Anesthesia and Analgesia in Reptiles

Craig A. E. Mosley, DVM, MSc, Dip. ACVA

Abstract

Reptiles are a diverse, complex group of animals that present unique challenges to the practitioner delivering anesthetic and analgesic care. A review of the current literature addressing the physiology and anatomy pertinent to the administration of anesthesia and analgesia to a wide variety of reptiles is presented in this article. Current clinical techniques in sedation and analgesia, the induction and maintenance of anesthesia, perianesthetic support, and monitoring are discussed. Copyright 2005 Elsevier Inc. All rights reserved.

Key words: **reptiles; anesthesia; analgesia; cardiopulmonary physiology; monitoring; perianesthetic support**

The anesthetic management of reptiles presents unique challenges, because their unique physiologic and anatomic adaptations can complicate anesthetic administration. The provision of anesthesia to this unique class of animals requires a thorough understanding of normal physiology, pathophysiology, the action and disposition of anesthetic and related drugs, and a familiarity with the design and use of related anesthetic equipment. Thorough pre-anesthetic assessment, a carefully designed anesthetic plan with attention to premedication, induction, maintenance, monitoring, supportive care, recovery, and ongoing postoperative support and analgesia all contribute to the reduction of risk associated with anesthesia.

Anatomy and Physiology

Reptiles have long been considered a class of animals that reflects the evolutionary transition between the aquatic and amphibious ectothermic vertebrates and endothermic birds and mammals. Many early investigations of reptilian physiology focused on the apparent "imperfections" of their physiology. More recently, investigators have begun to view reptilian physiologic adaptations as unique and advantageous, enabling ectothermic animals to inhabit almost all of the available nonpolar ecologic niches. Although many aspects of reptilian physiology are similar to those of endothermic vertebrates, significant differences remain. Such differences may alter both the action and disposition of anesthetics and analgesics.

Metabolism and Thermoregulation

The reptilian resting metabolic rate is one tenth to one third lower than the resting oxygen consumption rate of mammals of an equivalent size. Minimum and maximum oxygen consumption rates of individual reptilian species range from almost zero to values similar to those of a resting mammal.[1] A decrease in an animal's cellular metabolic rate may result in reductions in drug metabolism, leading to increases in both the latency of onset and duration of effect and time to recovery. The ambient environmental temperature is one of the

From the College of Veterinary Medicine, Oregon State University, Corvallis, OR 97331-4804 USA

Address correspondence to: Craig A. E. Mosley, DVM, MSc, Dip. ACVA, Department of Clinical Sciences, College of Veterinary Medicine, Oregon State University, Corvallis OR 97331-4801. E-mail: Craig.Mosley@oregonstate.edu

1055-937X/05/1404-$30.00

doi:10.1053/j.saep.2005.09.005

main determinants of metabolic rate in resting reptiles. As temperature decreases, oxygen demand and metabolic requirements of tissues decrease leading to a reduction in the metabolic capacity of various organ systems. There are significant interspecies and intra-individual variations in metabolic rate. Metabolic rate is also influenced by activity level and time since last feeding. Metabolic rate can increase 3 to 40 times the resting value after a meal and may remain elevated for up to 7 days.[2] However, it is unclear whether recent feeding has a clinically significant effect on anesthesia in reptiles.

In general, the varanid and lacertid lizards have relatively high metabolic rates, and boid snakes and chelonians have lower rates. Surface-dwelling squamates have higher metabolic rates than burrowing species, and species of lizards that eat insects or other vertebrates have higher metabolic rates than do herbivorous species.[3] Reptiles are ectothermic and derive their body temperature from the surrounding environment. However, some reptiles, such as, large pythons and leatherback sea turtles, derive some of their body heat from muscular activity. Such endothermic-like activity is only possible in larger reptile species. Reptiles can alter their body temperature through changes in cardiovascular function. During periods of warming some reptiles increase their heart rate and the degree of right-to-left shunting to increase the fraction of blood flow that is shunted to the periphery for heating and ultimate return to the body core. This adaptation facilitates more rapid and efficient warming of the animal.[4] Basking and shuttling between sun and shade are very important for temperature regulation in ectotherms. In all animals, the integration of physiology and behavior is affected by the internal thermal set point or preferred body temperature (PBT). In endotherms, the PBT generally remains constant. In reptiles, the PBT may vary in response to physiologic challenges such as fever. In the case of fever, many reptiles will alter their behavior and physiologic responses to maintain this higher body temperature. There is good evidence that reptiles downregulate their body temperature in response to hypoxia and/or inadequate tissue oxygen delivery. This is referred to as hypoxia-induced hypothermia.[5,6] Hypothermia induced by hypoxia decreases metabolic rate through the direct effect of temperature on tissue oxygen demand and through depression of the rate of aerobic metabolism.[5] The optimal body temperature can also be affected by hydration status. Reductions in hydration status lead to reductions in the PBT.[7] Reptiles undergoing anesthesia should be maintained at the average or the high end of their PBT range to ensure optimal metabolic function. Such values can be found in general husbandry references.

Cardiovascular System

The noncrocodilian reptile heart has three chambers, with two completely separate atria and a single anatomically continuous ventricle. The crocodilian heart is more typical of that seen in mammals and birds, with two completely divided atria and ventricles. In the crocodilian heart, the foramen of Panizza allows for some intravascular shunting under circumstances of breath holding, such as diving.

In noncrocodilian reptiles, the ventricle is divided into two main chambers by a septum-like structure called the Muskelleiste or muscular ridge. This ridge originates from the ventral ventricular wall and runs from the ventricular apex to base, dividing the ventricle into two main chambers: the cavum pulmonale and the cavum dorsale.[8,9] The cavum pulmonale and the cavum dorsale are comparable in function to the right and left ventricles of mammals, respectively. The dorsolateral border of the muscular ridge is free, permitting the flow of blood between the cavum pulmonale and cavum dorsale. However, during ventricular systole, the muscular ridge presses against the dorsal wall of the ventricle and separates the cavum pulmonale from the cavum dorsale; thus, although exhibiting anatomical continuity of the subchambers, in a functional sense, the heart is capable of acting as a two-circuit pump. Cardiac shunting occurs commonly in reptiles.[10-12] Cardiac shunts can occur in both directions and may occur simultaneously in both directions.[10,13,14] The direction of the net shunt determines whether the systemic or pulmonary circulation receives the majority of the cardiac output. Intracardiac shunting has three important functions. First, shunting serves to stabilize the oxygen content of the blood during respiratory pauses. Second, the right-to-left shunt is partly responsible for an increase in blood flow to the systemic circuit which can facilitate heating. Third, a right-to-left shunt directs blood away from the lungs during breath holding.

During anesthesia, cardiac shunting can affect systemic arterial oxygen content and the uptake and elimination of inhaled anesthetics. The size and direction of the shunts are ultimately controlled by pressure differences between the pulmonary and systemic circuits and washout of blood remaining in the cavum venosum (an anatomical subchamber of the cavum dorsale described in

many reptiles).[10,12,13,15] The pressure differences are principally controlled by cholinergic and adrenergic factors that regulate the vascular resistance of the pulmonary and systemic circulation.[10,16-21] Large right-to-left shunts limit the amount of anesthetic uptake early in the anesthetic period and slow anesthetic elimination at the end of anesthesia. Such shunts can delay the induction to and recovery from inhaled anesthesia. Changes in the level and direction of shunts may account for the unexpected awakening seen in some reptiles anesthetized with inhalant anesthetics. Intracardiac shunts also have implications for patient monitoring, in particular airway gas monitoring and pulse oximetry.

Blood pressure in reptiles is controlled by mechanisms similar to those described in mammals.[22] The cardiovascular system of reptiles responds to both cholinergic and adrenergic stimulation in a manner similar to mammals, and the presence of a baroreceptor reflex has been well described.[23] The resting blood pressures of reptiles tend to be stable in the absence of external stimuli but may vary with temperature, activity, or state of arousal.[24,25]

In contrast to mammals, systemic arterial blood pressures vary greatly among various reptilian species, making it difficult to identify a "normal" arterial blood pressure.[22] Normal blood pressure in reptiles may be more profoundly affected by environmental stresses such as habitat and temperature, species activity and size compared to the role of these factors on blood pressure in mammals. This greater variability may originate from a reptile's poor ability to regulate normal homeostasis independent of temperature and environment. Chelonians tend to have the lowest mean arterial pressures (15-30 mm Hg), whereas some varanids have resting arterial pressures (60-80 mm Hg) similar to mammals.[26] In the green iguana, normal resting systemic arterial blood pressures are reported to be in the range of 40 to 50 mm Hg, while pulmonary arterial pressures are in the range of 15 to 30 mm Hg.[26] The systemic blood pressures in snakes correspond to the gravitational stress they are likely to experience.[27-29] Snakes from arboreal habitats tend to have higher arterial pressures than those that are primarily aquatic. An allometric relationship between arterial blood pressure and body mass has also been described in snakes. As body mass increases, so does blood pressure.[30] Several anesthetics, such as sevoflurane, isoflurane, halothane, propofol, tiletamine-zolazepam, and ketamine, have been shown to induce cardiopulmonary changes in reptiles similar to those seen in mammals.[31-39]

Pulmonary System

The most significant difference between the respiratory physiology of reptiles, mammals, and birds is the lower oxygen consumption rate of reptiles. This difference reflects the lower reptilian metabolic rate. Reptile respiratory anatomy and physiology both vary markedly across species. The lungs of noncrocodilian reptiles are suspended freely in the common pleuroperitoneal cavity and are not located in a closed pleural space. In reptiles, the lungs tend to be sac-like with varying degrees of partitioning. Highly aerobic species such as the varanids (*Varanus exanthematicus* [Savannah monitor], *Varanus niloticus* [Nile monitor], and *Varanus dumerili* [Dumeril monitor]) tend to have highly partitioned lungs with numerous septae and invaginations that increase the surface area for gas exchange. Chelonians and lizards tend to have paired lungs where most snakes have a single, functional right lung. The functional units of the lung are referred to as ediculi and faveoli. Ediculi or faveoli are analogous structures to mammalian alveoli. Most reptile lungs exhibit areas of both type of parenchyma. There is little detail regarding the trachea and extrapulmonary bronchial tree system in reptiles. The tracheal rings of chelonians tend to be complete, necessitating care when placing an endotracheal tube. In addition, the trachea bifurcates proximally, so inadvertent endobronchial intubation may occur. Many snakes also possess a tracheal lung, the significance of which is unclear. The lungs of reptiles tend to have a larger tidal volume but a smaller respiratory surface area.

Because reptiles lack a diaphragm, they rely on the thoracic musculature for ventilation. Because both inspiration and expiration are active processes, the respiratory depression associated with anesthesia may be more profound than that observed in species in which expiration is a passive process. Because the muscles of ventilation include many of the same muscles used for locomotion, these two functions are relatively incompatible. Chelonians are faced with additional respiratory challenges, because expansion of the thoracic cavity by movement of the ribs is not possible. The dorsal surface of the lungs is attached to the carapace, and the ventral surface is attached to the abdominal viscera. Inspiration is accomplished by enlarging the visceral cavity, and expiration occurs by forcing the viscera up against the lungs, driving air out. This is accomplished by contraction of various posterior abdominal muscles and several pectoral girdle muscles.

Control of Respiration

The control of respiration in reptiles is poorly understood. Both peripheral receptor and centrally mediated control have been proposed. It seems more likely that there is an interaction between a central system, which generates the pattern of respiration, and afferent chemoreceptor input.[40,41] Both carbon dioxide and pH changes appear important for stimulating normal ventilation, but there is evidence that even under normoxic conditions, oxygen tension may play a role in normal ventilation.[42] Although there is some species variation, reptiles are generally viewed as episodic breathers.[43-45] Pulmonary vascular perfusion is also intermittent, and changes in perfusion are generally synchronous with changes in respiratory rate and rhythm.[17,46-48] Ambient temperature has variable effects on the frequency, tidal volume, and minute ventilation,[49] and due consideration should be given to maintaining the optimal temperature for a particular species.

Effects of Inspired CO_2 and O_2

The response of reptiles to inspired CO_2 is quite variable. Inspiration of more than 4% CO_2 in snakes and lizards produces an increase in tidal volume, a decrease in respiratory frequency, and an overall decrease in minute ventilation.[50,51] In turtles, specifically *Pseudemys scripta* and *Chrysemys picta,* the response to an increase in CO_2 is an increase in minute ventilation as a result of increases in both respiratory frequency and tidal volume.[17,52-54] In turtles, breathing less than 21% but more than 10% oxygen produces little change in the respiratory pattern. At inspired oxygen concentrations below 10%, some species increase ventilation, whereas others retain their resting minute ventilation and others may decrease ventilation.[45,50,55-57] In those species in which minute ventilation decreases or remains unchanged, metabolic oxygen consumption decreases. During anesthesia, most reptiles are maintained with an inhalant anesthetic delivered in 100% oxygen. The delivery of a high oxygen concentration may further compound respiratory depression by blunting the contribution of oxygen to stimulate normal ventilation. In several reptilian species, exposure to 100% oxygen significantly decreases minute ventilation,[50,52,58-60] suggesting that high inspired oxygen may be responsible for at least some of the respiratory depression seen during anesthesia. The magnitude of this effect is likely small compared with the effects of anesthetics on central control of respiration and the muscles of respiration. However, there is some evidence that in the green iguana, recoveries from isoflurane anesthesia may be faster when the animal is ventilated with room air rather than 100% oxygen, possibly by improving ventilation and the subsequent removal of the inhalant from the body.[61] Interestingly, in studies using Dumeril's monitors, no significant differences in recovery times from either isoflurane or sevoflurane anesthesia were found between animals ventilated with room air or those ventilated with 100% oxygen.[62] This may reflect differences in study methods or species differences.

Renal System

Reptiles cannot produce urine more concentrated than plasma, making the excretion of nitrogenous wastes more difficult for terrestrial reptiles. Most reptiles excrete nitrogenous waste as uric acid (uricotelic). Some turtles and crocodilians can also excrete urea. Uric acid is produced in the liver and, unlike ammonia and urea, it is very insoluble in water and is excreted as a semisolid. In the reptilian kidney tubule, urine is very dilute so that uric acid remains in the solution. Urine empties into the cloaca and then into the bladder or large intestine, where water is reabsorbed, causing the uric acid to precipitate. This results in the excretion of nitrogenous waste with relatively little water. The bladder of some reptiles can be used for the storage of water. Reptilian urine is not a good indicator of renal function. Many reptiles have specialized salt-excreting glands that allow for the excretion of very high concentrations of sodium, potassium, and chloride. Many reptiles living in extremely arid environments can tolerate the marked fluctuations in total body water and plasma osmolarity that can occur in these environments. When faced with limited water supplies, plasma osmolarity can rise to levels higher than those known in any other vertebrate species.

Hepatic System

The reptilian liver appears to be similar in structure and function to the liver of other vertebrates. Although there is little detail known about the reptilian liver, it is assumed that it probably plays important roles in tolerance to anaerobic metabolism, hypothermia, and adaptation to the physical environment. The liver of reptiles has a lower metabolic capacity compared with mammalian livers,[63] and the metabolic rate is very sensitive to changes in temperature.[64] The lower metabolic rates of reptilian liver probably account for at least some of the prolonged effects commonly seen with drugs such as antibiotics. This may partly contribute to the prolonged anesthetic recoveries seen when using drugs

that require extensive hepatic metabolism for termination of their clinical effect.

Clinical Anesthesia

Patient Assessment

Regardless of species or procedure, a thorough preanesthetic assessment should be performed on all patients. Patient assessment should include a complete history, species identification, and a full physical examination. Any additional supporting diagnostic tests such as blood work and imaging should be performed. Because most anesthetics produce some degree of cardiopulmonary depression, all animals should be physiologically stable before the induction of anesthesia. Unfortunately, in some reptiles, the size, disposition, or anatomy may prevent even the performance of a routine physical examination. In these animals, an assessment of body weight and general appearance may assist in determining the general health status of the animal. Species identification and information on the natural habitat of an animal may be useful when presented with a novel species. All animals should be kept at their PBT throughout the anesthetic period and recovery. Performing any anesthetic-related procedure early in the day allows animals predisposed to prolonged recoveries to recover during regular working hours rather than late into the night, when support staff and patient supervision may be reduced.[65]

Drug Administration Routes

The intramuscular route of drug administration is most common in reptiles. Historically, hindlimb and tail sites have been avoided because of concerns related to the first-pass effect associated with passage of any administered drug through the kidneys via the renal portal system. However, studies in some reptiles (turtles and green iguanas) suggest that this may be more of a theoretical than practical concern, because only a small amount of blood from the hindlimbs and tail passes through the kidney.[66,67] However, it is probably best to avoid hindlimb and tail administration of nephrotoxic drugs or those highly metabolized or excreted by the kidneys. The epaxial muscles provide a suitable injection site in most snakes. In lizards, the muscle mass of the forelimb (triceps and biceps), hindlimb (quadriceps, semimembranosus, and semitendinosus), and tail can be used. Caution should be used in species known to autotomize (drop) their tails (many geckos), because it is possible for an animal to "shed" its tail during handling. In chelonians, injections are most often administered in the triceps muscle. The cranial surface of the foreleg should be avoided, because the proximity of the radial nerve to injection sites in this area increases the risk of damage to this nerve. The pectoral muscles can also be used, although in many species there is a lack of significant muscle mass in this area.

Although intravenous drug administration is not always feasible in reptiles, the combination of good technique, practice, appropriate patient selection, and skilled physical restraint can facilitate predictable access to the ventral coccygeal vein in even very small snakes and lizards, and the dorsal coccygeal vein in tortoise and freshwater turtles. In sea turtles, the dorsal cervical sinus has also been used for intravenous administration of drugs.[68] Intravascular injection decreases the latency of onset of action of an administered drug. It also decreases the variability in uptake that is associated with intramuscular injections in reptiles. Some drugs produce tissue irritation after intramuscular irritation. Intravenous administration of these drugs may obviate such tissue irritation. Techniques for catheterization of the coccygeal vein in both lizards and crocodilians have been described.[69] Intravenous catheterization of the coccygeal or abdominal veins is mostly performed "blindly." In some species of turtles and tortoises, the jugular vein can be visualized, however; visualization of the jugular vein most often requires a skin incision and blunt dissection. Venous sinus sites are not ideal sites for intravenous catheter placement. Although over-the-needle catheters are most frequently used, a technique using a small gauge wire stylet through a needle (Seldinger technique) can be used to facilitate difficult catheterization. Cutdown procedures should be performed with a local anesthetic or general anesthesia, when required. Lidocaine diluted down to a 1% solution with sterile saline solution can be used for local infiltration. Although toxic doses have not been determined in reptiles, it is probably best to use less than 8 to 10 mg/kg. The most common sites for vascular access and associated technical tips are presented in Table 1.

Intraosseous catheterization is occasionally used to secure intravascular access in dogs, cats, and birds. Intraosseous catheter placement has been described in the green iguana and sea turtles.[33,70,71] This is a technique best suited for use in lizards and can be performed in most species. One study examining kidney function in green iguanas found similar renal uptake of the radioactive substance whether administered introsseously or in-

Table 1. Sites for Intravascular Access in Various Species of Reptiles

Squamates (snakes)

1) Coccygeal vein is located on the ventral midline of the tail. The needle should be inserted sufficiently caudal to the vent to avoid the hemipenes and anal sacs. The vessel is entered via a ventral midline approach, and the needle is advanced with gentle suction until the vein or a vertebral body is contacted.
2) Jugular vein can be used but requires a skin incision to visualize. An incision is made 4 to 7 scutes cranial to the heart at the junction of the ventral scutes and lateral body scales. The vein is then identified with blunt dissection just medial to the tips of the ribs.
3) Palatine vein is easily visualized in larger snakes and is located medial to the palatine teeth in the roof of the mouth. The technique is greatly facilitated by short-term anesthesia, but it is possible to collect blood from these vessels in awake animals using a mouth speculum.
4) Heart: Use of the heart for venipuncture is not recommended except in emergency situations.
5) Intraosseous: to this author's knowledge, these are no intraosseous sites described for drug administration in snakes.

Squamates (lizards)

1) Coccygeal vein is located on the ventral midline of the tail. The needle should be inserted sufficiently caudal to the vent to avoid the hemipenes. The vessel can be entered from either a ventral midline approach or laterally. The ventral approach is simple to perform: the needle is advanced with gentle suction until the vein or a vertebral body is contacted. The lateral technique involves inserting the needle just ventral to the transverse process of the vertebral body and walking the needle ventral until the vein is contacted.
2) Ventral abdominal vein is located on the ventral midline of the abdomen and can be entered percutaneuosly or via a small skin incision for direct visualization of the vessel.
3) Cephalic vein is located on the dorsal surface of the distal foreleg. A skin incision is generally required for visualization.
4) Jugular vein is located on the lateral surface of the neck at about the level of the tympanum and may be palpated in some species but is generally difficult to visualize. A small skin incision is often required for direct visualization. The jugular veins tend to be located more dorsal than those in mammals. There is a large lymphatic sinus close to the vein, and contamination with this lymph fluid occurs frequently.
5) Intraosseous techniques have been described for the distal femur, proximal tibia, and proximal humerus.[65] The techniques are similar to those described for other small animal patients.

Chelonian (turtles and tortoises)

1) Dorsal coccygeal vein is located midline dorsal to the coccygeal vertebrae. It is a technique requiring minimal restraint. The needle is introduced in a craniad direction at a 45° to 90° angle from the skin.
2) Dorsal cervical sinus (supravertebral) is located on the dorsolateral aspect of the neck in sea turtles. It is located one third the distance from the carapace to the head, cranial to the craniad edge of the carapace. The head is directed forward and down, and the needle is introduced lateral to midline on either side.
3) Occipital venous sinus has been described in freshwater turtles and is located midline below the occipitus. It requires that the head be restrained firmly and in an extended ventroflexed (45-90° angle from the carapace) position. The needle is then introduced midline just caudal to the occipitus and nearly perpendicular to the spine. Lymph contamination is a possibility.
4) Subcarpacal sinus or supravertebral sinus is located under the carapace just caudal to the last cervical vertebrae and craniad to the first thoracic vertebrae. This sinus can be approached by pressing the head into the shell and palpating for the first thoracic vertebrae (incorporated into the carapace). The needle should be directed through the skin just caudal to the juncture of the last cervical vertebrae up towards the carapace and first thoracic vertebrae.
5) Jugular veins are located on the lateral sides of the neck at about the level of the tympanum. In some species, venipuncture of the jugular vein is relatively straightforward and can be visualized, or a small skin incision can be made to facilitate direct visualization. Unfortunately, this technique requires the neck to be fully extended, and in uncooperative animals, a short-acting anesthetic or tranquilizer may be required.
6) Intraosseous techniques have been described using the carapace/plastron bridge, but like other authors,[65] this author has found most catheters end up in an intracoelomic, rather than intraosseous, position. The technique is descried as passing a needle at an angle through the bony bridge between the plastron and carapace.

Table 2. Dosages of anesthetic drugs used in chelonian spp

Drug	Route	Dosage	Comments	Reference
Glycopyrrolate	IV, IM, SC	0.01-0.04 mg/kg*	May increase viscosity of secretions, increasing risk of obstruction	Malley 1999[72]
Atropine	IM, IP	0.04 mg/kg*	May increase viscosity of secretions, increasing risk of obstruction	Schumacher 1996[106]
Acepromazine	IM	0.1-0.5 mg/kg*	Minimal effect	Millichamp 1988
Medetomidine	IM, IV	50-100 μg/kg (tortoises) 150-300 μg/kg (aquatic turtles)	Variable sedation when used alone, best combined with ketamine	Lock 1998[86] Sleeman 2000[84] Greer 2001[87] Chittick 2002[68] Dennis 2002[85]
Xylazine	IM	2 mg/kg	Did not improve anesthesia over ketamine alone in red-eared sliders (*Trachemys scripta elegans*)	Holz 1994[83]
Atipamezole	IM, IV	500 μg/kg	May be best to administer IM	Lock 1998[86] Sleeman 2000[84] Dennis 2002[85]
Midazolam	IM	1.5-2.0 mg/kg	May be unreliable on its own in some species Best in combination with ketamine	Bienzle 1992[80] Harvey-Clark 1993[82] Oppenheim 1995[81]
Ketamine	IM, IV	5-20 mg/kg (in combination)	Best combined with alpha$_2$ agonist or benzodiazepine Doses up 60 mg/kg have been used	Bienzle 1992[80] Holz 1994[83] Lock 1998[86] Greer 2001[87] Chittick 2002[68] Dennis 2002[85]
Tiletamine-zolazepam	IM	3.5-10 mg/kg	Prolonged recoveries likely	Gray 1974[79] Boever 1982[77]
Propofol*	IV, IO	3-5 mg/kg	Predictable effects and recovery, first choice for induction of anesthesia	Heard 2001[65]
Isoflurane*	Inhaled	2%-3% on vaporizer	MAC not determined	Heard 2001[65]
Sevoflurane	Inhaled	4%-5% on vaporizer	MAC not determined	Heard 2001[65]

**Dose anecdotal or determined by extrapolation from other species.*

travenously (IV).[70] This suggests that intraosseous drug administration is a suitable alternative to intravenous administration. To this author's knowledge, propofol is the only anesthetic drug that has been studied for intraosseous administration, but many other anesthetic and nonanesthetic drugs have been administered successfully via this route.

Premedication

Premedications are used to facilitate handling and intravenous catheterization, reduce handling stress, and reduce the negative side effects associated with the administration of higher doses of drugs used for the induction or maintenance of

Table 3. Dosages of Anesthetic Drugs Commonly Used in Lizards and Snakes

Drug	Route	Dosage	Comments	Reference
Glycopyrrolate	IV, IM, SC	0.01-0.04 mg/kg*	May increase viscosity of secretions increasing risk of obstruction	Malley 1999[72]
Atropine	IM, IP	0.04 mg/kg*	May increase viscosity of secretions increasing risk of obstruction	Schumacher 1996[106]
Acepromazine	IM	0.1-0.5 mg/kg*	Minimal effect	Millichamp 1988
Medetomidine	IM, IV, IO†	150 μg/kg*	Not commonly used	Heard 2001[65]
Midazolam	IM	0.5-2.0 mg/kg*	Minimal sedation	Redrobe 2004[73]
Ketamine	IM, IV, IO	22-88 mg/kg (alone) 10-15 mg/kg (combined with medetomidine)	Best used in combination with medetomidine	Glenn 1972[75] Cooper 1974[74] Wood 1982[76] Custer 1980[35] Arena 1988[32] Schumacher 1997[38]
Tiletamine-zolazepam	IM, IV, IO	3-6 mg/kg	Prolonged recoveries likely Even at high doses animals may remain responsive	Gray 1974[79] Boever 1982[77] Clyde 1994[78] Stirl 1994[39] Mauthe 2004[89]
Propofol	IV, IO	5-10 mg/kg	Predictable effects and recovery, first choice for induction of anesthesia	Bennett 1998[133]
Isoflurane	Inhaled	2-3% on vaporizer	MAC 1.5-2.1%	Maas 2002[99] Mosley 2003[100] Bertelsen 2005[98,99,90]
Sevoflurane	Inhaled	4-5% on vaporizer	MAC 2.5%	Bertelsen 2005[97]

**Dose anecdotal or determined by extrapolation from other species.*
†IO for lizards only.

anesthesia. Not all drugs administered before the induction of anesthesia will produce sedation, whereas others will not necessarily reduce the dose of drugs used for the induction or maintenance of anesthesia. Thus, the goal of premedication should be established when selecting appropriate drugs. If the primary goal of premedication is to facilitate restraint, it may be most appropriate to administer a combination of ketamine and an analgesic. If little chemical restraint is required, the premedication selection will be directed toward achieving preemptive analgesia.

Atropine and glycopyrrolate should probably not be used to decrease salivation but if bradycardia develops (Tables 2,3) may be indicated. Anticholinergics can increase salivary viscosity, and this may predispose the patient to obstructions from highly viscous mucous in airways or small-diameter endotracheal tubes. Anticholinergic drugs can alter intracardiac shunt fractions in reptiles. This may alter a patient's response to anesthetic drugs, particularly inhaled anesthetics.

Phenothiazines such as acepromazine tend to be relatively ineffective sedatives in reptiles (Tables 2,3). Their use requires the administration of large doses that are associated with prolonged effects. Acepromazine is not a very useful drug in reptile anesthesia.[65,72,73]

Ketamine, a phencylidine, is not routinely used as a premedication drug in most animals. Ketamine is regarded as an anesthetic, but at subanesthetic doses, ketamine produces analgesic effects and can produce profound restraint (Tables 2,3,4). At subanesthetic doses, ketamine induces a cataleptic state

characterized by the presence of uncoordinated voluntary and involuntary muscle movement that may appear in response to external stimuli. It is very important to recognize that an animal in this state should not be considered to be at a surgical plane of anesthesia. Ketamine is used frequently as a component of a premedication protocol to produce restraint in chelonians and other reptiles. Ketamine has also been used alone for restraint or the induction of anesthesia in a variety of reptiles.[74-76] In snakes, ketamine alone produces hypertension, tachycardia, bradypnea, and hypoventilation.[35,38] Similar effects on heart rate and respiratory rate have been observed in skinks (*Tiliqua rugosa* and *Egernia kingii*).[32] Because ketamine is also associated with muscle rigidity, it is most often combined with drugs that produce muscle relaxation (benzodiazepines, alpha$_2$ agonists).

Telazol (Fort Dodge Laboratories, Fort Dodge, IA) is a proprietary combination of tiletamine and zolazepam. Tiletamine is a long-acting phencyclidine similar to ketamine, whereas zolazepam is a long-acting benzodiazepine similar to diazepam. Telazol has been used in reptiles with variable results (Tables 2,3).[77-79] In the boa constrictor (species not identified), tiletamine-zolazepam (12.5 mg/kg intramuscularly [IM]) failed to produce surgical anesthesia, but produced safe immobilization associated with a transient increase in heart rate and an increase in respiratory rate that was not associated with changes in minute ventilation, systolic blood pressure, or arterial oxygen saturation.[39] The combination of tiletamine and zolazepam is a less desirable combination than ketamine and midazolam because of the longer duration of action of the tiletamine/zolazepam, which can lead to more prolonged recoveries. Telazol is occasionally used in very large reptiles to reduce the injected volume; however, prolonged recoveries may be observed.

Midazolam is a water-soluble benzodiazepine that can be administered both IM and IV. Diazepam is not recommended for intramuscular use, because it is very poorly absorbed via this route of administration. Midazolam (2 mg/kg) is used in combination with ketamine (20-40 mg/kg IM) to facilitate handling and to induce anesthesia in chelonians.[80] Midazolam (1.5 mg/kg IM) has also been used alone in freshwater turtles (*Trachemys scripta elegans*) with some success,[81] but fails to provide significant sedation when used alone in snapping turtles (*Chelydra serpentina;* 2.0 mg/kg IM)[80] and painted turtles (*Chrysemys picta;* 2.0 mg/kg IM).[82]

The alpha$_2$ agonists produce analgesia, sedation, and muscle relaxation in mammals. In reptiles, they appear to produce desirable levels of sedation and muscle relaxation. The analgesic effects of alpha$_2$ agonists have not been evaluated in reptiles, but clinical impressions suggest an analgesic effect as well. Xylazine (2 mg/kg IM), in combination with ketamine (60 mg/kg IM), produced a variable level of light anesthesia suitable for minor procedures only in red-eared sliders.[83] More recent reports describe the use of medetomidine rather than xylazine. Medetomidine has a higher alpha$_2$:alpha$_1$ binding ratio than xylazine. Medetomidine (150 μg/kg IM) is an effective sedative in desert tortoises (*Gopherus agassizii*).[84] Medetomidine, in combination with ketamine, produces anesthesia of a sufficient depth to allow endotracheal intubation in several species of tortoise,[85,86] red-eared slider turtles (*Trachemys scripta elegans*),[87] and loggerhead sea turtles (*Caretta caretta*).[68]

The administration of medetomidine to several mammalian species is known to be associated with marked cardiovascular side effects that include arrhythmias, a decrease in cardiac output, and an increase in systemic vascular resistance. It appears that some of these changes may also occur in reptiles. Medetomidine induces a significant decrease in heart rate, respiratory rate, and systolic, diastolic, and mean ventricular pressures, and a decrease in ventricular partial pressure of oxygen in desert tortoises (*Gopherus agassizii*).[84] Medetomidine, in combination with ketamine, produces a moderate increase in arterial pressure and moderate hypercapnia and hypoxemia in desert tortoises.[85] One advantage of using alpha$_2$ agonists is that they are reversible, a property that can be of benefit when faced with prolonged recoveries. After the administration of atipamezole, animals appear normal within 30 to 60 minutes. Atipamezole (500 μg/kg IV) produces marked arterial hypotension,[85] but intramuscular administration does not appear to produce significant alterations in ventricular pressures.[84] Thus, intramuscular, rather than intravenous, is the recommended route of administration of atipamezole.

Opioids are very poor sedatives in reptiles.[65] Although they are commonly used in the perianesthetic period to provide analgesia,[88] there are few studies evaluating the use of opioids for pain and analgesia. Regardless, it is strongly recommended that an analgesic be administered before any procedure that may be associated with significant tissue damage, regardless of whether additional sedation is required for the induction and maintenance of anesthesia.

Induction of Anesthesia

Both ketamine and tiletamine can be used alone to induce light anesthesia or a level of restraint adequate for endotracheal intubation. It is questionable whether satisfactory surgical anesthesia can be achieved with ketamine or telazol alone in reptiles.[32,39,74,75,77] Many reptiles maintain reflex movement even when administered very high doses of ketamine and tiletamine. To achieve a level of anesthesia appropriate for surgery, ketamine should be administered in combination with a drug that produces muscle relaxation (midazolam or medetomidine). In iguanas, tiletamine (10 mg/kg IM) has been evaluated as the sole drug for the induction and maintenance of short-term anesthesia. The mean induction time is 6.5 minutes, and a level of anesthesia sufficient to allow endotracheal intubation is produced.[89] Recoveries may be protracted. Telazol (33-44 mg/kg) produced surgical anesthesia in green iguanas, but in some animals anesthesia persisted for 12 hours or more.[77]

Propofol is an alkylphenol, structurally different from other anesthetics such as barbiturates, eugenols, or steroids. It is prepared in an intralipid solution intended for intravenous use. In mammals, propofol produces a rapid and smooth induction of anesthesia with a very predictable duration of action. The elimination of propofol involves both hepatic and nonhepatic sites, most likely the lung. Propofol (3-10 mg/kg IV) is the induction drug of choice when intravenous access is available. It is a reliable means of inducing anesthesia without unnecessarily prolonging recovery time. In mammals, the administration of propofol is commonly associated with apnea and hypotension. The intraosseous administration of propofol (5 and 10 mg/kg) has been evaluated in the green iguana. In this species, the administration of propofol is associated with prolonged periods of apnea.[33]

Inhaled anesthetics can be used for the induction of anesthesia. The least soluble of the inhalant anesthetics, sevoflurane, desflurane, or isoflurane, is preferred, because the solubility of an inhaled anesthetic is inversely related to the times for both induction of, and recovery from, anesthesia. In some reptiles, induction of anesthesia with an inhaled anesthetic can be very prolonged because of breath holding. Mask induction of chelonians can be very difficult because of breath holding and limited access to the head. The induction of anesthesia with inhaled anesthetics is generally easier in snakes and lizards, but prolonged periods of breath holding may occur in these species as well. In some species, breathing can sometimes be stimulated by stroking the lateral thorax. The average induction time for green iguanas using isoflurane in 100% oxygen administered by face mask is approximately 20 minutes. The prior administration of butorphanol does not effect the duration of induction.[90] In Dumeril's monitors, induction times with sevoflurane (11.20 ± 3.77 min) are significantly faster than the induction times using isoflurane (13.00 ± 4.55 min).[62] The addition of nitrous oxide (34% oxygen, 66% nitrous oxide) to the carrier gas significantly reduces the time to induction of anesthesia with sevoflurane.[62] In addition to mask induction with an inhaled anesthetic, many reptiles can be tracheally intubated while awake and then manually ventilated to induce anesthesia. This technique can reduce the time for induction of anesthesia, but it may be associated with high levels of stress and should be reserved for the exceptional circumstance. Topical administration of local anesthetic should be applied to the glottis if possible before an animal is intubated awake.

Muscle relaxants such as succinylcholine (depolarizing) and atracurium (nondepolarizing) are used in reptiles.[78,91-95] Muscle relaxants act by competitive inhibition of acetylcholine at the neuromuscular junction, leading to paralysis. They are used primarily to facilitate immobilization and tracheal intubation of crocodilians,[78,91,93,94] but are also used in chelonians.[95] Muscle relaxants are not anesthetics and have no analgesic or amnesic properties. The routine use of muscle relaxants for immobilization of reptiles should be avoided. Their use may be indicated (but always in combination with analgesic and amnestic drugs) for managing very dangerous and aggressive species or in field situations, when a very rapid immobilization is required to limit the potential for animal injury.

Endotracheal Intubation

Intubation is easily accomplished in most reptiles. In snakes, the glottis is located rostrally, and at the base of the tongue in lizards and chelonians. The glottis is easily visualized, and intubation is accomplished via direct visualization. A small drop of lidocaine (diluted to 1%) can be used to desensitize the glottis and may facilitate tracheal intubation. In some aquatic reptiles, anatomical modifications of glottal folds may obscure direct visualization of the glottis. The animal should be intubated with the largest diameter tube that can be placed easily. The mucous of reptiles tends to be very viscous, and mucoid plugs can form in endotracheal tubes during longer procedures. Attention to this possibility is important and can be recognized as an inability of the lungs to fully

deflate during expiration. The trachea of chelonians bifurcates quite rostrally, and single-lung intubation is possible. The tracheal rings in chelonians and crocodiles are complete, and in most reptiles, cuffed endotracheal tubes are avoided to prevent accidental over inflation and possible tracheal necrosis.

Maintenance of Anesthesia

Inhalant anesthesia is commonly used for maintenance of anesthesia in reptiles. The physical properties of the newer inhaled anesthetics afford minimal uptake and metabolism and predictable recovery. The administration of inhalant anesthetics is normally performed with oxygen as the carrier gas and can reduce the risk of hypoxia, despite the observation that reptiles are more tolerant of periods of hypoxemia than mammals or birds.[96]

Methoxyflurane and halothane are no longer readily available and are not inhalant anesthetics recommended for reptiles. Isoflurane, sevoflurane, and desflurane are more appropriate choices. Both isoflurane and sevoflurane have been evaluated in reptiles.[36,37,62,90,97-100] The minimal alveolar concentration (MAC) of sevoflurane in Dumeril's monitor has recently been found to be 2.51 ± 0.5%; this is similar to values in mammals (2.1%-2.3%).[97] The range of MAC values for isoflurane reported for reptiles (1.54%-3.14%) is more variable than that reported for mammals and birds. This may simply be a reflection of the techniques used for MAC determination, the body temperature of the patient, or actual species differences. Using comparable techniques, the MAC of isoflurane in the green iguana (2.1 ± 0.6%) and Dumeril's monitor (1.54 ± 0.17%) were found to be significantly different.[90,98] There is also greater variability in MAC values in green iguanas than those observed in Dumeril's monitors. The pronounced right-to-left intracardiac shunting in snakes, turtles, and nonvaranid lizards may account for some of these differences. In many aquatic reptiles that are capable of long periods of dive-induced breath holding, significant right-to-left shunting produces end-tidal anesthetic concentrations of inhaled anesthetics that may not be entirely reflective of those in the blood and hence the brain. Concentrations in the lung may substantially overestimate levels in the brain, leading to erroneously elevated MAC when using traditional methods of MAC determination.

That many reptiles either fail to become adequately anesthetized or induce to anesthesia very slowly with an inhaled anesthetic likely reflects the impact of significant right-to-left intracardiac shunting on the uptake of an inhaled anesthetic. A right-to-left intracardiac shunt results in a reduction of the volume of blood that is exposed to the inhalant at the gas exchange interface. In contrast, it is not uncommon to observe deep anesthesia in reptiles, even after very few breaths. This may be the result of the accumulation of inhaled anesthetic in the sac-like structure of reptilian lungs and the breathing patterns observed in most reptiles. Many reptiles are episodic breathers that take several breaths that are followed by a prolonged inspiratory pause. Such ventilation patterns are energetically efficient and may have developed to best meet the low metabolic oxygen demand of reptiles. This ventilation pattern, in association with the sac-like structure of the reptilian lung, affords continual access to oxygen without unnecessary energy expenditure. As a consequence, the lung may function as a reservoir of inhaled anesthetic that is available to the patient during breath holding. Thus, the extent of right-to-left cardiac shunting may have more of an impact on the speed of induction of anesthesia with an inhaled anesthetic than does ventilation rate.

Dose-dependent cardiovascular depression occurs during isoflurane anesthesia of the green iguana.[36] Both blood pressure and heart rate decrease in a dose-dependent manner. It is likely that similar cardiovascular depression occurs in other reptiles. However, the effects on heart rate are likely to be more variable. Ventricular blood pressures and heart rates in desert tortoises did not change with increasing dose of sevoflurane anesthesia.[37] Interestingly, the dose of isoflurane required to induce cardiovascular arrest in healthy green iguanas is much greater than the maximum percent delivered by most commercial isoflurane vaporizers (5%).[100] Even at levels 4 times greater than MAC (2.1%), isoflurane fails to induce cardiovascular arrest, suggesting a wide safety margin for this anesthetic when used in the healthy green iguana (See Tables 2 and 3).

Equipment Used during the Administration of Inhalant Anesthesia

Standard inhalant equipment used in small animal anesthesia is suitable for administering inhalant anesthetics to most reptiles. An anesthetic machine equipped with a flowmeter, precision vaporizer, and either a non-rebreathing circuit or a circle system is often used. In very small patients weighing less than 1 kg, a non-rebreathing or a pediatric circle system is preferred. The dead space associated with a standard adult circle system may lead to substantial rebreathing of expired gases. However, in reptiles it has been

shown that adding carbon dioxide to the inhaled gases may actually improve ventilation during inhalant anesthesia.[34,101] Oxygen flow rates should meet or exceed the oxygen consumption of the patient. The flow rates used for standard small animal patients are suitable for most reptiles: 50 to 100 mL/kg/min when using a rebreathing system and 200 to 300 mL/kg/min 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. Ventilators are useful when anesthetizing reptiles, because most, if not all, become apneic during general anesthesia. Most commercial ventilators are not well adapted to deliver the small tidal volumes required by many reptiles. It is important to recognize that, in addition to the ventilator-delivered tidal volume, the fresh gas flow rate contributes to the delivered tidal volume during inspiration. This is most significant in very small animals when high oxygen flow rates are used. Ventilators designed for small mammals are particularly useful when ventilating small reptiles.

Monitoring and Perianesthetic Support

The goal of anesthesia is to achieve and maintain a reasonable surgical plane of anesthesia while preventing anesthetic overdose. Safety during anesthesia is prevented by titration of the inhaled anesthetic in response to an individual animal's requirements. The necessity for such adjustments is determined by careful patient monitoring. Comprehensive monitoring includes assessment of several reflexes and a determination of the response of the cardiopulmonary system to anesthesia.

Monitoring of Reflexes

In 1957, Kaplan and Taylor[102] published a study involving the use of ether, nembutal (sodium pentobarbital), and urethane in adult turtles (*Pseudemys spp*). They recorded heart rates and rectal temperatures, and observed the degree of muscle tone, voluntary movements, pupillary diameter, and presence or loss of the corneal reflex to assess depth of anesthesia. They defined deep or surgical anesthesia as a plane of anesthesia associated with muscular relaxation, absence of response to painful stimuli, and loss of movement. Kaplan and Taylor were pioneers in this area; anesthetic depth in reptiles is still determined with some of the same qualitative parameters they defined. Interestingly, when reptiles are induced with inhalant anesthetics, muscle relaxation begins at midbody and moves cranially, then caudally. Tail tone is lost last. This has been demonstrated in lizards administered halothane and sevoflurane,[34,62] and in turtles administered ether.[103] These features can be used when assessing depth during induction and recovery.

Cardiovascular Monitoring

Direct auscultation of cardiac function is a simple method of assessing heart rate and rhythm. External auscultation is best performed using a stethoscope with a small pediatric bell, but this technique can be difficult because of interference from scales or the carapace and plastron in chelonians. A dampened gauze placed between the chest wall and the stethoscope bell can reduce interfering noise from scales. In anesthetized animals, a small esophageal stethoscope works very well for direct auscultation of the heart. The stethoscope tubing should be advanced in increments until the point of maximal sound intensity is reached. It is not uncommon for some reptiles to have heart rates of 20 beats per minute or less. If the esophageal stethoscope is not advanced slowly, it is easy to bypass the heart and place the stethoscope in the stomach. This may predispose the animal to regurgitation.

An excellent alternative to direct auscultation is the use of an ultrasonic Doppler device, which detects blood flow in major vessels and the heart itself. There are a variety of probes; adult and pediatric flat probes and pencil probes. These probes are most easily placed over the heart and held in place with tape. Alternatively, the carotid, coccygeal, or femoral arteries may be used as sites for probe placement. In chelonians, the shell generally precludes use of the heart. Pediatric probes have greater sensitivity in detecting flow in small vessels and are preferred for use in reptiles. In addition to providing an audible signal of blood flow through the vessels over which the probe is placed, the Doppler unit can also be used to assess blood pressure in a manner similar to that used during the anesthesia of nonreptilians. A small, inflatable cuff is placed around the limb or tail proximal to the probe. Blood pressure values obtained with this technique in reptiles have not been compared with direct arterial measurements; however, the technique is still useful for assessing trends in changes in blood pressure.

The electrocardiogram (ECG) can be used to monitor the electrical activity of the heart in reptiles. At the very least, the ECG provides an assessment of heart rate and rhythm. Electrical activity can con-

tinue in the heart despite loss of muscular activity, a condition known as pulseless electrical activity or electromechanical dissociation. Thus, it is best not to rely solely on an ECG for evaluation of cardiovascular function. The morphology of the reptilian ECG is similar to that of mammals with the addition of an SV wave proceeding the P wave.[44]

Although the ECG leads on reptiles are positioned similar to the standard 3-lead configuration in mammals, some modification in lead placement will improve signal strength and ECG quality. In lizards, the right and left forelimb leads are placed in the cervical region, because the heart is located in the pectoral girdle.[104] In snakes, the active leads are placed two heart-lengths cranial and caudal to the heart.[104] The heart in snakes is located 20% to 25% of the entire body length from the head and can often be identified by direct visualization of ventral scale movement caused by cardiac activity. In chelonians, the forelimb leads are placed on the skin between the neck and the forelimbs.[104] Stainless-steel suture loops or needles can be placed through the skin and attached to the leads and can improve signal strength.

Respiratory Monitoring

Direct visualization of respiratory movements can be extremely difficult in many reptiles, particularly chelonians and very small species. Additionally, chest and body wall excursions, bag movement, and fogging of the endotracheal tube can be misleading and may not always represent adequate ventilation. Because most reptiles require intermittent positive-pressure ventilation the utility of monitoring spontaneous respiration is reduced. Reptiles rarely breathe well when anesthetized,[33,65,105,106] making mechanical ventilation appropriate in most cases. Current recommendations for ventilatory support include rates of 2 to 6 breaths per minutes using tidal volumes ranging from 15 to 30 mL/kg, with peak airway pressures less than 10 cm H_2O. Manual intermittent positive-pressure ventilation is commonly performed, but several small animal-specific ventilators are now available.

Pulse oximetry is a noninvasive method used to assess functional hemoglobin saturation. Under normal circumstances, this value correlates closely with arterial hemoglobin saturation. Although pulse oximetry is used frequently during reptile anesthesia, the results should be interpreted with caution. Pulse oximetry was specifically developed for use in humans, using the oxygen-binding characteristics of mammalian hemoglobin to guide the development of the technology.[88] A reflectance probe for pulse oximetry in reptiles is most commonly placed in either the esophagus or cloaca. The heart rate reported by the pulse oximeter should correlate with the heart rate determined using direct methods (auscultation). The efficacy of this technology has only been assessed in a single reptilian species, the green iguana. In this species, values obtained during pulse oximetry with an esophageal reflectance probe placed in the esophagus (functional hemoglobin saturation) correlate closely with arterial hemoglobin saturation (arterial hemoglobin saturation) of blood taken from the abdominal aorta.[61] Other investigators have not been able to establish such a relationship between arterial hemoglobin saturation and hemoglobin saturations determined using pulse oximetry.[36]

Capnometry measures the amount of carbon dioxide in the expired gas during the ventilatory cycle. End tidal refers to the fact that the quantitative measurement derived during capnometry refers to the concentration of carbon dioxide in the last portion of the expired volume, the end-tidal volume. This gas most accurately reflects the gas contained in the gas exchange portions of the lung, rather than the gas in the conducting airways. End-tidal carbon dioxide concentrations are generally reflective of the carbon dioxide concentrations in arterial blood, although the level of carbon dioxide is generally lower because of the dilution of the expired carbon dioxide by noncarbon dioxide–containing gases in the conducting airways. Much more information can be obtained from a capnogram, a graphic representation of the end-tidal carbon dioxide concentrations over the entire respiratory cycle. Although capnography is a useful monitoring tool in mammals with normal lungs, the utility of capnography in monitoring respiratory function in reptiles has not been established. The presence of right-to-left intracardiac shunts and dead space ventilation associated with the unique structure of many reptilian lungs makes information gathered with this monitoring modality difficult to interpret.

Blood gas analysis in reptiles is subject to significant over-interpretation and misinterpretation. Numerous factors such as site of sampling, arterial versus venous blood, species, inspired oxygen concentration, thermoregulatory status, and the ventilatory status of the patient (spontaneous versus controlled) will all affect interpretation of blood gas values. Reptiles tend to be much more tolerant to alterations in pH, partial pressure of carbon dioxide, and partial pressure of oxygen (Po_2) than mammals, and thus normal values for mammals may not be applicable to reptiles. This said, in general, normal pH in reptiles

tends to be similar to that in mammals, provided comparisons are made at identical temperatures. Most reptiles have body temperatures below that of most mammals and, consequently, their normal pH values tend to be higher. Partial pressure of carbon dioxide and Po_2 tend to be lower in reptiles when compared with the same values in mammals. Po_2 values are lower as a result of intracardiac shunting and also intrapulmonary shunting and ventilation-perfusion mismatching. There is evidence that in some reptiles there may also be impairment to diffusion of oxygen from the lung into the blood.[42] Given our current state of knowledge, it is difficult to critically evaluate blood gas analysis in reptiles.

Fluid Therapy

Fluids should be administered before anesthesia if clinically significant dehydration is noted. Fluids are best administered IV or intraosseously, but they can also be given intraperitoneally (IP) or subcutaneously. Fluid movement, distribution, and homeostasis in reptiles vary significantly from mammals. Reptiles tend to have a greater proportion of total body water in the intracellular space (45%-58%).[107] For this reason, some have suggested using hypotonic replacement solutions. However, it is not clear that this is of benefit to the animal unless the dehydration is associated with pure water loss. It is probably best to use a standard balanced electrolyte solution. Some reptiles are capable of tolerating extreme alterations in total body water and plasma osmolarity when water resources are scarce. The significance of such an adaptation for fluid therapy is not clear. Each patient should be carefully assessed, and the fluid therapy plan should be tailored to meet the needs of the individual patient.

Thermal Support

Reptiles are ectothermic animals that derive nearly all their body heat from the external environment. Thermoregulation in reptiles is a complex interaction between the animal's internal environment and the external environment. Body temperature is regulated primarily through complex behavior patterns and alterations in the cardiovascular system. Most reptiles have a PBT range that is associated with optimal metabolic function. It is probably best to maintain animals in hospital care at the upper end of the PBT for that species. This is easily accomplished with circulating warm water blankets, warm water bottles, and warm forced air. Body temperatures below the PBT for the individual animal may be associated with prolonged drug effects and may impair the animal's immune system and healing.[32,34,39]

Recovery

Reptiles should be monitored throughout the recovery period. Because recovery from anesthesia in reptiles can be prolonged, inhaled anesthetics are often discontinued 15 to 20 minutes before completion of the procedure. Early discontinuation of anesthesia should be done cautiously as unexpectedly rapid recoveries may occur subjecting the patient to unnecessary risk. Delayed recoveries seem to be more common in less aerobic reptiles, which may be the result of significant right-to-left shunting and low cardiac output that lead to a protracted elimination of the inhalant from the body. Body temperature is also very important for facilitating recovery, and optimal body temperature should be maintained throughout the recovery period. Consideration for the postoperative analgesic needs of the animal should be made based on clinical signs and the anticipated degree of tissue damage associated with the procedure. Reducing the oxygen concentration by allowing the animal to breathe room air may help hasten recovery.[61]

Postoperative Analgesia

The benefits of providing adequate analgesia are well recognized. The consequences of untreated pain are consistent with impaired homeostasis and may impair the immune system and inhibit healing.[108,109] The benefits of preemptive analgesia have also been demonstrated and cannot only reduce postoperative pain by decreasing central sensitization but may also facilitate healing and prevent and/or limit the actions of detrimental neurohumoral responses to pain.[110,111] Additionally, many analgesics can be used as part of a balanced anesthesia to reduce the doses of other anesthetics. This can help reduce the cardiopulmonary effects of general anesthesia.[112-114] In a recent survey of the membership of the Association of Reptile and Amphibian Veterinarians, 98% of the respondents indicated their belief that reptiles do feel pain. However, only 39% of respondents in this survey reported using analgesics in >50% of their patients.[88]

The neuroanatomic components necessary for nociception have been described in reptiles.[115,116] Endogenous antinociceptive mechanisms[116,117] and a demonstrable modulation of pain with pharmacologic agents known to be analgesics in other species have also been identified in reptiles.[118-121] In lizards

(*Gekko gecko*), spinal projections originating in the brain stem region (nucleus raphes inferior) that project to the superficial layers of the dorsal horn have been identified. These structures suggest the presence of tracts similar to those found in mammals that mediate descending inhibition of nociception.[121] Neurotransmitters that are important in pain modulation in mammals have also been identified in reptiles.[122] Although endogenous opioids and opioid receptors involved in reproduction and thermoregulation have been identified in reptiles, there is little known about the role of opioids in nociception.[122-125] This information suggests, at the physiologic level at least, that reptiles respond to nociceptive stimuli in a manner very similar to mammals. The assumption that an animal's ability to experience pain is directly related to its position on the phylogenetic tree may be inaccurate. Rather, it may be that phylogenetic position is more determinant of an animal's ability to express pain (See Table 4).

Analgesic Therapy in Reptiles

As an extremely diverse group of animals, reptiles demonstrate a wide variation in interspecies and intraspecies behaviors. This makes the recognition of alterations in normal behavior that may be indicative of clinically significant pain and stress particularly difficult. Thus, successful treatment of pain in reptiles demands an intimate knowledge of normal species-specific behaviors. In the absence of such knowledge, the delivery of appropriate analgesic therapy is based on an assessment of the likelihood of tissue trauma associated with a particular procedure. This recommendation is not new and was suggested by Flecknell in 1984 and Morton in 1986.[126,127]

There are three primary classes of analgesic drugs used in reptiles: local anesthetics, nonsteroidal antiinflammatory drugs (NSAIDs), and opioids. Local anesthetics provide complete anesthesia by interrupting nociception from the level of the nociceptor to the spinal cord. NSAIDs act by modulating nociception in both the periphery and the spinal cord. Opioids act by modulating nociception in the periphery, the spinal cord, and supraspinal areas of the central nervous system. Because reptiles have a more primitive central nervous system, the central actions of analgesic medications, particularly opioids, may not be as predictable as the more peripherally acting drugs. However, it is well documented that reptiles have opioid receptors in the central nervous system,[122,123] and that the proopiomelanocortin system (one of the three molecular systems from which all naturally occurring opioids are derived) is well preserved among vertebrates.[128,129] The unknown actions of opioids and NSAIDs in the central nervous system of reptiles may result in unpredictable variations in the duration, potency, and side effects of these drugs when the doses are determined by extrapolation from mammalian doses. Despite the unpredictable central effects of NSAIDs and opioids, their administration may offer the advantage of an increased duration of effect compared with that associated with the administration of local anesthetics.

There are very few investigations that describe the assessment of analgesics in reptiles. The cardiopulmonary effects of several opioids have been studied in indigo snakes (*Drymarchon corais couperi*), bullsnakes (*Pituophis catenifer sayi*), and immature caiman (*Caiman crocodilus*).[130] In general, the administration of a variety of opioids to these species is not associated with significant changes in physiologic parameters (heart rate, respiratory rate) or behavior (sedation or excitement). Morphine (0.05-1.0 mg/kg IP) and meperidine (2-4 mg/kg IP) both induce statistically significant increased latency in response to a hot-plate test in crocodiles (*Crocodylus niloticus africana*).[119,120] A dose-dependent response is observed with both of these opioids. A ceiling for effect is observed after the administration of 0.3 mg/kg of morphine or 2 mg/kg of meperidine. In this species, the latency of onset of action is approximately 30 minutes, and the duration of effect is 2 to 2.5 hours. The hot-plate test assesses thermal nociception, which may not accurately reflect nociception associated with other stimulus modalities.[131]

There are no studies evaluating the efficacy of NSAIDs or local anesthetics in reptiles. Certainly, reported clinical experience supports the efficacy of local anesthetics and NSAIDs, and they continue to be recommended.[73,132-135] However, it is important to note that all NSAID and local anesthetic doses are anecdotal or extrapolated from mammals or birds.

Local anesthetic toxicity can be avoided by careful attention to total dose of local anesthetic administered to a patient. It must be kept in mind that many reptile patients are very small, and large doses can easily be administered. In general, the toxic dose of a local anesthetic in mammals (dogs) should not be exceeded; lidocaine 22 mg/kg and bupivacaine 5 mg/kg.[136] In addition, excessive dilution of local anesthetics will decrease their efficacy. Local anesthetics should not be diluted more than 50% of the concentration of the drug in the bottle.

The role of cyclooxygenase in the pathophysiology of pain and inflammation of reptiles has not been

Table 4. Dosages of Drugs Used for Analgesia in Reptiles

Drug	Route	Dosage	Comments	Reference
Butorphanol*	IM	1 mg/kg		Bennett 1998[133] Mosley 2003[100] Schumacher 1996[106]
Buprenorphine*	IM, IV, SC	0.4-1.0 mg/kg		Malley 1997[135]
Morphine	IC, IM	0.05-4.0 mg/kg	Ceiling effect seen at 0.3 mg/kg in Nile crocodiles (*Crocodylus niloticus africana*)	Kanui 1992[119]
Meperidine	IC	1-4 mg/kg	Ceiling effect seen at 2 mg/kg in Nile crocodiles (*Crocodylus niloticus africana*)	Kanui 1992[119]
Ketamine	IM, IV, SC	10-100 mg/kg	High doses are associated with anesthesia Low doses <10 mg/kg likely associated with analgesia without sedation	Glenn 1972[75] Cooper 1974[74] Bennett 1998[133] Malley 1999[72] Custer 1980[35] Schumacher 1997[38] Arena 1988[32]
Xylazine*	IM	1-1.25 mg/kg		Malley 1997[135]
Medetomidine	IM, IV, IO	50-100 μg/kg (tortoises) 150-300 μg/kg (aquatic) 150 μg/kg (snakes and lizards)	Dosages required for analgesia may be less	Sleeman 2000[84] Dennis 2002[85] Greer 2001[87] Chittick 2002[68] Lock 1998[86]
Meloxicam*	IM, IV, PO	0.1-0.2 mg/kg q 24 h		Malley 1997[135]
Carprofen*	IM, IV, SC	2-4 mg/kg followed by 1-2 mg/kg q24-72 h		Bennett 1998[133] Malley 1999[72]
Ketoprofen*	IM, SC	2 mg/kg q 24-48 h		Bennett 1998[133]
Flunixin meglumine*	IM	0.1-0.5 mg/kg q 24		Malley 1999[72]
Lidocaine (2%)*	Local infiltration	Toxic dose unknown, recommend <5 mg/kg	Dilute to 1% to increase volume	Bennett 1998[133] Malley 1999[72]
Bupivicaine (0.5%)*	Local infiltration	Toxic dose unknown, recommend <2 mg/kg	Dilute to 0.25% to increase volume	Redrobe 2004[73]

**Dose anecdotal or determined by extrapolation from other species.*

studied. There are at least two reports evaluating NSAIDs (ketorolac, indomethacin, and flunixin) in an amphibian model of pain, where a mild analgesic effect could be demonstrated but, as the authors comment, the model may not have been valid for testing NSAID-induced analgesia.[137,138] Until further studies in reptiles become available, it is probably best to consider the possibility that side effects similar to those seen in mammals (gastrointestinal irritation, renal compromise, and platelet inhibition) may also occur in reptiles. Therefore, hydration status, concurrent medications (steroids), presence of coagulopathy, gastrointestinal disease, and renal disease should all be addressed before administering these drugs.

References

1. Ultsch GR, Jackson DC: Long-term submergence at 3 degrees C of the turtle *Chrysemys picta bellii* in normoxic and severely hypoxic water. III. Effects of changes in ambient PO2 and subsequent air breathing J Exp Biol 97:87-99, 1982
2. Hicks JW, Bennett AF: Eat and run: prioritization of oxygen delivery during elevated metabolic states. Respir Physiol Neurobiol 144:215-224, 2004
3. Andrews RM, Pough FH: Metabolism of squamate reptiles: allometric and ecological relationships. Physiol Zool 58:214-231, 1985
4. Baker LA, White FN: Redistribution of cardiac output in response to heating in *Iguana iguana*. Comp Biochem Physiol 35:253-262, 1970
5. Hicks JW, Wang T: Hypometabolism in reptiles: behavioural and physiological mechanisms that reduce aerobic demands. Respir Physiol Neurobiol 141:261-271, 2004
6. Hicks JW, Wang T: Hypoxic hypometabolism in the anesthetized turtle, *Trachemys scripta*. Am J Physiol 277:R18-23, 1999
7. Ladyman M, Bradshaw D: The influence of dehydration on the thermal preferences of the Western tiger snake, *Notechis scutatus*. J Comp Physiol [B] 173:239-246, 2003
8. Van Mierop LHS, Kutsche M: Comparitive anatomy of the ventricular septum, in Wenick ACG (ed): The Ventricular Septum in the Heart. Boston, MA, Martinus Nijhoff, 1981, pp 35-46
9. Van Mierop LHS, Kutsche M: Some aspects of comparative anatomy of the heart, in Johansen K, Burggren WW (eds): Cardiovascular Shunts: Phylogenetic, Ontogenic and Clinical Aspects. Copenhagen, Munksgaard, 1985, p. 38-56
10. Comeau SG, Hicks JW: Regulation of central vascular blood flow in the turtle. Am J Physiol 267:R569-578, 1994
11. Herman J, Wang T, Smits AW, et al: The effects of artificial lung inflation on pulmonary blood flow and heart rate in the turtle, *Trachemys scripta*. J Exp Biol 200:2539-2545, 1997
12. Hicks JW, Ishimatsu A, Molloi S, et al: The mechanism of cardiac shunting in reptiles: a new synthesis. J Exp Biol 199:1435-1446, 1996
13. Heisler N, Neumann P, Maloiy GM: The mechanism of intracardiac shunting in the lizard, *Varanus exanthematicus*. J Exp Biol 105:15-31, 1983
14. Ishimatsu A, Hicks JW, Heisler N: Analysis of intracardiac shunting in the lizard, *Varanus niloticus*: a new model based on blood oxygen levels and microsphere distribution. Respir Physiol 71:83-100, 1988
15. Hicks JW, Malvin GM: Mechanism of intracardiac shunting in the turtle, *Pseudemys scripta*. Am J Physiol 262:R986-992, 1992
16. Berger PJ, Burnstock G: Autonomic nervous system, in Gans C (ed): Biology of the Reptilia. New York, NY, Academic Press, 1979, pp 1-57
17. Burggren WW, Glass ML, Johansen K: Pulmonary ventilation: perfusion relationships in terrestrial and aquatic chelonian reptiles. Can J Zool 55:2024-2034, 1977
18. Lillywhite HB, Donald JA: Pulmonary blood flow regulation in an aquatic snake. Science 245:293-295, 1989
19. Luckhardt AB, Carlson AJ: Studies on the visceral sensory nervous system. Am J Physiol 56:72-112, 1921
20. Milsom WK, Langille BL, Jones DR: Vagal control of pulmonary vascular resistance in the turtle, *Chrysemys scripta*. Can J Zool 55:359-367, 1977
21. White FN: Circulation, in Gans C, Dawson WR (eds): Biology of the Reptilia, Physiology A. New York, NY, Academic Press, 1976, pp 275-334
22. Burggren W, Farrell A, Lillywhite HB: Vertebrate cardiovascular systems, in Dantzler WH (ed): Handbook of Physiology. Section 13: Comparative Physiology. New York, NY, Oxford University Press, 1997, pp 254-267
23. Berger PJ: The reptilian baroreceptor and its role in cardiovascular control. Am Zool 27:111-120, 1987
24. Stinner JN: Cardiovascular and metabolic responses to temperature in, *Coluber constrictor*. Am J Physiol 253:R222-227, 1987
25. Stinner JN, Ely DL: Blood pressure during routine activity, stress, and feeding in black racer snakes, (*Coluber constrictor*). Am J Physiol 264:R79-84, 1993
26. Farrell AP: Introduction to cardica scope in lower vertebrates. Can J Zool 69:1981-1984, 1991
27. Seymour RS, Lillywhite HB: Blood pressure in snakes from different habitats. Nature 264:664-666, 1976
28. Lillywhite HB, Gallagher KP: Hemodynamic adjustments to head-up posture in the partly arboreal snake, *Elaphe obsoleta*. J Exp Zool 235:325-334, 1985
29. Lillywhite HB, Pough FH: Control of arterial pressure in aquatic sea snakes. Am J Physiol 244:R66-73, 1983
30. Seymour RE: Scaling of cardiovascular physiology in snakes. Am Zool 27:97-109, 1987
31. Anderson NL, Wack RF, Calloway L, et al: Cardiopulmonary effects and efficacy of propofol as an anesthetic in brown tree snakes (*Boiga irregularis*). Bull Assoc Reptilian Amphibian Vet 9:9-15, 1999
32. Arena PC, Richardson KC, Cullen LK: Anaesthesia in two species of large Australian skink. Vet Rec 123:155-158, 1988
33. Bennett RA, Schumacher J, Hedjazi-Haring K, et al: Cardiopulmonary and anesthetic effects of propofol administered intraosseously to green iguanas. J Am Vet Med Assoc 212:93-98, 1998
34. Bonath K: Halothane inhalation anaesthesia in reptiles and its clinical control. Intl Zoo Yearbook 19: 112-125, 1979
35. Custer RS, Bush M: Physiologic and acid-base measures of gopher snakes during ketamine or halothane-nitrous oxide anesthesia. J Am Vet Med Assoc 177:870-874, 1980
36. Mosley CA, Dyson D, Smith DA: The cardiovascular dose-response effects of isoflurane alone and combined with butorphanol in the green iguana, (*Iguana iguana*). Vet Anaesth Analg 31:64-72, 2004
37. Rooney MB, Levine G, Gaynor J, et al: Sevoflurane anesthesia in desert tortoises, (*Gopherus agassizii*). J Zoo Wildl Med 30:64-69, 1999
38. Schumacher J, Lillywhite HB, Norman WM, et al:

Effects of ketamine HCl on cardiopulmonary function in snakes. Copeia 395-400, 1997
39. Stirl R, Bonath KH: Cardiovascular, pulmonary and acid-base measurements in boa constrictors during tiletamine-zolazepam sedation. 5th International Congress of Veterinary Anesthesia, Guelph, Canada, 1994, Scientific Abstract 55
40. Milsom WK: Mechanoreceptor modulation of endogenous respiratory rhythms in vertebrates. Am J Physiol 259:R898-910, 1990
41. Smatresk NJ: Chemoreceptor modulation of endogenous respiratory rhythms in vertebrates. Am J Physiol 259:R887-897, 1990
42. Wang T, Smits AW, Burggren W: Pulmonary function in reptiles, in Gans C, Gaunt AS (eds): Biology of the Reptilia. Ithaca, NY, Society for the Study of Amphibians and Reptiles, 1998, pp 319
43. Shelton G, Jones DR, Milsom WK: Control of breathing in ectothermic vertebrates, in Geiger SR, Widdicombe JG (eds): Handbook of Physiology. Section 3: The Respiratory System. Bethesda, MD, American Physiological Society, 1986
44. Wood SC, Lenfant CJM: Respiration: mechanics, control and gas exchange, in Gans C, Dawson WR (eds): Biology of the Reptilia, Physiology A. New York, NY, Academic Press, 1976, pp 225-274
45. Glass ML, Wood SC: Gas exchange and control of breathing in reptiles. Physiol Rev 63:232-260, 1983
46. Johansen K, Hanson D, Lenfant C: Respiration in a primitive air breather, *Amia calva*. Respir Physiol 9:162-174, 1970
47. White FN: Redistribution of cardiac output in the diving alligator. Copeia 567-570, 1969
48. Shelton G, Burggren W: Cardiovascular dynamics of the chelonia during apnoea and lung ventilation. J Exp Biol 64:323-343, 1976
49. Perry SF: Structure and function of the reptilian respiratory system, in Lenfant C, Wood CM (eds): Comparative Pulmonary Physiology. Current Concepts. New York, NY, Marcel Dekker, 1989, pp 193-236
50. Glass ML, Johansen K: Control of breathing in *Acrochordus javanicus*, an aquatic snake. Physiol Zool 49:328-340, 1976
51. Templeton JR, Dawson WR: Respiration in the lizard *Crotaphytus collaris*. Physiol Zool 36:104-121, 1963
52. Glass ML, Burggren W, Johansen K: Ventilation in an aquatic and a terrestrial chelonian reptile. J Exp Biol 72:165-179, 1978
53. Jackson DC, Kraus DR, Prange HD: Ventilatory response to inspired CO2 in the sea turtle: effects of body size and temperature. Respir Physiol 38:71-81, 1979
54. Jackson DC, Palmer SE, Meadow WL: The effects of temperature and carbon dioxide breathing on ventilation and acid-base status of turtles. Respir Physiol 20:131-146, 1974
55. Boyer DR: Comparative effects of hypoxia on respiratory and cardiac function in reptiles. Physiol Zool 39:307-316, 1966
56. Hitzig BM, Allen JC, Jackson DC: Central chemical control of ventilation and response of turtles to inspired CO_2. Am J Physiol 249:R323-328, 1985
57. Jackson DC: Ventilatory response to hypoxia in turtles at various temperatures. Respir Physiol 18:178-187, 1973
58. Benchetrit G, Armand J, Dejours P: Ventilatory chemoreflex drive in the tortoise, *Testudo horsfieldi*. Respir Physiol 31:183-191, 1977
59. Benchetrit G, Dejours P: Ventilatory CO_2 drive in the tortoise Testudo horsfieldi. J Exp Biol 87:229-236, 1980
60. Frankel HM, Spitzer A, Blaine J, et al: Respiratory response of turtles (*Pseudemys scripta*) to changes in arterial blood gas composition. Comp Biochem Physiol 31:535-546, 1969
61. Diethelm G: The effect of oxygen content of inspiratory air (FIO_2) on recovery times in the green iguana (*Iguana iguana*). University of Zurich, Zurich, 2001
62. Bertelsen MF, Mosley CA, Crawshaw GJ, et al: Inhalation anesthesia in Dumeril's monitor (*Varanus dumerili*) with isoflurane, sevoflurane, and nitrous oxide: effects of inspired gases on inducion and recovery. J Zoo Wildl Med 36:62-68, 2005
63. Berner NJ: Oxygen consumption by mitochondria from an endotherm and an ectotherm. Comp Biochem Physiol B Biochem Mol Biol 124:25-31, 1999
64. Penick DN, Paladino FV, Steyermark AC, et al: Thermal dependence of tissue metabolism in the green turtle (*Chelonia mydas*). Comp Biochem Physiol 113A:293-296, 1996
65. Heard DJ: Reptile anesthesia. Vet Clin North Am Exot Anim Pract 4:83-117, 2001
66. Holz P, Barker IK, Burger JP, et al: The effect of the renal portal system on pharmacokinetic parameters in the red-eared slider, (*Trachemys scripta elegans*). J Zoo Wildl Med 28:386-393, 1997
67. Holz P, Barker IK, Crawshaw GJ, Dobson H: The anatomy and perfusion of the renal portal system in the red-eared slider, (*Trachemys scripta elegans*). J Zoo Wildl Med 28:378-385, 1997
68. Chittick EJ, Stamper MA, Beasley JF, et al: Medetomidine, ketamine, and sevoflurane for anesthesia of injured loggerhead sea turtles: 13 cases (1996-2000). J Am Vet Med Assoc 221:1019-1025, 2002
69. Wellehan JFX, Lafortune M, Gunkel C, et al: Coccygeal vascular catheterization in lizards and crocodilians. J Herpetological Med Surg 14:26-28, 2004
70. Maxwell LK, Jacobson ER: Allometric scaling of kidney function in green iguanas. Comp Biochem Physiol A Mol Integr Physiol 138:383-390, 2004
71. Whitaker BR, Krum H: Medical management of sea turtles in Fowler ME, Miller RE (eds): Zoo and Wild Animal Medicine (ed 4). Philadelphia, PA, W. B. Saunders, 1999, pp 217
72. Malley D: Reptiles, in Seymour C, Gleed R (eds): Manual of Small Animal Anaesthesia and Analgesia. Shurdington, United Kingdom, British Small Animal Veterinary Medical Association, 1999, pp 271-281
73. Redrobe S: Anaesthesia and analgesia, in Girling S, Raiti P (eds): BSAVA Manual of Reptiles. Shurdington, United Kingdom, British Small Animal Veterinary Association, 2004, pp 131-146
74. Cooper JE: Ketamine hydrochloride as an anaesthetic for East African reptiles. Vet Rec 95:37-41, 1974
75. Glenn JL, Straight R, Snyder CC: Clinical use of

ketamine hydrochloride as an anesthetic agent for snakes. Am J Vet Res 33:1901-1903, 1972
76. Wood FE, Critchley KH, Wood JR: Anesthesia in the green sea turtle, *Chelonia mydas*. Am J Vet Res 43: 1882-1883, 1982
77. Boever WJ, Caputo F: Telazol (CI 744) as an anesthetic agent in reptiles. J Zoo An Med 13:59-61, 1982
78. Clyde VL, Cardeilhac PT, Jacobson ER: Chemical restraint of american alligators (*Alligator mississippiensis*) with atracurium or tiletamine-zolazepam. J Zoo Wildl Med 25:525-530, 1994
79. Gray CW, Bush M, Beck CC: Clinical experience using CI-744 in chemical restraint and anesthesia of exotic specimens. J Zoo An Med 5:12-21, 1974
80. Bienzle D, Boyd CJ: Sedative effects of ketamine and midazolam in snapping turtles (*Chelydra serpentina*). J Zoo Wildl Med 23:201-204, 1992
81. Oppenheim YV, Moon PF: Sedative effects of midazolam in red-eared slider turtles (*Trachemys scripta elegans*). J Zoo Wildl Med 26:409-413, 1995
82. Harvey-Clark C: Midazolam fails to sedate painted turtles (*Chrysemys picta*). Bull Assoc Reptilian Amphibian Vet 3:7-8, 1993
83. Holz P, Holz RM: Evaluation of ketamine, ketamine/xylazine, and ketamine/midazolam anesthesia in red-eared sliders (*Trachemys scripta elegans*). J Zoo Wildl Med 25:531-537, 1994
84. Sleeman JM, Gaynor J: Sedative and cardiopulmonary effects of medetomidine and reversal with atipamezole in desert tortoises, (*Gopherus agassizii*). J Zoo Wildl Med 31:28-35, 2000
85. Dennis PM, Heard DJ: Cardiopulmonary effects of a medetomidine-ketamine combination administered intravenously in gopher tortoises. J Am Vet Med Assoc 220:1516-1519, 2002
86. Lock BA, Heard DJ, Dennis P: Preliminary evaluation of medetomidine/ketamine combinations for immobilization and reversal with atipamezole in three tortoise species. Bull Assoc Reptilian Amphibian Vet 8:6-9, 1998
87. Greer LL, Jenne KJ, Diggs HE: Medetomidine-ketamine anesthesia in red-eared slider turtles, (*Trachemys scripta elegans*). Contemp Top Lab Anim Sci 40:9-11, 2001
88. Read MR: Evaluation of the use of anesthesia and analgesia in reptiles. J Am Vet Med Assoc 224:547-552, 2004
89. Mauthe von Degerfeld M: Personal experiences in the use of association tiletamine/zolazepam for anaesthesia of the green iguana, (*Iguana iguana*). Vet Res Commun 28:351-353, 2004 (suppl 1)
90. Mosley CA, Dyson D, Smith DA: Minimum alveolar concentration of isoflurane in green iguanas and the effect of butorphanol on minimum alveolar concentration. J Am Vet Med Assoc 222:1559-1564, 2003
91. Brisaben LL: Reactions of the American alligator to several immobilizing drugs. Copeia 129-130, 1966
92. Klide AM, Klein LV: Chemical restraint if three reptilean species. J Zoo An Med 4:8-11, 1973
93. Messel H, Stephens DR: Drug immobilization of crocodiles. J Wildl Manage 44:295-296, 1980
94. Spiegel RA, Lane TJ, Larsen RE, et al: Diazepam and succinylcholine chloride for restraint of the American alligator. J Am Vet Med Assoc 185:1335-1336, 1984
95. Kaufman GE, Seymour RE, Bonner BB, et al: Use of rocuronium for endotracheal intubation of North American Gulf Coast box turtles. J Am Vet Med Assoc 222:1111-1115, 2003
96. Belkin DA: Anoxia: tolerance in reptiles. Science 139:492-493, 1963
97. Bertelsen MF, Mosley CA, Crawshaw GJ, et al: Anesthetic potency of sevoflurane and nitrous oxide in mechanically ventilated Dumeril's monitors (*Varanus dumerili*). J Am Vet Med Assoc 2005 (in press)
98. Bertelsen MF, Mosley CA, Crawshaw GJ, et al: Minimum alveolar concentration of isoflurane in mechanically ventilated Dumeril monitors. J Am Vet Med Assoc 226:1098-1101, 2005
99. Maas A, Brunson D. Comparison of anesthetic potency and cardiopulmonary effects of isoflurane and sevoflurane in colubrid snakes. Am Assoc Zoo Vet 306-308, 2002
100. Mosley CA, Dyson D, Smith DA: The cardiac anesthetic index of isoflurane in green iguanas. J Am Vet Med Assoc 222:1565-1568, 2003
101. Calderwood HW: Anesthesia for reptiles. J Am Vet Med Assoc 159:1618-1625, 1971
102. Kaplan HM: Anesthesia in amphibians and reptiles. Fed Proc 28:1541-1546, 1969
103. Bello AA, Bello-Klein A: A technique to anesthetize turtles with ether. Physiol Behav 50:847-848, 1991
104. Murray MJ: Cardiology and circulation, in Mader DR (ed): Reptile Medicine and Surgery. Toronto, Canada, W. B. Saunders, 1996, pp 95-103
105. Bennett RA, Divers SJ, Schumacher J, et al: Anesthesia. Bull Assoc Reptilian Amphibian Vet 9:20-27, 1999
106. Schumacher J: Reptiles and amphibians, in Thurmon JC, Tranquilli WJ, Benson GJ (eds): Lumb and Jones' Veterinary Anesthesia (ed 3). Philadelphia, PA, Williams & Wilkins, 1996, pp 670-685
107. Jarchow JL: Hospital care of the reptile patient, in Jacobson ER, Kollias GV (eds): Exotic Animals. New York, NY, Churchill Livingstone, 1988, pp 28-30
108. Kona-Boun JJ, Silim A, Troncy E: Immunologic aspects of veterinary anesthesia and analgesia. J Am Vet Med Assoc 226:355-363, 2005
109. Muir WW: Pain and stress, in Gaynor J, Muir WW (eds): Handbook of Veterinary Pain Management. Toronto, Canada, Mosby, 2002, pp 46-59
110. Lascelles BD, Waterman AE, Cripps PJ, et al: Central sensitization as a result of surgical pain: investigation of the pre-emptive value of pethidine for ovariohysterectomy in the rat. Pain 62:201-212, 1995
111. Woolf CJ, Chong MS: Preemptive analgesia–treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 77:362-379, 1993
112. Pascoe PJ, Steffey EP, Black WD, et al: Evaluation of the effect of alfentanil on the minimum alveolar concentration of halothane in horses. Am J Vet Res 54:1327-1332, 1993
113. Steffey EP, Baggot JD, Eisele JH, et al: Morphine-isoflurane interaction in dogs, swine and rhesus monkeys. J Vet Pharmacol Ther 17:202-210, 1994
114. Steffey EP, Martucci R, Howland D, et al: Meperi-

dine-halothane interaction in dogs. Can Anaesth Soc J 24:459-467, 1977
115. Liang YF, Terashima S: Physiological properties and morphological characteristics of cutaneous and mucosal mechanical nociceptive neurons with A-delta peripheral axons in the trigeminal ganglia of crotaline snakes. J Comp Neurol 328:88-102, 1993
116. Stoskopf MK: Pain and analgesia in birds, reptiles, amphibians, and fish. Invest Ophthalmol Vis Sci 35:775-780, 1994
117. Gans C, Gaunt AS: Muscle architecture and control demands. Brain Behav Evol 40:70-81, 1992
118. Mauk MD, Olson RD, LaHoste GJ, et al: Tonic immobility produces hyperalgesia and antagonizes morphine analgesia. Science 213:353-354, 1981
119. Kanui TI, Hole K: Morphine and pethidine antinociception in the crocodile. J Vet Pharmacol Ther 15:101-103, 1992
120. Kanui TI, Hole K, Miaron JO: Nociception in crocodiles: capsaicin instillation, formalin and hot plate tests. Zool Sci 7:537-540, 1990
121. ten Donkelaar HJ, de Boer-van Huizen R: A possible pain control system in a non-mammalian vertebrate (a lizard, Gekko gecko). Neurosci Lett 83:65-70, 1987
122. de la Iglesia JA, Martinez-Guijarro FI, Lopez-Garcia C: Neurons of the medial cortex outer plexiform layer of the lizard, *Podarcis hispanica*: Golgi and immunocytochemical studies. J Comp Neurol 341: 184-203, 1994
123. Reiner A: The distribution of proenkephalin-derived peptides in the central nervous system of turtles. J Comp Neurol 259:65-91, 1987
124. Lindberg I, White L: Reptilian enkephalins: implications for the evolution of proenkephalin. Arch Biochem Biophys 245:1-7, 1986
125. Ng TB, Hon WK, Cheng CH, et al: Evidence for the presence of adrenocorticotropic and opiate-like hormones in the brains of two sea snakes, *Hydrophis cyanocinctus* and *Lapemis hardwickii*. Gen Comp Endocrinol 63:31-37, 1986
126. Flecknell PA: The relief of pain in laboratory animals. Lab Anim 18:147-160, 1984
127. Morton DB: Assessment of pain. Vet Rec 119:435, 1986
128. Polzonetti-Magni A, Facchinetti F, Carnevali O, et al: Presence and steroidogenetic activity of beta-endorphin in the ovary of the lizard, *Podarcis s. sicula raf*. Biol Reprod 50:1059-1065, 1994
129. Zagon IS, Sassani JW, Allison G, et al: Conserved expression of the opioid growth factor, [Met5]enkephalin, and the zeta (zeta) opioid receptor in vertebrate cornea. Brain Res 671:105-111, 1995
130. Hinsch H, Gandal CP: The effects of etorphine (M-99), oxymorphone hydrochloride and meperidine hydrochloride in reptiles. Copeia 404-405, 1969
131. Waterman AE, Livingston A, Amin A: Analgesic activity and respiratory effects of butorphanol in sheep. Res Vet Sci 51:19-23, 1991
132. Bennett RA: Anesthesia, in Mader DR (ed): Reptile Medicine and Surgery. Toronto, Canada, W. B. Saunders, 1996, pp 241-247
133. Bennett RA: Reptile anesthesia. Sem Avian Exot Pet Med 7:30-40, 1998
134. Machin KL: Fish, amphibian, and reptile analgesia. Vet Clin North Am Exot Anim Pract 4:19-33, 2001
135. Malley D: Reptile anaesthesia and the practicing veterinarian. In Practice 19:351-368, 1997
136. Liu PL, Feldman HS, Giasi R, et al: Comparative CNS toxicity of lidocaine, etidocaine, bupivacaine, and tetracaine in awake dogs following rapid intravenous administration. Anesth Analg 62:375-379, 1983
137. Stevens CW, MacIver DN, Newman LC: Testing and comparison of non-opioid analgesics in amphibians. Contemp Top Lab Anim Sci 40:23-27, 2001
138. Terril-Robb LA, Suckow M, Grigdesby CF: Evaluation of the analgesic effects of butorphanol tartarate, xylazine hydrochloride, and flunixin meglumine in leopard frogs (*Rana pipiens*). Contemp Top Lab Anim Sci 35:54-56, 1996