Section 26

ARAV Anesthesia and Analgesia

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Snake Anesthesia and Analgesia: A Review

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Session #113

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Advances in anesthetic and analgesic management of lizards[1,2] may not directly benefit snakes despite their close relationship as members of the Order Squamata. Multiple formularies provide doses for practitioners as a starting point without all being based on pharmacokinetic studies and efficacy trials.[3-5]

Ketamine (5-20 mg/kg) is not routinely used alone and is typically combined with lower end doses of diazepam (0.2-0.8 mg/kg) or more commonly midazolam (0.1-2.0 mg/kg). These have been routinely used for sedation and surgical procedures on snakes. Ketamine is not reversible but midazolam can be reversed with flumazenil 0.05 mg/kg. Doses can be IV, IM or SC. Tiletamine and zolazepam (Telazol 100 mg/ml Zoetis, Kalamazoo, MI) has been used at 3-5 mg/kg IM in snakes to facilitate handling and intubation. Doses up to 10 mg/kg may be needed for surgeries. The primary disadvantage of these combinations has been the prolonged recoveries at higher doses necessary for surgical procedures.

Alfaxalone (Alfaxan 10 mg/ml Jurox/Pty Limited, Australia) has been used by one of the authors since 2010 at 1-5 mg/kg IV and provides rapid induction and ability to intubate provided IV access can be obtained. Administration (IM and SC) is effective in reptiles at higher doses of 5-10 mg/kg[6-7] (up to 30 mg/kg reported) and is being explored in combination with opioids. The current challenge with its use relates to label guidelines of single use after opening and cost related to a single individual bottle size.

Propofol (3-10 mg/kg) is also an excellent induction agent provided IV access can be obtained in a larger snake. This also is labeled for single use after opening, which limits extended use for multiple smaller snake patients. Its lipid characteristics result in a higher risk of contamination negating any extended use of a bottle.

General anesthesia with isoflurane or sevoflurane gas can be facilitated in venomous snakes with use of the Pro-Bagger system (Midwest Tongs, Inc, Greenwood, MO). Safety is maintained for the handler and the surgeon during mask induction utilizing a clear plastic handling tube.

Morphine, butorphenol, buprenorphine, hydromorphone and fentanyl are common opioid options available to practitioners. It does not appear that all reptiles share the same affinity for opioid receptors leading to much variability in effect. Butorphenol at 5 mg/kg failed to decrease physiologic stress responses in pythons.[8] Doses of 2 mg/kg had no response in corn snakes[9] but when dosed at 20 mg/kg blunted the response to heat 8 hours after administered. Morphine doses of 10-20 mg/kg that had analgesic properties in bearded dragons did not show benefit in the corn snakes even when increased to 40 mg/kg. Butorphenol doses of 10 mg/kg will produce sedation in pythons but did not provide analgesic effect 7 hours after administration.[10] Buprenorphine at doses

of 0.02-1 mg/kg had limited benefit in lizards and turtles[6] with studies on snakes needed. Fentanyl patches (12.5 µg/h) have shown analgesic efficacy in corn snakes and pythons to thermal stimuli.[11] The environmental temperature may affect absorption.

Regional blocks can be used as adjunctive analgesia during surgical procedures. Wellehan and colleagues reported use of mepivacaine at 1 mg/kg in crocodilians.[12] The authors have used mepivacaine at 2-10 mg/kg as a regional block at the site of radiotransmitter implantation in 71 snakes weighing between 400 g and 3 kg.[13] Dilutions may be required in small snakes to use lidocaine (2-5 mg/kg) or bupivacaine (1-2 mg/kg) for local and regional blocks.[14]

Meloxicam has gained routine use with reptiles needing NSAIDs for its anti-inflammatory and pain control properties. Empirical doses appear to be of limited benefit[8] or at too low of a dose. Published[3-5] intramuscular doses begin at 0.1 mg/kg and increase to 0.5 mg/kg in snakes, similar to use in other reptiles. Dose ranges of 0.5-1.0 mg/kg q24h are now routinely used by several of the authors. Hydration and renal status of the patients should be monitored.

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Comparison and Effect of Anesthetics in Lung Breathing Salamanders *(Ambystoma tigrinum)*

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Session #152

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Ambystomatid salamanders are generally robust in size, possess lungs and are capable of cutaneous (skin) respiration and pulmonary (lung) ventilation. As with most salamander species, the cutaneous route of respiration has been the focus of anesthetic studies, research, and medical treatments. However, noting their ability to use other forms of respiration, more avenues should be investigated. Three drugs were used in this study: tricaine mesylate (MS-222), isoflurane gas, and alfaxalone comparing 3 routes of administration injection, inhalation, and immersion. Times for anesthetic induction and recovery, heart rate, respiratory rate, righting reflex, and response to stimuli were recorded before, during and after. An initial preliminary study was performed to determine more accurate doses of alfaxalone since this information is novel for this species. Doses of 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, and 30 mg/kg were chosen in groups of 5 individuals each. The fastest induction periods with the least effect on vitals and shortest recovery were chosen for the second part of the study. Comparison of immersion drugs alfaxalone and MS-222 were compared as well. Alfaxalone at doses of 5 mg/L, and 2000 mg/L were compared to MS-22 at 55 mg/L, 1000 mg/L, 2000 mg/L, with a control. The best results from this group were also moved to the final comparison of all three drugs; MS-222 immersion, inhalation isoflurane, immersion alfaxalone and injectable alfaxalone.

Limiting Transmitter Associated Morbidity and Mortality in Snakes

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Session #321

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Mortality associated with implantation of radio transmitters has been recognized in snakes during conservation studies. Seasonal timing was demonstrated as one of the most significant causes of mortality by Rudolph and colleagues, with a higher risk in smaller snakes.[1] Snakes should not be implanted during the late season when mortality can approach 100%. Lentini and colleagues have reported concerns with radio transmitter morbidity exceeding 66% related to infections and inflammation.[2] This potentially raises concerns with behavior data validity related to decreased or increased movement and basking length and frequency. An Association of Zoos and Aquariums (AZA) task force has expanded specific guidelines for species like the Eastern massassauga rattlesnake (*Sistrurus catenatus catenatus*) advising to not place radio transmitters in snakes under 200 grams, limit transmitter size to less than 50% of snake width and 2.5% of weight in gravid females compared to 5% maximum in males.[3] This also advise to avoid implantation after June in gravid females of this species and after mid-August completely. Expansion to other species can help towards a conservation research goal of documenting post hibernacula survival rates the following spring and lessening any impact on reproduction.

This author seeks to increase dialogue on improving survival and limiting morbidity associated with snake transmitter diseases (STDs).[4,5] Many small transmitters only last a season, so many reports and papers lack any follow up on the snakes' health the following spring. Morbidity and mortality are not routinely published as data in the herpetologic summaries. King and colleagues reported almost 9.5% acute case fatality from anesthesia and post-surgical complications in his small northern population of Lake Erie Watersnakes (*Nerodia sipedon insularum)*.[6] Their surgical protocol maintained snakes in captivity for three days prior to release. Debate exists among herpetologists considering time in captivity an additional and unnecessary stressor and favoring immediate release upon recovery.[7] One AZA task force now stipulates that snakes should be kept at least 24 hours after surgery for observation and advises 3-6 days depending on the need for antibiotics considering environmental factors during release.[3] Concerns with a 19% transmitter (Holohil Systems Ltd., Carp, Ontario Canada) failure rate[6] were not observed by this author with their larger transmitters possessing a 2-3 year battery life, allowing multiple years of tracking. No acute mortality was noted in Timber Rattlesnakes (*Crotalus horridus)* with 71 coelomic surgeries and only a single overwintering mortality.[4] Enrofloxacin at 5-10 mg/kg IM q24h × 3 doses (Baytril 22.7 mg/ml. Bayer Healthcare LLC, Shawnee Mission, KS) was provided to all snakes during 48 hours in captivity. Two post-surgical infections were observed yet both snakes survived. One did not have any treatment and the other required transmitter removal and a month of topical and systemic wound therapy for an enrofloxacin resistant strain of Streptococcus.[4] Both snakes were identified alive outside their hibernacula the following spring.

Regional nerve blocks with mepivacaine HCl at 2-10 mg/kg (Carbocaine-V. 20 mg/ml. Pfizer. Pharmacia & Upjohn Company, New York, NY) and injectable meloxicam at 0.2 mg/kg IM q24h × 3 doses (Metacam 5 mg/ml. Boehringer Ingelheim. Fort Dodge, IA) were provided while the snakes were maintained in captivity to assist with pain control and as an anti-inflammatory.[4,5] GIS movement data for 22 snakes that received a replacement transmitter was compared 1 and 2 weeks pre- and post- surgery and found no statistical difference.[5]

ARAV members are encouraged to seek out collaborations and dialogue with herpetologists to improve compliance with IACUC welfare goals regarding surgical technique, asepsis and pain management. This will hopefully lead to reductions in morbidity and mortality and improvement in the conservation data gathered and reported in herpetologic species being studied.

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Chelonian Anesthesia

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Session #013

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Abstract: Chelonians can be a challenge to anesthetize because of their size, demeanor, uncooperative nature, ability to breath hold, and slower metabolism. Following the authors presentation of his approach to chelonian anesthesia, there will be time for questions/answers and discussion on the topic of chelonian anesthesia.

Introduction

There are over 7000 species of extant reptiles exhibiting considerable anatomic, physiologic and pharmacologic differences. The approach to anaesthetizing many pet reptiles is relatively straightforward because they are large enough for intravenous injections and endotracheal intubation, and yet small enough to be easily and safely handled; however, there are occasions when veterinarians are asked to deal with particularly small or large reptiles, and here modifications in standard procedures are often necessary.[1]

One important concept that is often of practical importance is the need to allometric scale drugs doses. For example, while 10 mg/kg propofol may be perfectly appropriate for a 1kg iguana it would probably be a significant overdose for a 75kg komodo dragon. Allometrically scaling the dose, however, provides a much safer and effective dose of 4 mg/kg for the dragon. Similar calculations result in a dose of 20 mg/kg for a 50g gecko.

Pre-Anesthetic Assessment and Stabilization

Fasting should be carried out before all elective surgery in order to reduce compression of lung(s) associated with large meals in carnivores as well as to reduce the chances of regurgitation. In general, 1-2 feeding cycles should be skipped. Fasting has less impact on the volume of hind gut fermenters, including most tortoises. A full history should be taken, assessing not only the animal's current and previous health status, but also paying attention to housing and feeding, since many reptilian ailments relate to sub-optimal environmental conditions or nutritional factors. Accurate identification of species is also essential; this may influence the choice of drugs administered and also the required hospitalization facilities. A full clinical examination should be performed, and the animal accurately weighed. For small reptiles weighing less than 100 grams, an accurate weight to the nearest 0.1 grams is preferred. When dealing with giant chelonians, it may not be possible to obtain an accurate weight or even perform a physical examination until after induction. Weight must therefore be estimated, and the anaesthesiologist should be prepared for under or over-dosing, and serious organ dysfunction that may only become apparent during anesthesia.

The fluid status of all reptiles should be assessed, especially if debilitated or post-hibernation. Determination of packed cell volume and total solids provides a quantitative measure of dehydration, especially if serial samples

are analysed. Normal values vary between species, but often lie between 20-35%. The total blood volume of reptiles is around 4-8% of body weight; of this, up to 10% may be withdrawn safely in healthy animals. While inconsequential for large reptiles, blood loss is often a critical factor in small specimens. For example, a 100-gram tortoise that has 0.5 ml of blood drawn for a pre-surgical biochemistry profile and haematology cannot afford to lose any blood during surgery. Therefore, when dealing with very small animals it may be necessary to stage blood collection 7-14 days prior to elective surgery, or forgo pre-surgical blood screens to maintain circulatory volume for non-elective surgery. Giant reptiles may simply be too strong and resist venipuncture even if multiple handlers are employed, or they may represent too great a danger to handle when conscious.

A range of intravenous routes are available for blood collection and the administration of anesthetic and other drugs. The jugular veins are preferred but subcarapacial site (dorsal midline, below cranial carapace), dorsal coccygeal vein (tail), and brachial plexus (deep to the medial tendon of the elbow).

For elective procedures (e.g., neutering), underweight, dehydrated or debilitated animals should be nursed for days, weeks or months until their condition improves. For non-elective surgery attempts to correct dehydration must be started prior to anesthesia. Even the most moribund egg-bound reptile will usually benefit from stabilization for at least 24 hours before embarking on surgery. Whilst oral fluids are non-invasive to administer and provide the most physiologically normal method of rehydration, they are sufficient only for mildly dehydrated animals and are contraindicated immediately prior to surgery due to the risks associated with regurgitation. Intracoelomic fluids are more suitable but uptake can take many hours and their use is obviously problematic if coeliotomy is planned. Thus for dehydrated surgical candidates, intravenous fluid therapy should be administered pre-, peri- and post-operatively as necessary. Fluids are administered at 20-35 ml/kg/day (rates of up to 5 ml/kg/hour may be initially used for the first 3 hours); the use of an infusion pump or syringe driver achieves accurate dosing but multiple bolus injections are a practical alternative. The placement of an indwelling jugular catheter, or better still, a long stay central line can greatly facilitate vascular access.

All reptiles should be hospitalized and maintained within their preferred optimum temperature zone to minimize physiologic disturbance and facilitate recovery and immunocompetence. While small animals can be easily housed in dedicated hospital vivaria, maintaining a 100 kg giant tortoise at 28ºC often presents practical difficulty. Hypothermia also affects the pharmacokinetics of administered drugs and greatly prolongs recovery. When dealing with large reptiles it is often necessary to plan ahead. It may be necessary to acquire additional personnel for lifting and moving the animal, and careful consideration needs to be given to access and movement around the hospital.

The calculation and print out of an emergency drug sheet is recommended (Table 1). Such documents are best prepared using EXCEL so that drug calculations are automatic, and they can simply be printed and attached to the patient's medical record.

Table 1. Reptile anesthesia and emergency drug calculator.

Insert reptile weight, print, and attached to anesthesia form.					
Patient name:	Tortie				
Patient number:	307892				
Patient weight (kg):	2.671				
Drug	Concentration (mg/ml)	Dose (mg/kg)	Route	Bolus	Units
Atropine	0.54	0.04	IV	0.20	ml
Epinephrine (1:1000)	1	0.1	IV	0.27	ml
Calcium gluconate	100	100	IV	2.67	ml
Furosemide	10	2	IV	0.53	ml
Maintenance fluids (ml/kg/day)		7.5	IV	0.83	ml/h
Intraoperative fluids (ml/kg/h)		3	IV, IO	8.01	ml/h
Shock fluid bolus (ml/kg/h)		10	IV, IO	27	ml/h
Hetastarch 6%		5	IV, IO	13	ml/h
Morphine	1	1.5	IM	4.01	ml
Hydromorphone	2	0.5	IM	0.67	ml
Propofol	10	10	IV	2.67	ml
Midazolam	5	2	IM	1.07	ml
Meloxicam	5	0.2	IM	0.11	ml
Lidocaine	20	2	Local	0.27	ml

Premedication and Analgesia

Premedication using midazolam may be useful, especially if combined with an opiate. Recent studies have shown that intramuscular injections can take an hour or more to reach peak levels. The author frequently uses intramuscular midazolam (1-2 mg/kg) and hydromorphone (0.5 mg/kg) for chelonians. There is still controversy concerning the use of opiate analgesics in reptiles, and taxa-specific effects have been documented; however, morphine, hydromorphone and tramadol appear effective for chelonians.[2-4] Meloxicam (0.2 mg/kg) is used routinely for all species, and may be repeated after 48 - 72 hours if necessary.

Induction of Anesthesia

Propofol, given intravenously at doses of 3-15 mg/kg depending upon size provides a rapid, controlled method of induction. It is relatively non-toxic and there is reduced risk of thrombophlebitis if injected perivascularly; this is of particular concern since intravenous access may be relatively difficult, especially in active animals undergoing elective procedures. Alfaxalone (also known as alphalaxone) is also FDA approved and is typically used at similar IV dose rates of 3-12 mg/kg; however, unlike propofol, alfaxalone can also be effective at higher IM doses of around 10-20 mg/kg (Table 2). These IM dose volumes are high and should be divided into several injection sites. Unfortunately, alfaxalone must be used or discarded within 6 hours which can make it cost-prohibitive.

The use of ketamine and (dex) medetomidine provides a reversible light to surgical plane of anesthesia in many chelonians. For intramuscular injections, the forelimb musculature is preferable. For small reptiles, accessing a muscle mass can be difficult, in which case subcutaneous administration may be the only option (although there does not appear to be a significant difference between induction times in most cases).

Table 2. Anesthesia drugs, dosages, and routes of administration.

Drug/Dosage	Route	Comments
Propofol (3-12 mg/kg)	IV	Dependent on intravascular administration; poor response often associated with partial perivascular injection. Must be discarded after 6 hours.
Alfaxalone (3-12 mg/kg)	IV	Similar results to propofol.
(10-20 mg/kg)	IM	Large volume must be divided into two or more injections.
Dexmedetomidine (0.025-0.075 mg/kg) plus Ketamine (5-25 mg/kg)	IM	Can produce inconsistent results in some species, especially terrestrial tortoises, long recoveries unless reversed using atipamezole; preferred for small chelonians where IV access and intubation are not possible.
Telazol (3-10 mg/kg)	IM	Prolonged recovery at higher doses.

Intubation

Chelonians, all aquatic and large terrestrial species, can have powerful bites, and a mouth gag should always be used. A stylet within the endotracheal tube also greatly facilitates placement. Airway resistance becomes increasing critical as endotracheal tube diameter decreases, because resistance, (Table 3).

Table 3. Relative airway resistance within endotracheal tubes from 1.0-4.5 mm in internal diameter.

Endotracheal tube diameter (mm)	Relative resistance
1.0	1000
1.5	198
2.0	63
2.5	26
3.0	12
3.5	7
4.0	4
4.5	2

Maintenance of Anesthesia

Isoflurane or sevoflurane are the agents of choice for maintenance of anesthesia. These volatile inhalation agents have quicker induction and recovery times than most gaseous alternatives. While the differentials in cost, and faster induction/recovery associated with sevoflurane, compared to isoflurane, are insignificant for small reptiles, there are increasingly significant for giant reptiles. Furthermore, the lack of reliance on hepatic metabolism or renal excretion further reduces the anesthetic risk to debilitated reptiles or those with questionable renal or hepatic function; however, both isoflurane and sevoflurane cause dose-dependent hypotension.

Following induction and intubation, chelonians, especially large animals, should be maintained in sternal until a surgical plane is achieved. Placing a large chelonian into lateral or dorsal recumbency can result in ventilation-perfusion mismatch.

Non-crocodilian reptiles lack a muscular diaphragm, instead relying on active gulps of air mediated by the action of skeletal intercostal muscles (squamata, crocodilia) or limb movements (chelonia). The action of these muscles is generally abolished at surgical planes of anesthesia; intermittent positive pressure ventilation (IPPV) should therefore be used routinely and will also help prevent small endotracheal tubes from becoming blocked. Ventilation every 10-120 seconds should typically be used and modified to maintain $ETCO_2$ levels of between 15-35 mmHg. Ideally, a pressure-cycle (e.g., BAS Vetronics, Bioanalytical Systems Inc, West Lafayette, IN, USA) for small reptiles, or a volume-cycle ventilator (e.g., Veterinary Anesthesia Ventilator 20021E, Hallowell Inc, Pittsfield, MA, USA) for large reptiles should be used. End-tidal CO_2 values <10mmHg tend to result in prolonged apnea and recovery.

For chelonians that are too small to intubate, the author relies on injectable agents (often ketamine-dexmedetomidine) and combination with local anesthesia (e.g., lidocaine).

Peri-operative fluid support, temperature control, and monitoring are important. Warm water circulating pads and forced warm air blankets are preferred to maintain the core body temperature within the species-specific preferred temperature range.

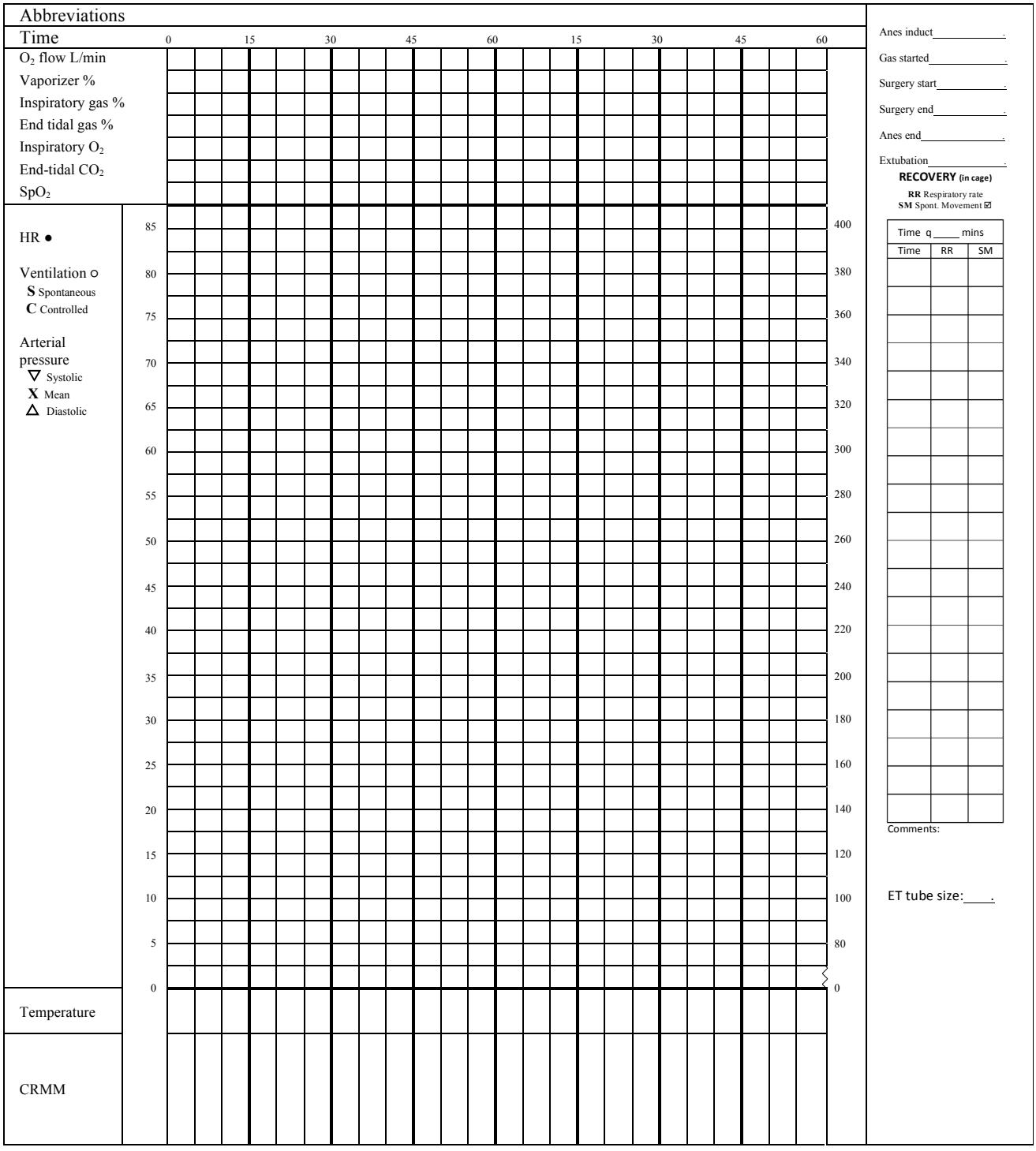
Monitoring During Anesthesia

A dedicated anesthesia recording form should be used routinely (Table 4). Palpebral and corneal reflexes are reliable in those species in which they can be elicited; however, corneal reflexes are abolished at toxic doses, and pupillary diameter bears little relation to the depth of anesthesia (unless fixed and dilated which indicates excessive anesthetic depth or brain anoxia and death); however, jaw tone (being careful not to get bitten!) and withdrawal reflexes (tongue, limb or tail) are useful, becoming abolished only at a surgical plane of anesthesia. This also correlates with full loss of righting reflex, loss of spontaneous movement and complete muscle relaxation. Cloacal reflex and tone is generally only abolished at excessive anesthetic depths.

Heart rate is often most reliably documented by doppler. Pulse oximetry, with an oesophageal or cloacal probe, is useful in monitoring pulse rate and strength. Although the spO_2 readings often under-estimate saO_2 values in most reptiles, monitoring the pulse oximetry trend may be more useful than the absolute values. Doppler can also be very effective and used over peripheral arteries or the heart; however, indirect blood pressure is inaccurate and untrustworthy compared to direct measures, and cannot be relied upon. $ETC0_2$ is especially useful to ensure appropriate ventilation. Using controlled ventilation and accurate cardiovascular monitoring it is possible to accurately control anesthesia. Arterial samples for blood gas evaluations are often difficult to obtain. Nevertheless, pH, PCO_2 and PO_2 are measured directly and can be trusted. Other values are calculated using human algorithms. Arterial samples are required for PO_2 and SaO_2 evaluation, but venous samples can be useful for other parameters including pH, lactate, bicarbonate, TCO_2, and BE.

Towards the end of surgery, the anaesthetic gas should be stopped while maintaining IPPV to facilitate inhalant drug excretion. Those under the influence of injectable agents should have them reversed (e.g., atipamezole for dexmedetomidine). Subsequently, ventilation should be reduced to every 1-5 minutes using room air to encourage mild hypoxia and hypercapnia, increase respiratory drive, and initiate a return to spontaneous breathing. It is also helpful to flex, extend and massage the limbs to encourage venous return and improved circulation. The administration of epinephrine at 0.1 mg/kg IM appears to reduce recovery periods significantly.

Table 4. Reptile anesthesia record.



Recovery and Post-Operative Support

Once the reptile is breathing spontaneously it can be returned to the hospital enclosure to fully recover. It is impractical to maintain the animal on the operating table until completely recovered as this may take many hours when giant reptiles are involved. Nevertheless, trained technicians should continue to monitor the reptile every 5-15 minutes until spontaneous movement and righting reflexes return. Only then is safe to leave the animal unsupervised. Aquatic species should not be returned to water for 12-24 hours. Oral and injectable tramadol has been shown to provide analgesia with less respiratory depression in chelonians, and should be considered for continued post-operative analgesia.[5]

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