Table 4 are specific to those etiologies.

Table 4. Gastrointestinal diseases of pet hedgehogs²⁰

Etiology	Signs	Diagnostics	Treatments
<i>Salmonella</i> sp., other bacteria	Clinically asymptomatic or diarrhea, weight loss, anorexia, dehydration, lethargy, death	Fecal culture and sensitivity, <i>Salmonella</i> special media	<i>Salmonella</i> : supportive care primarily, discuss zoonotic potential. Other bacteria: per sensitivity; supportive care
Candidiasis, alimentary	Weight loss, depression, blood in stool	Fecal cytology and culture and sensitivity	Appropriate antifungal per sensitivity, supportive care, decrease sugars in diet?
Cryptosporidiosis of ileum, jejunum, colon	Severe enteritis, wasting, death	Fecal cytology, biopsy, histology	No effective treatment.
Endoparasites	Unthriftiness, diarrhea	Fecal flotation, wet mount, history of exposure to wild-caught hedgehogs	Anthelmintics per parasite identified. Not seen much anymore with captive reared
Obstructions (foreign bodies)	Vomiting, diarrhea, non-specific weight loss, abdominal pain, lethargy, acute collapse	Radiology, contrast needed sometimes, laparotomy, exploratory	Surgical enterotomy or gastrotomy as indicated. Analgesics
Non-specific enteritis, gastrointestinal inflammation, ulcerations	Tenesmus, diarrhea, melena or frank blood, anorexia, weight loss, lethargy, dehydration	Radiology, contrast, ultrasonography, laparotomy, biopsy	Non-specific, antibiotics, supportive, antiinflammatories, gastrointestinal protectives
Diet-induced	Diarrhea	History of treat foods, milk, diet changes	Discontinue offending foods, stabilize diet, symptomatic antidiarrheals
Neoplasia	Diarrhea, weight loss, unthriftiness, non-specific pain, lethargy	Imaging, laparotomy with biopsy	Palliative or can try neoplasia therapies as in felids for specific diagnosis

The Sugar Glider and Virginia Opossum

Sugar gliders (*Petaurus breviceps*) have a simple gastrointestinal tract with the exception of a large cecum, for gum fermentation that is not present in other omnivore/carnivores. The sugar glider is considered an insectivore/gumivore, although its gastrointestinal morphology and dentition share features with carnivorous mammals. Sugar glider teeth have limited shearing action and can only compress insects not break them down into small pieces like a true carnivore. They can extract the hemolymph and soft tissues of insects through compression, then discard the exoskeleton.

Virginia opossums (*Didelphis virginiana*) have gastrointestinal tracts fairly similar to dogs. The Virginia Opossum is an insectivore/omnivore, with a primary diet in the wild of insects, mollusks, carrion, and plant material. The teeth are designed for shearing and tearing food material. In general, both the sugar glider and Virginia opossums have fairly simple gastrointestinal tracts, and antibiotic treatment guidelines follow those used for carnivores rather than herbivores. An interesting functional difference between eutherians (placental mammals) and marsupials concern the Brunner's glands of the duodenum. In eutherians, Brunner's glands are usually confined to the submucosa and the ducts empty into intestinal crypts of Lieberkuhn. In American marsupials, they drain into large mucosal depressions which are surrounded by more glands. In Australian marsupials, the ducts empty directly into

the duodenal lumen. No Australian marsupial carnivore has a cecum. The sugar glider has a well-developed cecum, needed for the fermentation of ingested gums and a short colon. Otherwise, their gastrointestinal tract is similar to the Virginia opossum. There are well-developed salivary glands that include large mandibular and smaller parotid and sublingual glands. The distal esophagus mucosa has raised transverse rugae. The stomach is simple and rather globular in form. The gastric mucosa is mostly fundic glands. There are some pyloric glands, and there is a narrow zone of cardiac glands at the cardiac sphincter. Enteroendocrine cells, along with endocrine cells in the pancreas control digestive functions. Secretions include gastric acid, gastrin, gastric-inhibitory polypeptide, secretin, cholecystokinin, and pancreozymin.²¹

The small intestine is about three times the length of the large intestine. The mesenteric attachments to the colon are loose. Just distal to the pylorus is the “collar” of Brunner’s glands in the submucosa. These secrete alkaline fluid and mucus.²¹

Gastrointestinal disease in omnivorous/insectivorous marsupials clinically presents most frequently with diarrhea and some degree of anorexia, weight loss, dehydration, lethargy and collapse. Vomiting may be seen in predominantly upper gastrointestinal illnesses. Bacterial, protozoal, and toxic etiologies have been found. Malnutrition or dietary changes may also play a role. Diagnostics and treatments follow regimens similar to that of other essentially carnivorous mammals.

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The Respiratory System: Exotic Companion Mammals

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Rabbits

Anatomy and Physiology

The nostrils of rabbits contain sensory pads at the entrance making the nose very sensitive to touch. The nostrils are still when totally relaxed, but can twitch up to 150 twitches per minute. Rabbits have an acute sense of smell due to turbinate bones with a vomeronasal organ and olfactory sensory epithelium. The glottis is small. Rabbits are obligate nose breathers. The thorax is small in contrast to the size of the abdomen. The thymus persists in the adult and lies ventral to the heart. It extends forward into the thoracic inlet. The lungs have cranial, middle, and caudal lobes. The left cranial lobe is smaller than the right due to the presence of the heart. The pleura is thin. There are no septa dividing the lungs into lobules. This accounts for pneumonia being generalized rather than localized. Normal at rest respiratory rate is 30 to 60 breaths per minute. At rest, the diaphragm is used for muscular contractions rather than the intercostal muscles.

Diseases

Respiratory diseases are a major cause of morbidity and mortality in rabbits. Pasteurellosis is the primary respiratory disease, but many other pathogens can play a role in the disease complex. The term “snuffles” can refer to any upper respiratory disease (URD). Comprehensive studies have shown that rabbits can resist infection even if housed with infected rabbits, spontaneously eliminate *Pasteurella multocida*, become chronic carriers, develop acute disease, develop bacteremia and pneumonia, or develop chronic disease. The pathogenesis depends on host resistance and virulence of the *P. multocida* strain. Many rabbits carry *Bordetella bronchiseptica* and *Moraxella catarrhalis* in the nares. The prevalence of *P. multocida* infection varies between rabbitries. It increases with the age of rabbits in facilities where the disease is endemic. There is an inverse relationship between *P. multocida* and *B. bronchiseptica* infections in rabbits. Weanlings have higher infection rates with *B. bronchiseptica* whereas *P. multocida* predominates in adults.

Pasteurellosis

Pasteurella multocida is a gram-negative, bipolar, nonmotile asporogenous coccobacillus from the family Pasteurellaceae which includes *Hemophilus*, *Actinobacillus*, and *Pasteurella* spp. Different strains require different specialized conditions for growth in the laboratory, which results in many cultures taken for diagnostic purposes failing to grow. *P. multocida* can be typed serologically with the use of indirect hemagglutination to identify capsular types (A,B,D,E, or F). The gel diffusion precipitin test has described 16 somatic antigen determinants of the capsule lipopolysaccharide. Antibiotic sensitivities are varied depending on the strain. Generally, *P. multocida* strains isolated from rabbits are sensitive to chloramphenicol, novobiocin, oxytetracycline, penicillin G, nitrofurazone, fluoroquinolones, and trimethoprim-sulfamethoxazole. Choice of antibiotic must be taken in consideration of the rabbit’s gastrointestinal flora. Recovery from acute disease and elimination of infection can occur, but spontaneous recovery from chronic infection is unlikely.

Virulence factors of *P. multocida* include adhesions, phagocyte resistance, endotoxin (lipopolysaccharide), exotoxin, and iron regulation. Some strains have pili or adhesin proteins on the outer membrane that enhance colonization. Type A strains are more adhesive to respiratory mucosa than are type D strains. Some type D strains

resist bactericidal activity of phagocytes. Leukotoxic enzymes may be produced. The availability of iron regulates the growth of some strains. Most strains produce iron-binding outer membrane proteins. *Pasteurella multocida* can invade and multiply because the capsule that is largely hyaluronic acid, inhibits phagocytosis and complement-activated bactericidal activity of serum. Endotoxin enhances resistance and stimulates the release of inflammatory mediators such as interleukin-1. Free endotoxin in the plasma during bacteremia causes fever, depression, and can induce shock. Some strains produce an exotoxin. The dermonecrotic toxin termed *P. multocida* toxin of some type D strains is similar to the toxin that causes atrophic rhinitis in pigs. A toxin has also been demonstrated for type A strains. Purified *P. multocida* toxin induces pneumonia, pleuritis, lymphoid atrophy, and possibly osteoclastic bone resorption in rabbits. Most Pasteurellaceae are commensal organisms on mucous membranes. Pathogenicity occurs under conditions of immunodeficiency and stress. Research into the role of the humoral immune response has shown that while immunization may protect the rabbit from the development of severe disease, infection was not prevented by antibody formation. Antibodies to antigens of *P. multocida* and other cross-reacting antigens of gram-negative bacteria notably other *Pasteurella* sp., *Yersinia* sp., and *Moraxella* spp., could enhance opsonization and phagocytosis. Rabbits that have chronic or severe infections usually have high titers of immunoglobulin G (IgG) to *P. multocida*. Secretory immunoglobulin (IgA) does not protect against nasal infection, but may play a role in limiting the spread. Cell-mediated immunity may play a role as a depressed T lymphocyte function has resulted in severe disease in infected rabbits. Several antigens associated with virulence have been identified, and in research studies, are recognized consistently by infected rabbits.

The clinical signs of pasteurellosis includes URD (rhinitis, sinusitis, conjunctivitis, dacryocystitis), otitis, pleuropneumonia, bacteremia, and abscesses (subcutaneous tissues, organs, bones, joints, genitalia). A serous nasal discharge precedes the typical white or yellowish mucopurulent discharge. Exudate adheres to the fur around the nares. The medial aspects of the forepaws will become matted and yellow-gray from grooming. Affected rabbits may make audible sonorous noises and have bouts of sneezing with discharge. The nasolacrimal duct can be infected and thereby involving the conjunctiva. Exudate occluding the duct may lead to excessive tearing, scalding of the face, alopecia, and pyoderma. In many rabbits, the signs of rhinitis subside or disappear as the infection continues into the paranasal sinuses or middle ears. Acute infection of the nares is accompanied by hyperemia and edema of the mucosa. Mucosal erosion and nasoturbinate atrophy occurs with chronic infection. Otitis media can be asymptomatic or if the inner ear is affected, torticollis, nystagmus, and ataxia can develop. The tympanic membrane may rupture. The rabbit may scratch persistently at the base of the ear. Radiographs may show an increased soft tissue density within the bulla with bone thickening. Pet rabbits however, presented with URD, otitis, or abscesses, are less likely than those from rabbitries, to have *P. multocida* as the causative agent. For pet rabbits, infection with *Bordetella bronchiseptica* or *Staphylococcus* spp. are more likely differential diagnoses. Chronic infection in the thoracic cavity may be subclinical long after the acute phase of the infection. If caused by *P. multocida* or *Staphylococcus* spp., pleuropneumonia, pericarditis, and abscessation around/in the lungs and heart may occur. The rabbit may be presented with non-specific signs such as anorexia, weight loss, depression, and fatigue. Dyspnea may only be noticeable upon exertion. Lung sounds may be absent due to consolidation or abscess. Rales must be differentiated from sounds heard from the upper respiratory tract. Radiography is needed to determine the extent of the disease process.

The main routes of transmission are by direct contact, airborne spread and fomites. It occurs more readily from rabbits with acute infections than from rabbits with chronic infections. Venereal transmission occurs if genital infection is present. Kits can be infected at birth from a doe with genital infection. The incubation period is difficult to assess because many rabbits are subclinically infected. Once *P. multocida* is established in the nasal tissues, infection spreads to contiguous tissues including the paranasal sinuses, nasolacrimal ducts, conjunctiva, Eustachian tubes, middle ears, trachea, bronchi and lungs. Hematogenous spread may also reach the middle ears, lungs, and internal organs.

Bordetellosis

Bordetella bronchiseptica is a common inhabitant of the respiratory tract of rabbits. The nares and bronchi become colonized. Usually respiratory disease is not associated with infection, but predominant recovery of this organism in a rabbit with URD points to it as the causative agent. The organism adheres to ciliated mucosa and resists

respiratory clearance. It induces ciliostasis, reduced macrophage adherence and phagocytosis. Some strains are cytotoxic and enhance colonization by toxigenic *P. multocida*. *Bordetella bronchiseptica* can be considered a co-pathogen or a pre-disposing factor in *P. multocida* infections.

Staphylococcosis

Staphylococcus aureus and *S. albus* are frequently isolated from the nares of both healthy and ill rabbits. *Staphylococcus* sp. infection can increase the inflammation of already compromised mucosa. Pathogenicity depends on host susceptibility and bacterial virulence. *Staphylococcus aureus* produces toxins lethal for rabbit neutrophils as well as protein A that binds the Fc portion of IgG, blocking host bactericidal mechanisms. Otitis media, fibrinous pneumonia or abscesses in the lungs or heart have been due to disseminated staphylococcosis. Grossly, the abscesses appear similar to ones caused by *P. multocida*. Antibiotic resistance is encountered more frequently with *S. aureus* than with *P. multocida*. Although culture and sensitivity testing is ideal, the abscess may be inaccessible. Blood culture may be helpful. Antibiotics of choice when a culture cannot be obtained include the fluoroquinolones, chloramphenicol, or trimethoprim-sulfamethoxazole.

Other Bacterial Pathogens

Moraxella catarrhalis (formerly *Micrococcus*, *Neisseria*, or *Branhamella catarrhalis*) is common in the normal nasal flora. It can be isolated from clinical cases of rhinitis or conjunctivitis. If it is isolated in pure culture from a symptomatic rabbit, it is implicated as the disease agent. However, it is more likely an opportunist on unhealthy mucosa. Treatment should be initiated only if there is clinical disease.

Mycobacterium spp. (*M. avium*, *M. bovis*, *M. tuberculosis*) have been isolated from cases of pneumonia in rabbits. *Moraxella bovis* and *Pseudomonas aeruginosa* have also been documented. *Pasteurella aeruginosa* can also cause abscesses similar to those of *P. multocida* as well as septicemia. *Francisella paratuberculosis* (pseudotuberculosis) and *Francisella tularensis* (tularemia) are rare in domestic rabbits but can occur in feral rabbits. Both will cause bacteremia, multiorgan fibrinopurulent disease, and pneumonia. Due to the zoonotic potential, caution should be taken when doing necropsies of wild or feral rabbits. *Chlamydophila* spp. (formerly *Chlamydia* spp) have been isolated from the lungs of domestic rabbits with pneumonia. Cilia-associated respiratory (CAR) bacillus have been recently characterized, and appear to be closely related to *Helicobacter* spp. This is not the same organism called CAR bacillus of rats which appear related to gliding bacteria of phylum Flavobacterium. Rabbit CAR bacillus is an opportunistic infection with organisms found between the cilia of the respiratory epithelium. Natural infections may show slight nasal discharge although histologically the lesions include slight hypertrophy and hyperplasia of the laryngeal, tracheal and bronchial epithelium. Treatment efficacy has not been evaluated.

Other Etiologies of Respiratory Disease

Viral diseases associated with primary respiratory disease have not been identified. Rhinitis and chronic bronchitis from exposure to allergens is seen commonly in pet rabbits. Identifying and eliminating the allergen may be difficult. Air filters are helpful during the spring pollen season in rabbits housed indoors. The differential diagnosis of pathogenic agents must be ruled out. Symptomatic treatment with antihistamines and limited use of ophthalmic corticosteroids may be helpful.

Neoplasia

Adenocarcinoma of the nasal turbinates should be a differential of URD. It progresses relatively rapidly and causes cavitation of the turbinates which is visible radiographically. Thymomas have been diagnosed in both young and old rabbits. Clinical signs may include tachypnea and moderate to severe dyspnea. Bilateral exophthalmos due to the interference of vascular return to the heart is also seen with thymoma. The mass is visible radiographically. Treatment may include surgical removal or chemotherapy. Lymphoma and thymoma may both cause dyspnea, lower respiratory rates and cyanosis on exertion. Lymphocytosis is usually present. Radiography and a chest tap with cytology will be useful to differentiate neoplasia from abscessation/infectious disease.

Guinea Pigs

Anatomy and Physiology

The caudodorsal part of the nasal cavity is lined by sensitive olfactory epithelium. The larynx has five cartilages (epiglottis, thyroid, cricoid and paired arytenoid) with no laryngeal ventricle. Although they have a wide variety of vocalizations, the vocal cords are poorly developed. The palatal ostium forms an aperture between the oropharynx and pharynx. The folds of soft palate around the ostium are called the velopharyngeal recess. The right lung has four lobes: cranial, middle, accessory, and caudal, separated by a deep fissure. The left lung has three lobes: cranial, middle, and caudal. Because the heart occupies a large portion of the thorax, the lungs are comparatively small.

Diseases

Vitamin C deficiency may be an underlying etiology or contribute to any infectious illness in the guinea pig. Additional Vitamin C should be included as part of any medical therapy. Streptococcal (*S. zooepidemicus*, *S. equi*, *S. pneumoniae*, *S. moniliformis*, etc.) infections are common in the form of pneumonia, cervical abscesses and joint abscesses. Cervical and joint abscesses should be surgically debrided. Antibiotics with only a gram positive spectrum should be avoided due to the potential for gastrointestinal tract flora disruption. *Streptococcus* spp, *S. aureus* and *Chlamydophila psittaci* are also common pathogens involved in conjunctivitis.

Bordetella bronchiseptica

Guinea pigs should not be housed with animal species which carry *Bordetella bronchiseptica* (rabbits, cats, dogs, pigs). It is a common etiology of conjunctivitis combined with Vitamin C deficiency. Bordetellosis will cause signs of respiratory distress, weight loss, and even sudden death. Bronchial, nasal, and/or ocular secretions should be cultured. Radiographs are useful to see the extent of pneumonia. Treatment is usually with an appropriate antibiotic such as enrofloxacin, trimethoprim-sulfamethoxazole, or injectable gentamicin. Repeated injections can be very stressful for the cavy. Supportive care includes fluids, gavage or assist-feeding, vitamins, bronchodilators, and nebulization. Large colonies may use vaccination with 0.2 ml of canine or porcine bordetellosis vaccine with a booster given in 2 to 3 weeks followed by semi-annual to annual revaccination. It has been reported that several drops of a canine intranasal vaccine affords similar protection. Vaccines used cannot contain aluminum hydroxide as cavies may have a sensitivity reaction. Vaccination may prevent clinical disease, but the cavies may develop an upper respiratory tract carrier state. In a large herd situation, it may be better to depopulate, disinfect the premises and replace stock.

Other Bacterial Pathogens

Chlamydial conjunctivitis can be diagnosed with conjunctival scraping and staining for elementary bodies. Treatment is with ophthalmic tetracycline preparations and systemic doxycycline. Pneumonias due to *Klebsiella pneumoniae* are usually severe and may result in sudden death. Gentamicin, tobramycin or enrofloxacin have been used along with supportive care. Rule-outs for cavies presented with torticollis, seizures, incoordination, and weakness include bacterial encephalitis, *Baylisascaris* infections, toxicosis, and inner ear infection (*Strep*, *Staph*). A full work-up including radiographs should be done as in other species.

Chinchilla

The respiratory anatomy of the chinchilla is similar to that of the guinea pig. However, the nasal cavity and cochlear/otic anatomy and physiology has been extensively studied as models for experimental infection with *Haemophilus influenzae* and various ear and vestibular disease in humans due to the relatively large tympanic bullae. The chinchilla has a palatal ostium similar to that of the guinea pig, making intubation and passage of a gastric tube difficult without the use of an endoscope or other means of direct visualization.

Diseases

Upper respiratory tract infections in chinchillas include infection with *Streptococcus* spp., *Pseudomonas aeruginosa*, *Pasteurella* sp. *Bordetella* spp. Clinical signs include rhinitis, nasal discharge, conjunctivitis. As with rabbits, there will be matting of the fur on the forearms due to increased grooming. Malocclusions and tooth root abscesses need to be ruled out. Diagnosis includes radiographs, culture and sensitive of discharges. Treatment includes broad spectrum but appropriate antibiotics, supportive care including fluids, topical ophthalmic preparations and antihistamines. Pneumonias may be due to *Streptococcus* spp. *Pasteurella*, spp., *Bordetella* spp. Signs include dyspnea, fever and usually anorexia. The chinchilla may become dehydrated and is lethargic. Diagnosis is with auscultation, radiographs, culture (tracheal, blood). Treatment includes appropriate broad spectrum antibiotics, bronchodilators, and supportive care.

Rats and Mice

Anatomy and Physiology

Over 50% of the nasal cavity is lined by olfactory epithelium. The vomeronasal organ lies about 10 mm from the vestibule in the ventral vomer bone. The rat has several well-developed nasal glands, the largest being Steno's gland. It lies in the rostral maxillary sinus with a duct emptying into the vestibule. It is homologous with the salt gland of marine birds. It produces a watery secretion at the nose helping to humidify inspired air and regulate mucus viscosity. The trachea is flattened and ovoid in cross-section. The right lung has a cranial, middle, caudal, and accessory lobe. The left is smaller, not divided into lobes.

Diseases

Many infectious agents affect both rats and mice. Few colonies that provide animals for the pet trade are respiratory-pathogen-free. A common cause of respiratory disease is mycoplasmosis due to *Mycoplasma pulmonis*. Signs include dyspnea, respiratory distress, nasal discharge, and torticollis (otitis interna). Diagnosis is through culture, serology, and histopathology of the lung and/or ear. Treatment is with doxycycline at 2.5 mg/kg PO q12h or 250 mg/liter drinking water. While the tetracyclines may control and manage the disease, it probably does not eliminate the *Mycoplasma* sp.. Tylosin has been used in the past, but it is no longer as effective. Sendai virus infections also present with respiratory distress. Diagnosis is through serology and histopathology of lung. Treatment is limited to supportive care. Usually it resolves within about a week in adults with complete recovery. It may exacerbate *M.pulmonis* infection. Another respiratory pathogen that is frequently present as well is the cilia-associated respiratory (CAR) bacillus. This bacillus now appears to be a member of the phylum Flavibacterium. Clinical signs include respiratory distress. Its pathogenicity without *M.pulmonis* co-infection is unclear. Diagnosis of the presence of this agent is through serology and special histopathology stains. Treatment is supportive and usually includes doxycycline or tetracycline to treat the concurrent *M.pulmonis* infection. It is considered a persistent infection that probably does not clear. *Corynebacterium kutscheri* infection in rats may just be respiratory while it is systemic in mice. Signs also include respiratory distress. Diagnosis is through culture and sensitivity and histopathology. Treatment usually is with doxycycline, tetracycline or chloramphenicol to control symptoms. This is also usually a persistent infection which is unlikely to be cleared with treatment, just managed. Owners with pet rats and mice that have respiratory problems need to know that periodically they will need to manage the clinical symptoms. They must recognize when symptoms occur as the symptoms need to be treated to make the animal comfortable and minimize chance of it become severe pneumonia. If they add a new rodent to the household, it is likely to trigger flare-ups in the resident rodents, plus the new animal may break with it too. Most rat owners learn how to work with this. Eventually, there is enough lung pathology that many succumb in older age to pneumonia/fibrosis (unless neoplasia or urolithiasis is the cause of death). Adjunctive therapy for dyspnea includes nebulization, bronchodilators, antihistamines, expectorants, and NSAIDs in addition to the antibiotics

Hamsters

Hamsters have well-developed nasal turbinates lined by mucosa that filter and humidify incoming air as well as warming the air before passage to the lungs. There are many nasal glands opening into the external nares. Like the rat, they have well-developed olfactory epithelium and bulbs. The lungs have a large single left lobe with 4 lobes on the right consisting of the cranial, middle, caudal and accessory lobes. The thymus has two lobes and lies in the cranial mediastinum. It decreases in size with age.

Diseases

Respiratory infections may be bacterial or due to Sendai virus, a paramyxovirus. Signs include respiratory distress and pneumonia. Diagnosis is usually through serology. Treatment is supportive. Bacterial pneumonia and/or rhinitis may be due to *Pasteurella* spp., *P. pneumotropica*, *S. pneumoniae*, *S. agalactiae*, *S. aureus*, *K. pneumoniae*, or *Bordetella* sp., etc. Signs include respiratory distress, coughing, sneezing, and matting of the fur on the forearms and nasal area. Diagnosis is through culture. Treatment includes appropriate antibiotic therapy with consideration to the gram positive gastrointestinal tract along with supportive care.

Gerbils

The gross respiratory anatomy and lung lobation is similar to that of mice and rats.

Diseases

Respiratory infections may involve various bacterial pathogens including *K. pneumoniae*. Upper respiratory disease is often primarily conjunctivitis. Culture, sensitivity testing and appropriate antibiotics along with supportive care are used to treat bacterial infections.

Prairie Dogs

Prairie dog gross respiratory system anatomy is similar to the guinea pig and clinically can be evaluated as with other rodents. The nasal cavity is similar to rats, as cheek teeth roots are closed.

Odontoma

Prairie dogs with odontoma are usually presented with dyspnea and/or open mouth breathing. On radiographs or rhinoscopy, there is often impingement, occlusion, or distortion of the nasal cavity, with or without signs of rhinitis, nasal discharge, or sneezing. As with other rodents, signs of nasal discharge may only be evident as matting of the fur on the forelegs from frequent grooming. Unlike with rats, there will not be porphyrin staining around the eyes. A few prairie dogs may sneeze, and owners will note snoring or honking noises when the prairie dog is at rest.

Ferrets

Anatomy and Physiology

The respiratory system of the ferret starts with nose and the nasal cavity. From here, air moves from the choana into the opening of the larynx, the rima glottis and then into the trachea. The skin of the nose is bare and often pigmented. The nasal cavity is divided into right and left nasal passages and has dorsal and ventral nasal conchae that have numerous folds to increase the surface area of the epithelial surface. The hard palate continues as the flexible soft palate that sits over the opening of the larynx. This opening is covered by the epiglottis which rests

above it. This arrangement allows air to move from the nasal cavity directly into the larynx. The larynx of the ferret is similar to that of the human larynx. It serves to close the airway to raise intra-abdominal pressure along with keeping ingesta from being aspirated into the respiratory tree and acts as an aid for vocalization. During the normal breathing cycle, the vocal cords remain relaxed. The larynx is innervated by the cranial and caudal laryngeal nerves that are branches of the vagus.

The trachea extends from the larynx to the bifurcation of the primary bronchi which divides at T 5-6. It is composed of C-shaped hyaline cartilages that are connected by smooth muscle. The mucosal surface of the trachea is composed of ciliated and nonciliated cells with mucus glands. There are submucosal glands with the numbers of glands closer to a human than a dog. These mucosal and submucosal glands are stimulated by nerves, acetylcholine and histamine. Secretions can be blocked with atropine, glycopyrrolate and antihistamines.

The thoracic cavity is cone shaped. The rib cage consists of 14 ribs with 9 sternbrae with the last several ribs not meeting the distal end of the sternum. The thoracic cage is divided into a cranial, middle and caudal mediastinal cavities.

Each primary bronchus divides into a lobar or secondary bronchus which further subdivides into small lobules of the lung. The lung extends from the 1 to 2nd to the 10 to 11th intercostal spaces. The left lung is divided into a cranial and caudal lobe while the right lung has a cranial, middle, caudal and accessory lobe. The accessory lobe of the right lung is irregular and conforms to the shape of the diaphragm and curves around the caudal vena cava. The number of generations of terminal bronchioles of the ferret (1 to 2) is intermediate between that of the dog (0 to 1 generations) with that of humans (3 to 4 generations).

The pulmonary arteries carry unoxygenated blood from the right ventricle to the parenchyma of the lungs. The pulmonary trunk divides into the right and left pulmonary arteries that supply the right and left lung fields. The pulmonary veins take oxygenated blood from each of the lobes to the left heart. The bronchial arteries supply blood to the parenchyma of the lung. They take origin from the first intercostal artery, close to the origin of the aorta.

The respiratory rate at rest is about 33 to 36 breaths/min. It tends to vary from 27 to 44 breaths/min when the ferret is under anesthesia. The total lung capacity is very large in ferrets and this capacity exceeds its predicted value by 297%. When the lung capacity was measured in 0.6 kg ferrets, the lung capacity compared to a 2.5-kg rabbit. The only other mammal with a similar comparative value is the sea otter. In addition to the large lung capacity, the chest wall is very compliant. It is thought that these two adaptations are important for successful subterranean hunting.

The ferret lung can adapt to changes in atmospheric pressures. With hypoxia, there is significant pulmonary vasoconstriction. This is similar to humans that in high altitudes develop pulmonary vasoconstriction.

Ferrets exhibit neurogenic inflammation as sensory nerve stimulation causes the release of tachykinins. These substances are found in the nerve terminals of the sensory nerves to the lung parenchyma. Their release causes smooth muscle contraction, submucosal gland secretion, increased vascular permeability, neutrophil adhesion and cough. Viral diseases, exposure to airborne toxins including nicotine and other agents can result in this neurogenic response. Nicotine has been shown to increase the ciliary beat frequency of the epithelial cells. Various air pollutants exacerbate pulmonary disease as it causes smooth muscle contraction and mucosal and submucosal gland secretion.

Studies have shown that there is a difference in the distribution of α -1 and β adrenergic receptors and muscarinic receptors in the pulmonary tree. In small bronchioles, α -1 receptors are more numerous but are sparse in the large airways. The β receptors are relatively high throughout the tree but are highest in the bronchioles. The cholinergic receptors are most dense in the bronchial muscle and decrease in density toward the distal bronchioles.

Diseases

Influenza

Ferrets are the only domestic animal species susceptible to human influenza viruses. They are often infected by their human owners. Signs are similar to those in humans: photophobia, catarrhal nasal discharge, sneezing, coughing, pyrexia, anorexia, and malaise. They may also act like they have a sore throat, with marked swallowing efforts. It may progress to pneumonia. Clinical course is usually 7 to 14 days. Treatment includes supportive care, antihistamines, cough suppressants, and prophylactic antibiotics. Preventive measures include separation of susceptible ferrets from ferrets or humans affected with influenza. It is recommended ferret owners get influenza vaccinations each year! At the present time, it is not recommended that ferrets be vaccinated, however, the human vaccines are efficacious in ferrets.

Pneumonia

Bruce Williams DVM, DACVP feels that the most common cause of pneumonia in ferrets is aspiration, either of orally administered medicants or of vomitus. Ferrets often resist liquid oral medication, and may involuntarily inhale part of the medication. Gross and microscopic pathology are similar to those found in other species with aspiration pneumonia. If aspiration is suspected, prophylaxis with broad spectrum antibiotics, rest, and supportive care are recommended.

Pneumonia due to *B. bronchiseptica* and *P. multocida* have been reported. *Bordetella bronchiseptica* causes upper respiratory signs which respond poorly to antibiotics, and occasionally as in dogs, will develop to severe pneumonia. Marshall Farms uses killed vaccine (Bronchicine, Pfizer, NY, NY) and feels it is safe and effective. Chloramphenicol and trimethoprim-sulfa may be helpful, along with supportive care. It is recommended that young ferrets be separated from dogs with respiratory disease. This is a concern in a veterinary hospital, or boarding facility that will take young ferrets as well as dogs.

Canine Distemper

This is a fatal disease in ferrets. Disease progression ranges from 12 days in ferret-adapted strains to approximately 42 in wild canine strains. Transmission is by direct contact, fomites, or aerosolization of urine, feces, or nasal exudate. The disease has been associated with ferret shows and the intermingling of ferrets that have not been properly vaccinated. The disease is profoundly immunosuppressive, and animals that survive the initial respiratory stages succumbing to neurologic dysfunction within several weeks. There is no treatment. Vaccination (Purevax Ferret, Merial, Duluth, GA) should begin when the ferret is 6 weeks old, a second vaccination at 10 weeks, and a third at 14 weeks of age with an annual booster. Early clinical signs include anorexia, pyrexia, chin dermatitis, photophobia, nasal and ocular discharge, and brown crusts around the face. Later clinical signs include bronchopneumonia, hyperkeratosis of the planum nasale and footpads, and central nervous system signs including tremors, convulsions, coma, and death. Histologically, eosinophilic viral inclusion bodies are both intracytoplasmic and intranuclear. They may be seen in a wide variety of epithelial cells, neurons, and occasionally in white blood cells and megakaryocytes. The urinary bladder, renal pelvis, and biliary epithelium are the most productive places to look for inclusions. A non-suppurative encephalitis with demyelination may be seen in animals showing neurologic disease.

Endogenous Lipid Pneumonia

This is a common incidental finding in mustelids at necropsy and is of no clinical significance. It has been called "foam cell foci" or "subpleural histiocytosis." It is mistaken at necropsy by practitioners as a dissemination neoplasm. The cause and origin of the lipid is unknown. Grossly multiple to coalescing white to yellow foci are present within the subpleural pulmonary parenchyma. A transverse cut through one of these foci will reveal its superficial nature. It is an aggregate of lipid-laden macrophages in the alveoli immediately subjacent to the pleura. As the lesions increase in size, they may include moderate numbers of lymphocytes and cholesterol clefts.

Non-specific Respiratory Conditions

A number of ferrets present with chronic sneezing and apparent upper respiratory irritation. Symptoms abate with antihistamines and/or topical ocular and nasal antibiotics and NSAIDs, but reoccur upon cessation of the

medications. Some ferrets exhibit seasonal symptoms similar to human allergies or hay fever. Cultures of discharges, nasal flushes, and conjunctival swabs usually contain a variety of bacteria considered normal flora, but nothing specific. A coughing condition has been noted in young ferrets recently shipped. Despite diagnostic testing including heartworm antigen, radiographs, echocardiography, transtracheal wash, culture, cytology, and endoscopy, no specific cause has been found. Some of these ferrets seem to grow out of it, while others have a congestive-sounding cough for years. The author (CJD) is pursuing the probable etiologic agent.

Dental disease and tooth root abscesses need to be investigated whenever a ferret is presented for nasal discharge, whether it is unilateral or bilateral. Intraoral and skull radiographs are useful to look at the tooth roots, as the tooth may seemingly appear healthy. Ferrets are also notorious for inhaling dusts, hair, spider webs and other particulates during their environmental investigations. Most of these result in acute paroxysmal sneezing with clearance of the irritant material. Occasionally the ferret will sneeze so hard that blood will be mixed with the mucousy discharge – if it continues, a more significant foreign body, rhinitis, or sinusitis may be involved.

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Diagnostic Laboratories

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- Charles River Laboratories, Inc. Research Animal Diagnostic Services, 1-800-338-9680, www.criver.com. Available testing: PCR, serology, parasitology histopathology, necropsy, microbiology
- Division of Laboratory Animal Medicine, LSU School of Vet Med, 225-578-9643. Available testing: rodent serology
- University of Miami Comparative Pathology Laboratory, 1-800-596-7390, <http://pathology.med.miami.edu>
Available testing: serology, histopathology, necropsy, microbiology, parasitology
- Research Animal Diagnostic Laboratory, University of Missouri, 1-800-669-0825, www.radil.missouri.edu. Available testing: PCR, serology, necropsy, histopathology, microbiology, clinical pathology, parasitology
- Zoologix, Inc. 1-818-717-8880, www.zoologix.com. Available testing: PCR
- Sound Diagnostics, Woodinville, WA. 1-206-363-0787. www.sounddiagnostics.com. Available testing: Rabbit serology
- Veterinary Molecular Diagnostics, Milford, OH. 1-513-576-1808. www.vmdlabs.com. Available testing: Small mammal PCR

FERRET NEOPLASIA

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INTRODUCTION TO COMMON NEOPLASIAS

The ferret has the highest incidence of spontaneous neoplastic disease of any mammal, rivaling genetically engineered rodents. Of significance is that frequently there are multiple types of tumors and that many are based in the endocrine system. Ferrets at any age may be affected. The multiple endocrine neoplasia (MEN) syndrome in ferrets includes adrenal adenoma/adenocarcinoma, islet cell carcinoma, lymphoma, and mast cell tumors. Other common tumors in ferrets include chordomas, sebaceous adenomas, fibromas, biliary cystic adenocarcinoma, and gastrointestinal carcinomas.

Splenomegaly

Splenomegaly is a common finding, particularly in middle-aged to older ferrets with other diseases, but can also be seen in young ferrets. Hypersplenism is most likely not a distinct entity. It has been linked with chronic inflammatory disease, chronic diseases, cardiomyopathy, anemia, and lymphoma/lymphosarcoma (and rarely, hemangiosarcoma). In a ferret under 3 years of age, a persistently enlarged spleen is most likely neoplastic. Grossly, the spleen may range up to 10 cm in length and weigh up to ¼ of the ferret's body weight. While most are diffusely enlarged, a small percentage of spleens contain single or multiple discrete nodules. Microscopically there may be marked congestion, extramedullary hematopoiesis, that is not typical of a "tumor," however it is neotissue and a cancerous process cannot be ruled out. Large areas of coagulative necrosis, often bordered by a combination of viable and degenerate neutrophils and various amounts of granulation tissue may be seen in grossly enlarged spleens. As enlarged spleens are prone to rupture, various signs of splenic trauma, including hematoma, siderotic plaques, and large areas of parenchymal fibrosis are commonly seen. Once a large spleen is identified, ultrasound examination is useful to differentiate parenchymal consistency, as occasionally splenic cysts are seen, which can be drained and may not reoccur. Prior to removal of a persistently enlarged spleen (greater than 30 days with no concurrent major disease process), a bone marrow biopsy and full CBC and serum chemistries should be done. In many cases, the bone marrow is no longer producing red cells, and even with exogenous erythropoietin administration may not be capable of returning to function. The author usually plans blood transfusions for the ferret post-splenectomy, as well as continued erythropoietin, and rechecks the CBC and reticulocyte counts every few weeks post surgery. Although early removal of the spleen if it is affected with lymphoma may slow metastasis, in the author's experience the spleen is often not the primary tumor site, and progression of lymphoma or metastasis may not be halted, just slowed. In ferrets with extramedullary hematopoiesis (EMH), the spleen may be the primary source of red blood cells. Primary EMH is seen frequently in ferrets with cardiomyopathy or chronic respiratory conditions.

Lymphoma/Lymphosarcoma

Lymphoma/lymphosarcoma (LSA) may occur virtually anywhere on the ferret. It may be localized or systemic. It may or may not be elucidated on a differential white blood cell count. The lymphoblastic form is the most common form in the gastrointestinal tract. Signs of LSA include anorexia, weight loss, splenomegaly, peripheral lymphadenopathy, small neoplasms of the skin or other tissues. Peripheral lymphocytosis of $\geq 55\%$, anemia, leukopenia, thrombocytopenia are sometimes seen. Histopathology of many tissues may reveal lymphocytic infiltration. Etiology of some forms are due to a Type C Retrovirus (Erdman, Susan presented at 1995 AALAS). The diagnostic work-up includes – history, physical examination, palpation, CBC, chemistries, radiographs, biopsy, ultrasonography. Treatments have been tried based on the feline regimen, although one study showed that ferrets treated with prednisone alone lived as long as those that had the full regimen, and many individuals did better with prednisone alone. In the author's experience, surgical debulking of the tumor mass when possible for comfort for the ferret, and low-dose prednisone along with supportive care results in longer and better quality of life than

administration of the chemotherapeutic regimen. There are a number of published therapeutic regimens for lymphoma/lymphosarcoma. The clinician should consult current literature regarding chemotherapeutic options and patient monitoring recommendations before choosing a course of treatment. One regimen that has been used for a number of years is as listed:

- Cyclophosphamide (do not give on same day as vincristine)- 1/4 of a 25 mg tablet/ferret once every three weeks PO for 3 doses (Cytosan, Mead Johnson, Glenview, IL)
- Vincristine sulfate - 0.05 mg for ferrets < 1 kg.; 0.10 mg for ferrets > 1 kg BW IV (Oncovin, Eli Lilly, Indianapolis, IN) For dosing regimens, please refer to current literature and formularies.
- Prednisone (2 mg/kg PO q24hr) treatment regimen as in cats

Melphalan has also been used (Alkeran, GlaxoWellcome, London, UK) - have the pharmacist pack into small capsules 0.10 mg and 0.05 mg amounts.

- **Regimen:** 0.10 mg capsule per ferret q24hr for 2 wks, then one 0.50 mg capsule per ferret for 2 weeks, then one 0.50 mg capsule per ferret q24hr for 2 weeks, finally wean off using 0.50 mg capsule per ferret every 2 days for 2 doses, then every 3 days for 2 doses, then every 5 days for 2 doses.
- Discontinue therapy if CBC shows changes (WBC drops below 2,000; thrombocytopenia or anemia occurs).

Islet Cell Neoplasia

Pancreatic insulin-secreting tumors (insulinomas or islet cell carcinomas) have been well-described.¹⁻⁵ The neoplastic pancreatic beta cells cause an increase in basal insulin secretion. They fail to respond to normal inhibitory stimuli and release excessive amounts of insulin in response to normal provocative stimuli. Continuous hyperinsulinemia inhibits hepatic gluconeogenesis and glycogenolysis, plus peripheral uptake of glucose by tissue cells is increased. The feedback mechanism to the glucoreceptors in the hindbrain and hypothalamus which release glucagon, cortisol, epinephrine and growth hormone, and in turn, act to raise blood glucose, is inoperative. The hyperglycemic effects of glucagon, epinephrine, cortisol, and growth hormone are inhibited, and blood glucose concentrations continue to decrease. Clinical signs of hypoglycemia are correlated to the rate of decline, concentration of blood glucose, and duration of hypoglycemia. Signs can be categorized as neuroglucopenic or adrenergic manifestations, or as a combination of both. Neuroglucopenic signs result from the effect of hypoglycemia on the central nervous system, as glucose is the primary energy source for these tissues. Glucose uptake in the brain occurs by diffusion and is not insulin dependent. Glucose deprivation of nervous tissue cells results in the signs of hypoglycemia: mental dullness, confusion, seizures, and coma. Adrenergic manifestations occur when blood glucose concentrations decrease rapidly, resulting in catecholamine release and increased sympathetic tone. These signs include tachycardia, hypothermia, tremors, nervousness, and irritability. Prolonged, severe hypoglycemia can result in cerebral hypoxia and possibly irreversible cerebral lesions.

Islet cell neoplasia has been reported in ferrets between the ages of three and eight years, with the most common onset being four to five years of age. Both sexes are affected. The history varies from acute onset to a chronic course of weeks to many months, with episodes that may last from several minutes to several hours. The episodes usually end with spontaneous recovery, or after administration of an oral sugar solution, fruit juice, or syrup by the owner. Owners will report the glazing over of the eyes, collapse, increased salivation, gagging, pawing at the mouth (due to nausea), weakness of the hind legs, and ataxia. There may be a gradual weight loss. Between episodes, the ferrets act normally. Physical examination may reveal no abnormalities, although many have varying degrees of splenomegaly. Other neoplasias occurring simultaneously are common: adrenal neoplasia, lymphoma, and various skin tumors. Additional disease such as cardiomyopathy may be present. Diagnosis of hypoglycemia can be confirmed with a blood glucose level. Fasting time should be fairly short (no more than four to six hours, or less if signs of hypoglycemia ensue) and done under close observation for signs of hypoglycemia. More than one test is usually done. Blood glucose concentrations lower than 60 to 70 mg/dl are suspected of islet cell neoplasia. (Normal fasting glucose is considered to be 90 to 125 mg/dl).⁵ Blood glucose taken during symptoms may be as low as 20 to 40 mg/dl. Serum insulin levels will be elevated. Because of different assays used by different laboratories,

normal values should be established per each laboratory, with clinical case levels compared to that normal. If the ferret with suspected islet cell neoplasia has an insulin level within the laboratory's "normal" range, repeat the assay at a later date or serially measure blood glucose concentrations to demonstrate a consistent pattern of hypoglycemia. Alternatively, measure the blood glucose and insulin levels following a controlled four hour fast.

A full diagnostic work-up of the ferret should be done, including a CBC and serum chemistries. Changes frequently seen included leukocytosis, neutrophilia, and monocytosis. There may be increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) which may reflect hepatic lipidosis secondary to chronically low blood glucose concentration or liver metastasis. Radiographs may show other changes, such as splenomegaly, or be useful in evaluating cardiac disease. Abdominal ultrasound may highlight unusually large tumors, but it is probably more useful as a pre-surgical evaluation of other organs. Hepatic lipidosis or infiltrates which may be indicative of metastasis, may be revealed. If this is the case, a liver biopsy at surgery would be recommended. Medical management includes using prednisone and/or diazoxide orally in conjunction with dietary management. Prednisone acts to increase peripheral blood glucose concentrations by inhibiting glucose uptake of peripheral tissues and increasing hepatic gluconeogenesis. Ferrets with mild to moderate clinical signs may be controlled by prednisone therapy alone, in dosages ranging from 0.5 to 2 mg/kg PO q12 hr. Start with the lower dosage, and increase if necessary. If an oral suspension is used, it should not contain alcohol. Diazoxide (Proglycem, Baker Norton Pharmaceuticals, Inc., Miami, FL) is a benzothiadiazine derivative which acts by inhibiting insulin release from the pancreatic beta cells, by promoting glyconeogenesis and gluconeogenesis by the liver, and by decreasing the cellular uptake of glucose. Usually diazoxide at 5 to 10 mg/kg PO q12 hr is added to the protocol when prednisone alone is not adequately controlling the hypoglycemia. The dosage may need to be increased gradually with the maximum of 60 mg/kg per 24 hours divided q 8 to 12 hours. Side effects of diazoxide include vomiting and anorexia. Compounding pharmacists can make a suspension from the tablet form, but then dosage consistency may be a problem. Recently doxorubicin has been tried and shows some promise. Famotidine at 2.5 mg/ferret 1 to 2 times a day may be helpful with the stomach upset and nausea which accompanies the islet cell disease.

One of the most helpful management schemes is just making sure the ferret eats frequently. Owners must be taught to see the very subtle signs of a hypoglycemic episode, and at that point, they need to induce the ferret to eat. It is not recommended to feed the ferret any foods with a high sugar or carbohydrate content, or give simple sugars such as honey or corn syrup because these foods tend to stimulate insulin secretion, which may precipitate an episode. A quality ferret food should be fed. Daily brewer's yeast with chromium picolinate, and B complex vitamins may help with appetite. Medical and dietary management may be effective in controlling signs for a number of months, or as an adjunct following surgery, but unfortunately the neoplastic process tends to progress. Other concomitant health problems may complicate the therapy. Surgery to excise neoplastic nodules or tissue is recommended. This may slow the progress and prolong life. Perioperative considerations include placement of an intravenous catheter before fasting and infusion of maintenance fluids with added 5% dextrose prior to and during surgery. Ferrets are only fasted minimally (usually no more than two to three hours) prior to surgery. Ferrets usually recover well from surgery, although fluid administration with dextrose needs to be continued until the ferret is euglycemic or eating. Food and water are normally withheld for 8 to 10 hours post surgery, but many ferrets act hungry before this time. A small meal with Nutri-Cal (Evsco Pharmaceuticals, Buena, NJ) and two to three pieces of ferret food within 3 to 4 hours of surgery has been well-tolerated in the author's experience. Post-operative analgesics such as butorphanol at 0.1 to 0.5 mg/kg IM q4h (Torbugesic, Aveco, Fort Dodge, IA) or buprenorphine at 0.03 mg/kg SC q 10 to 12 hr (Buprenex, Reckitt & Colman, UK) along with perioperative parenteral antibiotics complete the therapeutic regimen. Blood glucose should be monitored closely while the ferret is hospitalized. Many are euglycemic immediately after surgery, but many remain hypoglycemic for some time. A few may be hyperglycemic, although this appears to be only a transient rise which resolves in two-three weeks. Most ferrets treated surgically will require medical management for hypoglycemia again within two to six months. It is suggested that blood glucose be checked within two weeks of surgery, and then at two to three month intervals.⁵

Islet cell neoplasia although most often called "insulinoma" which denotes a benign tumor, should be considered to be malignant. Islet or beta cell carcinoma is frequently the histopathological conclusion. Occasionally the beta

cell carcinoma will be found in combination with beta cell hyperplasia or adenoma. Metastasis throughout the pancreatic tissue is common. Metastasis does occur to regional lymph nodes, the spleen, and/or the liver.⁵

Diabetes mellitus (DM) is uncommon, but has been diagnosed in ferrets. Some develop it secondarily to an aggressive debulking of the pancreas for islet cell neoplasia. The hyperglycemic ferrets show clinical signs similar to those of other species with hyperglycemia. Affected ferrets are polyuric, polydipsic, polyphagic, but may lose weight. They may appear lethargic, especially if they are ketoacidotic. Blood glucose will be elevated (consistently above 400 mg/dl), there will be a low blood insulin level, and consistently a glycosuria.⁶ In severe cases, ketones may be detected in urine samples. Glucagon concentration would be a good indicator to measure in ferrets with hyperglycemia, however it must be done at a laboratory with a validated assay for ferrets, and the test is not commercially available. Diabetes mellitus is either due to a lack of insulin or to a glucagonoma which causes an increase in blood glucose concentration. A normal or high insulin concentration could represent either an insulin-resistant DM or the presence of a glucagonoma. Treatment with insulin is usually instituted when blood glucose levels are consistently above 300 mg/dl and follows guidelines for cats. Therapy should be started in the hospital where blood glucose can be measured at regular intervals. An empirical dosage of 0.1 unit of NPH (neutral protamine Hagedorn) insulin per ferret twice daily may be tried, with the dosage adjusted based on blood glucose and urine glucose concentrations. Ultralente insulin given once daily has also been used.²⁷ Owners must learn to check the urine for glucose and ketones at home with urine dipsticks. If no glucose is present, no insulin should be given. If trace amounts are found, the dosage is not changed. If large amounts are found, the dosage is slightly increased. The snacking habits of ferrets seem to make regulation more difficult than in those species which will take a regular meal. Prognosis is guarded to poor as regulation is difficult.

Adrenal Neoplasia

We know how the physiology affects the disease manifestation: Ferrets are seasonal breeders, copulatory ovulators with a complex hormonal stimulation feedback system. In the absence of the gonads, the adrenal gland can respond similarly to a gonad. The adrenal gland has luteinizing hormone (LH) receptors (and in the disease, Dr. Nico Schoemaker has proven there are active LH receptors⁷) which enable the adrenal gland to produce sex steroids.⁷

At puberty and consequently breeding, sex hormone levels achieve peaks that “set the gonadostat” in the brain regulation areas (hypothalamus, pituitary). Neutering at puberty or in a breeding-age adult causes an LH surge which then acts similarly to breeding itself, which causes an LH surge. This LH surge followed by prolonged elevations of gonadotrophin releasing hormone (GNRH) due to inability to effect end-product hormone production, downregulates sex steroid production. It seems strange that prolonged elevation of GNRH causes downregulation, but that is what happens. Schoemaker examined the pituitary glands of intact or neutered ferrets, and ten neutered ferrets with hyperadrenocorticism. The ferret pituitary gland histologically was similar to the dog pituitary. In two of the ten, a tumor was detected in the pituitary gland, although these had characteristics of clinically non-functional gonadotroph tumors seen in man. In some of the ferrets, there was low pituitary immunoreactivity for gonadotrophic hormones, which was considered to be due to the feedback of autonomous steroid secretion by the neoplastic transformation of the adrenal cortex. This study concluded that the initially high concentrations of gonadotrophins resulting from castration initiated the hyperactivity of the adrenal cortex. The conclusion of this study was that because of the low incidence of pituitary tumors and the low density of gonadotropin-positive cells in non-affected pituitary tissue suggested that persistent hyperadrenocorticism was not dependent on persistent gonadotrophic stimulation.⁸ This finding contradicts the clinical finding that a medication sustaining gonadotrophin releasing hormone production in the pituitary depresses the production of sex steroids in the ferret, but explains the initial stimulation to the gland, and possibly why as the tumor progresses as it is not responsive to pituitary control. It would then follow that progression of anaplasia may be under a tumor suppressor gene control, rather than continuous pituitary stimulation. Episodic pituitary stimulation does explain why some ferrets will exhibit “rat tail” and pre-hyperadrenocorticism seasonally, before they are considered to have “adrenal disease.” In intact animals coitus triggers an LH surge, with subsequent ovulation or intromission. In males, the hormone feedback causes downregulation so the male goes out of season. In the female, pregnancy ensues in most cases. Hormonal feedback from the gonads is necessary to conclude the

breeding season. We also noted in our study using intact ferrets that 1 to 2 weeks of hot weather (over 80°F – no air conditioning) caused both the males and females to go out of season spontaneously. In the 3 years we followed intact ferrets, all would cycle out of season by late August, and none of the females developed estrogen toxicosis and anemia, despite monthly blood draws of 2 to 3 ml. (Johnson-Delaney, Oliver, unpublished)

Early spay/neutered (ES/N) animals have levels of sex steroid production seasonally similar to their intact counterparts. This was not anticipated when the longitudinal study began. Unlike intact animals that have gonadal production of sex steroids, and breed, which then down-regulates the system, the ES/N animals' adrenals respond and produce sex steroids, but no "breeding" occurs to shut the system down. The sex steroid levels continue to be produced throughout the year at a level appropriate to the breeding season level.

Post-puberty spayed/neutered ferrets have a markedly lessened hormonal cycle throughout the year, but it is still present. Sex steroids in all ferrets (altered or intact) rise at what can be considered the start of breeding season (late December - January for males; January – March for females – Seattle, WA latitude). Levels are lowest for males in late summer to early fall, and for females from September to November. Females lag behind the males sex steroid elevation by 1 to 2 months. Keeping ferrets on artificial light cycles, or supplying melatonin may suppress the sex steroid seasonal responses for awhile, but eventually the cycle continues. It may be out-of-synch with the calendar.

There is therefore a correlation between the timing of removing the gonads and the onset of "adrenal disease." Schoemaker proved this in his research.⁹ Schoemaker also explored some of the possible endocrine pathways for control (ACTH or alpha-melanocyte stimulating hormone (α -MSH)) by examining plasma levels of the hormones in neutered animals and intact animals. His conclusion was that ferrets with hyperadrenocorticism did not have detectable abnormalities in plasma concentrations of ACTH or α -MSH.¹⁰

The hypothesis therefore for the etiology of adrenal disease may be that stimulation from GNRH, LH from input via the pineal, pituitary and hypothalamus up-regulates sex steroid production in the adrenal tissue which then responds without a set-point for "shut-off": the tissue responds initially with hyperplasia.

The second hypothesis is that aberrant tumor suppressor gene(s) and/or their regulators are present, hyperplastic tissue will continue to progress to adenoma, then eventually adenocarcinoma, following models in other animals and humans. Peterson et al looked at tumor markers in ferrets, based on the work in gonadectomized DBA/2J mice that develop adrenocortical tumors expressing transcription factor GATA-4. Eighty-six percent of the ferret adrenocortical carcinomas, particularly in areas of myxoid differentiation expressed GATA-4. Normal adrenocortical cells lacked GATA-4 expression. Two other markers of adrenocortical tumors in gonadectomized mice that are co-expressed with GATA-4 are inhibin- α and LH receptor. These were co-expressed in some of the ferret tumors. No GATA-4 expression was observed in 3 cases of nodular hyperplasia, however patches of anaplastic cells expressed GATA-4 in 50% of the tumors classified as adenomas. The conclusion was that GATA-4 does function as a marker of anaplasia in ferret adrenocortical tumors.¹¹ The relevance of this shows that there may be a way of tracking and marking the tumors (prognostication), and pathways of cancer development in the ferrets is similar to that of other species. This also is suggestive of a genetic root to the development of the disease, as GATA-4 is a protein marker.

A point of management of the disease is to depress or suppress the stimulation to the adrenal gland thereby stopping sex steroid production. Likely the most crucial time to suppress the stimulation is the first stimulation that occurs at puberty (timing with first reproductive season). Blocking sex steroids from affecting other tissues can also be done, thereby decreasing clinical signs, but neither of these avenues may halt the progression of hyperplasia to adenoma to adenocarcinoma. Central (brain level) suppressive drugs such as leuprolide acetate depot formulations have been proven to down-regulate sex steroid production and decrease clinical symptoms. Melatonin implants in some ferrets have short-term suppressive effects. There are additional medications used for humans that work in ferrets for either central or peripheral sex steroid downregulation or blocking.^{12,13,14,15}

Leuprolide acetate 30-day depot formulation (Lupron 30 day, TAP Pharmaceutical Products, Inc., Lake Forest, IL) was effective in downregulating sex steroid production in intact ferrets in-season. Effects lasted 30 days. Lupron 3-month depot formulation was effective in the intact males for 75 to 90 days (January through April); but 2 females in one study returned to estrus by 60 to 75 days, so it is doubtful that the 3 month formulation will truly last for the full 3 months. (Johnson-Delaney, Oliver, unpublished).^{13,14}

Melatonin implants in one controlled study in intact males in season did not effectively decrease sex steroids.¹⁵ Others have reported clinical effects of regression of outward signs.¹⁶ Oral melatonin at 0.5 mg PO q24hr was administered to ferrets with clinical adrenal disease with elevated serum hormone levels, for one year. For up to eight months, there was clinical improvement with hair regrowth, decreased pruritus, decreased vulva/prostate size, and increase in activity level and appetite, the glands continued to grow and 17 α -hydroxyprogesterone, estradiol and androstenedione serum values continued to increase. Prolactin levels were decreased although prolactin does not appear to have a role in the disease process. The conclusion is that melatonin may have a positive effect on clinical manifestations of the disease, but it does not slow the progression. Additional therapeutics that suppress the pituitary-gonadal axis are being investigated. These include long-acting implants which may prevent the onset of the disease.

Surgery to debulk the glands may slow the progress by decreasing the tissue producing the sex steroids. A controlled clinical study has shown that without additional suppression of the hormone stimulation, ferrets who have debulking surgery as the only treatment did not live as long as those that had Lupron 30-day treatment alone. Surgery to debulk along with hormone suppression appears to have a slight edge over Lupron alone. This study followed ferrets until their deaths up to seven years post-surgery. All ferrets that had debulking surgery had rebound of increased sex steroid production by 6 to 12 months post-operatively, with return of clinical signs occurring sometime after the hormones were elevated. (Johnson-Delaney, Oliver unpublished). A recently published retrospective study of 130 cases showed that debulking was a sufficient surgical technique to allow a favorable long-term outcome when complete excision was not possible. The study did not evaluate serum hormones or if the ferrets remained disease-free.¹⁸ Both studies show that pathology of the adrenal glands at surgery did not correlate with longevity.

Data suggests that ES/N is detrimental for at least two reasons: (1) the set point in the sex steroid production feedback loop is not set – the ferret comes in to puberty and its first breeding season similarly to intact ferrets, but the system does not shut down. The stimulation has started the process. (2) time until onset of adrenal disease is shortened so that younger ferrets are affected. Adrenal disease has been documented by hormone level, ultrasound, and histopathology in ES/N ferrets as young as eight months of age (Johnson-Delaney, Oliver unpublished).

Mast Cell Tumors

Mast cell tumors appear primarily in the skin of ferrets over three years of age. They can range in size from less than 0.1 cm to 1 cm, may be raised, ulcerated, pigmented, pruritic, or just appear as an intense area of erythema. Many wax and wane. They do not seem to metastasize or be found internally. Initial treatment can be topical antihistamine cream or antibiotic ointment if the surface appears infected. If the ferret is bothered by their presence, excisional surgery can be done using a sedative and a local anesthetic infusion.

Chordomas

Masses at the end of the tail, or occasionally elsewhere on the tail or body may originate from neurologic tissue. These present as firm masses, often adherent to underlying bone. Excision is usually curative. If on the tail, it should be amputated 2 to 3 vertebrae proximal to the mass as it may not be possible on palpation and visualization alone to discern the proximal border of the tumor. Histopathology to determine complete excision is recommended.

Ferrets rarely bother sutures or incision lines, although incompletely removed tumors may cause altered healing at the site if neoplastic material is part of the closure.

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ESSENTIAL EXOTIC COMPANION MAMMAL SURGERIES

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Introduction

Whether you treat exotic companion mammals occasionally or often, there are certain surgical procedures that you will eventually be asked to perform. While the anesthesia and monitoring required for these surgeries is equally important, this lecture topic will focus on a handful of surgical procedures that are commonly encountered in practice. The emphasis will be on those concepts and practical matters that may be unfamiliar to the general practitioner. In all cases, however, gentle tissue handling and good pain control are important.

Ovariohysterectomy

Spaying is not only indicated for population control, but also to prevent aggressive behavior (rabbits, prairie dogs), urine marking and false pregnancy (rabbits), and to treat or prevent common pathologies such as uterine disease (rabbits, hedgehogs), mammary tumors (rats, rabbits), cystic ovaries (guinea pigs), and estrogen toxicity (ferrets).

Ovariohysterectomy (OVH) in these species is usually performed via ventral abdominal approach, the incision starting caudal to the umbilicus and ending cranial to the pubis. The cecum and bladder may be directly under the linea alba of herbivores and it is recommended that the body wall be elevated from the abdominal structures prior to making the initial incision. The incision should be large enough to see major landmarks and permit adequate access; a spay hook is not used so as to avoid perforating the cecum. Instead, Adson-Brown forceps are used to grasp and elevate the uterus, which is visible dorsal to (under) the cranial pole of the bladder. The surgeon must use caution in herbivores to avoid damaging the cecum, which usually lies just cranial to the bladder. To prevent blood loss in small mammals, the ovarian pedicles are individually ligated and not simply pulled from the body wall. The author uses 4-0 or 5-0 absorbable monofilament for most procedures, and occasionally uses hemostatic clips for ligation. Chromic gut suture is almost never used in small exotic mammals because of its tendency to cause caseous reactions (rabbits and rodents). Closure is generally two- or three-layer (linea/muscle, subcutaneous, and subcuticular). When properly performed, a subcuticular closure appears to cause minimal discomfort, and patients often seem unaware of its presence. Skin sutures are almost never used because rodents and rabbits tend to chew them out. Instead, tissue adhesive may be used for skin closure, and excellent pain control (buprenorphine and meloxicam) is provided.

Comments on Individual Species

Rabbit

Prone to uterine neoplasia after the age of three; endometritis, pyometra, hyperplasia, and uterine aneurysms are also reported. The mesometrium of rabbits is a site of fat storage, making it difficult to definitively find the ovarian and uterine vessels for ligation. The rabbit has two cervixes. To prevent vaginal remnant infection and the development of cervical or uterine stump aneurysms, some authors recommend ligation through the vaginal vault, removing as much of the vaginal body as possible. Oversewing the stump may prevent adhesion to the cecum or other organs. Spaying does also eliminate hormone-related aggression.

Hedgehog

Hedgehogs are prone to uterine hyperplasia and neoplasia. The uterus and ovaries are arranged like those of a cow, with the uterine horns coiled caudally, and the ovaries situated within the coil. Often, the OVH procedure can be quickly completed using 3 to 4 surgical clips.

Rat

Spaying reduces the incidence of mammary tumors in female rats from about 50% to less than 5%. The uterus and ovaries of the rat are easy to identify. Aside from the small size of some patients, the surgical procedure is simple to perform. Due to the rat's tendency to chew out sutures, some references recommend surgical staples for skin closure, however the author has not found this to be necessary, so long as good perioperative pain control is used.

Prairie Dogs

To prevent seasonal aggression, females should be spayed by the fall of their first year. The uterine horns and ovaries can be quite small, even in fully grown adults. Obesity is very common in prairie dogs, making identification of the reproductive tract difficult. However, with careful examination of the broad ligament and palpation of the periovarian fat, the uterus and ovaries can be located and removed in routine fashion.

Guinea Pigs

Ovarian cysts are common and can become extremely large. Medical therapy can provide temporary relief, but recurrence is likely without surgery. Having the first litter after six months of age (when the pubic symphysis becomes mineralized) is associated with a high rate of dystocia. Surgical sterilization may be indicated to prevent this potentially life-threatening complication. Ovariohysterectomy in guinea pigs is generally considered more difficult due to their ventrally located cecum and deep abdomen. The ovaries are extremely small may be difficult to distinguish. They may be located by first identifying the bifurcation, then tracing each uterine horn cranially. The ovaries are difficult to exteriorize, and care must be taken to avoid tearing the short ovarian ligament. Since the incidence of uterine disease in sows is comparatively low, an alternative approach advocated by some practitioners is to perform ovariectomy, removing each ovary through a small incision on the dorsolateral body wall caudal to the last rib. The advantages of this approach are that it avoids manipulation of the GI tract and improves access to the ovaries.

Chinchilla

Indications and surgical approach for ovariohysterectomy are similar to those in other small mammals: neoplasia, dystocia, and disease of the reproductive tract. As with other herbivores, care must be taken to avoid damaging the cecum. The ovarian vessels of the chinchilla are short and do not allow for exteriorization. Care must be taken to avoid tearing these vessels during ligation.

Ferret

A jill will remain in estrus until she is bred. Estrogen toxicity is likely to occur, resulting aplastic anemia, unless she is either spayed or allowed to breed. Surgical procedure is similar to that of other carnivores. Because ovariohysterectomy is usually performed by the breeder at a very young age, this procedure is rarely requested in the United States. Retained ovarian remnant is a (rare) differential diagnosis for swelling of the vulva, one of the prime indicators of adrenocortical disease in the female ferret.

Sugar Glider

The reproductive anatomy the female sugar glider is unusual: a single urogenital sinus branches into a single median and two lateral vaginas. The left and right lateral vaginas each encircle a ureter and then rejoin the median vagina proximally at the cervixes (as in the rabbit, each uterine horn has a separate cervix). Ovariohysterectomy therefore requires careful avoidance of the ureters. A midline abdominal approach is recommended, however it is complicated by the ventrally located pouch.

Castration

Indications for castration include: population control; the reduction of inappropriate urination, unwanted behavior, or aggression; odor reduction; and cosmetic purposes (sugar gliders). Unlike the situation in dogs,

castration is not indicated for the prevention of prostatic disease, but may be indicated for the treatment of testicular injury, tumor, or infection. Pet owners should be advised that sperm remaining in the vas deferens may be viable for weeks after surgery, and testosterone levels may take weeks to months to drop to negligible levels. The ideal surgical approach for orchidectomy differs greatly by species. As with spaying, 4-0 monofilament absorbable suture is the author's first choice (unless otherwise stated), and skin sutures are rarely indicated. Adequate postoperative pain control assists in preventing incisional self-trauma.

Comments on Individual Species

Rabbit

Castration prevents urine marking if performed before sexual maturity, and significantly reduces urine odor and undesirable sexual behavior. Disease of the testicle is rare, but includes trauma or abscesses (usually from bite wounds by other rabbits) and neoplasia. Tumors typically present as enlarged testis, occasionally with contralateral testicular atrophy. A midline prescrotal approach (as for the dog) is the author's preference, although a scrotal approach (as for the cat) has been described. A closed castration technique is best, and ligation of the spermatic cord close to the inguinal ring has been sufficient to prevent scrotal hernia in the author's experience. Cryptorchidism occasionally occurs in rabbits and requires a celiotomy approach.

Prairie Dog

Prevents or reduces seasonal aggression. Due to the inguinal location of the testicles outside of breeding season, an abdominal approach to surgery is usually preferred. An alternative method involves making incisions on either side of the prepuce, one over each testicle, and closing each inguinal ring afterwards.

Guinea Pig

Indicated mostly for population control, but will also control rare dominance aggression. An incision is made over each testicle, and the spermatic cord is ligated close to the body wall in closed fashion. About 50% of the testicular fat pad should be left in place and the inguinal ring should be carefully closed in order to prevent herniation of bladder, seminal vesicles, or other organs into the scrotal sac. Guinea pigs are anecdotally reported to be more prone to incisional infections than other species, thus perioperative antibiotics should be considered.

Chinchilla

Indicated to prevent reproduction and decrease undesirable sexual behavior. The surgical approach is identical to that used in guinea pigs. Additionally, however, male chinchillas should be checked for prepucial fur rings, which can accumulate and form a restrictive band.

Sugar Glider

Prohibits paired gliders from breeding. Also reduces odor and urine marking behavior, and prevents "balding" due to glandular development on the head and chest. The scrotum is located cranial to the penis, on the ventral abdomen. It is suspended on a long stalk, making scrotal ablation the preferred method by the author. However a scrotal approach to orchidectomy is also described.

Ferret

Hobs are castrated to reduce their strong odor and greasy skin secretion, and to prevent aggression toward males and unwanted sexual behavior toward females. A scrotal approach similar to that for cats is used.

Fracture Repair

Long bone fractures are most commonly encountered in the rabbit, chinchilla, and guinea pig. The principles of orthopedic repair in small mammals are very similar to those of dogs and cats, the major differences being the small size of the patient, and the ability of the patient to damage a fixation device by gnawing. Simple fractures with minimal displacement can be stabilized with splints or casts. However, where there is fracture displacement

and/or soft-tissue injury, internal fixation is indicated. Due to size limitations and lack of soft tissue, the use of plates and screws in exotic companion mammals is limited. The best solution for most long bone fractures in small mammals is external skeletal fixation (ESF). For fractures of the radius, ulna, and tibia, a Type I or Type II ESF may be applied. For humeral or femoral fractures, however, a Type I ESF is necessary due to the large muscle groups and interference from the body wall. Whenever applicable, the author prefers to combine a Type I ESF with an intramedullary (IM) pin to offer greater stability.

In the author's practice a mini hand chuck, a pin cutter, and a selection of K-wires and Steinmann pins are all that is generally needed. Using aseptic technique, an IM pin that is 40 to 50% of the diameter of the medullary canal is inserted, bringing the fracture into proper alignment. Then the proximal, extramedullary portion of the IM pin is bent over until it lies parallel with the bone, approximately 1.5 to 2 cm from the skin surface to allow for swelling and callous formation; this segment of the IM pin becomes the fixator bar. Fixation pins (K-wires, Steinmann pins, hypodermic needles) are then inserted proximal and distal to the fracture site(s), using the fixator bar as guide. Fixation pins should completely penetrate both cortices, and it is best to have two fixation pins on each side of a fracture. Where possible, fixation pins are bent until parallel with the bone and fixator bar. Once placed, the pins and IM pin/fixator bar are joined together with epoxy putty, polymethylmethacrylate, or thermoplastic mesh.

Intramedullary pinning and external fixation do not interfere with joint function and permit normal use of the limb. Patients often begin to use the limb within days of surgery, translating to faster healing. The fixator can be protected from damage by wrapping it with duct tape and/or providing an E-collar or yoke. Deterrents such as bad-tasting pastes and sprays appear to have no effect on rabbits and rodents. The fracture repair should be kept clean and dry; dust bathing (chinchillas) should be limited to the minimum required for normal grooming. Broad spectrum systemic antibiotics that reach effective levels in bone (e.g. chloramphenicol) are recommended, particularly with open, contaminated wounds. The hospital stay should be kept to a minimum, however fluid and nutritional support and analgesia are provided until the patient is eating and drinking voluntarily. Patients should be confined to a small, one-level area during convalescence. Follow up radiographs are made at 4 to 6 weeks postoperatively and every 2 weeks thereafter until there is radiographic evidence of fracture union.

Abscesses of Rabbits

Abscesses of rabbits are associated with a particularly high rate of recurrence. Rabbits form a thick abscess capsule that harbors bacteria isolating them from antibiotics, their thick caseous pus does not drain adequately and their skin wounds often heal before second intention healing can force out infection. As such, abscesses of rabbits should be resected *en bloc*, as one would remove a tumor. When a rabbit abscess occurs in an area that makes complete removal difficult (e.g. the head, distal limb), it is still best to treat the abscess like a locally invasive, non-metastatic tumor. Attempt to remove the abscess with minimal surgical margins and without rupturing it. If the abscess is in an anatomically difficult area where the surgeon is not comfortable trying to excise the entire capsule, then dissect and remove the abscess down to bone, curette the bone to remove affected hard tissue, and remove any teeth that are involved, if the jaw is the site of the infection. Copiously irrigate to decrease contamination from the ruptured abscess, and (very important!) remove all abnormal tissues, soft and hard. Residual microscopic disease is then treated by open wound management ("marsupialization") or wound packing with primary closure.

Marsupialization means to delay wound healing by suturing the skin to the abscess wall or whatever tissue is left surrounding the resection bed. The wound is packed with antimicrobials (povidone iodine ointment, granulated sugar, honey, etc.) and flushed daily, and the patient is placed on systemic antibiotics until the wound has completely healed. By allowing prolonged management of the open wound, residual necrotic tissue is debrided, and healing occurs gradually. Infection is eliminated before the wound closes, which takes days to weeks.

An alternative to this method is to implant antibiotic-impregnated polymethylmethacrylate beads (AIPMMA), which release a relatively high concentration of antibiotic locally with little systemic absorption. This allows primary closure of the site and eliminates the need for open wound care. The rabbit is still placed on systemic

antibiotics for two weeks, but long term therapy is not necessary as the beads release antibiotics for many months or even years. These beads are usually left in place however removal is indicated if infection reoccurs. Beads can be made in the hospital or purchased commercially.

Urolith Removal in Sows

Urolithiasis is particularly common in guinea pigs. Female guinea pigs with “urethral” stones may present with two distinct conditions: (1) bladder stones that lodge in the urethra, and (2) calculi that form in a prepuccial vestibule, the *praeputium clitoridis*, which lies distal to and covers the urethral orifice. The two conditions can be distinguished by subtle differences in presentation and radiographic appearance.

Guinea pigs with either condition may exhibit weight loss, anorexia, hematuria, or discomfort during urination (e.g. vocalization, erratic movements). Clinical signs are more common and severe with urethral stones, whereas prepuccial stones may be noticed as an incidental finding during exam or radiographs. A sow with a urethral stone will usually exhibit straining and have difficulty emptying the bladder. In contrast, a sow with a prepuccial stone can usually produce a normal urine stream and completely empty its bladder. Urethral stones may not be palpable, but prepuccial stones can often be palpated cranioventral to the urinary orifice. Radiographically, stones that form in the bladder and lodge in the urethra are oval or round, but prepuccial stones are typically flattened or concave along their dorsal surface, where they lie in contact with the clitoris and urethral orifice. Prepuccial stones also appear closer to the skin’s surface on radiographs than do urethral stones.

The clinical importance of distinguishing between the two presentations is that urethral stones may need to be retropulsed into the bladder for removal via cystotomy, but prepuccial stones will not. Prepuccial calculi, as well as urethral calculi that lodge in the distal urethra, can usually be removed via the urinary orifice using an ear curette, fine forceps, sterile lubricant, and sterile saline. Occasionally, it is necessary to incise over a vestibular stone in order to remove it. Closure of the incision is not mandatory; stricture of the urethra is unlikely so long as a longitudinal incision is used.

The etiology of urolithiasis in guinea pigs is unknown. A correlation with the “Pigloo” hide box suggests that affected guinea pigs may be sedentary and not drink enough water, promoting the formation of stones.

Adrenalectomy in Ferrets

Adrenocortical disease (ACD, adrenal gland disease, hyperadrenocorticism) is a common malady affecting middle-aged to older ferrets with no sex predilection. Adrenocortical disease can affect ferrets under a year old. First reported in ferrets in 1987, the prevalence of ACD is reported to range from 0.55% to 25%. Ferret adrenal disease is different from human, canine, and feline hyperadrenocorticism because in ferrets adrenal sex hormones are overproduced instead of cortisol.

Surgery is the treatment of choice for ACD in ferrets that are otherwise healthy. For the surgical approach, make a ventral midline incision, extending from the xyphoid as needed to allow a thorough examination of the abdomen. Both adrenal glands should be observed and palpated. They are often embedded in fat and lie at the cranial pole of the kidneys. Normal adrenal glands are whitish pink, 2 to 3 mm wide, and 6 to 8 mm long. Not all diseased adrenal glands are enlarged, and palpation alone is not enough to evaluate for disease. Thus, if the entire gland is not visible, use mosquito hemostats and cotton-tipped applicators to carefully dissect the thin layer of peritoneum and fat surrounding the gland. On the right side, incise the hepatorenal ligament and use it to retract the caudate lobe of the liver cranially. Cysts, yellow-brown discoloration, irregular texture, and enlargement are indications for removal of the gland.

If only one adrenal gland is diseased, there is debate as to whether it is best to leave the normal gland, to remove half of it, or to remove it entirely. If both glands are diseased, complete removal of both glands should be attempted. Often the left adrenal is completely removed and the right adrenal is debulked by placing hemostatic clips across it to allow for 50 to 75% removal. Alternatively, the capsule is incised and the glandular contents are shelled out. Subtotal adrenalectomy usually does not result in the need for long-term postoperative steroid therapy. If the right adrenal gland is debulked (less risky than complete removal) signs of ACD may return, necessitating repeat surgery or medical therapy.

Removal of the left adrenal gland is usually uncomplicated. The phrenicoabdominal vein (adrenolumbar vein) courses over the ventral surface of the gland. This is ligated at the cranio-lateral surface of the adrenal gland, and the cranial, lateral, and caudal aspects of the gland are dissected. The gland is elevated and gently undermined, and the phrenicoabdominal vein is traced to the vena cava and inspected for tumor invasion. If no tumor invasion is detected, the vein is ligated and the gland is removed.

Right adrenalectomy is often more difficult because of adherence of the gland to the wall of the vena cava and the greater potential for vascular invasion. Magnifying loupes, microsurgical instruments, and vascular clamps are often needed. If the tumor is small, often it can be almost completely freed from the wall of the vena cava with gentle dissection. If so, place hemostatic clips between the gland and the cava and resect the gland. Frequently, however, the gland cannot be freed from the vena cava because of tumor invasion, or it is located mostly on the dorsal aspect of the vessel. For these cases, more advanced surgical techniques may be needed.

Partial or total occlusion of the vena cava may be necessary to allow removal of the gland with a portion of the caval wall. Temporary occlusion can be accomplished with a small vascular clamp (neonatal Satinsky clamp) or with oversized braided suture material (e.g. 2-0 Vicryl) tied around the vessel in a "shoelace" knot. The defect in the caval wall can be sutured with 6-0 or smaller monofilament suture. The time that the vena cava is occluded should be limited. Before restoring blood flow, place a piece of gelatin sponge over the suture line.

With extensive vascular invasion of the vena cava, resection and anastomosis may be indicated. In some cases, complete ligation of the vena cava may be successful, however predicting whether a ferret will survive complete ligation at surgery is impossible. Approximately 25% of ferrets that undergo complete surgical ligation of the vena cava will experience acute venous hypertension and resultant renal failure. Therefore, surgical procedures that preserve the cava should be attempted before ligation. Research has demonstrated that in most ferrets tested there is collateral circulation branching from the vena cava, through the vertebral sinus, the azygos vein, and back to the vena cava cranial to the ligation. Why some ferrets survive ligation while others do not is unknown. One theory as to why some ferrets survive complete vena cava occlusion is that the adrenal tumor has already created a partial occlusion, allowing for collateral circulation to have gradually developed prior to vena cava ligation. Recently, a technique has been described wherein an ameroid constrictor ring is placed on the vena cava to provide more gradual occlusion. A second surgery is then performed weeks to months later to remove the right adrenal and vena cava segment intact.

Cryosurgery, laser surgery, and radiosurgical ablation of the right adrenal gland have been reported. With any of these methods, it may be difficult to evaluate how completely the adrenal tumor has been destroyed. Concerns about thermal damage to the vena cava exist with laser or radiosurgery, but not with cryosurgery. Freezing kills adrenal tumor cells. It also kills caval endothelium, however vessel wall integrity remains intact thanks to its elastic structure. After cellular death by freezing, elastic collagen serves as the matrix for new endothelial growth. Some controversy exists about cryosurgery of the adrenal gland as a recent study suggests that the addition of cryosurgery to partial resection has a negative prognostic indicator for long-term survival. Although complete tumor resection is the goal of surgical treatment, partial resection seems to be sufficient to achieve long-term survival, especially for tumors involving the right adrenal gland. Regardless of the method of tumor removal used, a surgical biopsy is recommended in order that histopathology of the tumor can be performed.

Insulinoma

Pancreatic islet beta cell tumors, more commonly known as insulinomas, have been well recognized and well documented in ferrets over the last 20 years. Insulinoma nodules within the pancreas secrete high levels of insulin and cause hypoglycemia. Clinical signs include lethargy, weight loss, weakness, ptyalism, bruxism, seizures, and death. Treatment modalities include medical therapy, chemotherapy, surgery, and dietary changes.

Surgical resection of pancreatic nodules or partial pancreatectomy is considered the treatment of choice for greater clinical resolution and longer survival times. An intravenous catheter should be placed prior to surgery, and 5% dextrose should be administered perioperatively to prevent a hypoglycemic crisis. A ventral midline incision is extended from the xyphoid caudally to allow adequate exposure. Careful visualization with gentle palpation of the pancreas is performed to locate pancreatic nodules. These may be removed individually or, in the case of multiple nodules, a partial pancreatectomy can be performed. Insulinoma nodules dissect easily from healthy pancreatic tissue. Bleeding is minimal and can be readily controlled with hemostatic sponge or surgical clips. Partial pancreatectomy—removal of one third to one half of the pancreatic mass—can be performed as a supplement to nodulectomy. Surgical debulking reduces the amount of pancreatic tissue available for future tumor development. The left limb of the ferret pancreas is easier to resect than the right limb, as the right limb lies within the mesoduodenum, closely associated with the duodenal vasculature. In one study, ferrets with partial pancreatectomy had longer survival times than those with nodulectomies. This is probably because microscopic tumors can be missed through nodulectomy alone. A full abdominal exploratory is recommended to evaluate for potential metastasis and concurrent conditions (e.g. adrenal disease). Biopsies of suspicious tissues should be collected for histologic evaluation.

The goal of surgery is to have patients normoglycemic following surgery, however some may remain hypoglycemic and many will have a recurrence of clinical signs within several months because of tumor metastasis. Case studies have demonstrated that as many as 52% of ferrets remain hypoglycemic following surgery, and reported disease-free intervals range from 0 to 23.5 months. Because of likely recurrence, owners should be advised that surgery is not curative but rather it may temporarily stop or slow the progression of disease and provide a longer disease-free interval than medical therapy alone. In one study, nodulectomy combined with partial pancreatectomy had a significantly longer median survival time (668 days), compared with nodulectomy alone (456 days) or medical treatment only (186 days).

Although some patients may need continued medical management of hypoglycemia postoperatively, clinical signs can usually be controlled on lower doses of medication than before surgery. In some patients, iatrogenic hyperglycemia may be exhibited after partial pancreatectomy, but this is usually transient and resolves within a few weeks without major treatment.

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