Techniques for Drug Delivery in Reptiles and Amphibians

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Abstract

Drug delivery in reptiles and amphibians can be challenging. The varied anatomical and physiologic adaptations of this diverse animal group must be considered when choosing routes of drug administration. This article will discuss specific techniques for delivering drugs via various routes of administration. Copyright 2006 Elsevier Inc. All rights reserved.

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General Considerations

Temperature

It is of critical importance that sick or debilitated reptiles and amphibians be kept in the correct temperature range, known as the preferred optimal temperature zone (POTZ). The POTZ varies by species and can often be found in reference materials or internet sources.[1] Studies have shown that reptile immune systems function best if they are kept in their POTZ.[2] In addition, drug absorption, metabolism, distribution, and excretion vary with ambient temperature.[3,4] No therapeutic plan will be successful or complete without providing the appropriate temperatures for these ectothermic patients.

Hydration

Many reptile patients present in various stages of dehydration. Rehydration, via one of the routes described below, is critical to successful therapy, particularly if potentially nephrotoxic drugs (such as aminoglycosides) are to be used. Changing the ambient humidity in the animal's enclosure with a humidifier or frequent misting may also help. Many reptiles may also be soaked in warm water, although care must be taken to tip the container if the animal is not able to hold its head out of the water.

The Renal Portal System

Unlike mammals, reptiles have a renal portal system that can direct blood returning from the caudal half of the body through the kidney before returning to the heart and general circulation.[5] Depending on the medication being delivered, this system may alter the pharmacokinetics of the medication and may potentially be more nephrotoxic when compared with injections made in the cranial half of the body. There have been few studies to define which drugs are safe to administer caudally and which are not,[6-8] so the current recommendation is to give parenteral drugs in the cranial half of the body until further studies are performed.

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Figure 1. Alzet osmotic pumps (model 1002 shown here) can deliver medications continuously without the need for periodic injections. They hold promise for future delivery options in reptiles.

On the Horizon

In some animals, particularly aggressive or venomous snakes, regular parenteral medication administration should be performed under extreme caution by the handler. Alzet osmotic pumps (Durect Corp., Cupertino, CA USA) are miniature cylindrical implants that operate on the basis of an osmotic pressure difference between the extracellular fluid and the osmotic agent in the pump (Fig 1). Any commonly used parenteral drug can be potentially delivered by these pumps, because they are loaded by the practitioner at the time of implantation. Osmotic pumps are fairly inexpensive and easy to use. There has been one report of using osmotic pumps in iguanas for hormone research.[9] The pharmacokinetics of amikacin using osmotic pumps in corn snakes has been investigated by one author (J. M. S.), and future studies are planned to develop dosages for other drugs.

Specific Administration Techniques

Restraint of the Head to Open the Mouth

In most species, the head is firmly grasped behind the mandible, while still allowing the mouth to open. In large animals, the thumb can be used to gently pull the skin over the mandible medially to partially open the mouth, and in smaller specimens, a cotton stick applicator works best when opening the mouth (Fig 2). Alternatively, a rubber spatula, metal avian speculum, tongue depressor, or credit card may be gently worked into the commissure of the mouth and then rotated to open the jaws (Figs 3 and 4). Regardless of the species and the instrument used, care must be taken not to damage the teeth. Teeth are directed caudally, so the instrument should not be drawn cranially when removed.

Grasping the head in turtles is easier when approaching the head from underneath the turtle, because their defensive reactions are based on threats from above and they quickly retreat into their shell if approached from that direction. With some turtles, applying pressure to the back end will cause them to extend their front half and give you an opportunity to access the head. Also, grabbing a leg and keeping it extended will prevent the turtle from "boxing up." Various techniques may be used to open the mouth, including holding the lower jaw with the fingers and applying steady downward pressure.[10] If the mouth of a turtle closes unexpectedly, it may sever and swallow the tube.

Most lizards can be restrained manually without gloves, but large, aggressive lizards may require leather or other puncture-resistant gloves. The vagal technique calms lizards momentarily and is used by applying gentle pressure to both eyes, either digitally or by taping cotton balls over the closed eyes (Fig 5). The dewlap on iguanas can be gently pulled to open a lizard's mouth, but it is best not to show clients this maneuver when training them, because excess force can damage the hyoid apparatus or permanently curve the lower lip downward in iguanas with metabolic bone disease. Amphibians should be handled with a wet latex or similar glove to prevent damage to their skin.

Figure 2. A cotton stick applicator may be used to gently open the mouth of snakes.

Figure 3. A rubber spatula may be used to open the mouth of a lizard, such as this bearded dragon (*Pogona vitticeps*).

Oral Route

Once the head is restrained and the mouth open, a red rubber flexible catheter or metal ball-tipped feeding tube may be passed down the esophagus into the stomach. The glottis in most species is located at the base of the tongue and is easily avoided. The tube should be passed into the stomach, which is generally located approximately half the distance from the head to the cloaca, and in snakes is just caudal to the heart. If the tube cannot be passed all the way to the stomach, then holding the animal vertically and giving small volumes can prevent regurgitation.

In snakes, a red rubber tube may be passed without opening the mouth. An oversized tube must be chosen to prevent passage into the trachea. The tube may be passed and removed at the center of the mouth, where there are generally no teeth (Fig 6). Alternatively, if the snake is eating, then the drug may be placed inside a small prey item. In lizards,

Figure 4. A plastic patient ID card is used to open the mouth of this eastern box turtle (*Terrapene carolina*).

Figure 5. SQ fluids may be given over the lateral body wall in lizards. The use of the vagal technique to facilitate restraint is shown; cotton balls are taped over closed eyes.

it is best to place food or drug directly in the mouth and let the lizard swallow the substance voluntarily. If the lizard is so debilitated that it cannot swallow, then the oral route of administration is inappropriate.

Placing a Pharyngostomy Tube in a Chelonian

A pharyngostomy tube may need to be placed in chelonians that will require frequent medication and extra nutritional support, or are difficult to tube feed. Once anesthetized, the head and neck should be extended, and curved hemostats placed down the throat and used to press the esophagus to the left side of the neck. A stab incision is then made over the points of the hemostats, with care taken to avoid vessels. The tip of a red rubber catheter is grasped with the tips of the hemostats and the tube pulled out through the mouth. The tube is then turned back into the mouth and passed down to the esophagus. The purpose of bringing the tube out of the mouth before passing it into the stomach is to prevent the tube from being passed through the subcutaneous (SQ) tissues along the side of the esophagus. The tube may then be sutured into place with a finger-trap pattern. Alternatively, tape may be applied to the catheter and the tape sutured to the skin. The tube is then flushed, capped, curled over the dorsum of the animal, and taped in place (Fig 7). An opioid or nonsteroidal antiinflammatory drug may be used help reduce pain or swelling.

Intramuscular Route

Intramuscular (IM) injections are easy to administer to reptiles, and clients can be instructed on how to perform this technique. The epaxial muscles are used in snakes and are located halfway between the dorsal midline and the lateral aspect of the snake (Fig 8). The front legs are the preferred sites of IM injections in chelonians and lizards, primarily the forearm or biceps area (Fig 9). One useful technique

Figure 6. A red rubber tube may be passed into the esophagus of snakes without opening the mouth. When using this technique, care must be taken to use a tube larger than the opening of the glottis to prevent accidental placement of the tube into the trachea.

Figure 7. An esophagostomy tube may be necessary for long-term nutritional support of chelonians. The tube should be secured at its exit from the skin by tape and sutures. Excess tubing may be coiled and taped to the carapace.

Figure 9. IM injections may be given in the forearm musculature of chelonians.

in chelonians is to draw the leg cranially and medially in front of the animal's face and inject in the caudal aspect of the biceps area (Fig 10). This prevents the animal from biting at the administrator during the injection. Although IM injections can be administered to amphibians, other routes are recommended that are not as traumatic to the underlying tissue.

Subcutaneous Route

The SQ route is an acceptable choice for fluid administration in reptiles that are minimally dehydrated. In snakes and lizards, the needle is inserted between the scales on the lateral aspect of the body. There is no need to tent the skin. The needle should be inserted more than half its length to decrease seepage from the injection site. A swelling of the area can be appreciated during injection, which expands cranially as more fluid is administered (Figs 5 and 11). In chelonians, the inguinal and ventral neck folds (Fig 12) are the preferred sites for SQ injections, although any available fold of skin is acceptable. Some turtles may have a thin strip of exposed tissue at the junction of their plastron and bridge, which is available for small volumes of medication even when the turtle is withdrawn into its shell.

Intracoelomic Route

The intracoelomic route is often reserved for fluid administration in critically ill and dehydrated reptiles and amphibians, but other medications may be administered via this route too. Care must be taken to avoid the lung or air sac, which lies in the cranial one half to three fourths of the coelomic cavity, just beyond the coelomic cavity membrane. This route should not be used if the integrity of the lungs is in question (that is, if carapacial fractures are present).

Figure 8. IM injections in snakes should be given in the epaxial muscles. Most medications are preferentially given in the cranial one-half of the body.

Figure 10. IM injections in chelonians may also be given in the triceps. A useful technique is to draw the limb across the animal's head to prevent the animal from biting the handler during injections.

Figure 11. SQ injections may be made along the lateral aspect of the body of snakes. The skin should easily expand both cranially and caudally from the injection site during administration.

Figure 13. Intracoelomic injections may be given cranial to the rear leg in chelonians. The needle must be directed ventrally to avoid the lungs, and it helps to hold the animal at an angle to allow coelomic organs to fall away from the injection site.

In snakes, the needle is passed into the caudal one fourth of the coelomic cavity at the junction between the lateral and ventral scutes. In chelonians and lizards, the needle is inserted cranial to the hind legs, directed toward the opposite shoulder, while being tipped on its side to allow internal organs to fall away from the injection site (Fig 13). Suction should be applied before injection; if suction produces air, the procedure should be aborted or retried.

Intravenous Route

Intravenous (IV) drug administration is typically limited to delivery of anesthetics, such as propofol, or imaging agents.[11]

In snakes, the routes are palatine vein, jugular vein, caudal tail vein, or directly into the heart. The palatine vein can be seen in the dorsal aspect of the mouth, although hemostasis after puncture of these vessels is very difficult and this route is generally not recommended. Accessing the jugular vein in snakes for venipuncture or catheter placement requires a cut-down procedure and is typically used for research rather than clinical purposes. The caudal tail vein in snakes and lizards is accessed by passing a needle or catheter at a 45° to 60° angle from the ventral midline dorsally toward the ventral aspect of the vertebra. The needle should be inserted approximately one-third to one-half the distance from the cloaca to the tail to avoid the hemipenes and anal

Figure 12. SQ injections in chelonians may be made in the ventral neck fold. The head must be well restrained before injection.

sacs, which, if aspirated, have a brown, fetid fluid. In snakes, drugs may be administered directly into the heart. The heart is located by visualization or palpation with the snake in dorsal recumbency. The needle is placed between the ventral scutes into the ventricle, while the heart is stabilized cranially with the forefinger and caudally with the thumb, although care must be taken to not obstruct blood to and from the heart. The needle tip must not move during injection, because administration of large volumes into the pericardial space can result in cardiac tamponade and death.

In chelonians, the IV route is usually reserved for nonresponsive or nonmotile animals. A cut-down procedure over the jugular vein is required, and the catheter is difficult to maintain if the animal can move its neck and feet. The jugular vein is on the lateral surface of the neck at the level of the tympanum. The subcarapacial sinus may be used for administration of euthanasia solution if required, and is accessed by passing a needle under the carapace, dorsal to the neck along the midline. Gentle aspiration while advancing the needle is required. The fluid in this site is often commingled with lymph and is not recommended for administration of medications other than euthanasia solutions.

The jugular vein in lizards is located between the ear and the point of the shoulder. A catheter can be placed in lizards in the jugular vein, the cephalic vein, or the tail vein. A catheter can also be placed intraosseously in the distal femur.[12] The ventral abdominal vein in lizards and amphibians is located intracoelomically on the ventral midline. The disadvantage of this site is the inability to apply direct pressure afterwards to prevent hemorrhage, and should not be used in a lizard with clotting difficulties. The IV route is difficult to access even in large amphibians. The femoral vein and sublingual vein are additional IV sites that can be used in amphibians.[13]

Figure 14. An Argentine horned frog (*Ceratophrys ornata*) is shown inhaling isoflurane through a face mask for induction of anesthesia.

Figure 15. After induction, an endotracheal tube may be used to continuously deliver isoflurane to amphibians.

Topical Treatments

Topical treatments for dermatologic diseases in reptiles are applied in a similar manner to those used for dogs and cats. A difference is that reptiles shed and actually have increased frequency of ecdysis with dermatologic or ophthalmologic diseases to assist healing. Amphibian skin is unique in that topical drugs are absorbed systemically through the epidermis. Drugs can be applied topically while keeping the amphibian moist, or the entire amphibian can be soaked in a bath of drug in solution. The liquid form of inhaled anesthetic agents can also be absorbed topically, but the unscavenged gas poses a risk to humans.

Nebulization or Inhaled

Respiratory diseases are common in reptiles. One effective way to deliver moisture and medications to the respiratory tract is via nebulization, although reptiles may need longer treatment times (up to 1 hour) compared with other animals because their respiratory rate is low and some species can hold their breath for extended periods of time. Nebulization is often used in conjunction with other treatments. Amphibians can be anesthetized with inhaled anesthetics via a mask and maintained via an endotracheal tube instead of using topical or injectable anesthetics (Figs 14 and 15).

Enema

Because of the unique physiology of the reptilian cloaca, it allows substantial fluid resorption from the colon, and therefore fluid can be administered via an enema. This same physiology, however, can cause a dangerous osmotic gradient to occur if castile soap or dioctyl sodium sulfosuccinate is administered, so these products are to be avoided in reptiles.

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