VENOMOUS REPTILES: VETERINARY PERSPECTIVES

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ABSTRACT

This lecture will discuss the venomous reptiles of the world. These include the helodermatid lizards (two species, the Gila monster (*Heloderma suspectum*) and the beaded lizard (*Heloderma horridum*)) and a wide variety of snakes. The taxonomy of the "higher" snakes, the Colubroidea, has been changing dramatically in recent years. In 2004, four families were recognized in this superfamily: Viperidae, Colubridae, Elapidae, and Atractaspididae.[40] A 2011 paper utilizing mitochondrial and nuclear genes has provided the most up-to-date and complete classification yet, and now recognizes the following seven families: Xenodermatidae, Pareatidae, Viperidae, Homalopsinae, Elapidae, Lamprophiidae, and Colubridae, five of which contain venomous species.[41] We will also discuss some attributes of venoms, human snakebites and antivenoms, and also vaccines that are commercially available. This includes CroFab Crotalidae Polyvalent Immune Fab antivenom for humans; the BioVeteria F(ab')2 crotalid canine antivenom and the MT Venom product Venom Vet polyvalent crotalid canine antivenom; and Red Rock Rattlesnake Vaccine for canines.

Key Words: venomous reptiles, snake venoms, snakebite, antivenom, rattlesnake vaccine, venomoid surgery, snake taxonomy

Introduction

Among the reptiles of this planet, the venomous species certainly are accorded a widespread notoriety in the public profile. Most areas that have reptile inhabitants also have one or more species that are venomous. The number of venomous snakebites received worldwide by humans remains in conjecture partly because many areas where snakebites occur are outside larger population centers where little or no medical help is available and no records are therefore kept.

Venomous reptiles traditionally have been thought to include two species of helodermatid lizards and a variety of snakes in four classical families. Recent work indicates that venoms may be more widespread than this, and also that as snake taxonomy continues to become more refined it is not so simple to characterize the venomous snakes as belonging to the four traditional groups. And other recent research suggests that venom has developed in only one clade of squamates, which includes all of the known venomous species, and that this has played a significant role in the diversification of the more advanced snakes.[15-16]

The slow-moving and stocky helodermatid lizards occur exclusively in North and Central

America. But among the venomous snakes are a wide variety of shapes and sizes, and they occupy a wide diversity of habitats including terrestrial, fossorial, aquatic, and even strictly marine species. Total length can vary from about 6 inches in the Peringuey's (or dwarf) adder (*Bitis peringueyi*) from Africa to the 18-foot king cobra (*Ophiophagus hannah*) of Southeast Asia. Many venomous snakes are quite beautiful and interesting.

Most zoos exhibit a variety of venomous reptiles. And at least in certain areas, private persons also keep and even breed venomous reptiles and these will sometimes be presented to the veterinarian for evaluation and care. You may choose not to treat such species, but rather refer them to someone else, but if you do, with care, caution and understanding, most can be handled safely.

Classification: Lizards

There is one family of venomous lizards, the Helodermatidae. The two species of helodermatid lizards both belong to the genus *Heloderma.* The Gila monster, *H. suspectum,* occurs with two subspecies in the Southwestern United States and adjacent Mexico. The larger beaded lizard, *H. horridum,* occurs from northwestern Mexico over 1600 miles to Guatemala. There currently are recognized four subspecies of beaded lizards and recent DNA work hints that at least a couple of these may be distinct species. The venom glands are located on the lower jaws, whereas in venomous snakes the venom glands are associated with the upper jaws. None of the teeth are modified into hollow fangs; the venom exits the gland by several ducts at the bases of the grooved sharp venom-conducting teeth. The glands are multi-lobed and each lobe has ducts. Their bites result in considerable pain but no fatalities have been reported. Other signs associated with their bites include hypotension, tachycardia, weakness, local edema and nausea. No antivenom is produced for their bites.

Heloderma venom has been found to contain over a dozen proteins and peptides including hyaluronidase, serotonin, phospholipase A_2, kallikreins, horridum toxin, helodermine, helospectin, exendin-3, and exendin-4. While it is thought that the venom serves a primary function in defense, horridum toxin can cause hemorrhage in visceral organs and exophthalmos, and helodermine in rats causes lethargy, partial limb paralysis, and hypothermia.[2-3] Neurotoxins are absent from helodermatid venoms.[34] Exendin-4 has a structural homology to human glucagon-like peptide-1 (GLP-1) which is a hormone that helps moderate blood glucose levels by stimulating the release of insulin; therefore it is being studied for its potential applications in treating human diabetes.[2]

Recently, a mandibular venom gland has been demonstrated in the Komodo dragon, *Varanus komodoensis,* that produces a venom which can cause hemorrhage and hypotension,[18] and other anguinomorph lizards have also been found to have toxic proteins in their secretions as well; seven protein families have been identified in these venoms[17] but none are thought to be of human medical consequence.

Classification: Snakes

Snake taxonomy continues to change as researchers delve more deeply into their anatomy, functional morphology, physiology, and DNA. It has been difficult to deduce relationships among many of the snakes partly because they have so few external features and the fossil record is meager. But all of the venomous snakes are considered to belong to several families in the superfamily Colubroidea. Venom production has evolved in several snake lineages, but only among the Colubroidea.

A popular herpetology text from 2004 summarized the classification of the 2500 species of snakes in the superfamily Colubroidea with the following families, all having venomous species among them, having not been much modified since about 1978: [40]

Family Viperidae Subfamily Crotalinae Subfamily Viperinae
Possibly Subfamily Causinae
Possibly Subfamily Azemiopinae
Family Colubridae
about nine subfamilies
Family Elapidae
Subfamily Elapinae
Subfamily Hydrophiinae
Family Atractaspididae

However, a more recent, comprehensive evaluation of the phylogeny of the Colubroidea also considers newer information from analysis of mitochondrial and nuclear genes and offers the following classification (*denotes groups containing venomous species): [41]

Family Xenodermatidae
Family Pareatidae
*Family Viperidae
*Subfamily Viperinae
*Subfamily Azemiopinae
*Subfamily Crotalinae
Family Homalopsidae
*Family Elapidae
*(other authors still divide this family into 3 subfamilies: Elapinae, Hydrophiinae, and Laticaudinae)
*Family Lamprophiidae
*Subfamily Pseudooxyrhinophinae
*Subfamily Aparallactinae
*Subfamily Atractaspidinae
Subfamily Lamprophiinae Subfamily Pseudaspidinae Subfamily Prosymninae
*Subfamily Psammophiinae
*Family Colubridae
*Subfamily Natricinae

*Subfamily Pseudoxenodontinae
*Subfamily Dipsadinae
Subfamily Scaphiodontophinae Subfamily Calamariinae Subfamily Grayinae
*Subfamily Colubrinae

Future work will likely serve to further clarify some of these relationships, but we can no longer think of the venomous snakes as belonging to the old traditional three or four families. Some of the above snakes are rarely if ever exhibited in U.S. collections.

Snake Dentition

There are four basic ways to describe and classify snake teeth:

1. aglyphous----these teeth are all basically similar with no fang-like enlargements (also termed homodont). This condition occurs in more primitive, non-venomous snakes.
2. opisthoglyphous---enlarged teeth posteriorly on the maxillary bones which may be grooved, the so-called rear-fanged snakes as in colubrids. Duvernoy's gland secretions are basically secreted and then chewed into prey as the snake bites and chews its victim.
3. proteroglyphous---with enlarged, true hollow fangs on the anterior of a long maxillary bone which is fixed and does not rotate; found in the elapids. The maxillary bone moves very little during a bite. These snakes have a true venom gland with a small lumen, musculature to compress the gland, and a duct that empties into the base of the fang. These snakes typically bite and hang onto the prey until it is immobilized. But mambas (*Dendroaspis* of Africa) and death adders (*Acanthophis* of Australia) have somewhat mobile maxillae.
4. solenoglyphous---elongated, hollow fangs on the anterior of a reduced maxillary bone which can rotate on the prefrontal for fang erection; the only teeth on the maxillas are the fangs. This is the condition in the viperids. These snakes have a true venom gland with well-developed compressor musculature, a large lumen and a duct that empties into the base of the functional fang. These snakes typically bite and release prey and then relocate it. The stiletto snakes (Atractaspidinae) have hollow solenoglyphic fangs with a cutting edge in which the maxillary bone pivots on a lateral, socket-like joint with the prefrontal bone. During a bite, a single fang is extended ventrolaterally from the closed mouth and jerked backwards. It is impossible for a human to hold one of these snakes and not get bitten.

Snake teeth are shed and replaced periodically including the fangs. Fangs when shed may be left in a prey animal and pass through the snake's gastrointestinal tract; they are sometimes visible in the feces. In elapids and viperids, there are lateral or posterior replacement fangs being formed to move into place when the functional fang is shed, and sometimes you can examine a snake and find two large fangs at a site which includes the currently-functional one and its immediate replacement.

Snake Venoms

Snake venoms are vey complex mixtures of a variety of active and inactive biological compounds, mostly proteins, including peptides and polypeptides, enzymes, glycoproteins, and other substances, which together can produce a number of pharmacologic activities in prey animals.[45] No two species have identical venoms. And even within some species, venom components can vary geographically or with the age or season. A particular venom may contain 30-100 protein toxins.[25] The proteins within venoms are designed to immobilize prey and potentially aid in prey digestion. Most venoms are yellowish in coloration. Among the most widespread snake venom enzymes are acetylcholinesterases, L-amino acid oxidases, serine proteinases, metalloproteinases, nucleotidases, hyaluronidases, and phospholipases A_2. [25] Some of the enzymes interact synergistically with nonenzymatic proteins, which increases their toxicity. Because of the variety of toxic compounds within snake venoms, they cannot be classified as either hemotoxic or neurotoxic, or myotoxic or cardiotoxic; such a classification is too simplistic and also dangerous. Most venoms have components capable of both tissue destruction and neurotoxic effects. Some venom components will be briefly discussed below.

Acetylcholinstrases are widespread in snake venoms but absent from viperines and crotalines. Although the amount present in snake venoms exceeds that found in any other biological fluid or tissue, their role in venoms is largely unknown.

Proteolytic enzymes are common in viperid venoms but much less so in elapids, and venoms rich in proteolytic enzymes exhibit considerable tissue destruction activity in prey.

L-Amino acid oxidases may comprise up to 30% of the total protein content of a venom, and these have an affinity for certain amino acids in the host. Some studies indicate a role in platelet aggregation and apoptosis in vascular endothelial cells.

Phospholipases A_2 interact with prey proteins, and many of the heterodimers are potent neurotoxins. Crotoxins including Mojave toxin are presynaptic toxins. Vipoxins are postsynaptic toxins. In the cobra *Naja naja,* fourteen isoenzymes have been identified. [45] Other phospholipase A_2s may be myotoxic, cardiotoxic, or block clotting cascades, and some are nontoxic active enzymes.[14,28] Many have digestive activities.

Snake venom serine proteinases interfere with the blood coagulation cascade, fibrinolysis, and activation of platelets. Various serine proteinases may be procoagulant, anticoagulant, activate the fibrinolytic system, or cause platelet aggregation. Some are commercially available for research into hemostasis, clotting or platelet function, and treatment of cardiovascular disease.

Snake venom metalloproteinases may constitute 30% or more the the total protein of viperine venoms, and these enzymes are largely responsible for local and systemic hemorrhage in prey animals by such mechanisms as procoagulant or anticoagulant activities, platelet aggregation, and apoptosis.

Hyaluronidases act as “spreading factors;” by breaking down the connective tissues they facilitate penetration of the tissues by other venom components.

Stiletto snakes (Atractaspidinae, often termed mole vipers in the older literature) have venoms that contain sarafotoxins, which cause vasoconstriction, cardiac arrest, tissue necrosis, and pain that may persist for years following a bite. [21]

Denmotoxin was recently described from the mangrove snake (*Boiga dendophila*) and is unique in having a bird-specific postsynaptic neuromuscular activity. [37]

Other enzymes may have mechanisms that act upon various sites in both the intrinsic and extrinsic blood coagulation pathways. [45] Russell's viper venom contains components for example that activate clotting factors V, IX, and X. Some elapids, colubrids, and viperines, but not crotalines, have venom components that activate prothrombin.

Crotalines and viperines have thrombin-like enzymes in their venoms. A venom may contain certain compounds with both coagulant or anticoagulant activities, their activities varying somewhat with concentration.

North American rattlesnake venoms have been reported to contain the following enzymes: proteolytic enzymes, arginine ester hydrolase, thrombin-like enzyme, collagenase, hyaluronidases, phospholipase A_2, phosphomonoesterase, phosphodiesterase, RNAse, DNAse, 5-nucleotidase, and L-amino acid oxidase. [45]

With so much variation in venom components it is difficult to compare venoms. A still-popular method of comparing relative toxicity is the LD_{50} or the dosage that will kill 50% of experimentally envenomated 20 gram mice within 24 hours. Utilizing this comparison, the most toxic venom is that of the inland taipan or fierce snake (*Oxyuranus microlepidotus*) of Australia; it has been said that one bite from this species has sufficient venom to kill 100 humans. In fact on most published lists (including those on the internet) of the most toxic snakes, the top 10 to 12 are Australian elapids. On an internet listing by the Australian Venom Research Unit of the top 25 most venomous snakes, the only U.S. snake comes in at 23, the eastern diamondbacked rattlesnake (*Crotalus adamanteus*). Of course, the LD_{50} has been extrapolated from mice to humans; no one has yet tested groups of humans for each of these venoms!

Antivenoms

Any venomous snakebite should be considered a medical emergency. Some will be dry bites in which case no venom was injected, but waiting to see may result in the appearance of serious symptoms. Antivenom is the only effective medical treatment for a venomous snakebite. Antivenoms are manufactured in various countries to help treat human snakebites, mainly from indigenous species. Monovalent antivenoms target bites from specific species while polyvalent antivenoms have the ability to treat several species. Basically, hoofed animals (equine, ovine) are injected with venoms from certain species, and later the serum is obtained to extract immune components, which can then be given to humans to help neutralize the effects of the designated snake species. Some of these have also been used off-label by veterinarians to treat pet animals.

In North America, currently the most widely used antivenom for human snakebites by native species is CroFab® Crotalidae Polyvalent Immune Fab (Ovine) (BTG International, Inc., www.crofab.com). It is apparently more efficacious than previous equine-origin antivenoms, with fewer allergic reactions, but is costly (patient cost about $4000/vial at Phoenix, AZ hospitals in 2012) and has a short half-life such that some medical physicians are now administering it as a CRI (constant rate infusion) for 2-3 days. During the summer of 2012, a 6-yr-old child in southern Arizona received 48 vials during treatment for a bite to the leg from a western diamondbacked rattlesnake, *Crotalus atrox.*

We cannot list here all of the antivenoms available throughout the world. One of the problems facing medical personnel is that persons who keep venomous snakes often keep exotic species and they do not have available the appropriate antivenoms. They erroneously assume that their local hospital and/or nearby zoo will have a suitable antivenom and that the available medical team will know how to treat the bite from an exotic species. An online Antivenom Index, maintained by the Association of Zoos and Aquariums (AZA) plus the American Association of Poison Control Centers, lists the antivenoms manufactured for various venomous snake species and their availability at various locations in the U.S. on the AZA website (wwww.aza.org) in the members-only section, to which local poison control centers have access. Additionally, the Miami- Dade Fire Rescue Antivenom Bank (in Florida) maintains an inventory of exotic antivenoms and lists these on their web site (www.miami-dadefirerescue.com). A national poison control hotline (800-222-1222) is available and has a listing of available medical experts that can provide assistance in guiding the treatment of a human snakebite.

Advice on human snakebite treatment is beyond the scope of this paper. But if you are keeping, working with, or treating venomous reptiles, you should familiarize yourself with the consequences of a snakebite and the basic first aid recommendations for treatment of such a bite, both for yourself, your staff, and your clients, as well as the availability of appropriate antivenoms. But never recommended are techniques for cutting at the bite sites and attempting to suck the venom out of a bite, tight ligatures (tourniquets), or applying electrical currents to a bite. Individual responses to a venomous snakebite can vary greatly depending upon such factors as the route of administration, the amount of venom injected, the absorption and distribution of the venom, the properties of that venom, the metabolism and excretion of the venom, activity of the person bitten, length of time until proper medical attention is available, and availability of the appropriate antivenom. Consequences of a snakebite can range from a dry bite with no effects, to rapid death. Rattlesnake bites in Arizona commonly involve males between the ages of 18 and 30, and alcoholic consumption is often a contributing factor.

You should have at hand your own protocol to use in the event of a venomous bite, and the AZA site given above presents a rational guideline for such a protocol. If you are the person bitten, it should also be available so that your staff may adhere to it and use it since you may not be able to. In my own clinic, no one handles a venomous snake unless I am in control and generally not unless that animal has been anesthetized. I do not allow clients to handle these animals in my clinic due to potential legal liability issues.

For treating pet companion animals, BioVeteria Life Sciences LLC produces a F(ab')2 Polyvalent Snake Antivenom manufactured from *Crotalus durissus* and *Bothrops asper* which is labeled for treatment of snake bites to dogs from North American pit vipers (www.BioVeteria.com). MT Venom LLC also is developing a polyvalent antivenom for use in crotaline bites in dogs (support@venomvet.com). Red Rock Biologics (P.O.Box 8630, Woodland, CA 95776 USA) manufactures a Rattlesnake Vaccine for use in canine pets, based on equine immunization with *Crotalus atrox* venom, that is labelled to stimulate a dog's immunity to rattlesnake bites.

Manipulating & Handling Venomous Reptiles

You must have the right equipment available to properly handle venomous reptiles. This equipment can include snake sticks, snake tongs, bagsticks, cloth snake bags, locking aquaria or commercial reptile cages, lock-top 5-gallon and 50-gallon plastic garbage cans, plastic restraint tubes, squeeze boxes, and goggles and face shields (for spitting cobras). The tongs are useful particularly in handling the other items or in preventing the escape of a fast-moving snake. Leather gloves are not recommended for handling venomous snakes of any size or species.

Snake hooks are useful for handling and manipulating the animals, and also in manipulating other equipment including bags and cans. They should not be used to pin a snake's head because: (1) its unnecessary; (2) its risky; (3) it overly-emphasizes the “negative;” (4) its potentially very hard on the snakes and can injure them including breaking skull bones; (5) they are not usually quite as dangerous as one might like to think; (6) there's no need to impress anyone by utilizing this technique. But helodermatid lizards may be gently pinned with a hook against a surface and then picked up with one hand around the neck and the second holding the body.

Reptiles are often transported in cloth bags, which are knotted (tied) on one end or ligated with a plastic “cable-tie.” Bagsticks make it safer and easier to place venomous snakes into a bag, as they have two flexible rods at one end, which hold the bag open so that the snake can be hooked or otherwise manipulated into the open bag. Snake sticks, bagsticks, and snake tongs, and other equipment, are available from Midwest Tongs (www.tongs.com).
Spitting cobras will aim for your eyes, and may spray venom on your face, so goggles and face shields are generally worn by personnel handling such animals. You should immediately wash off any venom that is sprayed on you and change clothing; venom can cause corneal ulceration if not immediately flushed.

Tube immobilization with plastic restraint tubes is a recommended technique for handling and treating many venomous snakes. They are available in varying sizes and can be safely used with practice. There is some risk involved, but with patience, any snake may be tubed with the right size tube. This technique involves sliding or slipping the tube over the snake's head, letting it enter the tube for a safe distance until the head and neck and a portion of the body are within the tube, and then grasping the tube and the snake together. Choose a tube that the snake can enter but in which it cannot turn around. Very active or agile individuals may be placed into a can or tub first and then tubed. Larger specimens may require a second person to help hold the body. Once safely tubed, you may proceed with your procedure, such as an injection, an examination, sexing by probing, venipuncture, etc. These tubes are also available from Midwest Tongs (www.tongs.com).

A squeeze box is used by many zoos to squeeze the snake between a foam pad in its bottom and a plexiglass top layer, to facilitate examination, measuring, or treating. Basically, a wooden box is constructed with sides and a foam pad in the bottom. The snake is placed into the box, on the foam pad, and the plexiglass top with handles is then lowered onto the snake, compressing it gently against the foam bottom.

Some zoos have shift-boxes constructed so that a snake may enter a box that can then be closed such that the box containing the snake can then be moved or the snake examined or treated. These may be attached to the outside of the snake's main enclosure, or inside the enclosure, and some elapid snakes have been trained with classical conditioning techniques to enter such boxes.[26]

Any cage or vivarium housing a captive venomous reptile should be secure and lockable and labeled as to identify its occupant(s) and the number of animals within. Most zoos will also attach a label indicating the appropriate antivenom to be used in the unfortunate event of a human bite. This also applies to captives housed in a veterinary hospital or private collection. Remember that snakes are expert escape artists.

Transportation of venomous snakes from one facility to another should include placing the animals in a double-secure container, such as a box within a box. Shipping via airlines is by air freight with specific guidelines for containers construction, and not all airlines will accept such shipments.

Sexing and venipuncture techniques involve identical methods used on other reptiles but with special attention to safety. These techniques can often be performed when a snake is tube-restrained.

Anesthesia and Surgery

All of the drugs we utilize in nonvenomous species can be applied to and used in venomous species. Patient handling will vary because we are working with venomous species. For administering premedications and sedatives, tube restraint is often appropriate. For very active or extremely dangerous species, some veterinarians will manipulate the animal into an anesthetic chamber and use an anesthetic gas exclusively until the snake is immobile; this can take an unpredictable length of time.

One difference with venomous snake anesthesia is that it is advisable to shield the head and fangs from any possible accidental accident involving the venom delivery system. This could involve placing a plastic cup around the head and securing it into place to shield the entire head. Closely monitor the plane of anesthesia as you would for any other anesthetized reptile.

Surgical techniques are the same for venomous snakes as they are for any other species. The only difference is in performing venomoid surgeries wherein the venom gland and duct are removed surgically to render the snake incapable of delivering a venomous bite. An intraoral approach is preferrable to a lateral approach. Philosophical controversies aside, this does allow a factor of safety in keeping such snakes in captivity. Venomoid snakes grow well, digest their food well, act normally, and can breed. When the surgery is performed by a veterinarian, there is no evidence of regeneration of the venom gland or duct. Positive permanent identification may be achieved by microchipping the snake.

Legal Considerations

Ownership of venomous reptiles varies in different regions. In some areas there may be no restrictions concerning venomous reptile ownership. In others, ownership may be available only to recognized institutions and researchers. Other areas allow possession only of native venomous reptiles and limitations on the numbers that can be held. Some venomous species are protected in certain areas. And regulations are continually changing. For those of us who work with and treat venomous reptiles, we must be aware of any regulations that apply to legal ownership. Treating an illegally-owned reptile may still be viewed as a violation of the law. Even venomoid snakes are still venomous species so most regulations would still be applicable.

With regard to a possible envenomation while a venomous snake is in your care, including being handled and treated as an outpatient, you and/or your hospital could potentially be judged legally liable for any injury to your client or support staff since you are the responsible party.

LITERATURE CITED

1. Altamari W. 1998. Venomous snakes: a safety guide for reptile keepers. SSAR Herpetol Circ 26:1-28
2. Beck D. 2004. Overview of the Family Helodermatidae for varanophiles. P. 517-520 *in* Pianka ER, DR King, RA Kings (eds.) Varanoid Lizards of theWorld. Indiana Univ Press, Bloomington.
3. Beck D. 2005. Biology of Gila Monsters and Beaded Lizards. Univ CA Press, Berkeley.
4. Bogert CM, R.Martin Del Campo. 1956. The Gila monster and its allies. The relationships, habits, and behavior of the lizards of the family Helodermatidae.
5. Bull Amer Mus Nat Hist 109:1-238.
6. Campbell JA, ED Brodie, Jr. (ed.) 1992. Biology of the Pitvipers. Selva, Tyler, TX.
7. Campbell JA, WW Lamar. 1989. The Venomous Reptiles of Latin America. Cornell Univ Press, Ithaca, NY.
8. Campbell JA, WW Lamar. 2004. The Venomous Reptiles of the Western Hemisphere. 2

vols. Comstock Publ Assoc, Ithaca, NY.
9. Cogger HG. 1992. Reptiles and Amphibians of Australia. Cornell Univ Press, Ithaca, NY.
10. David P, G Vogel. 2010. Venomous Snakes of Europe, Northern, Central, and WesternAsia. Ed Chimaira Terralog Vol. 16, Frankfurt am Main, Germany.
11. DeLisle HF. 1982. Venomous colubrid snakes. Bull Chicago Herpetol Soc 17(1):1-17.
12. Dobiey M, G Vogel. 2007. Venomous Snakes of Africa. Ed Chimaira Terralog Vol. 15, Frankfurt am Main, Germany.
13. Eidenmuller B, M Reisinger. 2011. Beaded Lizards & Gila monsters. Captive Care and Husbandry. Ed Chimaira, Frankfurt am Main, Germany.
14. Ernst CH. 1992. Venomous Reptiles of North America. Smithsonian Instit Press, Washington, DC.
15. Fry BG. 1999. Structure-function properties of venom components from Australian elapids. Toxicon 37:11-32.
16. Fry BG, H Scheib, L van der Weerd, B Young, J McNaughtan, SF Ramjan, N Vidal, RE Poelmann, JA Norman. 2008. Evolution of an arsenal. Structural and functional diversification of the venom system in the advanced snaakes (Caenophidia). Molec Cell Proteonomics 7.2:215-246.
17. Fry BG, N Vidal, JA Norman, FJ Vonk, H Scheib, SFR Ramjan, S Kuruppu, K Fung, MK Richardson, WC Hodgson, V Ignjatovic, R Summerhayes, E Kochva. 2006. Early evolution of the venom system in lizards and snakes. Nature 439:584-588.
18. Fry BG, K Winter, JA Norman, K Roelants, RJA Nabuurs, MJP van Osch, WM Teeuwisse, L van der Weerd, JE McNaughtan, HF Kwok, H Scheib, L Greisman, E Kochva, LJ Miller, F Gao, J Karas, D Scanlon, F Lin, S Kuruppu, C Shaw, L Wong, WC Hodgson. 2010. Functional and structural diversification of the Anguimorpha lizard venom system. Molec Cell Protemics 9.11:2369-2390.
19. Frye BG, S Wroe, W Teeuwisse, MJP van Osch, K Moreno, J Ingle, C McHenry, T Ferrrara, P Clausen, H Scheib, KL Winter, L Greisman, K Roelants, L van der Weerd, CJ Clemente, E Giannakis,WC Hodgson, S Luz, P Martelli, K Krishnasamy, E Kochva, HF Kwok, D Scanlon, J Karas, DM Citron, EJ Goldstein, JE VmcNaughtan, JA Norman. 2009. A central role for venom in *(Megalania) priscus.* Proc Nat Acad Sci 106(22):8969-8974.
20. Gloyd HK, R Conant. 1990. Snakes of the *Agkistrodon* complex. A Monographic Review. SSAR
21. Gold BS, RC Dart, RA Barish. 2002. Bites of venomous snakes. New England J Med 347(5):347-356.
22. Greene HW. 1997. Snakes. The Evolution of Mystery in Nature. Univ CA Press, Berkeley, CA.
23. Hardy DL. 1992. A review of first aid measures for pit viper bite in North America with an appraisal of extractor suction and stun gun electroshock. P. 405-414 *in* Campbell JA, ED Brodie Jr.(eds.) Biology of the Pit Vipers. Selva, Tyler, TX.
24. Hayes WK, KR Beaman, MD Cardwell, SP Bush (eds). 2008. The Biology of Rattlesnakes. Loma Linda Univ Press, CA.
25. Heatwole H. 1987. Sea Snakes. Krieger Publ Co., Malabar, FL. Kang TS, D Georgieva, N Genov, MT Myrakami, M Sinha, RP Kumar, P Kaur, S Kumar, S Dey, S Sharma, A Vrielink, C Betzel, S Takeda, RX Arm, TP Singh, RM Kini. 2011. Enzymatic toxins from snake venom: structural characteristics and method of catalysis. FEBS J 278:4544-4576.

26. Kipp SL, J Krebs, LG Simons. Venomous snake shift training at the Henry Doorly Zoo. J Medical Toxicol 2:39-40.
27. Klauber LM. 1997. Rattlesnakes. Their Habits, Life Histories, and Influence on Mankind. 2nd ed. 2 vols. Univ CA Press, Berkeley.
28. Kunsap S, N Pakmanee, O Khow, L Chanhome, V Sitprija, M Suntraval, SE Lucena, JC Perez, EE Sanchez. 2011. Purification of a phospholipase A_2 from *Daboia russelli siamensis* venom with anticancer effects. J Venom Res 2:42-51.
29. Lavonas EJ, A Ruha, W Banner, V Beharta, JN Bernstein, SP Bush, WP Kerns II, WH Richardson, SA Seifert, DA Tanen, SC Curry, RC Dart. 2011. Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-based consensus workshop. BMC Emerg Med 11(2):1-15.
30. Lock B. 2008. Venomous snake restraint and handling. J Exotic Pet Med 17(4):273-284.
31. Lowe, CH, CR Schwalbe, TB Johnson. 1986. The Venomous Reptiles of Arizona. AZ Game and Fish Dept., Phoenix, AZ.
32. Minton SA, MR Minton. 1990. Venomous Reptiles. Rev Ed. Charles Scribners Sons, NY, NY.
33. Najman L, R Seshardi. 2007. Rattlesnake envenomation. Compendium Cont Ed Pract Vet 29:166-177.
34. Norris R. 2004. Venom poisoning by North American reptiles. P. 683-708 *in* Campbell JA, WW Lamar (eds). The Venomous Reptiles of theWestern Hemisphere. 2 vols. Comstock Publ Assoc., Ithaca, NY.
35. Norris R, SA Minton. 1995. Snake venom poisoning: what the herpetologist needs to know. Vivarium 6(6):4-22.
36. O'Shea M. 2005. Venomous Snakes of the World. Princeton Univ Ptress, Princeton, NJ.
37. Servent, R Menez, E Sturla, A Menez, RM Kini. 2006. Denmotoxin, a three- finger toxin from the colubrid snake *Boiga dendrophila* (Mangrove catsnake) with bird-specific activity. J Biol Chem 281(39):29030-29041.
38. Phelps T. 1989. Poisonous Snakes. Rev Ed. Blanford Press,London.
39. Phelps T. 2010. Old World Vipers. A Natural History of the Azemiopinae and Viperinae. Ed Chimaira, Frankfurt am Main, Germany.
40. Pough FH, RM Andrews, JE Cadle, ML Crump, AH Savitzky, KDWells. 2004. Herpetology, 3rd Ed. Pearson, Prentice Hall, Upper Saddle River, NJ.
41. Pyron RA, FT Burbrink, GR Colli, AN Montes de Oca, LJ Vitt, CA Kuczyski, JJ Wiens. 2011. The phylogeny of advanced snakes (Colubroidea), with discovery of a new subfamily and comparison of support methods for liklihood trees. Molec Phylogen Evol 58:329-342.
42. Roze JA. 1996. Coral Snakes of the Americas. Biology, Identification, and Venoms. Krieger Publ. Co., Malabar, FL.
43. Rubio M. 1998. Rattlesnake. Portrait of a Predator. Smithsonian Univ Press, Washington, DC.
44. Rubio M. 2010. Guide to the Rattlesnakes of the United States and Canada. ECO Herpetol Publ Distrib, Rodeo, NM
45. Russell FE. 1983. Snake Venom Poisoning. 2nd Ed. Scholcum Intl Inc., NY, NY.
46. Schuett GW, M Goggren, ME Douglas, HW Greene (eds.). 2002. Biology of the Vipers. Eagle Mountain Publ., Eagle Mountain,UT.
47. Vogel G. 2006. Venomous Snakes of Asia. Ed Chimaira, Terralog Vol.14, Frankfurt am

Main, Germany.
48. Whitaker BR, BS Gold. 2006. Working with venomous species: emergency protocols. P. 1051-1061 *in* Mader DR (ed.). Reptile Medicine and Surgery. 2nd Ed. Saunders Elsevier, St.Louis, MO.
49. Willey JR, M Schaer. 2005. Eastern diamondback rattlesnake (*Crotalus adamanteus*) envenomation of dogs: 31 cases (1982-2002). J Am Anim Hospital Assoc 41:22-29.