Journal of the American Association for Laboratory Animal Science
Copyright 2017
by the American Association for Laboratory Animal Science

Vol 56, No 3
May 2017
Pages 244-253

Uses and Doses of Local Anesthetics in Fish, Amphibians, and Reptiles

Frederic Chatigny,[1,*] Collins Kamunde,[1] Catherine M Creighton,[2] and E Don Stevens[1]

Local anesthetics are an integral part of routine pain management in mammals, yet their use is relatively limited in fish, amphibians and reptiles. These animals frequently undergo potentially painful surgical procedures and therefore could possibly benefit from those drugs. Some recommendations are currently available in the literature concerning analgesic use in these animals. However the pharmacological properties, safety and often efficacy of local anesthetic drugs have not been investigated yet in fish, amphibians, or reptiles. This review compiled current information concerning the use of those agents in fish, reptiles and amphibians to help clinicians make an informed decision as to which dose and drug to use. The resulting literature search showed that the literature concerning use of local analgesics in fish and amphibians is very limited while the literature for reptiles is more extensive. We found few experimental studies evaluating the efficacy of local anesthetics. Further studies would provide additional information for developing guidelines to improve the welfare of fish, amphibians and reptiles.

Minimizing pain is a fundamental principle of veterinary medicine.[3] However, the capacity of lower vertebrates (fish, amphibians, and reptiles) to experience pain is a topic of debate (see references 7 and 72 for both sides of the argument regarding fishes). Despite this controversy, a generally accepted fact is that these animals respond to noxious stimuli with a nocifensive response. Therefore veterinarians should make efforts to minimize these responses. Nocifensive responses often are associated with surgical procedures and can generally best be reduced by providing appropriate pre- and perioperative care[52,61] through the use of a multimodal approach combining anesthetic and analgesic drugs.[6,39,52] One family of analgesic drugs, local anesthetics, alleviates pain by interrupting nerve conduction in a specific region of the body, thus temporarily preventing the sensation of the noxious stimulus from being conducted to the CNS. Local anesthetics interrupt nerve conduction by inhibiting the influx of sodium ions at voltage-gated sodium channels in axonal membranes. The mechanism involves binding of the drug to the H-(or inactivation) gate of the channel.[79] The appropriate use of local anesthetics can reduce the amount of anesthetic required and decrease the overall requirements for systemic analgesia, in addition to providing sufficient localized desensitization for many minor surgical procedures.[41]

Although often said to provide 'analgesia,' local anesthetics produce only anesthesia because they block all nerve activity, whereas analgesic agents block only nociceptive transmission. Local anesthetics are used mainly in 4 ways: to induce anesthesia of the skin or mucosa (topical anesthesia), anesthesia of tissues locally (local infiltration), regional anesthesia, and intravenous anesthesia.[47] These chemicals tend to have a low cost, minimal side effects, and brief recovery period when used appropriately.[46] This group of drugs has the potential to cause toxicity to both the CNS and cardiovascular system, and this feature may be of concern in smaller animals.[40] The main disadvantage of local anesthetics is that they do not have a sedative effect to assist restraint, thus they often need to be combined with sedation or general anesthesia, except for minor procedures. The most frequently used local anesthetics in veterinary medicine are the amide-linked drugs such as lidocaine hydrochloride (for example, Xylocaine) and bupivacaine hydrochloride (for example, Marcaine).[41]

Local anesthetics routinely are used in mammals, yet their use is still limited in 'exotic' species, such as fish, amphibians, and reptiles.[12,28,46,58] Furthermore, these species frequently undergo potentially painful surgical procedures. In addition to being important research models, fish (such as koi) and amphibians are often pets; whereas reptiles are common in zoos and are increasingly seen in veterinary clinics.[68,92] According to the latest animal data report from the Canadian Council for Animal Care, fish are the second largest among the 15 groups of animals used in research, and amphibians are the sixth.[11] Common surgical procedures for fish include fin biopsy,[26,64,69] hypophysectomy, gonadectomy, implantation of telemetric devices, catheterization of the dorsal aorta, and marking procedures such as tattooing.[28] Common surgical procedures for amphibians and reptiles include wound debridement and repair, skin biopsy, abscess/neoplasm/parasite removal, prolapse replacement/repair, celiotomy,[83] digit and leg amputation, enucleation, and lens surgery.[12,21]

Local anesthetics generally are not used to provide local anesthesia in fish and amphibians; instead they are regularly used to produce and maintain general anesthesia. The main anesthetic agent used in aquatic medicine is the local anesthetic tricaine methanesulfonate (commonly known as MS222 [Western Chemical, Ferndale, WA]). MS222 acts in the same manner as other local anesthetics, but because it is water-soluble, it enters fish (through the gills) and amphibians (through the skin) to act on the CNS instead of acting locally. The exact mechanism of this central action has not been explained completely.[95] This use of local anesthetics is widespread and is already the subject of multiple articles and reviews[12,60] and therefore will not be

Received: 09 Nov 2016. Revision requested: 06 Dec 2016. Accepted: 07 Dec 2016.
Departments of [1]Biomedical Sciences and [2]Companion Animals, Atlantic Veterinary College, University of Prince Edward, Charlottetown, Prince Edward, Canada
[*]Corresponding author. Email: fchatigny@upei.ca

covered here. Instead the focus of the present review is the use of these drugs specifically as local (rather than general) anesthetics.

Although the pharmacologic properties, safety, and often efficacy of local anesthetic drugs have not yet been investigated in fish, amphibians, or reptiles, the literature contains recommendations concerning their use as analgesics.[10,42,58,81] However, this information generally is not extensive and can be difficult to find. In particular, it is difficult to locate original sources that form the basis of the recommendations in general reference texts. Therefore, one goal of the present review was to compile the current knowledge, practices, and recommendations concerning the use of local anesthetics for local anesthesia in fish, amphibians, and reptiles.

Materials and Methods

We searched the online databases PubMed, Science Direct, and One Search by using the keywords 'fish «local anesthetic»,' 'fish lidocaine,' 'fish benzocaine,' 'fish procaine,' 'fish bupivacaine,' 'fish mepivacaine,' and 'fish analgesia,' as well as the same combinations but replacing 'fish' with 'amphibian' or 'reptile.' Articles were included if they mentioned the use of local anesthetics explicitly for local anesthesia or analgesia. To keep the focus of this review on local anesthesia, any use of local anesthetics to produce general anesthesia (for example, as a bath treatment for fish or amphibians) was excluded. Only the use of local anesthetics on live animals was included; that is, we excluded studies using isolated tissues. Only articles presenting original information were included. 'Original information' was defined as the article presenting information based on an experiment or case study or not referencing another article when mentioning the local anesthetic use. However, some chapters referencing local anesthetics used for local anesthesia from the main veterinary reference textbooks were exceptions to this rule and were included. The rationale for this inclusion was to provide contrast with the other sources despite the fact that these reference books do sometimes refer to dated sources or personal experiences. The books chosen and included were: *Exotic Animal Formulary*,[9] *Reptile Medicine and Surgery*,[45] *Fowler's Zoo and Wild Animal Medicine*,[57] and *Lumb and Jones' Veterinary Anesthesia*.[24]

We tabulated the results for each animal class separately, and within each class we categorized articles as experimental studies, case studies, texts or general references, standard operating procedures, and others. Articles classified as 'experimental studies' reported research regarding the efficacy or side effects of local anesthetics. 'Case studies' were articles in which a local anesthetic was used for a reported procedure but its particular efficacy was not evaluated, such that the outcome of the procedure was the main focus of the article. Sources classified as 'others' were articles in which the use of a local anesthetic for local anesthesia was mentioned in the study's protocol, but very few details were provided and its efficacy was not evaluated. This classification of sources is used in the tables to highlight the potential value of the reported dose because, as previously mentioned, studies thoroughly investigating the use of local anesthetics for local anesthesia in fish, amphibians, and reptiles have yet to be performed. Therefore an official optimal dose for most species is often unavailable, and knowing the information source will help clinicians to make an informed choice regarding which drug and dosage to use.

The concentration of the agent was included whenever it was reported in the original source, but many reports did not include this information. When the original source reported a volume of agent instead of a dose in 'mg/kg' format, dose was calculated based on the average weight of the animals in the study and presented in the table; the volume reported is cited in parentheses. When the average weight of the animals was not reported, only the volume of the agent is included in the table.

Results and Discussion

None of the 3 databases used located all of the articles presented here. Most searches resulted in a high number of nonrelevant sources, especially when searching the literature for amphibians, because their eggs are used extensively as models but very few papers involve the amphibians themselves. In addition, as another review reported, "PubMed does not index the herpetological journals in which the most relevant papers [for reptile literature are] published."[2] Furthermore, some relevant information for reptiles was presented in conference proceedings and was difficult to locate.

Another problem with the search for reptilian literature was that some articles from Brazil were in Portuguese and were challenging to locate; some—but not all of these articles—had an English abstract. Although the details of their protocols were difficult to assess, the articles contain useful information from case studies and experiments.[19,25,31,74]

Overall, there were considerably more original references concerning local anesthetics for reptiles (35 articles) compared with amphibians (8) and fish (12). The reptile literature included a relatively high number of case studies (6) and experimental studies (5) compared with those for fish or amphibians. Only 2 experimental studies were found for fish and only one for amphibians; no case studies were found for either fish or amphibians. In addition, we found more mentions of the use of local anesthetics in articles for fish (8) compared with amphibians (2).

Fish. Lidocaine was the main local anesthetic mentioned in association with fish in the literature (Table 1), with only one article involving a different agent, novocaine. The species were varied, but the majority of fish in the selected sources were salmonids. The other species were white sea cod, skipjack and yellowfin tuna, zebrafish, African catfish, mormyrids species, and species of the genus *Eigenmannia*. No study involved elasmobranchs, a result perhaps explained by the fact that no nociceptors have been found in those species yet.[72]

Experimental studies. We found only 2 experimental studies on the use of local anesthetics as analgesics in fish, and in both studies, local anesthetics were one class among several drugs tested as potential analgesics.[13,14,55]

One 1997 study[14] (data were reported again in a 2004 publication[13]) tested novocanium (procaine or novocaine) on cod (*Gadus morhua marisalbi*, 100 to 300 g). The noxious stimulus was a series of electrical pulses applied by using implanted electrodes in the tail, and the response measured was movement of the tail. In the earlier article,[14] the authors stated "injection of 0.25 mL of 2% novocaine solution (fully blocking the axonal conductivity) to epithelial tissue of fins or subcutaneously in the area of application of the stimulus fully blocked up nociceptive responses;" the 2004 publication[13] stated that "local subcutaneous injections of 2% solution of novocanium [dose not given] blocked the nociceptive reactions."

The authors of the other study[55] tested lidocaine by using the injection of acetic acid (0.1 mL of 0.1%, corresponding to an average dose of 9 mg/kg) as the noxious stimulus, and the lips as the tested site. The authors reported no delay in feeding for saline-control fish, whereas acid injection resulted in a feeding delay in 2 of 5 fish; acid also resulted in a decrease in activity and an increase in ventilation rate. Although they recommended the use of lidocaine, their experimental results do not support their recommendation. None of the 4 metrics they used (delay

Table 1. The use of local anesthetics for local anesthesia in fishes

Agent	Dose	Route	Species	Comments	Reference(s)
Textbooks					
Lidocaine	1–2 mg/kg (maximum)	LI	ND	Care must be taken not to overdose small fish	9, 28
Experimental studies					
Procaine 2% (Novocaine)	25 mg/kg (0.25 mL)	LI	White sea cod (*G. m. marisalbi*)	Blocked sensation	13
Lidocaine	9 mg/kg (1 mg/fish)	In lips	Rainbow trout (*O. mykiss*)	Lidocaine was deemed more effective than buprenorphine or carprofen	55
Other documents					
Lidocaine 2%	1.7 mg/kg (0.1 mL/site)[36]	LI	Atlantic salmon (*S. salar*)[36] *Eigenmannia*[57]	Used at surgical site	36, 56
Lidocaine 2%	15 mg/kg (0.1 mL/site)	SI	Brown trout (*S. trutta*) Rainbow trout (*O. mykiss*)	Immobilization occurred in 5 min; recovery took 45–50 min	62
Lidocaine 2% with 1 ppm epinephrine	30 µL	LI	Mormyrids (*P. isidori*, *P. adspersus*)	Inhibited acoustic courtship displays when infiltrated into swimbladder muscles	17
Lidocaine 10% (Xylocaine spray)	—	T	African catfish (*C. gariepinus*)	To numb area of electrode implantation	38
Lidocaine	—	SI	Skipjack tuna (*K. pelamis*) Yellowfin tuna (*T. albacares*)	Used to provide additional restraint during experiment	8
Lidocaine	—	LI	Lacustrine sockeye salmon (*O. nerka*) Masu salmon (*O. masou*)	Used at surgical site	75
Lidocaine gel (50 mg/g)	—	T	Zebrafish (*D. rerio*)	Topical use of lidocaine in the nares to block smell	1

LI, local infiltration; ND, no data; SI, spinal infiltration; T, topical.
Reference citations have been included after their respective comments or as needed if some information is not common to all sources in a row.
If concentrations are not specified, the information was not provided in the original source.

in feeding, activity 30 min after the stimulus, ventilation rate 30 min after the stimulus, rate of recovery of respiration after the stimulus) was significantly different after the noxious stimulus without or with lidocaine at any of the 3 doses. Although unclear from the methods, the authors imply that they administered both lidocaine and acetic acid at the same time rather than giving the lidocaine sufficient time to block before administering the noxious stimulus. The sample size of the study was small (5 fish per group), and the statistical tests not always appropriate; for example, the *P* values were not corrected for the large number of comparisons.

Textbooks, standard operating procedures, and other documents. In recommendations in textbooks and standard operating procedures, the doses used for local infiltration of fish ranged from 1 mg/kg[35] to 9 mg/kg.[55] Most textbooks (for example, Carpenter[9] and Fowler[57]) recommend a lidocaine dose of 1 to 2 mg/kg, similar to those used in mammals.[41] Both texts refer to the same source,[27] but that source does not mention local anesthetics. A 1999 work[29] warns that "care must be taken not to overdose small fish with local injections" when using lidocaine as a general anesthetic rather than as a local. However, our laboratory has used 20 mg/kg locally infiltrated in rainbow trout with no detectable side effects or mortality. One group of scientists in Norway uses 0.1 mL lidocaine at the surgical site in their protocol for dorsal aorta cannulation[18,34,35] but provides no evidence for efficacy or rationale for the dose. The 2008 text *Anesthetic and Sedative Techniques for Aquatic Animals*[73] has only one mention of local anesthetics: lidocaine as a spinal block based on the minimal information presented in a 1978 publication.[62] Interestingly, the most extensive and intensive recent reviews on fish surgery do not mention local anesthetics.[60,80]

Clearly, further studies are needed to assess the efficacy, ideal dose, and maximal safe dose of lidocaine in fish, as well as to test a wide range of species.

Amphibians. As in fish, lidocaine was the main local anesthetic mentioned in association with amphibians in the literature (Table 2), with only one article mentioning a different agent, bupivacaine.[12] Specific species were mentioned in only 3 sources: frogs in 2 sources[59,84] and a salamander in the other.[37]

Experimental studies. Very few original references address local anesthetics for amphibians, and we found only one experimental study.[37] This study compared amphibian marking techniques to assess toe-clipping using 4 treatments (control with handling only, no anesthesia or local anesthetic, general

Table 2. Use of local anesthetics for local anesthesia in amphibians

	Dose	Maximal dose	Route	Species	Comments
Textbooks					
Lidocaine (1% to 2%)	—	—	LI[9,47] T[92]	ND	All/local anesthesia with or without epinephrine; lidocaine in combination with ketamine has been used for minor surgeries; use with caution;[9,46] minor surgeries can be performed by using local anesthesia through direct application of lidocaine 2% to the surgical site[93]
Experimental studies					
Lidocaine	—	—	T	Salamander (*Desmognathus*)	Used for toe-clipping[37]
Others					
Bupivacaine	2	5 mg/kg	T, LI	ND	Duration 3 h; use diluted 3:1 with sodium bicarbonate solution[12]
Lidocaine	2	5 mg/kg	T, LI	ND	Duration 30–60 min; use diluted 3:1 with sodium bicarbonate solution[12]
Lidocaine 2%	<1 mg/kg	1 mg/kg	—	ND	Recommended for minor surgeries[21]
Lidocaine 2%	286 mg/kg (0.5 mL per site)	—	LI	Grass frogs (*R. pipiens*)	Used at surgical site[83]
Lidocaine 4%	—	—	T	Tree frogs (*E. coqui*)	Used at surgical site; "Frequent additional swabs were applied during surgery"[59]

LI, local infiltration; ND, no data; SI, spinal infiltration; T, topical.
Reference citations have been included after their respective comments or as needed if some information is not common to all sources in a row.
If concentrations are not specified, the information was not provided in the original source.

anesthesia only, and local anesthetic only [lidocaine dose not mentioned]) in salamanders as models. Efficacy of the lidocaine treatment was assessed by absence of toe retraction when pinched. The authors reported no statistical difference in stress hormone responses (adrenaline and noradrenaline levels), locomotion, infection rates or general behavior during the 2 wk after toe-clipping. The investigators concluded that toe-clipping without anesthesia or local anesthesia was a "viable and humane field technique."[37]

Textbooks, standard operating procedures, and other papers. Only one mention of the use of local anesthetics in a study[84] was obtained. In the methods section, the author states that "animals were administered a local anesthetic (0.5 mL, 2% lidocaine) suffused just under the skin of the skull region" at 15 min prior to surgery. However, the efficacy of the procedure was not assessed.

Doses cited in textbooks, 1 to 2 mg/kg, are similar to those used in mammals.[41] The only maximal dose recommended was 5 mg/kg for both bupivacaine and lidocaine.[12] However, the source for this dose is unclear, because the only mention of local anesthetics in the reference cited in the article[21] is: "It is possible to perform minor procedures using no more than 1.0 mg/kg total dose of 2% lidocaine as a local anesthetic." Bupivacaine is not mentioned at all in the cited publication,[21] and a maximum dose of 1 mg/kg for lidocaine, rather than 5 mg/kg, is implied.[12] The stated maximal dose of 5 mg/kg[12] appears to be based on values for mammals[41,40] rather than on actual tests in amphibians.

A study involving surgery in the roof of the mouth of tree frogs[59] used injections of pentobarbital sodium for general anesthesia and added "a generous topical application of lidocaine (4%)" to "desensitize the area near the incision." The authors commented that "frequent additional swabs of topical anesthetic were applied during surgery, which could proceed only with adequate numbing of the wound area," but do not explain how the numbing of the area was evaluated. Such an application of highly concentrated lidocaine potentially could cause general anesthesia instead of a localized one (see the additional explanation following), and perhaps even death, considering that the investigators report repeating the injection of pentobarbital "every 3–4 h to maintain immobility," yet no mortalities were reported.

We also looked for standard operating procedures and guidelines from universities where amphibians are used for research. Some universities have protocols that recommend the use of a swab of local anesthetic, often bupivacaine, to provide additional anesthesia at the incision site of a laparotomy once the animal is under general anesthesia.[86,87] None of the studies obtained evaluated the benefits of such a procedure. In addition, the presence of any such benefits is doubtful because, as previously mentioned, general anesthesia of an amphibian typically is produced by immersing the animal in MS222, a local anesthetic. The characteristic permeability of amphibians' skin is such that drugs placed in contact with their skin pass through it and become systemic.[15,21] On this basis, general anesthesia is achieved by using a local anesthetic as a bath treatment. This same characteristic makes localized anesthesia difficult with those animals, but it is possible on the extremities, usually for toe-clipping.[93] This recommendation was based on the fact that local anesthetics can be used without general anesthesia for minor procedures.[21,93] The benefits of topically adding a small quantity of a local anesthetic to the skin of an animal that was just bathed in a large quantity of another local anesthetic is therefore questionable. Furthermore, the previously mentioned study[37] that evaluated different types of anesthesia in salamanders found no difference in adrenaline or noradrenaline levels between general anesthesia (MS222) and a local swab of lidocaine during toe-clipping. These results raise doubts regarding the benefits of using local anesthetics alone in amphibians, because the stress of handling is perhaps equivalent to that of inducing full anesthesia. However, because the authors did not use any other parameters to evaluate stress, further studies are necessary to confirm their conclusions regarding the benefits of local anesthetics in amphibians shortly after immersion in a local anesthetic solution.

Reptiles. The local anesthetic drugs mentioned for use in reptiles (Table 3) were more varied than in fish or amphibians, adding tetracaine, mepivacaine, EMLA (lidocaine–prilocaine) cream, Cetacaine spray (a combination of benzocaine, butamben, and tetracaine; Cetylite, Pennsauken, NJ), and a mixture of lidocaine–bupivacaine to the previously mentioned lidocaine, bupivacaine, and procaine (Table 3). Some studies disproved the popular belief that mixing lidocaine and bupivacaine provides the advantages of both drugs.[70,88] The range of species found in the literature search was wide, representing all extant clades of reptiles, including Archosauria (that is, crocodilians),[90] Testudinata, (that is, turtles),[30,31,43,49,71,74,85] and Squamata including both lizards[4,25] and snakes.[54,94]

Experimental studies. We found 5 experimental studies on the use of local anesthetics as analgesics in reptiles.[16,30,31,48,50,74] Most evaluated only lidocaine, with the exception of one group,[74] who studied bupivacaine also. Four studies involved chelonians, and one study involved snakes. Most of the studies concerned spinal anesthesia of chelonians, using similar doses of lidocaine ranging from 3[31] to 4.6 mg/kg.[74] One group[30] used lidocaine as local infiltration at the surgical site during a celioscopy for sex identification and found that it was not sufficient for anesthesia when used alone. Other investigators[16] "anesthetized the facial pits [of rattlesnakes (*C. viridis*)] with a drop of 2% [lidocaine] placed into each pit chamber; this treatment completely blocked trigeminal responses to cooling or heating of the pits, even with extreme stimuli such as ice or a hot soldering iron." A more specific dose was not described.

Case studies. Six experimental studies involved the use of local anesthetics as analgesics in reptiles.[19,22,25,71,82,90] One study[82] determined that EMLA (lidocaine–prilocaine) cream was of practical use when combined with tramadol analgesia for the surgical treatment of prolapsed penis in various chelonians. Two other studies[19,71] used lidocaine to provide spinal anesthesia in chelonians: 0.8 mg/kg in Galapagos tortoises (*G. nigra*) and 4 to 8 mg/kg in red-footed tortoise (*C. carbonaria*). Other authors used lidocaine as local infiltration (5 mg/kg) to improve desensitization of an area during surgery involving a Tegu lizard (*T. merianae*) and a python (*P. molurus*).[22,25] In addition, mepivacaine provided mandibular block for dental surgeries in restrained crocodilians that were given systemic analgesics (ketoprofen or meloxicam); efficacy was estimated using a nerve locator and absence of motor response.[90]

Textbooks, standard operating procedures, and other documents. The doses reported were generally similar, staying within the range given in textbooks for mammals (lidocaine, 2 to 5 mg/kg; bupivacaine, 1 to 2 mg/kg). There were 2 exceptions,[4,94] which used doses as high as 15 mg/kg lidocaine in Tegu lizards and Brazilian rattlesnakes (*C. durissus terrificus*) and reported no side effects. Local anesthetics were used for varied purposes, mainly at surgical sites and for endotracheal intubation as well as for desensitizing the cloacal region and for spinal or dental blocks.

According to the literature, the use of local anesthetics is widespread in reptiles than in amphibians or fish. Apparently supporting this trend, a 2002 survey of members of the Association of Reptile and Amphibian Veterinarians revealed that nearly one third of participants reported using local anesthetics.[67] Information concerning local anesthetics and their use in reptiles has continued to grow. This more prevalent use of local anesthetics in reptiles might be associated with the fact that information concerning these drugs is more readily available in the literature through many references in textbooks as well as case studies, conference proceedings, and clinical experiments. The value of clinical experiments and case studies should not be underestimated, and we believe that they can be especially practical for clinicians because they report a very precise and applicable use of local anesthetics in a specific context. However, the data are only useful if efficacy and dose are actually tested and reported.

Conclusions

In most textbooks and case reports, the recommended doses of local anesthetics for use in for fish, amphibians, and reptiles is the same as that in mammals. However, very little evidence was available that supported the appropriateness of this recommendation for these animals. Moreover, the actual doses used in research studies and case reports vary widely and are often higher than those recommended in textbooks. Thus it is impossible to provide a table that contains the recommended doses of these drugs for these animals.

The amphibian and fish literature concerning local anesthetics is very sparse. The reptilian literature is more extensive and shows that local anesthetics are used in some routine procedures, such as endotracheal intubation.[78] Local anesthetics were used without any epinephrine additive in all cases in fish except one.[17] Lidocaine was the most commonly mentioned local anesthetic for use in amphibians, fish, or reptiles and was almost the sole agent for amphibians and fish, with the exceptions of bupivacaine and procaine, respectively. The reptilian literature also includes mepivacaine, tetracaine, EMLA cream, and a mixture of lidocaine-bupivacaine in addition to bupivacaine, procaine, and lidocaine.

None of the information collected here is based on pharmacokinetic or pharmacodynamic data from the target species. These data on local anesthetics are not yet available for any species of fish, amphibian, or reptile and have been obtained only for mammalian species. Regardless, local anesthetics are used or recommended for use in fish, amphibians, and reptiles due to their perceived benefit and based on rare mentions of clinician's personal experience and even rarer case studies. Caution is advised in light of the important difference in biologic characteristics between mammals and the 3 groups of animals discussed here as well as key differences between species within each group. Those differences influence the way those animals respond to and metabolize drugs. Furthermore, we know that the structure of the voltage-gated sodium channels on which local anesthetics act varies between species as well as within species acclimated to different temperatures.[91] Therefore the binding of these drugs and thus the effective dose likely will differ between species, making it important to report efficacy in different species as well as to gather detailed pharmacodynamic information about local anesthetics in those animals. Doing so would improve our knowledge of the properties of local anesthetics in fish, amphibians, and reptiles and therefore

Table 3. Reptiles: Results of a literature search for use of local anesthetics for local anesthesia in reptiles.

Agent	Dose	Maximal dose (mg/kg)	Route	Species	Comments
Textbooks					
Bupivacaine	1–2 mg/kg	4 10[77]	T[77] LI	ND; chelonians[58]	Repeat every 4-12 h[9,46,57,78]
Lidocaine (0.5% to 2%)	2–5 mg/kg	4[77] 10	T[9,47,75,77] LI	ND	Infiltrate to effect; often used in conjunction with chemical immobilization;[9] repeat every 4–12 h;[46,78] used for desensitization of glottis 2–3 min before intubation; good with manual restraint for minor procedures in most reptiles, but additional drugs should be used for venomous snakes and large crocodilians[76,77]
Lidocaine (0.5% to 2%)	— 1 mg/kg	2 —	LI SI	Chelonians	May be used as adjunct to general anesthesia; epithecal anesthesia may be used alone or in conjunction with general anesthesia for surgeries of the cloaca and tail[57]
Lidocaine 2%	—	—	LI	ND[23] American alligators (*A. mississippiensis*)[20]	Line blocks are effective for minor procedures if adequate restraint is provided; digital amputations and a midfemur amputation on alligators performed by using only lidocaine for anesthesia and physical restraint;[20] good alternative for general anesthesia for minor procedures[23]
Procaine 1%	—	—	LI	ND	Good alternative for general anesthesia for minor procedures[23]
Experimental studies					
Bupivacaine	1.15 mg/kg		SI	Red-footed tortoise (*C. carbonaria*)	Applied 0.2 mL per 5 cm of carapace[74]
Lidocaine 2%	—	—	T	Prairie rattlesnakes (*C. viridis*)	Anesthetized the facial pits: this treatment completely blocked trigeminal responses to cooling or heating of the pits, even with extreme stimuli such as ice or a hot soldering iron; duration of 25 min[16]
Lidocaine 2%	1 mg/kg	—	LI	Chelonians	Not sufficient anesthesia for celioscopy when used alone[30]
Lidocaine 2%	3 mg/kg	—	SI	D'Orbigny's slider turtle (*T. dorbignyi*)	Anesthesia and muscle relaxation of the tail, cloaca, and pelvic members; average duration of anesthesia of 82 min; no side effects or significant heart rate change[31]
Lidocaine 2%	4 mg/kg	—	SI	Red-eared sliders (*T. s. elegans*)	Motor block of the tail, cloaca, and hindlimbs; duration of 1 h[50]
Lidocaine 2%	4.6 mg/kg	—	SI	Red-footed tortoise (*C. carbonaria*)	Applied 0.2 mL per 5 cm of carapace[74]
Case studies					
EMLA cream (lidocaine-prilocaine)	1 g/10 cm^2	—	T	Chelonians	Surgical anesthesia was reached within 19.22 ± 4.36 min; full recovery of the tail and hind limb withdrawal reflex and the full response to pinching was recorded at 40.8 ± 7.7 min after application[82]
Lidocaine 2%	4–8 mg/kg	—	SI	Red-footed tortoise (*G. carbonaria*)	Provided an anesthetic period of 45 to 206 min[19]
Lidocaine 2%	10 mL	—	LI	Python (*P. molurus*)	Used to desensitize cloacal mass[22]

Table 3. Continued

Agent	Dose	Maximal dose (mg/kg)	Route	Species	Comments
Lidocaine 2%	5 mg/kg	—	LI	Tegu lizard (*T. merianae*)	Used at surgical site[25]
Lidocaine 2%	0.8 mg/kg	—	SI	Galapagos tortoises (*G. nigra*)	Allowed phallectomy in conscious tortoises[71]
Mepivacaine 2%	1	25–29	LI	Crocodilians	Used as a mandibular nerve block in alligators[90]
Others					
Bupivacaine 0.25%	<2 mg/kg	2	LI	ND	Useful when the critical nature of a patient precludes general anesthesia[51]
Bupivacaine Lidocaine	—	—	T LI	ND	Local anesthetics (lidocaine and bupivacaine) are 1 of the 5 most used analgesic drugs in reptiles in 2004[67]
Cetacaine spray (benzocaine, butamben, tetracaine)	—	—	T	American alligators (*A. mississippiensis*)	Used at the surgical site[63]
Lidocaine	—	—	LI	ND	Manual restraint supplemented with local infiltration around the surgical site is satisfactory for minor surgical procedures[89]
Lidocaine 1%	4 mL	—	LI	Loggerhead sea turtles (*C. caretta*)	Used at incision site for laparoscopy[43]
Lidocaine 1%	20 µL[55]	—	T, LI[55]	Female red-sided garter snakes (*T. s. parietalis*)	Numbed the cloacal region[53,54]
Lidocaine 1%	15	—	LI	Brazilian rattlesnake (*C. d. terrificus*)	Dose was diluted to a total volume of 1.0 mL in normal saline and divided between 4 injection sites (0.25 mL/site) anterior to the cloaca[94]
Lidocaine 1% to 2%	—	—	T LI	ND	Can be used on glottis to help intubation or as a local infiltration for minor procedures; restraint is still required[32]
Lidocaine 1% to 2%	0.1–0.2 mL	—	LI	Multiple snake species	Combined with general anesthesia (ketamine, hypothermia) for venom gland adenectomy[33]
Lidocaine 2%	2–15 mg/kg (0.2–1.0 mL)	—	LI	Tegu lizard (*T. merianae*)	Used at surgical site[4]
Lidocaine 2%	—	—	LI	ND	Effective in providing anesthesia for laceration repair, abscess therapy, and other minor procedures[5]
Lidocaine 2%	<2 mg/kg	2 mg/kg	LI	ND	Useful when the critical nature of a patient precludes general anesthesia[51]
Lidocaine 2%	—	—	LI	American alligators (*A. mississippiensis*)	Use on incision line and to block a heart valve[85]
Lidocaine 5%	—	—	T	Pond turtle (*P. scripta*)	Used for postoperative anesthesia of a wound[65]
Lidocaine 2% + bupivacaine 0.25%	2 mg/kg + 1 mg/kg	<2 mg/kg	LI	ND	Can help to reduce or negate the need for anesthetic drug in critical patients[51]

Table 3. Continued

Agent	Dose	Maximal dose (mg/kg)	Route	Species	Comments
Lidocaine 2% + bupivacaine 0.25%	2 mg/kg + 1 mg/kg	—	—	ND	Use as needed[66]
Procaine 1%	—	250 mg/kg (lethal dose, based on dogs)	LI	ND	Effective in providing anesthesia for laceration repair, abscess therapy, and other minor procedures[5]
Tetracaine 1%	20 µL[55]	—	T LI[55]	Female red-sided garter snakes (*T. s. parietalis*)	Numbed the cloacal region[53,54]

improve our use of these drugs in those species. In the meantime, clinicians must make educated decisions, basing them on the available literature while taking into account the source they are using, especially whether the source evaluated the efficacy of the drug. To facilitate this process, we have collected and categorized publications in the current review according to the source's type.

Although personal communication between clinicians is a common way to share information, publication in scientific journals remains the best way to disseminate knowledge. Performing an in-depth experiment involving the collection of pharmacologic data to assess the efficacy of analgesic drugs like local anesthetics is not the only way to help improve our knowledge of such drugs. Presenting at conferences and publishing case studies of the use of such drugs in 'exotic' species can be greatly beneficial; the reptile literature is a good example of this. Clinicians in laboratory settings as well as zoological institutions often have many fish and amphibians in their care. Some clinicians already may be using local anesthetics to treat various cases yet have not shared their experience through publication. We encourage clinicians and researchers to investigate and publish information regarding local anesthetics to broaden their use in improving animal health.

Acknowledgments

We thank the Sir James Dunn Animal Welfare Centre and NSERC for providing the funding for the main author's current research.

References

1. **Abreu MS, Giacomini AC, Kalueff AV, Barcellos LJ.** 2016. The smell of 'anxiety': behavioral modulation by experimental anosmia in zebrafish. Physiol Behav **157:**67–71.
2. **Alpi KM, Stringer E, Devoe RS, Stoskopf M.** 2009. Clinical and research searching on the wild side: exploring the veterinary literature. J Med Libr Assoc **97:**169–177.
3. **American College of Veterinary Anesthesiologists.** [Internet]. 2006. American College of Veterinary Anesthesiologists' position paper on the treatment of pain in animals. [Cited 30 September 2016]. Available at: http://www.acvaa.org/docs/Pain_Treatment.
4. **Andrade DV, Brito SP, Toledo LF, Abe AS.** 2004. Seasonal changes in blood oxygen transport and acid–base status in the tegu lizard, *Tupinambis merianae.* Respir Physiol Neurobiol **140:**197–208.
5. **Bennett RA.** 1998. Reptile anesthesia. Semin Avian Exot Pet Med **7:**30–40.
6. **Bodenham AR, Howell SJ.** 2009. General anaesthesia compared with local anaesthesia: an ongoing story. Br J Anaesth **103:**785–789.
7. **Braithwaite V.** 2010. Do fish feel pain? Oxford: Oxford University Press.
8. **Bushnell PG, Brill RW.** 1992. Oxygen transport and cardiovascular responses in skipjack tuna (*Katsuwonus pelamis*) and yellowfin tuna (*Thunnus albacares*) exposed to acute hypoxia. J Comp Physiol B **162:**131–143.
9. **Carpenter JW, Marion CJ, editors.** 2013. Exotic animal formulary. 4th ed. St. Louis (MO): Elsevier.
10. **Canadian Council on Animal Care.** [Internet]. 2004. CCAC species-specific recommendations on: Amphibians and reptiles, p 1–30. [Cited 23 May 2016]. Available at: http://www.ccac.ca/Documents/Standards/Guidelines/Add_PDFs/Wildlife_Amphibians_Reptiles.pdf.
11. **Canadian Council on Animal Care.** [Internet]. 2013.CCAC animal data report. [Cited 23 May 2016]. Available at: http://www.ccac.ca/Documents/AUD/2013-Animal-Data-Report.pdf.
12. **Chai N.** 2016. Surgery in amphibians. Vet Clin North Am Exot Anim Pract **19:**77–95.
13. **Chervova LS.** 1997. Pain sensitivity and behavior of fishes. J Ichthyol **3:**98–102.
14. **Chervova LS, Lapshin DN.** 2004. Pain sensitivity of fishes and analgesia induced by opioid and nonopioid agents. Presentation presented at the 4th International Iran and Russia Conference, ShahreKord, Iran, 8–10 September 2004. Proc 4th Intl Iran Russia Conf **1:**1420–1425.
15. **Chinnadurai SK, Kane LP.** 2014. Advances in amphibian clinical therapeutics. J Exot Pet Med **23:**50–55.
16. **Chiszar D, Dickman D, Colton J.** 1986. Sensitivity to thermal stimulation in prairie rattlesnakes (*Crotalus viridis*) after bilateral anesthetization of the facial pits. Behav Neural Biol **45:** 143–149.
17. **Crawford JD, Huang X.** 1999. Communication signals and sound production mechanisms of mormyrid electric fish. J Exp Biol **202:**1417–1426.
18. **Djordjevic B, Kristensen T, Øverli Ø, Rosseland BO, Kiessling A.** 2012. Effect of nutritional status and sampling intensity on recovery after dorsal aorta cannulation in free-swimming Atlantic salmon (*Salmo salar L.*). Fish Physiol Biochem **38:**259–272.
19. **Fontenelle J, Carvalho do Nascimento C, Lozano Cruz M, Stélio PLL, Adauto LVN.** 2000. [Epidural Anesthesia of Amazonian tortoises (*Geochelone carbonaria*)]. Abstract presented at IV Congresso e IX Encontro da ABRAVAS, São Pedro, São Paulo 7 January 2000. [Abstract in Portuguese].
20. **Frye FL.** 1973. Surgery and pathology, p 112–134. In: Frye FL, editor. Husbandry, medicine, and surgery in captive reptiles. Bonner Springs (KS): VM Publishing.
21. **Gentz EJ.** 2007. Medicine and surgery of amphibians. ILAR J **48:**255–259.
22. **George PL, Joseph J.** 1989. Prolapse of cloaca in a python (*Python molurus*). Indian Vet J **66:**648–649.
23. **Girling S, Raiti P, editors.** 2004. BSAVA manual of reptiles. Quedgeley (Gloucester): British Small Animal Veterinary Association.
24. **Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, editors.** 2015. Veterinary anesthesia and analgesia: the 5th edition of Lumb and Jones. Ames (IA): Wiley Blackwell.
25. **Guirro ECB dP, Cunha O d, Santos AP, Toffanetto L, Moreira eN.** 2010. [Multimodal anesthesia in tegu lizard *Tupinambis merianae*: case report]. Ciência animal brasileira **11:**458-460. [Article in Portuguese] DOI 10.526/cab.v11i2.3134

26. **Hansen LP.** 1988. Effects of carlin tagging and fin clipping on survival of Atlantic salmon (*Salmo salar L.*) released as smolts. Aquaculture **70:**391–394.
27. **Harms CA.** 1999. Anesthesia in fish, p 158–163. In: Fowler ME, Miller RE, editors. Zoo and wild animal medicine: current therapy 4. Philadelphia (PA): WB Saunders.
28. **Harms CA.** 2005. Surgery in fish research: common procedures and postoperative care. Lab Anim(NY) **34:**28–34.
29. **Harms CA, Lewbart GA.** 2000. Surgery in fish. Vet Clin North Am Exot Anim Pract **3:**759–774.
30. **Hernandez-Divers SJ, Stahl SJ, Farrell R.** 2009. An endoscopic method for identifying sex of hatchling Chinese box turtles and comparison of general versus local anesthesia for coelioscopy. J Am Vet Med Assoc **234:**800–804.
31. **Hirano LQL, Santos ALQ, Silva JMM, Simone SBS, Andrade MB.** 2012. [Spinal anesthesia in D'Orbigny's slider turtle, *Trachemys dorbignyi*]. Ciência animal brasileira **22:**53–58. [Article in Portuguese].
32. **Johnson JH.** 1991. Anesthesia, analgesia, and euthanasia of reptiles and amphibians. Presentation at the 24th Annual Meeting of American Association of Zoo Veterinarians, Calgary, Canada, September 29–3 October 1991. AAZV 132–139.
33. **Kiel JL.** 1984. Long-term effects of venom gland adenectomy of snakes. Avian Exotic Pract **1:**35-41.
34. **Kiessling A, Dosanjh B, Higgs D, Deacon G, Rowshandeli N.** 1995. Dorsal aorta cannulation: a method to monitor changes in blood levels of astaxanthin in voluntarily feeding Atlantic salmon, *Salmo salar L.* Aquacult Nutr **1:**43–50.
35. **Kiessling A, Johansson D, Zahl IH, Samuelsen OB.** 2009. Pharmacokinetics, plasma cortisol, and effectiveness of benzocaine, MS-222, and isoeugenol measured in individual dorsal aorta-cannulated Atlantic salmon (*Salmo salar*) following bath administration. Aquaculture **286:**301–308.
36. **Kiessling A, Olsen R-E, Buttle L.** 2003. Given the same dietary carotenoid inclusion, Atlantic salmon, *Salmo salar* (*L.*), display higher blood levels of canthaxanthin than astaxanthin. Aquacult Nutr **9:**253–261.
37. **Kinkead KE, Lanham JD, Montanucci RR.** 2006. Comparison of anesthesia and marking techniques on stress and behavioral responses in 2 *Desmognathus* salamander. J Herpetol **40:**323–328.
38. **Lambooij E, Kloosterboer RJ, Pieterse C, Gerritzen MA, Van de vis JW.** 2003. Stunning of farmed African catfish (*Clarias gariepinus*) using a captive needle pistol: assessment of welfare aspects. Aquacult Res **34:**1353–1358.
39. **Lamont LA.** 2008. Multimodal pain management in veterinary medicine: the thysiologic basis of pharmacologic therapies. Vet Clin North Am Small Anim Pract **38:**1173–1186.
40. **Lemke KA.** 2007. Pain management II: local and regional anaesthetic techniques, p 101–114. In: Seymoura C, Duke-Novakovskia T, editors. BSAVA manual of canine and feline anaesthesia. 2nd ed. Gloucester: BSAVA.
41. **Lemke KA, Dawson SD.** 2000. Local and regional anesthesia. Vet Clin North Am Small Anim Pract **30:**839–857.
42. **Longley L.** 2008. Amphibian anaesthesia, p 245–260, Chapter 17. In: Longley L, editor. Anaesthesia of exotic pets. London (United Kingdom): Elsevier.
43. **MacLean RA, Harms CA, Braun-McNeill J.** 2008. Propofol anesthesia in loggerhead (*Caretta caretta*) sea turtles. J Wildl Dis **44:**143–150.
44. **Mader DR.** 1998. Understanding local analgesics: practical use in the green iguana (*Iguana iguana*). Presentation at the 5th Annual Meeting of the Association of Reptilian and Amphibian Veterinarians, Kansas City, Missouri, 26–29 September 1998. Proc Assoc Rept Amphib Vet 1:7–10.
45. **Mader DR, editor.** 2006. Reptile medicine and surgery. St Louis (MO): Saunders Elsevier.
46. **Mader DR.** 2013. Practical use of loco-regional analgesia in reptile medicine, in proceedings. Presentation presented at the 12th Annual Meeting of the Association of Reptilian and Amphibian Veterinarians, Indianapolis, Indiana, 14–19 September 2013. Proc Assoc Amphib Rept Vet 1:61–65.
47. **Mader DR, Divers SJ, editors.** 2014. Current therapy in reptile medicine and surgery. St Louis (MO): Elsevier.
48. **Mans C.** 2014. Clinical technique: intrathecal drug administration in turtles and tortoises. J Exot Pet Med **23:**67–70.
49. **Mans C, Lahner LL, Steagall PVM, Johnson SM, Sladky KK.** 2013. Feasibility, efficacy and inter-operator variability of spinal anaesthesia in female red-eared slider turtles (*Trachemys scripta elegans*). Presentation at the 1st International Conference on Avian, Herpetological, and Exotic Mammal Medicine, Wiesbaden, Germany, 20–26 April 2013. Exotic Anim Med 162.
50. **Mans C, Steagall PVM, Lahner LL.** 2011. Efficacy of intrathecal lidocaine, bupivacaine, and morphine for spinal anesthesia and analgesia in red-eared slider turtles (*Trachemys scripta elegans*). Presentation presented at the Annual Conference of the American Association of Zoo Veterinarians, Kansas City, Missouri, 23–28 October 2011. Proc Annu Conf Am Assoc Zoo Vet 135.
51. **Martinez-Jimenez D, Hernandez-Divers SJ.** 2007. Emergency care of reptiles. Vet Clin North Am Exot Anim Pract **10:**557–585.
52. **Mathews K, Kronen PW, Lascelles D, Nolan A, Robertson S, Steagall P, Wright B, Yamashita K.** 2014. Guidelines for recognition, assessment, and treatment of pain. J Small Anim Pract **55:**E10–E68.
53. **Mendonça MT, Crews D.** 1990. Mating-induced ovarian recrudescence in the red-sided garter snake. J Comp Physiol A **166:**629–632.
54. **Mendonça MT, Crews D.** 2001. Control of attractivity and receptivity in female red-sided garter snakes. Horm Behav **40:**43–50.
55. **Mettam JJ, Oulton LJ, McCrohan CR, Sneddon LU.** 2011. The efficacy of 3 types of analgesic drugs in reducing pain in the rainbow trout, *Oncorhynchus mykiss.* Appl Anim Behav Sci **133:**265–274.
56. **Metzner W, Koch C, Wessel R, Gabbiani F.** 1998. Feature extraction by burst-like spike patterns in multiple sensory maps. J Neurosci **18:**2283–2300.
57. **Miller RE, Fowler ME, editors.** 2015. Fowler's zoo and wild animal medicine. 8th ed. St Louis (MO): Saunders Elsevier.
58. **Mosley C.** 2011. Pain and nociception in reptiles. Vet Clin North Am Exot Anim Pract **14:**45–60.
59. **Narins PM, Wagner I.** 1989. Noise susceptibility and immunity of phase locking in amphibian auditory-nerve fibers. J Acoust Soc Am **85:**1255–1265.
60. **Neiffer DL, Stamper MA.** 2009. Fish sedation, anesthesia, analgesia, and euthanasia: considerations, methods, and types of drugs. ILAR J **50:**343–360.
61. **Ong CK-S, Lirk P, Seymour RA, Jenkins B.** 2005. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg **100:**757–773.
62. **Oswald RL.** 1978. Injection anaesthesia for experimental studies in fish. Comp Biochem Physiol C **60:**19–26.
63. **Powell FL, Milsom WK, Mitchell GS.** 1988. Effects of intrapulmonary CO_2 and airway pressure on pulmonary vagal afferent activity in the alligator. Respir Physiol **74:**285–298.
64. **Pratt TC, Fox MG.** 2002. Effect of fin clipping on overwinter growth and survival of age-0 walleyes. N Am J Fish Manage **22:**1290–1294.
65. **Prechtl JC, Bullock TH.** 1992. Barbiturate sensitive components of visual ERPs in a reptile. Neuroreport **3:**801–804.
66. **Raftery A.** 2011. Reptile orthopedic medicine and surgery. J Exot Pet Med **20:**107–116.
67. **Read MR.** 2004. Evaluation of the use of anesthesia and analgesia in reptiles. J Am Vet Med Assoc **224:**547–552.
68. **Reavill DR, Griffin C.** 2014. Common pathology and diseases seen in pet store reptiles, p 13–19. In: Mader DR, Divers SJ, editors. Current therapy in reptile medicine and surgery. St Louis (MO): Elsevier.
69. **Reed B, Jennings M.** 2011. Guidance on the housing and care of zebrafish (*Danio rerio*). West Sussex (United Kingdom): RSPCA
70. **Ribotsky BM, Berkowitz KD, Montague JR.** 1996. Local anesthetics: is there an advantage to mixing solutions? J Am Podiatr Med Assoc **86:**487–491.
71. **Rivera S, Divers SJ, Knafo SE, Martinez P, Cayot LJ, Tapia-Aguilera W, Flanagan J.** 2011. Sterilisation of hybrid Galapagos tortoises (*Geochelone nigra*) for island restoration. Part 2: Phallectomy of males under intrathecal anaesthesia with lidocaine. Vet Rec **168:**78.
72. **Rose JD, Arlinghaus R, Cooke SJ, Diggles BK, Sawynok W, Stevens ED, Wynne CDL.** 2012. Can fish really feel pain? Fish Fish **15:**97–133.

73. **Ross LG, Ross B**. 2008. Anaesthetic and sedative techniques for aquatic animals. 3rd ed. Ames (IA): Blackwell Publishing.
74. **Santos ALQ, Menezes LT, Kaminishi APS, Leonardo TG, Nascimento LR.** 2011. [Comparative study of spinal administration of lidocaine or bupivacaine in red-footed tortoise *Chelonoidis carbonaria* (Spix, 1824)] PubVet **5:**12 [Article in Portuguese].
75. **Sato K, Shoji T, Ueda H.** 2000. Olfactory discriminating ability of lacustrine sockeye and masu salmon in various freshwaters. Zoolog Sci **17:**313–317.
76. **Schumacher J.** 1996. Reptiles and amphibians, p 670–685. In: Thurman J, Tranquilli W, Benson G, editors. Lumb and Jones' veterinary anesthesia. 4th ed. Ames (IA): Blackwell Publishing.
77. **Schumacher J.** 2007. Chelonians (turtles, tortoises, and terrapins), p 259–266. In: West G, Heard. D, Caulkett N, editors. Zoo animal and wildlife immobilization and anaesthesia. Ames (IA): Blackwell Publishing.
78. **Schumacher J, Yelen T.** 2006. Anesthesia and Analgesia, p 442–454. In: Mader DR, editor. Reptile medicine and surgery. 2nd ed. St Louis (MO): Elsevier.
79. **Schwarz W, Palade PT, Hille B.** 1977. Local anesthetics. Effect of pH on use-dependent block of sodium channels in frog muscle. Biophys J **20:**343–368.
80. **Sladky KK, Clarke EO,** 3rd 2016. Fish surgery: presurgical preparation and common surgical procedures. Vet Clin North Am Exot Anim Pract **19:**55–76.
81. **Sneddon LU.** 2012. Clinical anesthesia and analgesia in fish. J Exot Pet Med **21:**32–43.
82. **Spadola F, Morici M, Knotek Z.** 2015. Combination of lidocaine/prilocaine with tramadol for short-time anaesthesia–analgesia in chelonians: 18 cases. Acta Vet (Beogr) **84:**71–75.
83. **Stevens CW, Rothe KS.** 1997. Supraspinal administration of opioids with selectivity for μ-, δ-, and κ-opioid receptors produces analgesia in amphibians. Eur J Pharmacol **331:**15–21.
84. **Stevens CW.** 2011. Analgesia in amphibians: preclinical studies and clinical applications. Vet Clin North Am Exot Anim Pract **14:**33–44.
85. **Syme DA, Gamperl K, Jones DR.** 2002. Delayed depolarization of the cog-wheel valve and pulmonary-to-systemic shunting in alligators. J Exp Biol **205:**1843–1851.
86. **University of California at San Francisco IACUC.** [Internet]. 2015. Oocyte collection. [Cited 19 August 2016]. Available at: http://iacuc.ucsf.edu/Policies/Oocytecollxenopus.doc.
87. **University of Rochester.** [Internet]. 2015. Policy on oocyte harvest (a major invasive surgery) in frogs. [Cited 19 August 2016]. Available at: https://www.urmc.rochester.edu/MediaLibraries/URMCMedia/ucar/policies/documents/UCAR-Approved-Frog-Policy-Major-Invasive-Surgery-6-17-15.pdf.
88. **Valvano MN, Leffler S.** 1996. Comparison of bupivacaine and lidocaine/bupivacaine for local anesthesia/digital nerve block. Ann Emerg Med **27:**490–492.
89. **Wallach JD.** 1969. Medical care of reptiles. J Am Vet Med Assoc **155:**1017–1034.
90. **Wellehan JFX, Gunkel CI, Kledzik D, Robertson SA, Heard DJ.** 2006. Use of a nerve locator to facilitate administration of mandibular nerve blocks in crocodilians. J Zoo Wildl Med **37:** 405–408.
91. **Widmark J, Sundström G, Ocampo Daza D, Larhammar D.** 2011. Differential evolution of voltage-gated sodium channels in tetrapods and teleost fishes. Mol Biol Evol **28:**859–871.
92. **Wilkinson SL.** 2015. Reptile wellness management. Vet Clin North Am Exot Anim Pract **18:**281–304.
93. **Wright KM, Whitaker BR**, **editors.** 2001. Amphibian medicine and captive husbandry. Melbourne (FL): Krieger Publishing Company.
94. **Zacariotti RL, Grego KF, Fernandes W, Sant'anna SS, de Barros Vaz Guimarães MA.** 2007. Semen collection and evaluation in free-ranging Brazilian rattlesnakes (*Crotalus durissus terrificus*). Zoo Biol **26:**155–160.
95. **Zahl IH, Samuelsen O, Kiessling A.** 2012. Anaesthesia of farmed fish: implications for welfare. Fish Physiol Biochem **38:** 201–218.