ANESTHESIA IN REPTILES

Part 1: injection anesthesia

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ABSTRACT

The first part of the article gives a review of injection anesthesia in reptiles. The specific anatomy and physiology of reptiles are briefly described, along with their pre-anesthetic evaluation. Drugs used for premedication, muscle relaxation, local anesthesia and the induction of general anesthesia are discussed. The last section deals with analgesia in reptiles.

***Chelonians* are relatively difficult to anesthetize so injection anesthesia is of great value in this species. Midazolam/ketamine or an α_2-agonist (medetomidine, xylazine) / ketamine combination can be used successfully. Propofol I.V. or I.O. is the agent of choice for induction and minor surgeries not exceeding 20 minutes. In large tortoises (eg. *Aldabrachelys gigantea*) a muscle relaxant may be indicated to facilitate handling of the head and intubation. Ketamine and zolazepam/tiletamine (zoletil, tilazol) I.M. are indicated as premedication in snakes. Propofol I.V. and even methoxital I.M. or S.C can be used for induction and small interventions. In lizards, easy access to the tail and abdominal veins assure intravenous access. For this reason, propofol is mostly used for induction and smaller surgical interventions. Ketamine and alphaloxone/alphadolone I.M. are good alternatives. Since problems often occur with gas induction, injection anesthesia is usually obligatory in these species before inhalation anesthesia can be performed.**

SAMENVATTING

In het eerste deel van dit artikel wordt een overzicht gegeven van de injectieanesthesie bij reptielen. Vooraf worden de specifieke anatomie and fysiologie samen met het pre-anesthetisch onderzoek bij deze dieren belicht. De mogelijke farmaca voor premedicatie, spierrelaxatie, lokale anesthesie en inductie van een algemene anesthesie worden toegelicht. In het laatste deel wordt de analgesie bij deze dieren besproken.

Hagedissen zijn behoorlijk moeilijk te verdoven. De injectieanesthesie biedt hierbij een bruikbare oplossing. De combinatie van een α-2 agonist (medetomidine, xylazine) of midazolam met ketamine kan gebruikt worden bij deze species. Propofol IV of IO is te verkiezen voor relatief korte ingrepen (maximaal 20 minuten). Een spierrelaxans kan gebruikt worden om de kop van grotere schildpadden uit het schild te halen en intubatie toe te laten. Bij slangen kan ketamine of zolazepam/tiletamine aangewend worden als premedicatie. Propofol IV of IO en methohexital IM of SC zijn eveneens geschikt voor de inductie van de anesthesie of voor kleinere ingrepen. De staart en abdominale vene van hagedissen kunnen gebruikt worden als IV-toegangsweg. Propofol is aangewezen bij deze dieren; ketamine en eventueel alphaloxone alphadolone IM zijn mogelijke alternatieven. Aangezien er vaak problemen voorkomen bij hagedissen tijdens de gasinductie, is injectieanesthesie onmisbaar als inductie voor een inhalatieanesthesie.

INTRODUCTION

The numbers of reptiles being referred for consultation in small animal practice has been increasing in recent years. These animals are often difficult to handle and chemical restraint is sometime necessary for clinical examination. In some turtles, for instance, chemical restraint may be necessary to protrude the head from the shell. Reptile surgery has also come a long way, and over the years good anesthetic protocols have became increasingly important.

The drugs reported in reptile medicine are often for 'off label' use because almost no drugs have been ap-

proved for use in reptiles. However, a lot of clinical research has been performed on the drugs that are now currently used in reptiles.

This article is the first of two articles in which the different aspects of injection anesthesia in reptiles will be discussed. The anatomy and physiology of reptiles, the pre-anesthetic examination, the different injectable drugs and analgesia will be discussed. The second article will focus on gas anesthesia and monitoring.

The two articles will discuss only reptiles (including lizards, snakes and chelonians) referred or presented in small animal practices. Crocodiles will not be discussed. A simplified classification of reptiles can be found in Table 1. Specific problems encountered when anesthetizing different species of reptiles are summarized in Table 2.

ANATOMY AND PHYSIOLOGY

Most reptiles (except crocodiles) have a heart that is anatomically three-chambered but functions as five chambers. The ventricle is divided into the *cavum pulmonale* and the *cavum venosum* by an incomplete septum. A third compartment of the ventricle is the so-called *cavum arteriosum* (Heard, 2001). The fact that the monoventricle contracts first on one side and then on the other results in separate pulmonary and general circulation (Burke, 1978).

Chelonians (tortoises and turtles) have a renal portal system whereby part of the blood from the hind limbs and pelvic region is drained towards the kidneys. This renal portal blood perfuses only the tubules and not the glomeruli so the renal tubules receive mixed venous and arterial blood (Mallley, 1999). In normal healthy reptiles, only a small amount of the blood is diverted through the kidney. This phenomenon implicates that almost no problems can be encountered when drugs are injected into the hind legs. However, the renal portal valves close under the influence of the parasympathetic nervous system and so more of the blood flow is directed through the kidneys. A stress response induced, for example, by an injection, triggers a sympathetic response and opens the portal valves, making the renal portal system of little importance (Malley, 1998, 1999). Despite the relatively minor importance of the renal portal system, injection into the hind limbs, especially with drugs having possible nephrotoxic effects, is not recommended.

In dehydrated reptiles the afferent glomerular arterioles constrict and the renal portal system continues to supply blood to the tubules, thus preventing ischaemic necrosis. This protective mechanism can end in

Table 1. Classification of reptiles (Adapted from EMBL reptile database).

Order	Remarks
Crocodilia	Crocodiles, alligators, caimans, garials, *23 species*
Testudines	Turtles, tortoises, terrapins, sea-turtles, *26 species*
Squamata	
Suborder:	
Rhynchocephalia	Tuatara (New Zealand), *2 species*
Sauria	Lizards, *4610 species*
Amphisbaenia	Worm lizards, *160 species*
Serpentes	Snakes, *2900 species*

Reference: http:// www.embl-heidelberg.de/~vetz/LivingReptiles.html

Table 2. Problems encountered in anesthetizing reptiles.

Order	Problems
Chelonians	Holding breath (up to 27 hours)
	Biting
	Withdrawing head into shell
	Withdrawal of tail and hindlimbs in "bar turtles" (genera Terrapene, Cuora)
Snakes	Venomous (injection) / Non venomous (gas induction)
	Aggressiveness
	Size (Large: injection / small: gas induction)
Lizards	Breath holding (up to 4.5 hours)
	Biting

the rapid excretion of drugs injected into the hind legs of dehydrated reptiles. Alternatively, drugs can be administered using the front legs in dehydrated animals (Holz, 1999).

The different possible injection sites in different kind of reptiles are represented in Table 3. Most reptiles (excluding crocodiles and some varanes, which have a kind of pseudo-membraneous structure) do not have a diaphragm, so the thoracic and abdominal cavities are combined into the so-called thoraco-abdominal or coelomic cavity (Calderwood, 1971).

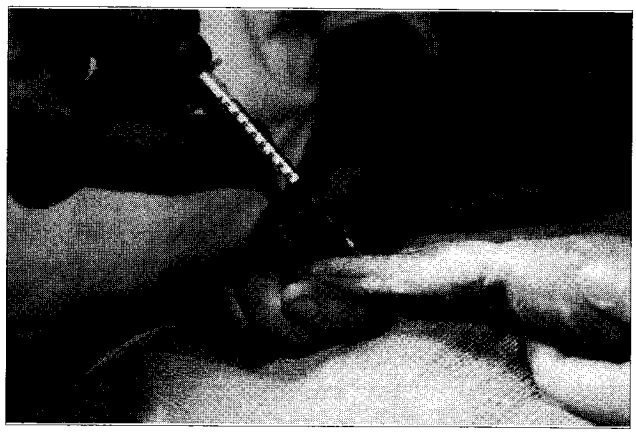

Figure 1. Blood sampling in ventral tail vein in a tree monitor (Varanus prasinus).

PRE-ANESTHETIC PREPARATION/EXAMINATION

A thorough anamnesis is of major importance in reptile medicine. The animal should be weighed very accurately since body weight is easily overestimated in smaller animals. Body weight is very important for calculating the exact doses of anesthetics and other medication. Only small volumes of blood can be withdrawn safely from smaller reptiles (Schumacher, 1996) (Figure 1).

It is important to observe the animal for respiratory and circulatory abnormalities and possible clinical signs of sepsis (Heard, 2001). Drugs eliminated by the kidneys such as ketamine are not justified in reptiles with a renal dysfunction (Frye, 1981). Samples from faeces, aspirates, tracheal fluids or blood can help in making an accurate pre-anesthetic diagnosis. The determination of packed cell volume, white blood cell count, total protein content and a biochemistry panel can sometimes be of help (Bennet *et al.*, 1999).

Throughout the entire anesthetic procedure, it is crucial to maintain reptiles at their preferred body temperature (PBT), which differs from species to species. The PBT is the most important factor affecting heart and respiration frequencies (Bennet, 1991; Schildger *et al.*, 1993; Malley, 1998).

Stress in reptiles should be minimized since rough handling, together with poor muscle relaxation, can cause a drop in blood pressure, hypoxaemia and hypercapnea. Even more importantly, if the sympathetic nervous system is overstimulated cardiac arrhythmias can occur. In snakes, inadequate handling was also reported to induce a fatal myositis (Malley, 1998).

Table 3. Injection sites in reptiles (adapted from Malley, 1998).

	Intravenous	Intracoelomic	Intracardiac	Subcutaneous	Intramuscular	Intra-osseous
Chelonians	Jugular vein Caudal vein (dorsal)	Axillary or inguinal approach	Junction of pectoral and abdominal scutes	Axillae Inguinae	Pectorals Quadriceps	Tibia
Lizards	Ventral caudal vein Ventral abdominal vein	Ventrolateral 80% craniocaudal from pectoral to pelvic girdle	Ventral third of chest caudal to the left front leg extended cranially	Paramedian and midline dorsum	Limbs	Tibia
Snakes	Ventral caudal vein Palatine vein	Ventrolateral 80% craniocaudal from nose to vent, paramedian	Palpate the heart (25-30% from nose to vent)	Paramedian and midline dorsum	Paravertebral tail Dorsum	none

Prophylactic antibiotics and adequate pain management are justified if surgery is planned (Malley, 1998).

PREMEDICATION/SEDATION

Parasympatholytic drugs

In mammals, parasympatholytic drugs suppress the vagal activity in the body by blocking acetylcholine at the postganglionic nerves. Oral, pharyngeal and respiratory tract secretions are decreased and a bronchodilatation can be observed. Vagal or centrally induced arrhythmias and bradycardia can thus be effectively counteracted (Thurmon *et al.*, 1996a).

The use of parasympatholytic drugs in reptiles remains controversial. Atropine sulphate (0.01 to 0.04 mg/kg I.M. or I.P.) or glycopyrrolate (0.01 mg/kg I.M. or S.C.) given 10 to 15 minutes before induction of anesthesia, were reported to decrease salivation and the risk of bradycardia. A small amount of saliva can induce a life-threatening obstruction of the endotracheal tube in smaller reptiles (Bennet *et al.*, 1991). However, Schildger *et al.* (1993) reported that salivation in reptiles is rarely observed and that bradycardia only occurs in very deep stages of inhalation anesthesia. Atropine administered at the end of barbiturate anesthesia was also reported to prevent or treat pulmonary edema (Kuen, 1974).

Sedatives

Sedative drugs, including major and minor tranquilizers and α_2-agonists, decrease the amount of the induction agent and reduce possible excitement of the patient during handling (Bennet, 1991).

Major tranquilizers

Phenothiazines and butyrophenones are major tranquilizers. They are mainly antagonists of the D_2 dopamine receptor. They are primarily used to prevent anxiety. In addition they can be used to sedate a patient for physical examination and transport. These drugs have a clear α-sympathicolytic effect so they are not indicated in anemic patients or animals in shock (Thurmon *et al.*, 1996a).

Although phenothiazines can be used in reptiles, little information about these drugs is available for

these species. Acepromazine (0.1 to 0.5 mg/kg I.M.) has been used 1 hour prior to anesthesia in order to decrease the quantity of induction agent needed. Chlorpromazine in chelonians (*Pseudemys genus*) (10 mg/kg I.M.) was reported to decrease the induction time of a barbiturate anesthesia (Frye, 1981; Bennet, 1991; Schildger *et al.*, 1993).

Minor tranquilizers

The minor tranquilizers (benzodiazepines) have anxiolytic, sedative, muscle relaxing and anticonvulsant properties. The effects of benzodiazepines occur in neuronal pathways in which gamma-aminobutyric acid (GABA) is the primary neurotransmitter. Sedation and anticonvulsant activity are mediated by GABA in the cerebral cortex and motoric centers (Thurmon *et al.*, 1996a). Diazepam is seldom used in reptiles because of the propylene glycol solvent, which can produce irritation and even cardiogenic disorders when given I.V. (Thurmon *et al.*, 1996a).

Oppenheim and Moon (1995) reported the optimum dose of midazolam (1.5 mg/kg) in red-eared slider turtles *(Trachemys scripta elegans)* for manual extension of the head. Onset of sedation appeared after approximately 5 minutes and sedation lasted for about 80 minutes. Recovery was complete 40 minutes later. Although many individual differences were observed, midazolam was reported to be an effective and safe sedative. Reversal of sedation with flumazenil was possible.

Bienzle and Boyd (1992) investigated the sedative effects of midazolam and ketamine in snapping turtles *(Chelydra serpentina)*. Midazolam (2 mg/kg I.M.) or ketamine (40 mg/kg I.M.) alone did not produce an adequate sedation. The combination of the two drugs provided an effective sedation in less than 5 minutes and a complete recovery in 3 hours.

At the current time, zolazepam, another benzodiazepine, is available only in combination with tiletamine (1:1 Tilazol, Zoletil). The addition of zolazepam potentiates the anesthetic effects of tiletamine and provides better muscle relaxation. Boever and Caputo (1982) tested this combination in snakes, iguanas and turtles. In turtles, the doses ranged from 4.4 mg/kg to 88 mg/kg I.M. At all dosages, the turtles seemed to be depressed but were easily aroused. Few signs of the presence of an adequate analgesia were observed. This makes Tilazol of little value for use in turtles. In snakes, dosages from 22 to 77 mg/kg I.M. were administered. At low dosages a deep sedation was observed but a standard stimulation still induced movement, making surgical procedures impossible. At high dosages, all snakes died. Tilazol was reported to be justified at low dosages for sedation of poisonous and difficult to handle snakes before inhalation anesthesia. In iguanas, 11 to 22 mg/kg allowed physical examination but long recoveries were reported (12 hours). Dosages from 33 to 44 mg/kg induced good surgical anesthesia in these species but, again, recoveries were prolonged (approximately 22 hours).

α_2-agonists

α_2-agonists are potent sedatives that stimulate the α_2-receptors, mainly presynaptic, decreasing the release of norepinephrine. In mammals these products provide good sedation, visceral analgesia and moderate muscle relaxation. Because of the centrally mediated decrease of noradrenaline, there is a possible danger of bradycardia and cardiac blocks (second degree A-V and sinus blocks). These problems can be partially avoided by the use of parasympatholytic drugs (atropine, glycopyrrolate). However, care should be taken when using a combination of these drugs because important hypertension have been reported to occur in mammals (Alibhai *et al.*, 1996). Over the years many α_2-agonists have become available (xylazine, romifidine, detomidine, medetomidine, dexmedetomidine).

Only xylazine and medetomidine are currently used in reptile anesthesia. Xylazine can be used in reptiles at dosages of 0.10 to 6 mg/kg. It produces different stages of unconsciousness in reptiles, ranging from light sedation to surgical anesthesia. Induction times were reported to be between 10 and 60 minutes and the duration of sedation lasted from less than one hour to over 12 hours. One advantage is that xylazine can be antagonized with yohimbine, even when combined with ketamine (Frye, 1981).

Medetomidine is mainly used in combination with ketamine (10 mg/kg) at a dosage of 150 µg/kg I.M. in tortoises and 300 µg/kg I.M. in aquatic chelonians. In the Californian king snake (*Lampropelti getulus*), 100 µg/kg medetomidine I.M. prior to ketamine (50 mg/kg) was effective (Malley, 1998). Medetomidine can be antagonized with atipamezole (5 times the dose of the medetomidine) (Bennet *et al.*, 1999).

MUSCLE RELAXANTS

Muscle relaxants have no anesthetic or analgesic properties, but rather provide immobilization. When

using these products for surgical interventions, they must be supplemented with drugs that assure hypnosis and analgesia.

Depolarizing muscle relaxants

Succinylcholine (two acetylcholine molecules joined together) is a depolarizing muscle relaxant. Initially, this drug stimulates cholino-receptors at the neuromuscular junction to open the ion channel, allowing the inflow of sodium and calcium ions and the outflow of potassium ions. Depolarization occurs at the end plate, leading to muscle contractions. After a period of depolarization the muscle membranes become insensitive and relaxation occurs (Heavner, 1996). This drug cannot be antagonized.

Succinylcholine (0.3 to 1.5 mg/kg I.M.) can be used in chelonians to prevent the withdrawal of heads and necks into the shell. The effect has been reported to begin approximately 4 to 6 minutes after injection and to last for up to 20 minutes. If larger doses are given, spontaneous respiration stops, so chelonians must be intubated and artificially ventilated (Frye, 1981). Schildger *et al.* (1993) tested succinylcholine in 13 tortoises (8 *Testudo hermanni* and 5 *Testudo graeca*) in combination with ketamine (50 mg/kg I.M.). Succinylcholine was administered in male and female tortoises at a dose of respectively 1.0 mg/kg and 0.5 mg/kg I.M. Anesthesia was satisfactory and muscle relaxation was excellent.

Non-depolarizing muscle relaxants

Competitive or non-depolarizing muscle relaxants prevent acetylcholine from occupying the triggering sites of the receptors by reacting dynamically with receptor recognition sites (Heavner, 1996). One of the non-depolarizing muscle relaxants used in reptile immobilization is d-tubocurarine. This drug was tested in venomous Australian tiger snakes *(Notechis scutatus)* (6.0 mg/kg I.M.), a Northern Territory rock python *(Liasis olivaceous)* (1.8 mg/kg I.M.) and a Cunningham's skink *(Egernia cunninghami)* (0.9 mg/kg I.M.) (Frye, 1981; Schildger *et al.*, 1993; Bennet, 1991; Malley, 1998). The tiger snakes and the skink had to be intubated and artificially ventilated. Apparently venomous snakes require more d-tubocurarine than non-venomous ones. No information is available about the use of newer curare derivatives such as cisatracurium and pancuronium in reptiles.

LOCAL ANESTHETICS

Local anesthesia can be an alternative for small surgical interventions in reptiles (repair of small lacerations, curettage of abscesses, removal of small tumors). In reptiles, 2% lidocaine or 1% procaine is recommended (Bennet, 1996; Schildger *et al.*, 1993). In mammals, the toxic dosage of lidocaine varies from 5-20 mg/kg. The toxic dose of lidocaine in reptiles has not been established yet (Heard, 2001). The lethal dose of procaine in reptiles was reported to be 250 mg/kg S.C. (Bennet, 1991; Schildger *et al.*, 1993).

INDUCTION OF INJECTION ANESTHESIA

Narcotics

Opioids or narcotics are drugs that bind to opioid receptors, producing a morphine-like agonist action. Normally, their analgesic effects are not accompanied by loss of proprioception or consciousness unless excessive doses are given. Etorphine is a narcotic that is chemically related to morphine but 10,000 times more potent. It has analgesic and catatonic actions, produces a severe respiratory depression, reduces gastro-intestinal motility and blocks conditioned reflexes. Etorphine has been combined with acepromazine (LA Immobilon, 2.45 mg etorphine/ml and 10.0 mg acepromazine/ml) for use in wild and zoo animals (Thurmon *et al.*, 1996a). LA Immobilon has been used in chelonians and snakes at a dose of 0.25 to 5 mg/kg I.M. These dosages are very high compared to mammals but were reported to induce an acceptable chemical restraint without a proper surgical anesthetic level (Bennet, 1991; Schildger *et al.*, 1993). Etorphine can be antagonized by diprenorphine; the dose for all species is 0.0272 mg/kg I.V. by slow injection (Thurmon *et al.*, 1996a). The legal implications and the danger for man must be kept in mind, so the question can be raised as to whether these drugs should be used at all in reptiles.

Barbiturates

Barbiturates can be used as hypnotics, sedatives, anti-epileptics and general anesthetics. They interfere with the passage of impulses to the cerebral cortex and act directly on CNS neurons in a manner similar to that of the inhibitory transmitter GABA (Thurman *et al.*, 1996b).

The barbiturates have been classified into four groups: the ultrashort-acting (methoxital), the short-

acting (thiobarbiturates), the middle-long-acting (pentobarbital) and the long-acting (phenobarbital). Ultrashort and short-acting are mainly used as anesthetics, while middle-long and long-acting barbiturates are indicated for use as sedatives and anticonvulsives (Thurman *et al.*, 1996b).

Barbiturates can be administered in reptiles by different injection routes (I.M, I.P., I.V. and S.C.). When not given I.V., the concentration should be lower than 2.5% because of the irritating characteristic of the drug (Bennet, 1991; Schildger *et al.*, 1993). Thiobarbiturates and middle-long-acting barbiturates induce in reptiles comparable induction times, duration of anesthesia and recovery times. This can be explained by the fact that reptiles rely on their metabolism for the elimination of both middle-long-acting and short-acting barbiturates. In mammals, redistribution for the elimination of short-acting barbiturates is of major importance. When the environmental temperature is increased, recovery time can be shortened (Bennet, 1991). Many barbiturates have a narrow safety margin and produce long, unpredictable inductions and recoveries (Frye, 1981).

Methoxital is an ultrashort-acting barbiturate that detoxifies very rapidly in mammals and in reptiles. It is three times more potent than thiopental and the onset of action is three times faster. The recommended dose in reptiles is 5 to 20 mg/kg S.C., but there are significant interspecies variations (see Table 4). In young animals it is better to decrease the dose by 20 to 30% because these subadults seem to be very sensitive to the drug (Bennet, 1991; Bennet, 1996). Its rapid onset and short duration makes methoxital a good drug for induction and intubation before gas anesthesia (Bennet, 1991; Schildger *et al.*, 1993). The concentration of the solution should be adjusted to the weight of the reptile (Table 4) (Bennet *et al.*, 1991; Bennet, 1996).

Thiopental and thiamylal can be administered in reptiles at a dose of 15 to 30 mg/kg I.M or I.P. with similar effects as pentobarbital (Frye, 1981; Bennet, 1991; Schildger *et al.*, 1993). However, a 5% thiopental solution injected I.P. in snakes was reported to produce mesenteric oedema (Bennet, 1991).

Pentobarbital is a middle-long-acting barbiturate that can be used in all reptiles, though with variable results. In snakes, dosages from 15 to 30 mg/kg I.M. (Schildger *et al.*, 1991) and up to 30 mg/kg intracoelomically were recommended (Frye, 1981). Karlstom and Cook (1955) reported that dosages of 60 to 100 mg/kg were fatal in snakes. Bonath (1977) noted also that dosages exceeding 50 mg/ kg proved to be fatal in some snakes. Venomous snakes were reported to require twice the dosages that non-venomous snakes require (Calderwood, 1971). Induction after pentobarbital anesthesia occurs within 40 to 60 minutes and recovery may require from two days up to one week. The surgical stage of anesthesia lasts 22 to 45 minutes. Schildger *et al.* (1993) recommended a dose of 10 to 18 mg/kg I.M in chelonians. One paper described the use of 18.2 mg/kg I.P. to induce 2 to 4 hours of anesthesia (Jones, 1977). Another study reported a dosage of 10 to 26 mg/kg I.V. into the dorsal cervical sinus of green sea turtles *(Chelonia mydas)* (Wood *et*

Table 4. Available data of methohexital in reptiles (adapted from Bennet, 1991). Doses of methoxital in different species and concentration of methoxital according to body weight.of reptiles.

Species	Dose	Body weight	Concentration
Common Garter Snake *Tamnophis sp.*	15 mg/kg SC	< 5 grams *(all reptiles)*	0.125%
Common Water Snake *Nerodia sp.*	15 mg/kg SC	4.5 – 9 grams *(lizards)*	0.25%
Anole Lizard *Anolis sp.*	20 mg/kg SC	5-100 grams *(snakes)*	0.5%
Other Lizards	10 mg/kg SC	>100 grams *(all reptiles)*	1.0%

al., 1982). This dosage resulted in an induction time of 14 to 120 minutes, a surgical anesthesia of 40 to 240 minutes and a recovery of 4 to 24 hours. It was recommended to start with the lowest dose (10 mg/kg) I.V. and give supplemental dosages of 5 mg/kg every 15 to 30 minutes with a maximum of 25 mg/kg. Pentobarbital was ineffective in 10 % of turtles, however (Wood *et al.*, 1982).

Dissociative anesthetics

Dissociative anesthetics are specific drugs that produce a dissociation between the thalamus/neocortex and the limbic system. When used alone, they induce cataleptic effects and muscle rigidity (Lin, 1996). The catalepsy can be prevented by giving adequate premedication (midazolam, xylazine) (Green *et al.*, 1981; Bienzle and Boyd, 1992). Dissociative anesthetics provide good peripheral analgesia but the visceral analgesia is doubtful (Bennet, 1996).

The best known and most commonly used dissociative anesthetic in reptiles is ketamine. One of its biggest advantages is the high therapeutic range it displays in conjunction with its wide margin of safety. Ketamine can be used as a sedative, an induction agent and for maintaining anesthesia. In general, when used as a sedative, a dosage of 22 to 44 mg/kg I.M. or S.C. was recommended. For surgical anesthesia a dose of 55 to 88 mg/kg I.M. or S.C. was advised (Jones, 1977; Bennet, 1991; Schildger *et al.*, 1993; Bennet, 1996). The response to ketamine is not only dose dependent but also differs from species to species and individual to individual (Table 5). When combined with xylazine, a reduced dose of ketamine (to 20 mg/kg) can be used for example for surgical interventions in certain iguanas. Recovery periods can vary widely but were reported to be approximately 24 to 72 hours (Cooper, 1974).

At high doses of less than 88 mg/kg, a minor respiratory depression and cardiac stimulation were observed, while extremely high doses (more than 110 mg/kg) induced respiratory arrest and bradycardia. Artificial respiration is required to overcome the respiratory arrest (Bennet, 1991).

Cooper (1974) reported that injection of ketamine was painful in snakes but few pain reactions were observed by Schildger *et al.* (1993) in these animals.

In mammals, ketamine is known to be metabolized in the liver and eliminated through the kidneys. Although in reptiles the exact mechanism for excretion

Table 5. Reported differences in species with regard to ketamine in reptiles.

Author	species	doses	remarks
Cooper (1974)	East African reptiles	40-60 mg/kg I.M. or S.C.	< 50 mg/kg → sedation > 50 mg/kg → anesthesia
		Induction: snakes: 50 mg/kg lizards: 40 mg/kg	Additional doses of 10 mg/kg every 30 minutes, if necessary
Green et al. (1981)	Snakes	40-80 mg/kg I.M.	
	Chelonians	60-80 mg/kg I.M.	
Wood et al. (1982)	Green sea turtles	50-71 mg/kg I.P.	I.M and I.V. not effective Induction: 2-10 minutes Recovery: < 2 hours
Schildger et al. (1993)	Monitor lizards	50-100 mg/kg I.M.	In boids (except royal python) Ketamine not sufficient for surgical anesthesia
	Snakes	50-75 mg/kg I.M.	
	Chelonians	40-90 mg/kg I.M.	

is not known, renal elimination is most likely in view of the fact that recovery in dehydrated animals is prolonged and I.V. infusion together with furosemide speed up recovery (Bennet, 1991; Schildger *et al.*, 1993).

Aggressiveness was observed during recovery in ketamine anesthetized reptiles. Snakes handled during recovery from the cataleptic state presumably felt themselves to be in danger, which naturally resulted in aggressive behavior (Lawrence and Jackson, 1983).

Tiletamine is another dissociative drug commercially available in combination with zolazepam (Tilazol or Zoletil). This combination can not be used as an induction agent but can be useful as a sedative before intubation for gas anesthesia. This drug combination has already been discussed (see above).

Alphaloxone/alphadolone

The preparation (Saffan) of this steroid combination (9 mg alphaxalone and 3 mg alphadone acetate/ml) is commercially available for cats in the U.K. Lawrence and Jackson (1983) tested this combination in 40 reptiles of 13 different species. The doses varied from 9 to 18 mg total steroid/kg bodyweight I.M. They reported that this combination was a safe and successful anesthetic in lizards and chelonians but that it was unreliable in snakes. The induction time was 25 to 40 minutes (average of 35 minutes) and surgical anesthesia lasted 15 to 35 minutes (average of 25 minutes). Recovery was complete in 1.5 to 4 hours (average of 2.5 hours). During anesthesia there was good muscle relaxation, and no signs of respiratory or cardiac depression were observed. Reactions during injection were not noticed. Care should be taken when using this combination in animals with hepatic problems.

Frye (1981) obtained satisfactory anesthesia in snakes giving 6 to 9 mg total steroid/kg I.V. Schildger *et al.* (1993) tested this product in a boa constrictor *(Boa constrictor)* and a royal python *(Python regius)*. Acceptable results were obtained giving the product I.M.(!). Induction was 20 minutes, duration of the anesthesia was 30 to 60 minutes, and recovery was also 30 to 60 minutes. Muscle relaxation was equal to the effect produced by isoflurane anesthesia and better than with ketamine anesthesia.

Propofol

Propofol (2,6-diisopropylphenol) is an oily anesthetic emulsion without preservatives. This drug induces depression by enhancing the effects of the inhibitory neurotransmitter GABA and decreasing the brain's metabolic activity. Apnea and hypercapnia may occur after bolus injection. In mammals, propofol is primarily excreted by the kidneys. However, renal insufficiency has little or no effect on the clinical response (Thurmon *et al.*, 1996b).

Propofol has become the agent of choice for induction of general anesthesia and small surgical interventions in lizards, snakes and chelonians. Its biggest advantages are the rapid onset of anesthesia, the short duration of action, and rapid recovery (Anderson *et al.*, 1999). Moreover, accidental perivascular injection causes no irritation and the drug is non-cumulative. Repeated injections or continuous infusions can be used. Propofol has to be administered I.V. or intra osseous (I.O.), which makes it very difficult for use in smaller reptiles (Bennet *et al.*, 1998). Moreover, propofol has poor analgesic properties (Heard, 2001).

Bennet *et al.* (1998) tested the intra osseous use of propofol in green iguanas *(Iguana iguana)* (Figure 2). Single injection of 10 mg/kg I.O. gave a mean induction time of 1.2 minutes and a mean duration of anesthesia of 27 minutes. In the group of 5 mg/kg I.O. followed by an infusion of 0.5 mg/kg/min propofol, mean induction time was 3 minutes. A significant decrease in heart rate was observed after 35 minutes and lasted for 120 minutes. The bradycardia was probably due to the constant infusion rather than the induction bolus. All animals showed apnea but started to breath again after 5 minutes. Intubation of the iguanas and artificial ventilation were recommended.

Propofol was also tested in brown tree snakes *(Boiga irregularis)*. The snakes were given 5 mg/kg propofol intracardiacally (I.C.) and were intubated (breathing room air). Intubation was easy within 30 seconds after the administration of propofol. The period of unconsciousness lasted approximately 24 mi-

Figure 2. Intra-osseous catheter placed in the tibia of a common Iguana *(Iguana iguana)*.

Figure 3. Intra-osseous catheter for fluid administration placed in the tibia in commun readed dreagon (Amphibolurus barbatus).

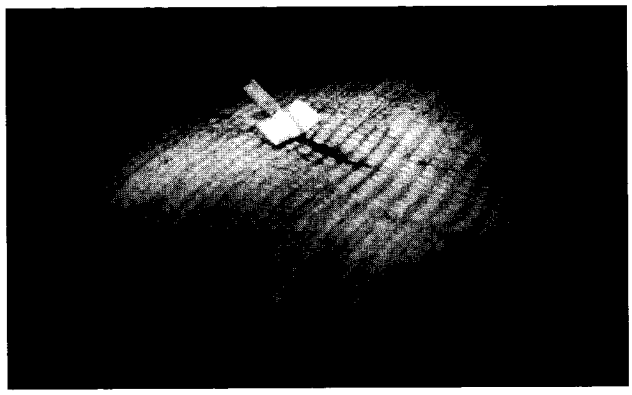

Figure 4. Catheter placed in the abdominal vein of a tree monitor (Varanus prasinus).

nutes. After induction, almost all snakes had a self limiting apnea, which lasted for 30 to 60 seconds. The respiratory rate was still significantly lower 2 minutes after injection. The first 15 minutes after I.C. injection, an increase in heart rate was observed but this was probably of no clinical importance. It was observed that agitated snakes and snakes with the greatest fat reserves had the shortest duration of anesthesia. Apparently obese reptiles needed a higher dosage of propofol. When the dose was increased to 6 mg/kg propofol I.C., better results were obtained in agitated or obese snakes (anesthesia of approximately 10 minutes). Doses greater than 6 mg/kg propofol I.C. induced apnea lasting up to an hour. When prolonging the anesthesia, a dose of 2.5 mg/kg was advised. Necropsy 7 months after anesthesia revealed a mild hemosiderosis in the heart, probably as a result of the intracardiac injection (Anderson *et al.*, 1999).

Fonda (1999) tested the intra osseous (I.O.) use of propofol in red-eared sliders *(Trachemys scripta elegans)*. The administration of 15 mg/kg I.O. was not sufficient to produce anesthesia although slightly better results were found when the body temperature was higher (27.1°C. 22.9 °C.). The use of 30 mg/kg I.O. (T: 26.4 °C.) proved to be satisfactory in red-eared sliders. The mean induction time was 115 seconds, and the duration of anesthesia and recovery time were 47 minutes. The results showed that propofol can be used I.O. in *Trachemys* at higher dosages than in I.V. administration (7 mg/kg), and body temperature seems to have a certain influence.

Divers (1996) recommends the following doses of propofol I.V. in unpremedicated reptiles: in lizards 10 to 14 mg/kg, in snakes 10 to 12 mg/kg and in chelonians 12 to 15 mg/kg. The induction times were less than 1 minute, except in chelonians where they can be more than 5 minutes. One possible explanation is that the injected fluids went into the lymphatic vessels close to the caudal vein. Surgical anesthesia lasts 15 to 25 minutes and recovery 25 to 40 minutes. For longer interventions, additional injections or gas anesthesia may be used.

Rooney *et al.* (1999) tested different doses of propofol in desert tortoises *(Gopherus agassizii)*. A low dose (2 to 4 mg/kg I.V.) produced a light sedation sufficient for examination. A moderate dose (5 to 8 mg/kg I.V.) allowed intubation in the tortoises and a high dose (9 to 12 mg/kg I.V.) produced surgical anesthesia. The recoveries were approximately 25, 45 and 120 minutes, respectively. Dilution of the propofol was recommended (2 parts NaCl 0.9 % + 1 part propofol) to prevent respiratory depression.

ANALGESIA

It is assumed that reptiles, like mammals, can experience pain. This assumption is supported by the presence of neurological components that evoke an action potential in response to a nociceptive stimulus, endogenous mechanisms for pain modulation and a demonstrable modulation of pain. Therefore an analgesic should be administered before surgery. (Heard, 2001).

In reptiles, two classes of analgesics can be used: the opiates and the non-steroidal anti-inflammatory drugs (NSAID's). Opioids raise the pain threshold or decrease the perception of pain by acting at receptors in the dorsal horn of the spinal cord and mesolimbic system, midbrain grey matter and several thalamic and hypothalamic nuclei. They must be used carefully in animals with pulmonary problems (Thurmon *et al.*, 1996c). The opiates are classified in two groups: the pure agonists (morphine, methadone, fentanyl) and

Table 6. Drugs used for analgesia in reptiles (adapted from Heard, 2001).

	Drug	Dosage	Administration route
Opioid's	Butorphanol	0.4 mg/kg every 4 hours	IM
		0.2 – 0.5 mg/kg q 24 h	IV or IO
	Buprenorphine	0.01mg/kg q 24h	IM
NSAIDS's	Ketoprofen	0.022 mg/kg q 24-48h	IM or SC
	Carprofen	2-4 mg/kg initially followed by 1-2 mg/kg q 24-72h	IM, IV, SC or PO
	Flunixin meglumine	0.1-05 mg/kg q 24h for 2-3 days	IM
		2mg/kg q 24h	IM or SC
		for 1-2 days	

(NSAID's = non steroidal anti-inflammatory drugs).

the agonist-antagonists (butorphanol, buprenorphine). Opiates currently used in reptile medicine are mainly agonist-antagonists (Table 6). These drugs can be antagonized by naloxone.

The NSAID's work mainly peripherally by decreasing prostanoids that facilitate the generation and conduction of pain impulses. When administered prior to tissue damage, analgesia is produced by suppressing the production of kinines and prostaglandins. NSAID's are useful for treating pain of somatic origin (Thurmon *et al.*, 1996c). This group of drugs can be used in reptiles as per-operative analgesics (Table 6).

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