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Options for analgesia and anaesthesia in reptiles



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Reptiles are an increasing component of small animal practice, whether they are animals belonging to private owners or zoological collections, or, occasionally, wildlife casualties. The provision of analgesia and anaesthesia in these species is notoriously difficult due to differences in metabolism compared with other animals and their ability to bypass the pulmonary circuit. This article discusses the use of analgesics and anaesthetics in reptiles, and outlines the requirements for appropriate monitoring and recovery.

Thermoregulation and metabolism

Reptiles are ectothermic and their metabolic rate is determined by their ability to thermoregulate. This means that animals can choose to select a body temperature that is optimal for the metabolic processes occurring at that time. Therefore, when dealing with such animals, an appropriate environment with a thermal gradient should be provided. If a patient is too collapsed to thermoregulate, a suitable even temperature will help to optimise metabolism. Metabolic rate has a huge influence on drug therapy. Studies in tortoises, for example, have shown differences in the uptake and clearance of therapeutic agents. Thus, the first rule of medicine and surgery in reptiles is to warm the patient to its optimal temperature before examination and drug therapy.

Analgesia

Reducing anxiety in patients can help to facilitate analgesia. Therefore, providing a suitable thermal environment away from predator species, including small hiding boxes or towelling, is important. Where possible, painful areas should be immobilised.

Many agents used in exotic animals are not specifically licensed for these patients. Note that none of the injectable drug therapies mentioned in this article are licensed for use in reptiles.

Assessing pain

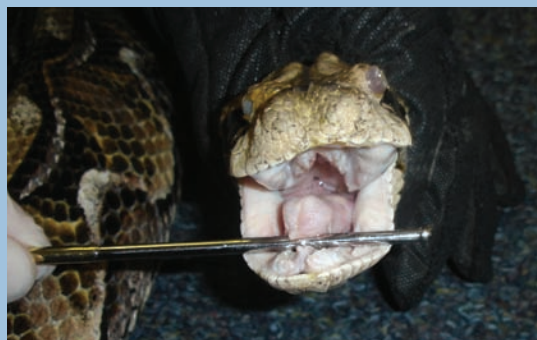
Lesions that are painful in mammals are also likely to cause pain in lower vertebrates, but the mechanism of pain perception may differ. Therefore, while reptiles do possess an opioid system, their responses to opioids vary from the mammalian model.

Clinical signs of pain can be limited in reptiles. For this reason, analgesia is sometimes overlooked in these animals and it can be difficult to clinically quantify the benefits of analgesia. Acute pain often results in vigorous activity at the time of the insult (eg, trying to bite when injected) but, subsequently, or in the case of chronic pain, reptiles may become immobile (eg, after surgery). In addition, prey species may show less overt signs of pain, so remote observation of such patients can help to identify subtle behaviours.

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Handling venomous species

Venomous species require careful experienced handling and it is best to send these patients to specialised facilities for treatment. Hooks and snake tubes are essential for the safe handling of venomous snakes, which can either be induced in these tubes using a gaseous agent or given intravenous anaesthetics via the ventral tail vein. Venomous lizards can be masked down.



Some reptiles, such as this gaboan viper, are best handled at specialist units



Spur-thighed tortoise showing an acute pain response to ketamine inadvertently injected subcutaneously

Acute pain

Signs of acute pain includes withdrawal of painful limbs (eg, in chelonians and lizards), escape behaviour, avoidance, restlessness, aggression and increased respiratory rate. In those species with melanophores, acute pain can be identified by a darkening of the skin over the affected areas. This can be seen following injections in chameleons or water dragons, for example, and owners should be made aware of this. In some cases, florid displays of pain can be seen with biting or scratching of the region in question, and vocalisation.

Chronic pain

More chronic pain is less likely to evoke marked clinical signs. Instead, immobility or stunting of the area may be seen (eg, snakes may not curl in the affected region), and some animals may become aggressive if handling or manipulation is attempted (ie, acute pain overlying chronic pain).

Analgesic protocols

Local anaesthesia

Local anaesthesia is hugely underutilised but should not be overlooked in reptiles. Both lidocaine and bupivacaine can be used. Mixing these two agents improves the duration of action while ensuring prompt induction and should, ideally, be given before any painful procedure. These products act at the site of the painful focus and so prevent any sensitisation. The maximum doses are 10 mg/kg for lidocaine and 4 mg/kg bupivacaine. However, the author prefers to reduce these by 50 per cent and use both drugs together. Patients should be weighed accurately and dilution in saline may be required to facilitate administration.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) should be used as a matter of routine. There have been some studies on pharmacokinetics in reptiles using ketoprofen and meloxicam, which are currently the agents of choice. Recommended doses are 0.2 mg/kg meloxicam given every 48 hours by injection, or 2 mg/kg ketoprofen administered every 36 hours by injection (Hernandez-Divers and others 2004, Tuttle and others 2006). Long-term studies have not been performed. For oral use, meloxicam given at a rate of

Measuring efficacy of analgesics in reptiles

Quantifying the need for analgesics and their efficacy in reptiles is difficult. Historically, research into analgesia in these species has usually focused on thermal stimuli to determine their pain threshold. However, reptiles appear unable to detect focal heat sources as their thermoregulatory set point is determined by hypothalamic temperature. This means that the need to achieve the optimal core temperature for metabolism overrides local hyperthermia, which can lead to focal burns. Thus, studies investigating pain in reptiles should be critically analysed before any conclusions are drawn, particularly if a focal thermal stimulus was used.

0.2 mg/kg daily for five days may achieve therapeutic levels over a few days. Subsequent dosing should be 0.2 mg/kg every other day. However, one study in ball pythons failed to demonstrate analgesic effects when meloxicam was used at 0.3 mg/kg (Oleson and others 2008).

Opioids

Opioid analgesics are used frequently in reptiles. However, while their effectiveness has been judged by anaesthetic sparing effects or pain studies, numerous reports provide conflicting results and the efficacy of many agents remains in question.

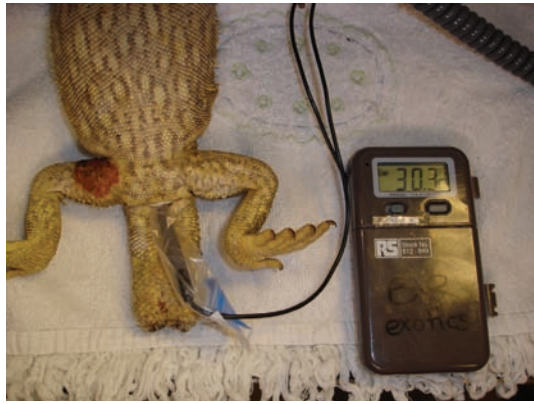
Butorphanol has been used at doses of 0.4 to 28 mg/kg in a variety of species. One report using electrical stimulation found that a dose of 1.5 or 8 mg/kg was effective in providing analgesia. Buprenorphine failed to provide analgesia at doses of 0.02 or 0.1 mg/kg (Greenacre and others 2006). Morphine has been shown to be effective in both lizards and crocodylians at doses of 1 to 2 mg/kg. Gamble (2009) found that serum levels following the use of transdermal fentanyl patches in skinks were comparable to those providing analgesia in humans.

Alpha-2 agonists and ketamine

Alpha-2 agonists and ketamine also provide some analgesic effects and are worth including in the anaesthetic regimen.



(left) Bearded dragon following ventral coeliotomy. This animal has lifted its body off the ground, which suggests it is agitated. (right) The same case after the administration of local analgesia. The dragon is lying down and is now more relaxed



Continuous monitoring of the cloacal temperature of a bearded dragon throughout anaesthesia



Induction of a spur-thighed tortoise using alfaxalone injected via the subcarapacial vein

Anaesthesia

Cardiovascular and respiratory anatomy, and physiology all influence the method of anaesthesia used in reptiles, and all reptiles have a number of adaptations that are vital to their survival. For example, the following all affect how anaesthesia is conducted:

- Reptiles have a high anaerobic tolerance combined with a low metabolic rate, which means they are capable of breath-holding for long periods of time;
- Reptiles have a three-chambered heart, which allows blood to flow selectively around the pulmonary circuit (increased by sympathetic stimulation) or bypass the lungs (increased with parasympathetic stimulation).

There is some mixing of the pulmonary and systemic circuits in all cases. The parasympathetic tone is activated in response to diving in many aquatic species, so red-eared terrapins, for instance, can survive in a nitrogen environment for 27 hours, while Mediterranean tortoises can easily survive falling into a pond overnight. Therefore, mask or chamber induction is not appropriate for chelonian anaesthesia, but is suitable for many squamate species.

Preanaesthetic preparation

Reptiles must be warmed to their optimal (and thus metabolically active) temperature before anaesthesia. In addition, they should have their cloacal or oesophageal temperature monitored throughout the procedure and recovery. Measuring the temperature of animals in the vivarium can be used as a benchmark.



Intubation of a conscious carpet python. Ventilation is provided using a mechanical ventilator to induce anaesthesia

Induction

Induction in squamates is typically performed using a gaseous agent such as isoflurane or sevoflurane. Sevoflurane has been shown to have quicker induction times compared with isoflurane. Prolonged induction times in reptiles (10 to 20 minutes) using gaseous agents by mask has health and safety implications for staff and can be stressful for reptiles as they resent physical restraint for long periods of time. Direct intubation with positive pressure ventilation to induce anaesthesia is commonly employed in snakes (and chelonians), but can also be stressful for patients.

The author prefers to use ziplock bags for the induction of small lizards and snakes of up to 1 kg in size. This reduces the amount of inhalational gas needed. These bags are usually strong enough to avoid being punctured by the reptile. The bag should be emptied of air and the animal placed inside, after which it is filled with oxygen and either 5 per cent isoflurane or 8 per cent sevoflurane, and then closed. It is possible to monitor respiration and heart rate, and assess both the righting and pinch reflexes through the bag to determine induction. Once a suitable plane of anaesthesia has been achieved, the bag can be opened (preferably outdoors to avoid inhalation) and the animal removed. Anaesthetic scavenging is not required as the volume of gas involved is relatively small. This method of induction is usually quicker than using a mask as breath-holding is minimal.

Anaesthetic protocols

Intubation

Following induction, intubation can be performed.



Induction of a mangrove snake using a ziplock bag filled with 5 per cent isoflurane in 100 per cent oxygen



Intravenous catheters can be modified and securely attached to a cut-off 2 ml syringe and an 8 mm endotracheal tube connector

In larger squamates and chelonians, injectable anaesthetic agents are required before intubation.

Commercially available endotracheal tubes can be as small as 1 mm in diameter. However, custom homemade endotracheal tubes may be required for smaller patients. Intravenous catheters as small as 26 gauge can be used with a tube size of 0.64 mm.

Intubation can be difficult in lizards and chelonians due to the small size of the glottis, which only opens during inspiration, but should be possible with care. Intubation is much easier in snakes. Tracheal rings in reptiles can either be complete or incomplete, and uncuffed endotracheal tubes are therefore recommended. The length of the endotracheal tube used depends on the species. For example, chelonians have a proximal tracheal bifurcation, which in some species can be just behind the angle of the jaw, and so need short endotracheal tubes. A focal light source can be helpful for visualising the glottis. Local anaesthetic is unnecessary.

Intravenous administration

Intravenous administration is possible in most chelonians. This can be carried out using propofol (10 mg/kg), alfaxalone (5 to 10 mg/kg), medetomidine (0.15 mg/kg) or ketamine (5 to 15 mg/kg). Medetomidine and ketamine have also been used in combination. The author's agent of choice is alfaxalone. Many of these products can be given to effect; lower doses can be administered to patients that require heavy sedation for radiography, ocular examination or oesophagostomy tube placement without having to resort to intubation and prolonged anaesthesia. Propofol and alfaxalone provide



Box turtle that has retreated into its carapace. This leaves the anaesthetist no option but to consider intramuscular administration, which should be given in the pectoral musculature to one side of the hinge



Spur-thighed tortoise intubated and attached to a mechanical ventilator. In this case, a tongue depressor is being used to keep everything in place

20 minutes of surgical time, although at low dosages, stimulation by physical manipulation can reduce their effect. Jugular veins, the subcarapacial vein and the dorsal tail vein can all be used for intravenous access. The subcarapacial vein is the easiest to access, even in very small chelonians, using a 27 gauge needle.

The ventral tail vein is commonly used for intravenous induction in squamates. Propofol or alfaxalone can typically be administered in these animals at similar doses to those given in chelonians.

Intraosseous administration

If intravenous therapy is impractical (eg, in lizards and some chelonians), the intraosseous route can be considered using an intraosseous needle. However, unless critically collapsed, such patients require sedation in addition to local anaesthesia to facilitate needle placement.

Intramuscular administration

Intramuscular administration of agents is generally appropriate for recalcitrant animals. Medetomidine and ketamine with or without the addition of butorphanol have been used. Alfaxalone at 10 to 20 mg/kg is also a suitable alternative. Dexmedetomidine has similar cardiovascular effects to medetomidine and can be used as an alternative to racemic medetomidine at half the dose. Intramuscular administration requires 30 minutes to take effect, during which time the reptile should be returned to a warm environment. In snakes, ketamine has been used somewhat historically at high doses (up to 100 mg/kg) but can lead to protracted recovery periods (up to three days has been reported). A better approach is to use sufficient intramuscular agent to facilitate direct or gaseous induction, or intravenous access, both of which reduce recovery time.

Maintenance

Once a reptile has attained a surgical plane of anaesthesia, all voluntary respiratory activity is lost. Positive pressure ventilation is therefore necessary for all patients. Inspiration and expiration are active processes, as reptiles do not possess a diaphragm and air

movement is generated by the skeletal muscles of the body wall or by movement of the limbs in chelonians.

Following successful intubation, the reptile should be connected to an appropriate breathing circuit, such as a T-piece. Intermittent positive pressure ventilation can then be provided manually or, alternatively, a mechanical ventilator can be used to control the rate and depth of respiration more precisely. Lung anatomy is highly variable between species but, generally, the more proximal lung has greater vascularisation and tissue differentiation. Therefore, when ventilating patients, the proximal part of the lung fields should not be compromised. Low pressure should be used initially but this can be gradually increased while observing the patient's ventilation until a 'normal' depth of respiration is achieved. Pressures are in the order of about 8 cm H₂O. In chelonians, successful respiration is gauged by movement of the forelimbs. Respiration rate in many reptiles can be as low as two breaths per minute. However, initially, higher ventilation rates should be considered until the reptile is at the required plane of anaesthesia.

After a reptile is at the required plane of anaesthesia, the concentration of the gaseous agent and the rate of respiration are both reduced. For isoflurane, a concentration of 3 per cent is usually necessary. Although pulmonary bypass is possible in all reptiles, one study observed that the parasympathetic tone is reduced once anaesthetic has been induced, thus increasing the blood flow to the pulmonary circuit. As a result, gaseous anaesthesia is suitable for the maintenance of anaesthesia in chelonian species, but it is important to ensure that adequate ventilation is provided to limit the risk of mismatching. Some authors prefer to use injectable agents such as propofol or alfaxalone as intravenous top-up agents instead of a gaseous agent (while still leaving patients on intermittent positive pressure ventilation oxygen) and report no prolonged recoveries as a consequence.

Isoflurane is routinely used by the author for maintaining anaesthesia. Studies have shown sevoflurane to have some advantages in reducing recovery times, but these reports are not consistent.



Carpet python with the location of its heart marked to facilitate repeat measurement of the heart rate using a Doppler probe

Monitoring

Doppler monitoring

Anaesthesia is best monitored using a Doppler probe. Heart rate can be predicted by metabolic scaling using the following formula:

$$\text{Estimated heart rate (bpm)} = 34 \times \text{Weight}^{-0.25} \text{ (kg)}$$

However, practically, most conscious reptiles have a heart rate of approximately 70 beats per minute (bpm) at their optimal temperature. Anaesthetised reptiles have a rate of 30 to 40 bpm. Respiration and heart rates, and temperature should be recorded on the patient's anaesthetic sheet.

Doppler units can be left running throughout anaesthesia and provide an audible output. Changes in heart rate and rhythm can therefore be easily detected by the user without quantification. Flat or pencil probes can be used to monitor the major vessels or heart, or the peripheral pulses via the jugular or carotid arteries. Probes are best placed as follows, depending on the species:

- **Chelonians.** At the thoracic inlet or on the plastron at the junction between the pectoral and abdominal scutes (in small individuals);
- **Snakes.** On the apex beat, which is situated at about 22 to 33 per cent of the length of the snout vent when viewing the snake ventrally. The heart should be marked to facilitate repeat examination;
- **Lizards.** At the thoracic inlet, over the thoracic girdle or aimed close from behind. Monitor lizards have a more caudally placed heart than other lizards and this should be taken into account during monitoring.

It can be difficult to obtain a vessel peripheral enough to obtain a reading in larger patients. The author has also used ultrasonography to record heart rate and motility during anaesthesia.

Electrocardiography

Electrocardiography can be used as a monitoring tool. As reptiles have thick skin and low electrical activity, conduction can be improved by placing needles subcutaneously. This modality records electrical activity only, whereas Doppler probes record just mechanical activity. That said, a reptile can be dead with no cortical function but can still have a heart beat.

Pulse oximetry

Pulse oximetry may be carried out using cloacal or oesophageal probes. It has been used in reptiles and has been validated in the green iguana. Capnography has limited use in reptiles as the concentration of carbon dioxide in the respiratory tract may correlate poorly with arterial levels due to the shunting of blood away from the respiratory tract and the mixing of blood. Some studies have reported no correlation (Hernandez-Divers and others 2005) but more recent unpublished work suggests there may be some merit in measuring end tidal CO₂ and keeping this at 50 to 60 mmHg. Trends in the level of carbon dioxide may subsequently be identified and may be of some use.



Ventilation of a spur-thighed tortoise with room air using a small animal constant volume resuscitator

Reflexes

Reflexes such as the toe/tail pinch, head withdrawal (chelonians), tongue withdrawal reflex (snakes), rib stimulation (snakes) and jaw tone can be used to assess the depth of anaesthesia.

Recovery

Recovery in reptiles can be protracted, so it is best to perform anaesthesia in these animals early in the day. A number of studies have investigated what influences recovery rates in reptiles. The first and most significant point is to keep the reptile at its optimal temperature throughout the procedure, so continuous monitoring of cloacal temperature is critically important. Any signs of hypothermia can therefore be corrected immediately.

The author prefers to maintain a warm room temperature of 24 to 26°C using an external heat source. This provides heat by conduction by warming the air. Anaesthetised reptiles can also be provided with additional external heat sources that generate heat by conduction (eg, water recirculating heat mats) and by radiation (eg, overhead theatre lighting). If cloacal temperature decreases, a hair drier can be used to provide heat by convection.

Hypoxia has been shown to elevate the respiratory rate of reptiles, while hypercapnia increases both the rate and depth of respiration. Under anaesthesia, many reptiles are provided with 100 per cent oxygen and many are probably hyperventilated throughout anaesthesia. One study considering the differences of sevoflurane over isoflurane in green iguanas demonstrated quicker recoveries with sevoflurane (Hernandez-Divers and others 2005), but other studies have failed to show significant differences (Bertelsen and others 2005). However, the use of room air, as opposed to oxygen, during recovery had a much greater impact in the iguana study (Hernandez-Divers and others 2005). Thus, Ambu bags or a constant delivery animal resuscitator can be used. Breathing into an endotracheal tube is not advised due to the zoonotic risks! Many authors reduce the rate of ventilation and pressure as surgery draws to a close. Some also rapidly reduce the concentration of the anaesthetic agent early on in shorter procedures.

It is important to remember that reptiles in the immediate postoperative period are unable to thermo-

regulate and should be kept at an even temperature (typically 28°C although this varies with species), but should not be placed under a heat lamp, as they run the risk of hyperthermia. A hot spot should only be used when animals are mobile.

Extubation can occur once jaw tone increases and voluntary respiration occurs. Doppler and cloacal probes can be left in place to continuously monitor the patient until recovery. Once mobile, reptiles can be transferred to their usual cage and allowed to thermoregulate.

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