Zoological small mammal species are commonly encountered in veterinary practice and include those kept as pets, maintained by laboratories and zoological collections, and those encountered as free-living species. Effective protocols for analgesia and anesthesia are critical to the provision of a high level of medical and surgical care for these species. Pain can have serious negative implications for healing and well-being in small mammals, especially those susceptible to stress-associated morbidity. Pharmacologic protocols customized to small mammal species in order to control noxious stimuli at multiple points within the pain pathway are useful tools when providing analgesia. Additionally, sedation and anesthesia can provide a safe and effective means to facilitate diagnostic testing and to perform treatments that would otherwise be difficult or unsafe to perform.

When developing practice protocols for anesthesia of exotic mammals, factors pertaining to equipment availability and skill level of the animal care team must be considered. The small size of most exotic mammals often correlates with increased metabolic rates compared to dog and cat patients which can predispose them to hypothermia and hypoglycemia during anesthesia. Additionally, responses to medications and anesthesia are less predictable in small mammals. Maintaining a patent airway via endotracheal intubation, achieving vascular access for fluid and drug administration, and close patient monitoring is optimal but often difficult to achieve in these patients. Development and implementation of established, well-practiced protocols will minimize time and risk to the patient associated with anesthesia.

Pre-anesthesia: Patient evaluation and preparation
Prior to anesthetizing a patient, a complete medical history, including assessment of husbandry, should be collected. Obtaining a detailed description of the patient’s husbandry, including information pertaining to diet and enclosure, may provide valuable clues as to the cause of the pet’s presenting complaint which should be considered prior to anesthesia. Additionally, questions should be posed to the owner as to the signs the animal has been exhibiting, the duration and progression, as well as any therapies or care that have been implemented at home or by another veterinarian. Whenever possible, a complete physical examination should be performed. It is important to visually assess the patient prior to a hands-on physical exam. Many small mammals are stressed when in unusual situations and are intolerant of handling. As patients in critical condition may decompensate from a simple physical examination, decisions must be made as to how much the animal can tolerate at any given time during treatment. It may be necessary to perform diagnostic testing and treatment administration in a stepwise fashion, allowing the patient recuperation time between handling periods.

A balance must be achieved which minimizes the stress of the patient while allowing a thorough, efficient physical assessment. Sedation or general anesthesia may be warranted but is not without challenge or risk. At a minimum, an accurate weight on a gram scale and assessment of biological parameters including heart rate and respiratory rate should be obtained. Measurement of body temperature should also be recorded if feasible.

Ideally, pre-anesthetic assessment would include a complete blood count and biochemical profile. Minimally, the packed cell volume, total protein, and blood glucose should be measured. A volume corresponding to 1% of the total body weight (kg) can be collected safely from small mammal patients and commercially available analyzers have the ability to process small samples. However, consideration of the expected blood loss during upcoming surgical procedures may dictate that pre-anesthetic laboratory assessment be performed in advance of planned surgery to allow for replenishment of total blood volume and components. Additionally, sample collection in non-anesthetized patients is difficult or unsafe in certain species, such as small rodents and hedgehogs, making pre-anesthetic hematology impractical.

Patient fasting prior to anesthesia is neither practical nor necessary when working with exotic mammals. Rabbits and rodents lack the ability to vomit, although regurgitation can occur. Therefore, the goal of limiting food consumption prior to anesthesia is to keep the mouth clear of food which might be aspirated during intubation or during anesthetic maintenance. Small exotic carnivores should be fasted, but the fast is limited to 2-4 hours prior to anesthesia which allows the stomach to empty while avoiding complications associated with hypoglycemia. The pre and post anesthetic environment should be quiet, warm, with minimal visual and auditory stimulation to prevent stress induced catecholamine release. If blood loss is expected during the procedure, administration of fluids, usually by subcutaneous route, is recommended 2-3 hours prior to anesthesia (10 ml/Kg). If the procedure is likely to cause pain or if the patient’s condition warrants analgesia, preemptive pain management is implemented ½-1 hours prior to anesthesia. Pain should be managed post operatively at the same dosages. Frequency of dosing depends on the level of pain and sedation of the patient but is usually every 4-8 hours.

Establishing vascular access for parenteral fluid and drug administration is necessary based on the patient’s condition and length of anesthesia. Ideally placed prior to anesthetic induction, placement of catheters in non-sedated, fractious animals may not be feasible. In those cases, pre-anesthetic sedation may be used or the catheter should be placed after induction. Intraosseous catheter placement is
Anesthetic induction and maintenance

Sedation protocols may provide enough of a calming effect on exotic mammal patients to allow necessary exams, testing, and procedures. Therapeutic combinations using an opioid with a short-acting benzodiazepine, such as midazolam, are well tolerated. Clinical effects are generally apparent within 15 minutes after administration and last 1-2 hours. Sedation protocols may be used in lieu of anesthesia or may be used as a premedication to decrease the amount of inhalation agent necessary for anesthetic maintenance.

Due to the small size of many of these patients and the need for rapid adjustment of anesthetic depth or recovery, inhalation agents are preferred for use in exotic mammal patients. Isoflurane gas is well tolerated, cost effective, and readily available. Sevoflurane is also commonly used and offers more rapid induction. Mask induction is preferred in small mammals as it allows for close control of the patient. Rabbits will breath-hold during induction if exposed to high concentrations of isoflurane. To minimize this effect, induction is best done with incremental increases in isoflurane concentration. Many exotic mammals display an excitation phase when being induced. Secure restraint of the patient is required to prevent injury during this period. Conversely, anesthetic chambers may be used for induction of stressed or fractious animals but should only be used in well ventilated areas. Sterile ophthalmic lubricant should be applied to the eyes of the anesthetized patient to prevent corneal drying or abrasion.

Mask administration of maintenance anesthesia is acceptable in exotic mammals if the total anesthetic time is brief or if intubation of the patient is impractical. However, if an extended duration of anesthesia is necessary or if there is any concern regarding the patient’s ability to self-ventilate, intubation should be performed. Intubation of ferrets is performed in the same manner as in cats, using a 2.0-3.0 ID endotracheal tube. Because of the long, narrow oral cavity in rabbits, visualization of the larynx is difficult. Intubation may be performed blindly or with the aid of an endoscope using a non-cuffed, transparent, 2.0-3.0 ID endotracheal tube. The endotracheal tube is secured in place routinely but care should be taken to avoid impinging on the tube diameter. Alternatively, a tape butterfly secured to the tube can be sutured to the patient’s lip to prevent the tube from being displaced during patient manipulation. Intubation of rodents is often not feasible due to their small size. Small rubber tubing or large IV catheters can be converted into micro-endotracheal tubes for these patients. Laryngeal masks, developed to be inserted into the oropharynx of small mammals and fit over the larynx, have been used with some success in patients where intubation was not possible. Rabbits and rodents are obligate nasal breathers. Administration of inhalation agents via a mask covering the nose allows for access to the oral cavity during dental and other oral procedures. If a mask is used and assisted ventilation is necessary, the mask should fit tightly around the nose and mouth as manual ventilation is performed. In these instances, gas is likely to enter the stomach and will need to be expelled.

Injectable anesthetic agents

Injectable anesthetic agents are often used in combinations to achieve muscle relaxation, loss of consciousness, as well as anesthesia in small mammal patients. Drugs such as ketamine, telazol, dexmedetomidine, xylazine, and propofol are easy to administer, cost effective and require little equipment to use. However, disadvantages to injectable protocols include the inability to modify anesthetic depth once the drugs are administered and relatively long anesthetic recovery times if reversal agents are not administered. Additionally, many anesthetic pharmaceuticals are controlled, requiring specific storage and licensing. Dosing is available for many common anesthetic agents used in exotic mammal practice and practitioners should consult an appropriate formulary when developing individual patient protocols.

Anesthetic monitoring

Cardiopulmonary arrest associated with anesthesia is often treatable in veterinary patients if detected rapidly. Trained personnel dedicated to patient monitoring is critical to safe anesthesia. The same basic principles of monitoring anesthesia in domestic animals apply to monitoring of exotic mammals. Reflexes are often good indicators of anesthetic depth including the pedal withdrawal reflex and auricular reflex (rabbits). The loss of the palpebral reflex indicates medium anesthetic levels. Eye position is also an indication of
anesthetic depth. As the animal is induced, the pupil is centrally located. As anesthetic depth reaches a light to medium level, the pupils move ventrally. Once deep surgical anesthetic depth is achieved, the pupil returns to a central location. This may indicate a depth that is deeper than needed for the actual procedure.

Monitoring of the patient is begun at the onset of induction or as soon as practical. Equipment used for monitoring small mammal patients includes an ECG, thermometer, pulse oximetry, Doppler monitor, pediatric stethoscope, +/- esophageal stethoscope. Charting anesthetic parameters helps the anesthesiologist to identify trends in the patient which could foretell a problem. Emergency resuscitation medications should be available as well as any reversal agents if injectable anesthetic agents are being used. Doses are either posted or calculated for the patient prior to anesthesia. Emergency medications used for resuscitative measures in small mammals are the same as those used for other species. However, glycopyrrolate is used in rabbits suffering from bradycardia as they are less responsive to atropine.

Anesthetic recovery and post-operative care
Following anesthesia, patients should be monitored closely and securely restrained until they can maintain a sternal posture and are responsive to mild stimuli. The oral cavity should be cleared of debris or mucus that may have accumulated during the procedure. Once fully recovered, food should be offered. Patients that do not self-feed within a few hours should receive assisted feedings. Small herbivores will also benefit from gastrointestinal prokinetic agents if fecal production does not resume. Analgesia, antibiotics, and other therapeutics should be provided as necessary including continued fluid therapy and supplemental heat.

The pain pathway
As an unpleasant sensory, and emotional, experience associated with actual or potential tissue damage, pain is associated with surgery and trauma, but is also associated with many disorders and diseases of small mammal patients. Physiologically, individuals feel pain to allow for behavioral responses to avoid painful stimuli and to identify physical ailments. However pain also has negative effects on homeostasis and healing, including immune system modulation and decreased food consumption. Ongoing pain results in guarding or altered use of the injured area leading to disuse atrophy. Pain may also lead to hypoventilation, causing hypoxia and respiratory acidosis.

Recognition of pain in small mammal patients
Assessment of pain is affected by species differences, individual tolerances, and the ability of animals to mask signs of pain. Many times the only indication of pain in small mammals is a behavioral change. Behaviors associated commonly with pain in ferrets and rabbits include depression, immobility, hiding, and decrease in grooming activities. Anorexia and disinterest in the surrounding environment may also be noted. Small herbivores will sometimes exhibit bruxism in response to pain. Recognition of pain is often underestimated due to the reliance upon observed behaviors to detect pain and the subjective nature of these observations.

Palpation is a useful tool for pain detection. The fleshy part of the 2nd and 3rd fingers are best suited for palpation due to the more sensitive nature of these digits and digital pressure required to blanch the ends of the fingernails should be applied. A systematic approach to palpation will allow for detection of areas that generate a reaction which should then be explored through additional palpation, range of motion manipulations, or other diagnostic modality. It is important to learn the normal behaviors of the species being evaluated so that deviations from this behavior can be recognized. Ideally, a pain scoring system should be developed for consistent patient evaluation and staff use. As patient status changes, so can pain perception making re-evaluation necessary. In general, if an animal’s lesion would be painful to a human with the same lesion, if the lesion is damaging to the tissues, or if the animal is displaying behavior that may be indicative of pain, then the presence of pain should be assumed and analgesia provided to the patient.

Approach to analgesia
Analgesic modalities target the pain pathway at one or more levels. A multimodal approach to analgesia provides optimal pain management by impacting multiple steps along the pain pathway including the transduction, transmission, modulation, and perception of a noxious stimulus. Multimodal analgesia allows individual analgesic modalities to become synergistic, or additive, when used together which prevents unwanted side effects associated with larger drug doses necessary for one drug to achieve the same effect. Thermal therapy (ice, heat) and massage therapy target the pathway at the level of transduction of the noxious stimulus, preventing the conversion and perpetuation of the electrical impulse. Local anesthesia impedes transmission of the impulse from the periphery to the spinal cord. Nonsteroidal anti-inflammatory drugs modify both transduction and transmission by inhibiting steps in the arachidonic acid inflammatory pathway. Opioid analgesics have effects at all levels of the pain cascade. Administration of analgesia before pain is perceived by the patient helps to stabilize the maintenance phase of anesthesia, reduces the total amount of analgesic medication needed to control pain, prevents wind-up pain, and decreases patient morbidity associated with surgery or anesthesia.
Analgesic drugs used in small mammals

Opioids – Three types of opioid receptors are expressed in veterinary patients; μ (mu), κ (kappa), and δ (delta). Understanding the distribution of these receptors helps guide analgesic protocols however continual patient assessment and therapeutic adjustment is warranted when working with individual cases. When administered appropriately, opioid analgesics are safe and effective in managing pain. Fentanyl, hydromorphone, morphine, buprenorphine, and butorphanol are the most commonly used opioids in veterinary medicine. Tramadol, a synthetic opioid, is also gaining popularity as an effective analgesic. Opioid analgesics tend to have a rapid onset and are reversible, making them ideal for controlling pain in critical patients. Butorphanol, an agonist-antagonist, is a short acting, fast-onset opioid that provides analgesia for visceral pain but not somatic pain. Due to its short action, re-dosing is frequent (2-4 hours); otherwise a constant rate infusion is necessary for prolonged analgesic effect. Buprenorphine is a mixed agonist-antagonist that is slow in onset but longer acting, generally re-dosed every 4-8 hours. Transmucosal dosing has been reported in small mammals but the efficacy of buprenorphine administered by this route is questionable and the dose administered is significantly higher than parenteral routes. Tramadol provides an oral option for opioid administration and may be compounded into suspension but is bitter tasting, requiring use of a strong flavoring for oral dosing to small mammals. While all opioids may have sedative effects in small mammal patients, buprenorphine is associated with decreased gastrointestinal motility. Despite historical concerns however, opioid analgesics do not cause respiratory depression in small mammal patients if dosed appropriately.

NSAIDS – Nonsteroidal anti-inflammatory drugs inhibit cyclo-oxygenase (COX) enzyme in the arachidonic acid pathway, thereby inhibiting production of inflammatory mediators such as prostaglandin. COX-1 has historically been associated with homeostatic functions in the body such as protecting the gastrointestinal tract and kidneys, maintaining platelet function and macrophage differentiation. COX-2 is involved in inducing prostaglandins that mediate inflammation, pain, and pyrexia. This clear functional distinction between these enzymes is unlikely but the negative side effects associated with NSAID administration that include gastrointestinal ulceration, renal damage, and bleeding, are associated with COX-1 inhibition. Therefore, many NSAIDS used today are COX-2 specific (COX-1 sparing). NSAIDs should not be used in small mammals with known renal disease or those with gastrointestinal bleeding. Meloxicam is the most commonly used NSAID in small mammals and it has primarily COX-2 inhibition. Oral and injectable formulations are available. Dosing is variable but published doses are available for all small mammals. Ferrets possess limited ability for glucuronide conjugation which prolongs the duration of action of NSAIDs, therefore caution must be used when using these products in ferrets. Carprofen is available in both oral and injectable form and has weak inhibition of both COX-1 and COX-2 pathways. However, it has good anti-inflammatory activity and is safe for use in ferrets, rabbits, and rodents. Ibuprofen is well tolerated by rabbits and rodents, but should not be administered to ferrets. Gabapentin is used primarily for neuropathic pain and is synergistic with other NSAIDs when used concurrently.

Local Anesthetics – Local anesthetics, such as lidocaine and bupivacaine, provide good regional analgesia as well as local anesthesia. These can be used as an infiltrate at an incision site, in ring blocks, as a tissue infusion or topical wash, and in epidural application. The total dose used should not exceed published doses for systemic administration of either drug (1 mg/kg). The addition of an opioid to the infusion may also extend the duration of the local anesthesia provided. Preservative-free morphine (0.1 mg/kg) combined with bupivacaine 0.123% (0.1 mg/kg) is used for epidural anesthesia which is performed routinely.

Nerve Blocks – Dental disease is common in rabbits and rodents, often necessitating oral surgery and dental extractions. Dental blocks administered using lidocaine and bupivacaine are an important component of multimodal analgesia perioperatively. Controlling pain in these patients will allow them to recover faster and return to self-feeding. Regional anesthesia is achieved through 5 nerve blocks in the rabbit patient; infraorbital, mental, mandibular, maxillary, and palatine. Techniques for applying these blocks are described in Lichtenberger and Ko.

Ancillary therapy

Thermal therapy, using both heat and cold, provides targeted therapy to painful tissue. Cryotherapy is often used during the first 24-48 hours post tissue injury to provide analgesia and control inflammation. Ice packs applied to a surgical incision or inflamed tissue for 10-15 minutes 3-4 times daily controls edema and postoperative swelling. Applying heat to damaged tissue will promote tissue healing and increase circulation once the acute inflammatory phase has resolved. Thermal therapy is especially useful when preparing a patient for physical therapy. Both heat (prior to) and cold (following) can be used in conjunction with physical therapy to improve function and build strength in a limb following an injury. Passive range of motion exercises helps preserve normal joint function while the patient is recovering from an injury but care must be taken to prevent exacerbation of the injury or discomfort to the patient. Message therapy provides pain relief, reduces stress, and can reduce edema. It should be performed in a controlled, gentle manner. In small herbivores, gentle massage of the abdominal wall increases vagal activity which improves gastric motility. Acupuncture has modulating activity on the peripheral, central, and autonomic nervous system with studies in animals showing that those patient undergoing treatment experienced analgesia and more rapid return to function. Therapeutic laser therapy has been shown to have a positive impact on wound and bone healing by altering oxygen utilization in mitochondria, blood flow through angiogenesis and
vasodilation, and axonal sprouting both centrally and peripherally. Associated with few risks, this modality controls pain and inflammation while encouraging normal neurological function.

References
Emergency Assessment and Critical Care of Exotic Herbivores
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Providing veterinary care to exotic pets is both rewarding and challenging, offering the veterinary care team the chance to work with a wide variety of species while also requiring species-specific knowledge in order to provide quality care. Veterinary hospitals engaged in providing routine and critical care for exotic pets must adopt special accommodations and a commitment to educating all members of the veterinary care team about these unique pets. Physical assessment and diagnostic evaluation of exotic pets is often time intensive due to the need to obtain an in-depth history and the sometimes fragile state of these patients. Critical care is an integral part of disease management of exotic pets. The nature of these species and the fact that they are fairly recently domesticated dictates that they hide their illness until they have decompensated. Owners need to be aware that their pet is in serious condition but by providing critical care, the veterinary care team is able to provide them with the best chance for their pet’s recovery.

Preparedness
Many exotic pets requiring hospitalization and nursing care are presented in critical condition. Immediate and efficient implementation of triage and care protocols requires a dedicated, well-stocked, and organized clinical space with established roles and protocols for care team members. These preparations should be established well before the first critical patient is presented. Work with your care staff to create a plan to respond to medical emergencies. Most of the supplies and equipment used for emergency care of traditional pets can be used to care for exotic pets, but some additional supplies will be needed. Prepare a space in your facility that is ready to care for exotics. Include small gauge needles and small syringes, small endotracheal tubes, and drug doses for exotic species in your crash cart. Organize and hold training sessions to practice emergency techniques on exotic species, using cadavers or models to hone your skills and those of your support staff. Every good team has members that know their role in an emergency and are prepared to perform it. Make sure your team members are ready.

Critical care of the exotic small mammal herbivore
Rabbits and rodents, such as guinea pigs, chinchillas, degus, prairie dogs, rats, mice, hamsters, and gerbils, are often presented to small animal or exotic animal practices for routine care, basic and advanced surgical procedures, as well as for critical care. An important component of veterinary care is providing the owner with information regarding appropriate husbandry, dietary needs, preventative health care, and discussing clinical signs that, when observed in their pet, constitute the need for emergency and critical care. Small exotic herbivores, such as rabbits, guinea pigs, and chinchillas, are exquisitely sensitive to environmental and physiological stressors. Because of the resultant catecholamine induced physiology, gastrointestinal motility disorders often compound the animal’s clinical condition, regardless of the underlying pathology or etiology. In these situations, implementation of critical care early after the onset of clinical signs can improve the patient’s chances of stabilization and effective disease management.

Husbandry and history
Obtaining a detailed description of the patient’s husbandry, including information pertaining to diet, enclosure, and environment, may seem minimally important in the face of an emergency, but valuable clues as to the cause of the pet’s presenting complaint may be gleaned from the information provided. Additionally, questions should be posed to the owners as to the signs the animal has been exhibiting, their duration and progression, as well as any therapies or care that have been implemented at home or by another veterinarian. A detailed history can be collected by hospital staff while a triage exam is performed so as not to delay the provision of care to a critical patient. Developing a pre-printed history form will facilitate this process by identifying problems in husbandry to help focus your exam and make specific care recommendations. Additionally, if concerns regarding the patient’s husbandry are addressed prior to the onset of problems, you have provided your client with excellent preventative health care for their pet.

Triage exam
Patient assessment is part of a good triage examination whether the patient has just arrived for an emergency or it is being evaluated after a night of hospitalization and care. It is important to visually assess the patient prior to a hands-on physical exam. Many exotic herbivores are stressed when in unusual situations and are intolerant of handling and the stress it induces. As patients in critical condition may decompensate from a simple physical examination, decisions must be made as to how much the animal can tolerate at any given time during treatment. It may be necessary to perform diagnostic testing and treatment administration in a stepwise fashion, allowing the patient recuperation time between handling periods. Some animals benefit from sedation or anesthesia to minimize perceived stress.

Physical examination should be performed with the animal resting on a firm, stable surface. Wrapping the patient in a towel can provide comfortable restraint. Small rodents such as mice and hamsters may need to be scruffed to achieve secure restraint but this...
will also increase the patient’s stress level. Conversely, the handler may wear a pair of thin leather or thick gardening gloves to handle particularly fractious rodents. While rodent teeth can still penetrate through these gloves, the animal is more likely to bite the glove and not the examiners hand. A balance must be achieved which minimizes the stress of the patient while allowing a thorough, efficient physical assessment. Sedation or general anesthesia may be warranted. Unfortunately, anesthesia of these small patients is not without challenge or risk. In all but the larger patients, intubation is not feasible and it is more difficult to achieve vascular access, prevent hypothermia, and generally monitor the patient while under anesthesia. Inhalant anesthetic agents, such as isoflurane or sevoflurane, offer the advantage of allowing rapid adjustments to anesthetic depth and patient recovery but are also associated with potential cardiopulmonary depression.1 Combining inhalant anesthesia with sedatives helps to ‘balance’ the anesthesia to provide desired affect (unconsciousness, decreased response to pain, muscle relaxation) while minimizing potential adverse effects. Midazolam, a short-acting benzodiazepine, is useful in rabbits and rodents as a pre-anesthetic agent or as a sedative for non-painful procedures or handling. When combined with an opioid analgesic such as buprenorphine or butorphanol, many small herbivores will become calm and comfortable enough to allow for diagnostic sample collection, positioning for imaging, and catheter placement. Alpha-2 agonists such as dexmedetomidine may also be used to provide good muscle relaxation but are associated with respiratory depression and bradycardia.

Basic biological parameters including heart rate, respiratory rate, body temperature, mucus membrane color, capillary refill time, and blood pressure should be evaluated, if feasible, to assess the patient’s overall condition and perfusion status. Table 1 summarizes biological parameters for common small herbivore pet species. Obtaining an accurate weight, best performed with the use of a digital gram scale, is essential for complete patient assessment and for implementing medical therapy.

Table 1: Biological parameters for exotic pet herbivore species.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Life Expectancy</th>
<th>Heart Rate (beats/min)</th>
<th>Respiratory Rate (breaths/min)</th>
<th>Temperature degrees F (C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbits2</td>
<td>6-13 years</td>
<td>130-325</td>
<td>30-60</td>
<td>100-103° (37.8-39.4°)</td>
</tr>
<tr>
<td>Guinea pigs3</td>
<td>5-7 years</td>
<td>240-310</td>
<td>80-120</td>
<td>99-103° (37.2-39.5°)</td>
</tr>
<tr>
<td>Chinchillas3</td>
<td>10-20 years</td>
<td>100-150</td>
<td>80-120</td>
<td>98.6-100.4° (37-38°)</td>
</tr>
<tr>
<td>Prairie dog4</td>
<td>6-10 years</td>
<td>83-318</td>
<td>40-60</td>
<td>95.7-102.3° (35.4-39.1°)</td>
</tr>
<tr>
<td>Hamsters4</td>
<td>1.5-2 years</td>
<td>250-500</td>
<td>35-135</td>
<td>-98.6-100.4 (37-38)</td>
</tr>
<tr>
<td>Gerbils4</td>
<td>3-4 years</td>
<td>360</td>
<td>90</td>
<td>98.6-101.3 (37.0-38.5°)</td>
</tr>
<tr>
<td>Mice and Rats4</td>
<td>1.5-3.5 years</td>
<td>250-780</td>
<td>35-135</td>
<td>96.6-103.1° (35.9-39.5°)</td>
</tr>
</tbody>
</table>

Skin tenting and moistness of mucous membranes give indications of the hydration status of the animal. Small herbivores with increased skin tenting, dry oral mucus membranes, but normal pulses may be considered to be 4-6% dehydrated. Those patients with more pronounced skin tenting, very dry mucous membranes and dry, sunken eyes are closer to 10% dehydrated. Hypovolemic shock accompanies dehydration greater than 10%. Small herbivores are less likely to demonstrate clinical signs associated with compensatory shock, making detection of even mild dehydration states critically important. In rabbits, once bradycardia (<200 beats/min, ref. range 80-240 beats/min), hypothermia (<98.0° F, ref. range 100-102° F), and hypotension (<90 mm Hg, ref. range 90-120 mm Hg systolic) is detected, the patient is in early decompensatory hypovolemic shock and in need of aggressive fluid resuscitation.5

Mentation and respiratory character can be assessed prior to handling, in addition to stance and gait in the ambulatory patient. As obligate nasal breathers, rabbits and rodents with respiratory disease should be observed closely for nasal and thoracic movement. Signs of dyspnea generally correspond with a poorer prognosis. Physical assessment of small herbivores is performed in a routine manner but must include examination of the oral cavity and palpation of the gastrointestinal structures. A transilluminator or other light source and nasal speculum will facilitate a through oral exam in rabbits, chinchillas, prairie dogs, and guinea pigs. When a nasal speculum is not available, an otoscope may be used. In small rodents, oral exam is limited to the incisor teeth unless the patient is anesthetized. Digital palpation or the maxilla and mandible will allow for detection of apical elongation of the cheek teeth which is a common finding in patients with dental disease. Abdominal palpation should include detection of the location and degree of distension of the stomach, detection of bloating in the intestines, and presence of fecal material in the colon. Many exotic herbivores suffering from GI disease will demonstrate a pain response during abdominal palpation. While any gastrointestinal disease can lead to life-threatening complications in small herbivores with hind-gut fermentation, the presence of diarrhea or fluid accumulation in the gastrointestinal tract are poor prognostic indicators.

**Stabilization and resuscitation**

Critically ill small herbivore patients often present in early or late stages of decompensatory shock and require aggressive therapy to stabilize and reverse their declining condition. Animals exhibiting bradycardia will have low cardiac output resulting in hypothermia which in turn exacerbates the bradycardia and perpetuates the worsening of clinical signs. Fluid resuscitation as well as providing thermal and respiratory support are the hallmarks of management of shock.
Complete fluid therapy protocols provide for administration of fluids for resuscitation to correct perfusion deficits and restore oxygenation of tissues, rehydration to correct interstitial deficits, and subsequently maintenance to support body functions and replace ongoing loses until the patient is eating and drinking normally. Crystalloids fluids are preferred for rehydration and maintenance. Combination therapy using a crystalloid and a colloid is preferred for treatment of shock in small herbivores. Physiological data of the patient should be frequently monitored throughout therapy including assessment of mentation, capillary filling and mucous membrane color, pulse quality, heart rate, respiratory rate, body temperature, and production of urine. A small mammal suffering from hypovolemic shock requires placement of an intravenous or intraosseous catheter. Resuscitation should be initiated with administration of an isotonic crystalloid (10-15 mL/kg) bolus infusion followed with a colloid (5mL/kg) infused over 5-10 minutes. Thermal therapy should be implemented concurrently. The resuscitation fluid boluses are repeated every 15 minutes until systolic blood pressure is >90 mm Hg. Patients that demonstrate persistent hypotension in spite of therapy may be administered hypertonic saline (5 mL/kg) by bolus infusion over 10 minutes. Due to its hyperosmotic property, hypertonic saline pulls fluid from the interstitial and intracellular spaces to increase intravascular volume. Because of its effect on the extravascular tissue, however, it should be administered concurrently with crystalloids to prevent worsening of dehydration. Once the patient has stabilized, with normal physiologic parameters, rehydration therapy can begin. Rehydration fluids take into account the degree of patient dehydration and body weight. The volume to be administered equals the hydration deficit (%) multiplied by the patient weight (kg) multiplied by 1000 mL. A rabbit weighing 1.2 kg that is 8% dehydrated will require 96 ml (0.08 x 1.2 x 1000=96) to correct its deficit, 80% (76.8 ml) of which can be administered in the first 24 hours after resuscitation. Hetastarch can also be continued as a constant rate infusion (20 mL/kg/day) for those animals that require intravascular osmotic pressure. In general, maintenance fluid therapy for small herbivores is 3-4 mL/kg/hr or 75-100 mL/kg/day.5

Severe hypothermia in small herbivores indicates that the animal is in decompensatory shock and is a poor prognostic indicator. Aggressive, rapid warming of the patient should be performed over the initial 1-2 hours after presentation. Administration of warmed fluids will help heat the body core while external heat sources provide environmental warmth. Caution should be exercised when using a focal heat source such as a lamp or heating pad as a non-ambulatory animal will not remove itself from the heat source and may suffer burns. Assessment of body temperature should be performed frequently to ensure that the animal does not become hyperthermic.

As obligate nasal breathers, rabbits and rodents will become respiratory compromised rapidly when suffering from both upper and lower airway diseases. Oxygen supplementation is indicated for patients experiencing respiratory distress. The small size of exotic herbivores is well suited for oxygen chambers however oxygen cages are expensive and often unavailable. Oxygen concentrators absorb nitrogen from room air to increase the concentration of oxygen emitted, often >95% fractional inspired oxygen (FiO₂), and can be used to achieve therapeutic levels of oxygen (>40% FiO₂) in small enclosures used to hospitalize exotic patients.

Nebulization as an adjunct therapy for management of respiratory is not only beneficial in delivering medications directly into the airways, it helps maintain the hydration status of respiratory membranes to allow clearance of secretions. Nebulizing hypertonic saline decreases edema associated with the pulmonary tissue resulting in an opening of the airways. Albuterol inhalation solution developed for children with asthma has also been effective for management of respiratory disease in rabbits and rodents. Its bronchodilator action opens airways and alleviates bronchospasm. Dosing is empirical and extrapolated from human use (0.042% Albuterol Sulfate Inhalation Solution or 0.083% solution diluted with 3 ml saline, 15 min. q8-12h for 14 days). Antimicrobial therapy may be incorporated into nebulization therapy.

Nutritional support must be provided to hospitalized patients, especially those with high metabolic rates where anorexia rapidly results in cachexia. The caloric requirements of the patients must be calculated and those requirements met on a daily basis through self or supplemental feeding. As in domestic species, metabolic rates are measured in kilocalories per day (kcal/day). Once the number of kilocalories needed is determined, the amount of food needed to meet that requirement can be calculated and divided over the day’s feedings. The best way to determine if a patient is receiving appropriate nutrition is to weigh the patient daily on an accurate gram scale. Supplemental feeding can then be adjusted as appropriate. Oral administration of a gruel diet will also help hydrate the patient. Several commercial diets are available. Patients should be fed approximately 50 ml/kg/day divided into feedings every 4-6 hours.

References
Ferret Endocrinology: What’s New in the World of Hormones

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The ferret, Mustela putorius furo, is a small mammal belonging to the order Carnivora and is a probable descendant of the European polecat. Although kept as domesticated animals since 400 BC, the popularity of ferrets as pets is well established in North America and Europe. Female ferrets, jills, reach sexual maturity at 8-12 months of age. Jills are seasonal induced ovulators, remaining in estrus for extended periods of time if not bred. Male ferrets, hobs, reach sexual maturity at 8-12 months of age. Hobs have a prepuce on the ventral abdomen and have an os penis that is ‘J’ shaped, rendering urinary catheterization difficult. Kits are born in litters of 5-10 after 42 days gestation. They open their eyes at around 4 weeks of age and are weaned at 6-8 weeks. The average life expectancy of a ferret is 5-8 years although some ferrets may reach 10-12 years of age.

Endocrine disorders are common in pet ferrets and treatment recommendations have evolved with the availability of new therapies.

Adrenal disease

Adrenal-associated endocrinopathy in ferrets, known as adrenal disease, affects ferrets from 1-8 years-of-age, although the average age of onset in ferrets is 3-4 years-of-age. First described in the 1980’s, the etiology of adrenal disease remains elusive. Suggested etiologies include early sterilization of ferrets, consistent and prolonged exposure to protracted photoperiods or lack of variation (seasonality) of photoperiods, and genetics. It has been proposed that in the United States, the prevalence of adrenal disease in ferrets is 20-25%, with age of onset an average of 3.5 years after sterilization surgery.

Clinical signs in affected ferrets are associated with hyperadrenogenemia and hyperestrogenemia, with cortisol elevations rarely seen. The most common presenting clinical sign of adrenal disease is progressive bilaterally symmetrical alopecia, usually starting at the tail and dorsal lumbosacral region. Hair loss may initially be seasonal before becoming persistent. Other signs may include vulva swelling in females (55-89%), stranguria or dysuria in males with prostatic tissue swelling 1-7%, pruritis (9-40%), and muscle atrophy (4-56%). Aggression and/or sexual behavior, lethargy, and polyuria/polydipsia have also been associated with adrenal disease in ferrets.

Many clinicians are comfortable diagnosing adrenal disease in ferrets based on history and clinical presentation. Ancillary testing helps to support the diagnosis and histopathology of the adrenal tissue is confirmatory. Studies evaluating the circulating blood levels of sex hormones in ferrets with adrenal disease have demonstrated that concentrations of estradiol, 17-hydroxyprogesterone, androstenedione, and dehydroepiandrosterone may be independently or concurrently elevated. A commercial serum hormone assay which measures estradiol, androstenedione, and 17-hydroxyprogesterone is available (Clinical Endocrinology Laboratory, University of Tennessee College of Veterinary Medicine). Elevations in one, or more, of the three hormones has a reported 96% sensitivity for diagnosing adrenal disease in affected ferrets.

Cortisone levels and adrenal stimulation tests are not helpful in diagnosing adrenal disease in ferrets as this condition is not associated with hypercortisolemia. Anemia and thrombocytopenia may be found on hematological evaluation in chronic cases due to the prolonged presence of circulating estradiol hormones, however serum biochemistry evaluation is typically normal. Cytology of the prepuce in male ferrets may be a useful screening test for adrenal disease as there is a correlation between adrenal disease and the presence of >70% cornified preputial epithelial cells.

Radiographic imaging is rarely diagnostic for adrenal disease but is useful for screening patients for concurrent disease. Ultrasound evaluation is useful for evaluation of the size, shape, and parenchymal architecture of the adrenal glands, as well as evaluating the animal for unilateral versus bilateral disease. Measurement reference ranges have been established for normal adrenal glands in ferrets. Normal adrenal glands are larger in males than in females but may be challenging to locate using ultrasound. In one study of normal ferrets, size is reported as length (7.2 ± 1.8 mm left, 7.6 ± 1.8 mm right) and thickness or width (2.8 ± 0.5 mm left, 2.6 ± 0.4 mm right), with glands tending to be ovoid. Abnormal adrenal glands become rounded, with enlargement of one or both poles. Normally hypoechoic to the surrounding retroperitoneal tissue, diseased adrenal glands may display a heterogenous structure and increased echogenicity. It is important to evaluate both adrenal glands to determine the presence of unilateral or bilateral disease as this will affect treatment planning.

Histologic evaluation of adrenal gland tissue from affected ferrets demonstrates a range of lesions, from hyperplasia to adenoma to adenocarcinoma, with some evidence of progression. Intact unbred female ferrets may present with clinical signs consistent with adrenal disease, as will those jills with remnant ovarian tissue. However, in these cases, the age of onset of clinical signs is associated with the onset of estrus, usually at a year-of-age. Likewise, male ferrets may demonstrate seasonal alopecia that is unrelated to adrenal disease, making this a differential diagnosis to consider.

Historically, an adrenalectomy of the affected gland is the preferred treatment for unilateral disease, however medical management may be preferred due to economic reasons or for ferrets with concurrent disease that makes them an unsuitable surgical candidate. The
right adrenal gland is more difficult to remove than the left due to its close proximity to, and possible involvement with, the vena cava. Surgical debulking, cryosurgery, and laser surgery are other options in these difficult cases. When bilateral disease is present, removal of the larger gland and debulking of the smaller gland is recommended. Serious complications and death can occur after bilateral adrenalectomy surgery. Up to 8% of ferrets, and perhaps more, possess accessory adrenal tissue as encapsulated nodules comprised of cortical tissue embedded in the perirenal fat, however temporary administration of glucocorticoids and/or mineralocorticoids may be necessary following adrenalectomy. Hobs with urinary obstruction secondary to prostatic cysts improve rapidly (1-2 days) post-surgery and should remain catheterized while obstruction of the urethra is resolving. Recurrence of disease within 3-18 months occurs in 17-38% of ferrets undergoing unilateral adrenalectomy.

Medical management of adrenal disease is palliative. Therapies developed for treating Cushing’s disease in dogs are ineffective and potentially dangerous in ferrets. Melatonin administration has been shown to temporarily ameliorate clinical signs. GnRH analogs have proven effective in temporarily relieving the clinical signs of adrenal disease. GnRH agonists, such as leuprolide and deslorelin, initially stimulate LH release, but subsequently promote negative feedback inhibition to downregulate GnRH receptors in the pituitary gland due to their binding properties. This leads to decreased LH release and decreased sex hormone production by the adrenal tissues. Leuprolide acetate (Lupron – Abbott Laboratories, Northbrook, IL) is a long-acting GnRH agonist depot that alleviates clinical signs beginning about 2 weeks post injection. Dosing of 100-150 μg/kg IM every 4-8 weeks is recommended. Higher doses (250 mg) have been used without adverse effects on ferrets suffering from prostatic disease. Lupron can be divided into aliquots and frozen for at least a year. Deslorelin acetate was developed as a canine contraceptive and comes as a slow-release subcutaneous implant in two sizes (3 mg and 4.7 mg). Suprelorin F (Virbac Animal Health, Inc., Fort Worth, TX) is available in the United States. The implant is inserted subcutaneously on the dorsum over the shoulders and is associated with alleviation of clinical signs within 2 weeks and a duration averaging 17.6 months. Anesthesia or heavy sedation may be necessary when placing the implant due to its large size and the associated discomfort of placement. Adrenal disease in ferrets is not a life threatening disease except in the case of a hob with urinary obstruction. Both medical and surgical treatment options are expensive and owners may elect benign neglect as a treatment for their ferret.

**Insulinoma**

Insulinomas are tumors of insulin-secreting pancreatic islet cells and is considered one of the most common neoplasm affecting ferrets. There is no sex predilection but the average age of onset is 4-5 years. Contributing factors to the development of insulinomas in ferrets include genetic factors as well as diet. Metastasis is uncommon but possible. In a normal ferret, a low blood sugar level stimulates the release of glucagon, cortisol, epinephrine and growth hormone. These in turn stimulate gluconeogenesis and glycogenolysis in the liver to raise the blood sugar. In addition, these hormones inhibit the release of insulin and decrease the utilization of glucose by cells. Once blood sugar rises, pancreatic beta cells secrete insulin to provide negative feedback and stimulate the uptake of glucose by cells. A ferret with an insulinoma secretes excessive amounts of insulin which inhibits gluconeogenesis and glycogenolysis while stimulating the uptake of glucose by tissues, which results in hypoglycemia.

Clinical signs of insulinoma may develop over weeks to months. Conversely, owners may be unaware of any manifestation of disease until a hypoglycemic crisis occurs. Clinical signs of this disease include lethargy, weakness, ptymal, pawing at the mouth, weight loss, peripheral neuropathies, collapse, ataxia, and seizures. Seizures occur in the majority of dogs suffering from insulinomas, however only 14% of ferrets develop seizures. This may be reflective of the ferret’s relative tolerance of hypoglycemia and the slow onset of this disease. Diagnosis is based on a fasting blood glucose level, correlated with clinical signs.

Most practitioners agree that a level of 60 mg/dl is suggestive of an insulinoma although other causes of hypoglycemia must be ruled out (hepatic disease, sepsis, paraneoplastic syndrome, hypoadrenocorticism). Hand-held glucometers may be inaccurate, generally providing a value lower than the actual blood glucose level. Additionally, glucometers are inaccurate in patients with high hematocrits making this tool problematic for use in ferrets. Suspected hypoglycemic samples should be confirmed with conventional laboratory methods. Fructosamine, a glycosylated protein, has been used in dogs to measure the degree of glycosylation which would be expected to be low in hypoglycemic patients. However, these proteins have not been measured in ferrets and the results are unreliable. Biochemical testing, with the exception of glucose levels, as well as hematology are usually unremarkable. Additionally, diagnostic imaging has low sensitivity for diagnosing insulinoma. Serum insulin levels can be measured and must be simultaneously compared to a fasting glucose level. A normal or high insulin level in the face of hypoglycemia is diagnostic.

Ferrets presenting for emergency complications of hypoglycemia must be treated symptomatically until stable. A slow bolus of 50% dextrose followed by a constant rate infusion of 5% dextrose spiked fluids will stabilize the hypoglycemia. Diazepam (1mg/ferret IV) may be needed to control seizure activity. Once stabilized dietary, medical and surgical therapy is indicated singularly or in combination. The specific therapy implemented is dependent on severity of signs, age of patient, presence of concurrent disease, and owner’s wishes. The recent consensus is that surgical treatment is preferred to extend the patient’s expected life span. An exploratory laparotomy is performed and both lobes of the pancreas are visually and manually examined. While care should be exercised when handling pancreatic tissue, the ferret pancreas tolerates manipulation well. Insulinomas may be solitary or multiple,
and can range from non-detectable to 2 cm in size. Individual nodules can be locally resected. Diffuse disease is best treated with pancreatic lobectomy or partial pancreatectomy. Post-operative fasting for 12 hours is indicated. A blood glucose level, measured post operatively, will often be high and will stabilize over the next few days. Serial glucose testing each day will determine the need for implementation of medical management. Medical management controls clinical signs by blocking the effects of insulin, not by treating the neoplasia. Prednisone (0.5-2.0mg/kg q 12 hrs.) is started at the lowest dose and raised as needed to maintain normal blood glucose levels and control clinical signs. If prednisone therapy is unable to control the disease, diazoxide (Proglycem, Baker Norton Pharmaceuticals, Inc. Miami, FL) can be added starting at an initial dose of 5mg/kg q 12 hrs and can be increased as needed to a maximum dose of 60mg/kg divided BID. Regardless of medical or surgical therapy, ferrets diagnosed with insulinoma should be fed many small meals throughout the day containing high quality protein and moderate to high levels of fat. Carbohydrates and treat food should be avoided. Due to the microscopic nature of some insulinomas, cure is generally not possible. Ferrets that undergo surgery tend to have longer survival times (1-3 years) than ferrets managed with medical therapy (6-12 months). Fasting (4 hr.) blood glucose levels should be evaluated regularly in these ferrets.

References
Antibiotic usage is widespread in veterinary medicine and is indicated for a variety of reasons ranging from prophylactic prevention of bacterial colonization during surgery to treatment of systemic bacterial infections. The choice of antibiotic is based on factors pertaining to the patient, the clinic, the medication, and the individual practitioner. The location of infection, ease of handling of the patient, frequency of administration, and route of administration must be considered prior to developing antibiotic use protocols.

**Questions to answer prior to implementing antibiotic therapy**

Prior to electing to implement therapy with antimicrobial medications, several questions must be answered in order to judiciously select and use these drugs.

*“Does this patient have a treatable bacterial infection?”*

While seemingly obvious, this is the most important question to be asked. There are certainly some instances where antibiotic therapy is warranted when the animal is not suffering from a bacterial infection but this should not be the norm. Prophylactic use of antibiotics may be indicated peri-operatively, when surgical contamination is likely and unavoidable. Practitioners may also elect to implement antibiotic therapy when the patient is immunocompromised or severely debilitated and therefore exquisitely susceptible to opportunistic infections. However, antibiotics should only be used when necessary to treat a specific and susceptible condition. In healthy hosts, the body’s natural defenses are often sufficient to ward off infection. It is only when these mechanisms become compromised, or there is a change in pathogenicity of the microbe that infection develops. Signs of bacterial infection include suppurative exudate, inflammation, odor, and dysfunction of the affected tissue.

*“Where is the infection and can I effectively treat this animal?”*

The answer to these questions will allow the clinician to begin evaluating the treatment options at their disposal. Many antibiotics have a variety of formulations allowing for diverse routes of administration. Others are very limited in how they may be administered and what tissues they penetrate to reach therapeutic doses. Animals with skin infections may be treated systemically or topically, depending on the severity of the lesion. In some cases, patient handling will be the limiting factor. Particularly fractious or stressed patients will be better treated with longer acting therapeutics, while patients that are amenable to handling may be treated more frequently without adverse effects. Owner compliance and potential complications must always be considered when implementing antibiotic therapy.

*“What pathogen is most likely involved?”*

Bacteria are classified as gram positive or gram negative based on their appearance after being exposed to the staining process. The peptidoglycan layer of the cell wall is not covered by a cell membrane in gram-positive cells so the methylene blue stain is retained and these bacteria appear blue-purple. Gram-negative cells do have a cell membrane which prevents the stain from being retained. The methylene blue stain is washed off and replaced by the safranin in gram-negative cells resulting in their pink-red appearance. Bacteria are also classified by their use of oxygen; aerobic organisms requiring oxygen to reproduce and anaerobic organisms requiring little to no oxygen to multiply. When possible, a sample collected from the infected tissue should be evaluated by Gram staining to provide the clinician with expedient and inexpensive preliminary clues pertaining to the causative organisms. Gram staining does not replace the need for culture microbiore, nor does it provide clues regarding antibiotic susceptibility.

In addition to staining techniques and culture, certain characteristics of the host, affected tissues, and environment provide insight regarding pathogen involvement. Many skin infections involve gram-positive cocci including Staphylococcus and Streptococcus. Respiratory infections often involve aerobic gram-negative organisms such as Pasteurella or Klebsiella, and Bordatella. Animals living in aquatic habitats may have wounds that colonize with Pseudomonas or Enterococcus. Granivorous birds, such as parrots, normally have GI flora populated predominantly with gram-positive cocci and rods. In these species, most opportunistic infections are caused by gram-negative organisms. By understanding these relationships, the clinician may judiciously select an antibiotic to initiate treatment pending definitive testing.

*Which brings us to our final question…”What antibiotic should be used?”*

Whenever possible, a culture and bacterial sensitivity should be performed so that the causative bacteria can be identified and antibiotic selection can be based on susceptibility of the organism to a specific drug. However, not all drugs are readily available and useful in exotic animal patients. The selected antibiotic should target the microbe causing the infection as specifically as possible to prevent negatively impacting the commensal microbiota.

Focused antibiotic therapy directed against gram-positive organisms may include the beta-lactam antibiotics in the penicillin and cephalosporin classes. Antibiotics with specific efficacy against gram-negative organisms include the fluoroquinolones, 3rd generation cephalosporins, aminoglycosides, and phenicols. Anaerobic organisms are susceptible to metronidazole, penicillins, cephalosporins, phenicols, and macrolides. When sepsis is suspected, broad-spectrum antimicrobial therapy is indicated. Relatively few...
pharmacokinetic (PK) and pharmacodynamics (PD) studies have been done using these drugs in exotic animals and most dosing information is anecdotal. However, what has been elucidated by the studies that have been performed is that there can be significant species differences in PK and PD parameters when administered the same drug. Reported dosing ranges are often broad and caution must be exercised when extrapolating between species. In general, animals with a larger mass require lower doses and less frequent dosing than those with small mass. Likewise, dosing tends to be higher in animals with high metabolic rates compared to those with lower basal metabolism. Rabbits, rodents, and ferrets are often used as animal models for human drug studies making dosing information for these species more available. However, absorption, distribution, metabolism, and elimination are dependent on the health status of the animal, anatomical and physiological parameters, and variability in drug metabolites, enzymes, and protein binding properties.

Extra label drug use
Few drugs are approved for use in exotic animals. The U.S. Food and Drug Administration oversees the use and administration of pharmaceutical agents in animals through the Federal Food, Drug, and Cosmetic Act (CFR 21 USC 360) and the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994 (CFR 21, Chapter 1, Part 530) which outlines the parameters for extra-label drug use.

"Extra-label use" is defined as the "Actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease and other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from labeled withdrawal time based on these different uses."

Off-label administration must be administered under oversight of veterinarian, there must be a valid veterinarian-client-patient relationship, the use is limited to cases where health of animal is threatened and suffering/death will result if not treated. Compounding of approved animal and human drugs is legal but is regulated under 21 CFR 530.13.

Wildlife with defined hunting seasons are considered food animals and have additional AMDUCA regulations: 1) Extra-label drugs may be used only when no approved drug is available 2) Requires veterinary assessment of patient 3) Extended withdrawal period for animal products should be established based on known withdrawal times for domestic species 4) Identification protocols must be Institutes to ID treated animals and 5) Measures to ensure that withdrawal time frames are met prior to release must be taken. Extra-label drug use is strictly regulated for poultry and game birds as well. The food animal drug residue database may be found at http://www.farad.org/eldu/prohibit.asp.

What’s new
Long-acting formulations
As new antibiotics are developed, efforts continue to increase their efficacy, duration of action, and spectrum. Several long-acting antibiotics have been developed for use in companion animals however their PK/PD parameters are unknown when used in exotic species. It has long been known that some antibiotics that are short-acting in domestic animals have long-acting properties when used in extra-label species (i.e. 3rd generation cephalosporins in reptiles). The definition of ‘long-acting’ is somewhat ambiguous and applies only to those species for which the drug is labeled. In most cases, the duration of long-acting antibiotics ranges from 48 to 150 hours depending on the drug and the species receiving it. Time-dependent antibiotics are most often suited for long-acting formulations as their mechanism of action requires that tissue levels remain above a minimum therapeutic threshold for an extended period of time rather than reaching a specific peak. Beta lactam antibiotics have been targeted because of these properties. In order to make a formulation long-acting, the drug must be changed in some manner; either in its chemical structure, its protein binding capability, or its carrier which keeps it in tissues.

One of the first long-acting antibiotic formulations that has recently been developed is a 3rd generation cephalosporin, cefovecin (Convenia, Zoetis). In dogs and cats, an 8 mg/kg dose provides therapeutic levels for 14 days. The duration of action in exotic species has been variable, with the formulation not having long-acting effect in reptilian and avian species. Conversely, another 3rd generation cephalosporin, ceftiofur crystalline free acid (Excede, Zoetis) does have long-acting properties in birds and reptiles. This formulation has decreased water solubility, retarding dissolution of drug particles and the injection site. In helmeted guinea fowl and American black ducks, a 10 mg/kg dose administered in muscles produced therapeutic levels for 3 days. A 15 mg/kg dose in ball pythons resulted in 5 day dosing recommendations.

Tulathromycin (Draxxin, Zoetis) is a long-acting bacteriostatic semisynthetic macrolide that achieves long-acting properties through extensive absorption and tissue distribution which results in decreased clearance. This product has some potential as an intralecular antibiotic for treatment of abscesses although it is labeled for small ruminants and pigs.

Azithromycin (Zithromax, Pfizer) is a macrolide that concentrates in the host’s cells. In ball pythons, 10 mg/kg oral dosing provided therapeutic levels for 2-7 days. Dosing in Amazon parrots and blue and gold macaws for uncomplicated, non-intracellular infections is 10-20 mg/kg every 48 hours for five doses. However, dose and duration of therapy increases for intracellular infections such as Chlamydiosis, with dosing frequency increased to every 24 hours. Azithromycin has also been used as a component of
antibiotic therapy to treat Mycobacteriosis in birds, in combination with rifabutin and ethambutol, although treatment is controversial due to the pathogens zoonotic potential. Use of azithromycin has not been studied in passerine species.

Tetracycline is bacteriostatic, with good oral absorption and tissue penetration, however its use in treating bacterial infections has declined over time due to the development of antimicrobial resistance. Long-acting tetracycline, LA-200 (Liquamycin) contains oxytetracycline with a co-solvent (2-pyrrolidone). When injected into muscle, the solvent is carried away while the drug precipitates at the injection site and is slowly dissolved to provide minimum inhibitory concentrations of antibiotic for a minimum of 72 hours in approved species. Tissue necrosis has been reported at the site of injection. Dosing of 20 mg/kg in a macropod species (tammar wallaby) did not provide reliable data regarding duration of efficacy. Five day dosing, using 10 mg/kg, has been recommended for American alligators. Recently, studies in humans have shown efficacy of long-acting tetracyclines in treating methicillin-resistant Staphylococcus aureus infections.

Florfenicol (Nuflor, Merck Animal Health) is a long-acting bactericidal phenicol labeled for large animals. It contains polyethylene glycol, propylene glycol, n-methyl pyrrolidone as solvents. When used in cattle, minimum inhibitory concentrations of drug are achieved for a minimum of 48 hours. Phenicol antibiotics provide broad spectrum antibacterial coverage, including anaerobic spectrum, making these drugs particularly useful in some small herbivores in which β-lactam antibiotics have limited use. However, chloramphenicol administered orally may result in anorexia in those patients. Florfenicol administered at 30 mg/kg every 24 hours as a subcutaneous injection in guinea pigs produced no adverse effects in this author’s experience.

### Formulation and delivery
A significant amount of work has been done evaluating the efficacy and usefulness of antibiotic-impregnated beads for the delivery of sustained release of antimicrobials. New work is being performed to evaluate the potential of this method for delivery of other therapeutics including chemotherapeutics and anti-fungals. Antibiotic-impregnated beads embedded into tissues elute high concentrations of the antimicrobial at the implant site. A wide array of antibiotics have been used including aminoglycosides, β-lactams, macrolides, metronidazole, fluoroquinolones, and neomycin. Antibiotic powder may be incorporated into polymethylmethacrylate (PMMA) or plaster of Paris (calcium sulfate) to customize spectrum and size of implant. Care must be taken to use aseptic technique and gas sterilization is needed to avoid decreasing antibiotic potency.

Enrofloxacin, a fluoroquinolone, has long been used as an extra-label antibiotic in exotic species due to its efficacy against gram-negative bacteria. As a concentration-dependent antibiotic, less frequent dosing is permitted as compared to other antibiotics. Enrofloxacin is available as an injectable solution in two concentrations (22.7 mg/ml and 100 mg/ml) or as a tablet in three sizes (22.7 mg, 68 mg, 136 mg), but no oral liquid formulation is available. However, compounded oral suspensions or solutions remain stable at room temperature for 8 weeks. The 2.27% injectable solution may be administered by oral route. The large animal injectable product may be used to create compounded solutions but should not be administered orally undiluted as oral ulcerations have been observed. Extra-label use of fluoroquinolones is prohibited in food-producing animals. Besides enrofloxacin, few studies have been done using fluoroquinolones in exotic animals.

Aminoglycosides, including amikacin and gentamicin, are concentration dependent, bactericidal antibiotics with broad gram-negative spectrum. The lack of oral bioavailability and association with nephrotoxicity of these drugs make this class of antibiotic not ideal for use in exotic animals. Nebulization therapy is an effective means of administering therapeutics into the large and small airways. Incorporating an aminoglycoside into nebulized solutions delivers antibiotic to the site of infection allowing for local treatment without systemic absorption.

### References
Staying Outside the Box: Strategies for Managing Unusual Exotic Pets

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Provision of quality care to zoological species requires familiarity of the clinician with the unique natural history, husbandry, anatomy and physiology of individual species. However, application of the principles of veterinary medicine transcends species differences. More and more people in today’s society are choosing to own exotic pets in addition to or in lieu of the traditional dogs and cats commonly seen in veterinary practice. Their small size and housing, ease of care, and human-animal bond potential are optimal for some pet owners. Often owners of exotic pets will make every effort to provide their pet with the best veterinary medicine has to offer. By offering service to exotic animal patients, you are meeting a tremendous demand that will be highly valued by your clients and/or employers.

Role of the veterinary team
Exotic pet practice offers the practitioner an opportunity to work with a large variety of species. While professionally rewarding, this also represents a significant challenge. The diversity of exotic pets kept in captivity dictates that the veterinary practitioner be versed with the health and husbandry of a wide array of species commonly kept as pets. Husbandry factors are often at the root of medical conditions seen in these animals. A thorough history, including husbandry information, is necessary for appropriate case management. Training of veterinary support staff will enhance the veterinarian’s ability to accommodate these species in a busy schedule. Providing adequate time for acquisition of a thorough history requires a minimum appointment time of 30 minutes. Longer appointment times minimize stress to the patient and allow necessary time for client education. Knowledgeable front office staffs are also critical in facilitating exotic pet care. Staff should be familiar with the species being seen and should demonstrate their interest to your clients. Statements that are derogatory regarding ownership of certain species or the decisions of owners to spend money on pets that are deemed “inexpensive” should be avoided.

Natural history and husbandry
It is important to educate yourself regarding species identification and the natural history of the species you’re seeing. Certainly years can be spent learning all there is to know about every species kept as a pet, but a general working knowledge of those commonly kept will lend confidence to your client interactions. In addition, knowing the natural history of the species presented to you will help you identify the husbandry requirements of that animal when kept in captivity. The goal in keeping any exotic pet is to maintain it in an environment that is as close as possible to that it would be living in if it were free-ranging. Often the problem that an exotic pet presents for is related to deficiencies or excesses of environmental conditions or their diet. Being familiar with the husbandry requirements of a species will help you identify potential problems and give insight in implementing treatment recommendations. It will also allow you to help your clients determine if that particular species would make a good pet for them based on their circumstances.

The internet provides a readily available means to search for information helpful in identifying an unknown species. While this is not often a concern when working with exotic mammals, or even birds, reptiles kept as pets range from the common bearded dragon to those unfamiliar to the practitioner such as the uromastyx. Unfortunately, in some situations, the owner may not even be aware of what species they own. Internet sources range in the accuracy of the information they provide but many zoos, nature organizations, and species interest groups maintain sites that provide images and basic natural history information that provide clues to the species. Additionally, field guides or other texts are useful when seeking this information. Once the species is known, determine where that animal is found in nature and how it utilizes its environment. Species natural history includes information regarding the geography, diet, and behavior associated with that species. Geography provides important details about the animal’s climate, including temperature range, humidity, light cycles and seasonality. It also provides details regarding the terrain. Behavioral characteristics are important for determining the social nature of the species, social hierarchies, diurnal or nocturnal activity, and whether seasonal variation in activity should be expected.

The details gained from reviewing a species natural history allow practitioners to critically evaluate their patient’s husbandry, even if the practitioner is relatively unfamiliar with the species. Husbandry refers to the conditions under which the animal is maintained in captivity. It includes information pertaining to caging, including the substrate that is used, the size and ventilation of the cage, temperature and humidity of the environment, exercise opportunities that are provided including furniture or other structures within the cage, what lighting is provided and by what means, and how often is cage cleaning performed. Husbandry also pertains to the diet consumed by the animal including treat foods. Exposure to conspecifics, other animals, and the source of the animal are also important aspects of husbandry. An animal that is normally found free-living in a desert habitat eating an invertebrate diet may likely develop clinical disease if kept in a manner that is not reflective of that natural history.