*Occasional Papers of the Cape Fear Serpentarium*

# Ontogeny of the Bushmaster Shock Death in Human Beings*

by Dean Ripa © 2007 (abridged version)

**Figure 1.** At 9-months old this South American bushmaster (*Lachesis muta*) is still a fairly small snake, less than 1 meter long and a slender 450 grams in weight—about the size of an adult American copperhead (*Agkistrodon contortrix*). It has even less available venom than a copperhead of that size, about 0.2 cc (or 40 mg when dried). It would probably not inject more than a third of this supply even in a full bite. Yet its bite can produce grave effects in minutes! The lethal dose of bushmaster venom for man is therefore quite small (Chapters 25 - 26 review the probabilities). Note the enormous fangs of this little snake, already as long as those of an adult *Crotalus adamanteus* outweighing it by 10 times! Photo Regina Ripa. Cape Fear Serpentarium.

THE VISCOUS, YELLOWISH proteinaceous secretion of the relatively small serous glands of *Lachesis* species gives no hint in appearance of the dissimilar and perhaps much more dangerous properties it presents upon comparison with the also thick, yellowish, serous secretions of other vipers. Most viperine venoms kill or cause harm by disrupting normal hemostasis, and are lethal to man in several consistent ways: through interference with coagulation (e.g., hemorrhagic syndromes that produce free bleeding), vascular thrombosis (leading to cellular anoxia), tissue hydrolysis, and other predominately localized effects. These advance slowly, requiring a period of time before overwhelming a large animal like a human being.

The story of bushmaster venom till now has been almost entirely of these, as it were, "digestive" components; being all those agents responsible for the breaking down of the blood and tissue of prey, to prepare it for gastric consumption. Hypotheses of lethality in man rest largely on the venom's fibrinogen-clotting and hemorrhagic effects (though occasionally reported neurotoxicity; e.g., Magalhaes et al., 2003). Those agents in bushmaster venom that digest the prey are implicated as the thing that kills the human being. As noted in Estevao-Costa et al. (2000), "features of bushmaster envenomation are serious hemorrhage, blood coagulation disorders, and renal failure." While no doubt these factors have occurred clinically (and geographic variation in these and all snake venoms makes broad statements incautious), they are probably not the first order of importance when treating bushmaster bite. For example, death from renal failure is usually a development of several days, not hours; nor is bleeding to death any quick pro-

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cess. Blood and tissue derailing agents require time to work their destructive magic on the cardiovascular system. But a bushmaster bite can kill you in minutes.

It is true that a number of fatalities have required such an appropriate time period as proteolytic effects can produce. Bolaños (1982) records 4 such deaths, and Hardy and Silva Haad (1997) another. These cases present the classically deranged coagulation of many other *Crotalid* bites; but the cause of death cannot be ascribed to these factors specifically. Without exception the victims died from shock (or something resembling shock). It is given that excessive hemorrhage can, or should, produce shock; after all, the ultimate effects are not dissimilar; both involve vascular depressurization. However, these examples should usually exhibit some form of organ damage (from hemorrhage) as well, and this, apparently, was not the problem: shock was. Thus we see a dissimilarity in means not primarily proteolytic in kind.

The lethal action of bushmaster venom in man is due to its ability to produce a rapid and fatal "shock syndrome" resulting in an irreversible hypotension. This shock-state (often called hypovolemia) proceeds from origins distinct, say, from those multifactorial processes seen in the *Bothrops* bite, where the patient may already have been severely bleeding for several days, and whose constitution is worn away by necrosis and infection, etc.; or from the *Crotalus* bite, where again, hemodynamic alterations affecting the integrity of the tissue produce a gradual degradation to the whole system that may end in a fatal shock state. This is not to say that bushmaster venom does not also do these things, but they appear to be less profound and are not the first order of emergency in treatment. To date, no bushmaster bite victim—at least no victim who has received enough antivenom—has succumbed to the bleeding disorders common to envenomings of conspecifics like *Bothrops*. On the contrary, bushmaster bite victims die unanimously from shock, and often in spite of prompt antivenom treatment.

Clinical reports of bushmaster envenoming describe edema (believed caused by plasminogen activation [e.g., Sanchez et al., 2000]); inflammatory action (caused by numerous agents including serine proteinases, phospholipase $A_2$ [$PLA_2$], metalloproteinases, serotonin, nitric oxide, histamine, &c., some of these by-products of the victim's own metabolism and immune system (e.g., Silva et al., 1985); hemorrhage (due to metalloproteinases which degrade the capillaries [e.g., Rucavado et al., 1999]); hemolysis (mediated by lectin, therefore disruption of the cell wall is not direct in kind [e.g., Silva Haad, 1981; Otero et al., 1998]); myotoxicity (applicable to the muscle only in direct intramuscular inoculation and believed due to the action of specialized enzymes and proteinases in conjunction with leukocytes and macrophages infiltrated by the inflammatory response [e.g., Otero et al., 1998; Fuly et al., 2000]); incoagulability (from defibrinating activity due to effects of thrombin on fibrinogen, with enzymatic activity like $PLA_2$ and proteinases preventing bloodclotting (e.g., Yarleque et al. 1989); coagulant activity (resulting in clots obstructing capillary blood flow [e.g., Magalhaes and Diniz, 1979]; but I know of no directly attributable case of this happening); proteolytic activity (specifically the attack of thrombin-like proteases, metalloproteinases, cytolytic and myotoxic [e.g., Otero et al. 1998], rarely seen with prompt antivenom [Ripa, 1999]); neurotoxicity (affecting the Vagus, 10th cranial nerve, disrupting the muscles of speech and swallowing [dysphagia and dysphonia], interrupting transmissions to the heart and smooth muscles of the visceral organs (Fan and Cardoso, 1995); this, further exaggerated by shock, results in convulsive abdominal pain, projectile vomiting and diarrhea [e.g., Ripa, 1999, 2002]); and finally, most importantly, hypotensive shock itself (potentiated by kininogen and kallikrein-like proteinase, releasing bradykinin and kallikrein, inspiring rapid hypotension [e.g., Silva, 1980-81; Diniz and Oliveira, 1992; Felicori et al., 2003]).

It is the latter, almost invariably, that kills the victim. This occurs in a quick fashion (within the first 24 hours) as a seemingly "autopharmacological response" (Ripa, 1999) or over the course of about four days, where its evolution would seem little mediated by antivenom. Thus I have posed two fatal outcomes in bushmaster envenoming, one the *catastrophic* (based on a sudden shock-syndrome) and the other, a *progressive*, which may be a process of these, and other, multiplying factors.[1] Whether occurring "within minutes" as Ditmars reported, or within hours (see newspaper account in Chapter 23), or delayed till the third and fourth day (as reported in Bolaños, 1982) these are most certainly shock-deaths, hypovolemic and/or vasodilative in kind. Abundant explanations can be proposed: diminished fluid volume resulting from excessive fluid demands in other parts of the body, inhibiting the heart's ability to move the blood (e.g., due to the rapidly expanding edema of the bitten extremity; or

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[1] It may not be a coincidence that serum sickness also commences on about the 3rd or 4th day after antivenom, an additional burden on the patient. It is an intriguing premise, though not a necessary one, to think that two similar but distinct pathologies may be working on the patient simultaneously at this critical time!

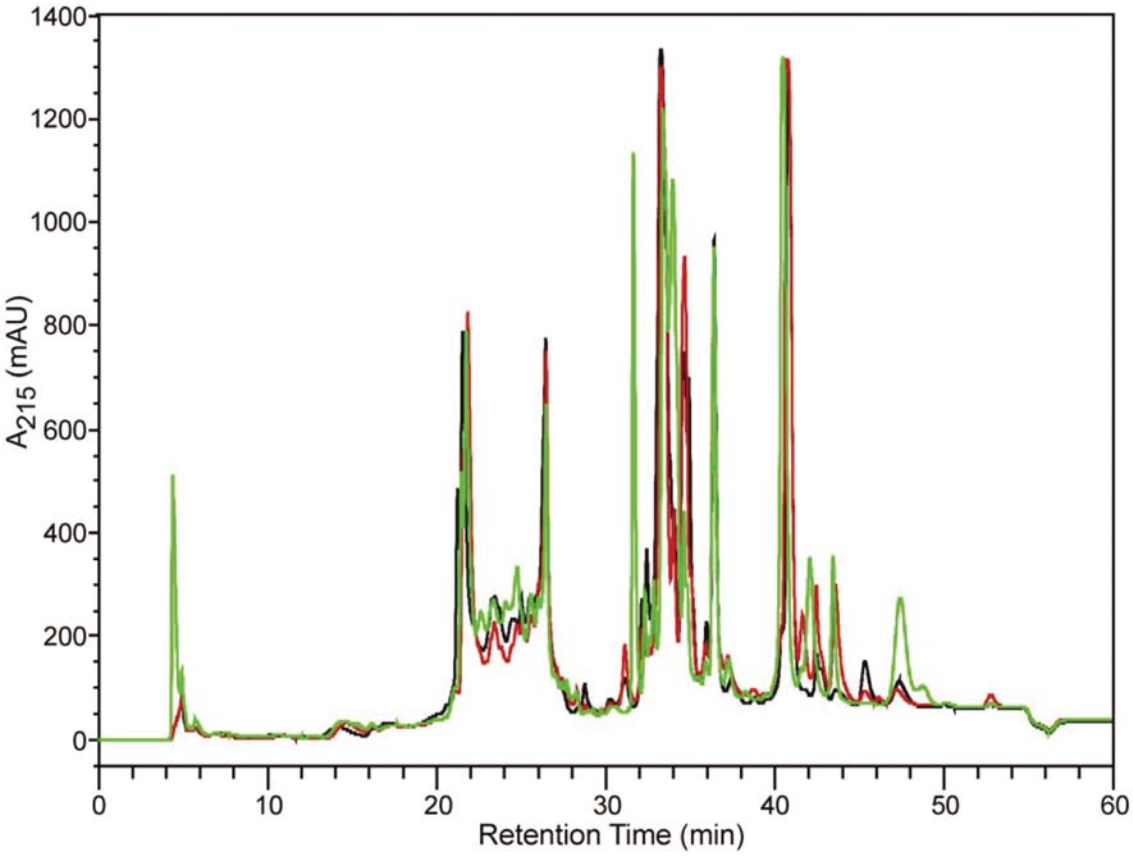



**Figure 2. Illus. 1.** HPLC chromatogram of venoms from different species of Bushmaster snakes. Venom from *Lachesis melanocephala* is in black. Venom from *Lachesis stenophrys* is in red. Venom from *Lachesis muta muta* is in green. One milligram of venom was loaded onto the column in each case. From Ripa, Boomershine and Ripa (in prep); HPLC by Will Boomershine.

from a less centralized vascular dilation also leeching blood from the heart), or the main arteries of the heart itself may be pooling blood. Hence the increased heart rate within the first few minutes of bushmaster bite (Ripa, 1999; Chapter 22) is probably an attempt by the heart to compensate, with the subsequent slowing of the heart (as the pulse falls and grows faint) from blood deprivation, from having less and less blood to beat. The result is the "*Lachesis* Syndrome," the fatal shock-state typical of bushmaster bite. There are other significant effects, such as hemorrhage, also bringing blood loss, and hemolysis, which, of course, affects the very integrity of the blood itself. Finally (and this must be considered very significant in the cases so far seen) we have the type of medical treatment, which may include surgery (fasciotomy). The latter is a sure recipe for a funeral. While common sense would tell you that the last thing you should do is operate on somebody who is bleeding to death, this has not stopped many doctors so far (who are merely parroting the remarks they have read in their medical books, and have no direct experience with the alleged effects of the "compartment syndrome" bugaboo they allege themselves to be preventing; Chapter 23). In such cases (e.g., Bolaños, 1982) we have seen previously managed shock-states return and, with redoubled strength in the weakened victim, end fatally.

Most snake envenomings respond well enough to immunotherapy that you start to see some good results soon after administering it. The complex processes of hemorrhage, hemolysis, neurotoxicity, &c., cease and in little while the body begins restoring itself. Not so with the "L-syndrome," which, like an exploding bomb keeps on spreading shrapnel from its own inertial thrust. The fact of defusing "the bomb" (with immunotherapy) does not soon reverse the effects of the explosion which continues its cascade. Other mediations must be attempted. As with catastrophic necrosis (where the most minute sums of certain venoms, though early neutralized, trick the immune system into mimicking the chemical invader in its effort to repel it and ends up murdering its own cells), the L-syndrome is self-perpetuating, because the body itself has been recruited to enact the deadly program. The venom, which originated the process, has ceased being the active agent and neutralization of its chemistry will not certainly alter the paradigm. If surgery is attempted during this critical period the effects will be enhanced, and even if having abated, will

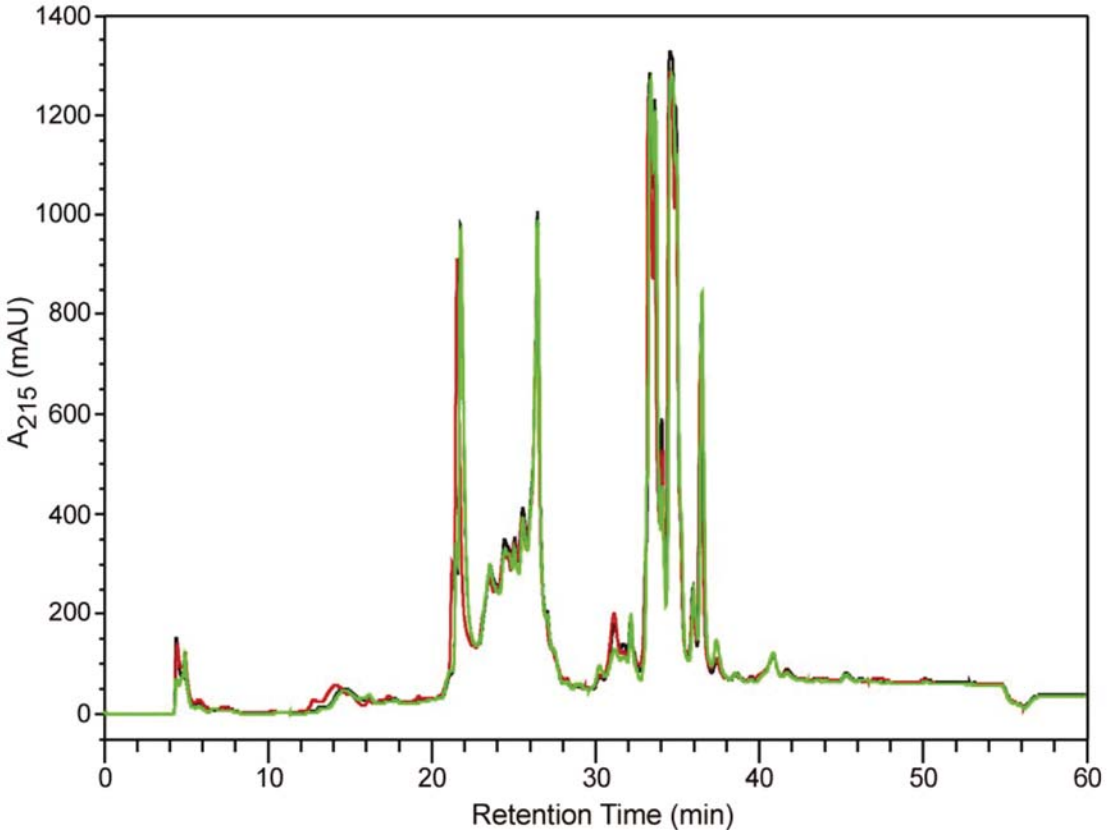



**Figure 3. Illus. 2.** HPLC chromatogram of venoms obtained from specimens of *Lachesis melanocephala* of different ages. Venom from 2 week old specimens is in black. Venom from 4 week old specimens is in red. Venom from 3 month old specimens is in green. One milligram of venom was loaded onto the column in each case. From Ripa, Boomershine and Ripa, (in prep); HPLC by Will Boomershine.

probably return full on and the patient will die. In modern cases of bushmaster bite, most fatalities that have been recorded have involved surgery (Chapter 23).

The Gaboon viper (*Bitis gabonica*) is another species whose venom produces a quick and deadly shock effect in human beings. Mallow et al. (2003) summarizes: "Abrupt hypotension develops *within seconds* in i.v.-injected anesthetized dogs. Profound peripheral vasodilation and reduced aortic impedance cause an increase in stroke volume, thereby increasing ventricular discharge."

In bushmaster bite I have insisted that the first course of treatment should be to address the "shock effect," even to the detriment of restoring normal coagulation if these means are not available; and by all means to avoid invasive means to correct edema (e.g., fasciotomy) and necrosis, as these efforts will only enhance and prolong the shock state. If the patient is going to perish from a bushmaster bite, it is the shock that is going to do it, and hemostatic changes, while occurring in consort, are by comparison a less urgent problem. This is quite unlike the sympatric *Bothrops* with which bushmaster bite is often confused.

What is the chemical action of the L-syndrome? Previous studies (e.g., Felicori et al, 2003) reveal significant levels of kallikrein-like proteinase and kininogenin, both bradykinin releasers, in bushmaster venom. Bradykinin has been linked repeatedly to hypotension in other snakebites, and Silva, on the basis of symptoms, made the correlation with *Lachesis* more than twenty-five years ago (Silva, 1981). My analysis (from Ripa, Boomershine and Ripa, in prep) confirms the presence of these releasers in three species of bushmaster; however, it reveals something entirely new. The concentration and proportion of these toxins is overwhelmingly concurrent with the snake's age.

What is most lethal in bushmaster venom has so far been misinterpreted in test animals as a proteolytic (digestive) component, agents that are not very potent in bushmaster venom. On this basis, neonate bushmasters were previously considered by some authorities (e.g., Gutiérrez et al., 1990) to be "not very dangerous." In-

deed, my analysis adjourns with quite the opposite conclusion. What is most surprising is the disproportion of the shock-producing agents in the venom of the neonate, more than double that of the adult.

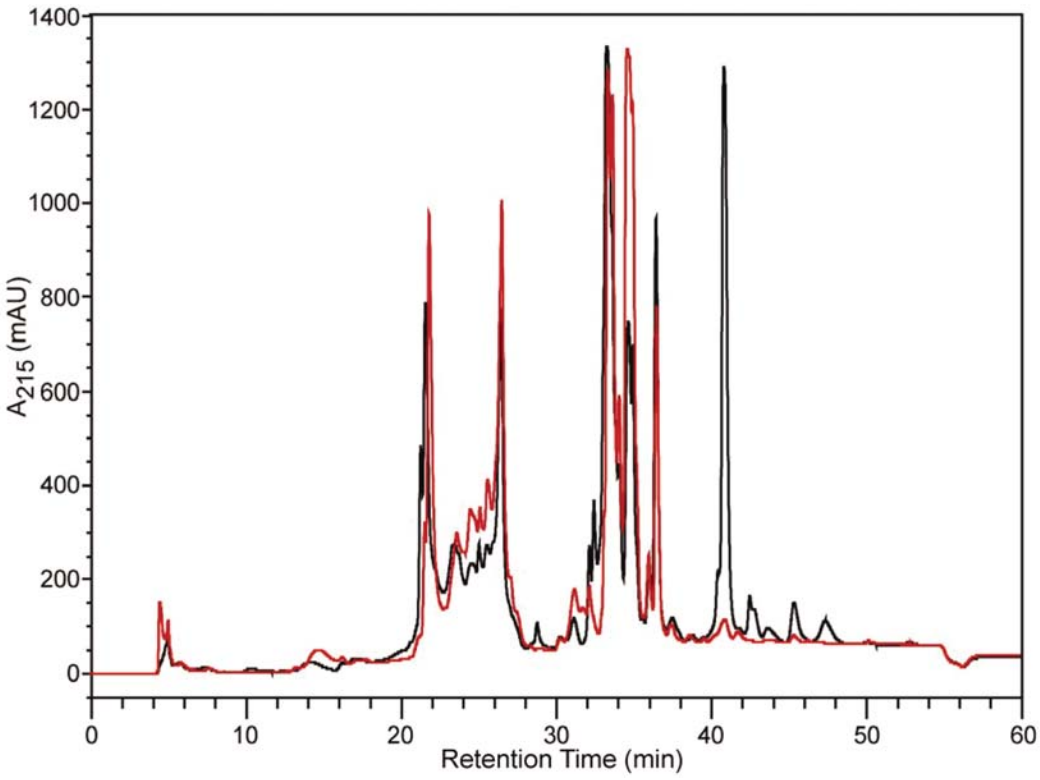
Gutiérrez et al. (1990) noted a curious absence of "toxic" agents in the venom of neonate *Lachesis stenophrys*, emphasizing the low hemorrhagic, myonecrotic, and inflammatory effects of that venom (Chapter 21 discusses this data further). Believing these actions to be the explicitly lethal effects of the venom ensemble, and noting their greater lack in the neonate, they concluded that the neonate needed to mechanically overpower its prey (e.g., restraint and constriction in the jaws) and that its venom must not be very dangerous to man. The problem with their model was in the definition of toxicity, or rather the kind of toxicity they analyzed, which did not account for an L-syndrome-like effect. In their model, bushmaster venom gained in toxicity as the snakes reached maturity, but when the snake was a baby it was hardly venomous at all.

The data assembled in Chapter 21 show how untrue this idea is. Newborn bushmasters efficiently dispatched their prey through the use of venom alone, and in a rapid time-frame. Mechanical restraint of the prey was unnecessary. The prey died almost equally rapidly when strike-released.

The dichotomy is this: Gutiérrez et al. (1990) correctly adduces the low blood/tissue destructive effects (e.g., the hemorrhage, necrosis, &c., of classic viperine envenomation) of the baby venom in prey; but did not recognize that these are not the effects that actually kill the prey. Nor are these the effects that most seriously endanger the lives of human beings in a modern world where antivenom is, or should be, readily available in time to treat most pitviper bite. Where antivenom and other support treatment is readily available, there is simply no reason to die from proteolytic factors in a bushmaster bite. Indeed, it may be impossible to do so even without antivenom, for proposing such an intense envenoming as would kill a human being from hemorrhagic effects is to pose a concomitant L-syndrome reaction of such magnitude that the shock-death would surely precede them. This sounds incautious, but, contradicting presumptive assertions in the literature till now, no such fatality has ever been shown (at least we cannot say positively that the culprit was not really a *Bothrops*).

The fatality rate from bushmaster bite remains one of the highest of any snake. Chapters 22 - 24 provide a range of venomous effects and symptoms, and shows

**Figure 4. Illus 3.** HPLC chromatogram of venoms from specimens of *Lachesis melanocephala* of different ages. Venom from adult specimens is in black. Venom from two-week old specimens is in red. One milligram of venom was loaded onto the column in each case. From Ripa, Boomershine and Ripa (in prep); HPLC by Will Boomershine.



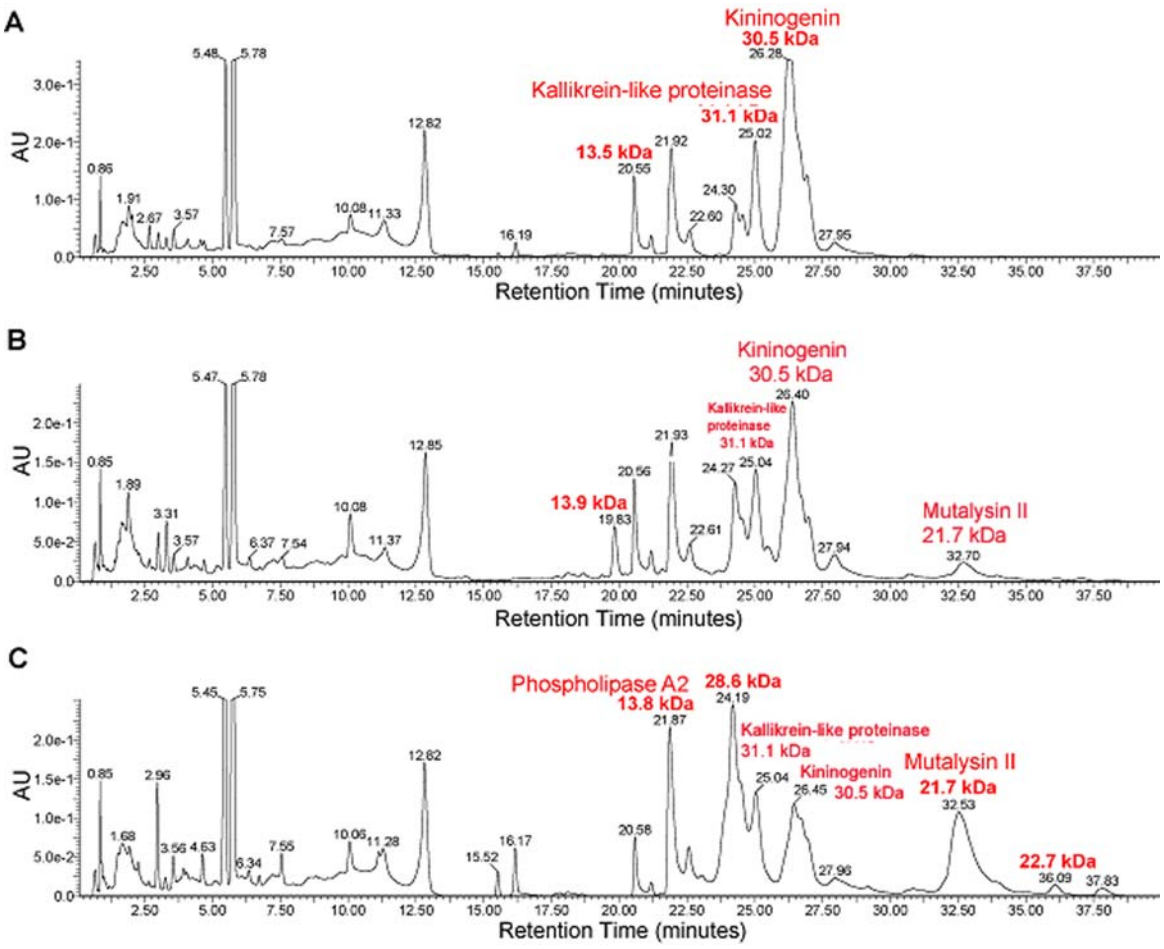



**Figure 5. Illus. 4.** UPLC chromatograms of venom from *L. melanocephala* of various ages. A is neonate, B is 10 month old juvenile, and C is mature adult. Small black numbers indicate retention time in minutes. Red labels indicate the molecular weight of protein in that peak as determined by electrospray-time-of-flight (ToF) mass spectrometry and in some cases indicate the identity of the protein based on molecular weight. Peaks labeled in red indicate that this age of snake contains more of this component of venom than other ages. Note preponderance of "K-complex" in neonate and juvenile (however decreasing somewhat in juvenile), and dramatic reduction in adult. Note dramatic increase of Mutalysin 2 (absent in neonate, nearly absent in juvenile) to adult. The venom is shifting from almost total "shock-syndrome" production toward greater proteolytic (exodigestive) activity. The peak represented by 28.6kDa is an unidentified protein typical of *L. melanocephala* and less abundant in *L. stenophrys*. From Ripa, Boomershine and Ripa (in prep); UPLC by Will Boomershine.

which are most explicitly dangerous in the bushmaster bite. None of them are "proteolytic" in the classic sense (as blood and tissue destructive), except insofar as vasodilation could enhance tissue destructive effects through increasing venous permeability.

In this chapter I explore why bushmaster venom is quickly lethal to prey, and conclude—quite the reverse of Gutiérrez et al. (1990)—that not only is the neonate venom fully toxic, but drop for drop it is significantly more toxic to prey animals and human beings than the venom of the adult snakes. The difference is in the action of the lethality, which in other writing has been variously misunderstood as cytologically destructive in kind.

**What's the toxicity?**

The venom of adult bushmasters shows a significantly higher proteolytic action than that of neonates in mice (Gutiérrez et al., 1990), and this can be demonstrated clinically in the record of damage in adult vis-à-vis neonate bites on human beings (e.g., Ripa, 1999; Chapter 22). These effects, while potentially dangerous if left untreated, should not be confused with a much more dangerous action, one serving no explicitly digestive function, and which constitutes the venom's single most lethal agent: the ability to instigate rapid shock.

In my model, "lethality" is equated with those actions that are most directly toxic to the organism, that is, the agents that actually kill the prey. The classically pro-

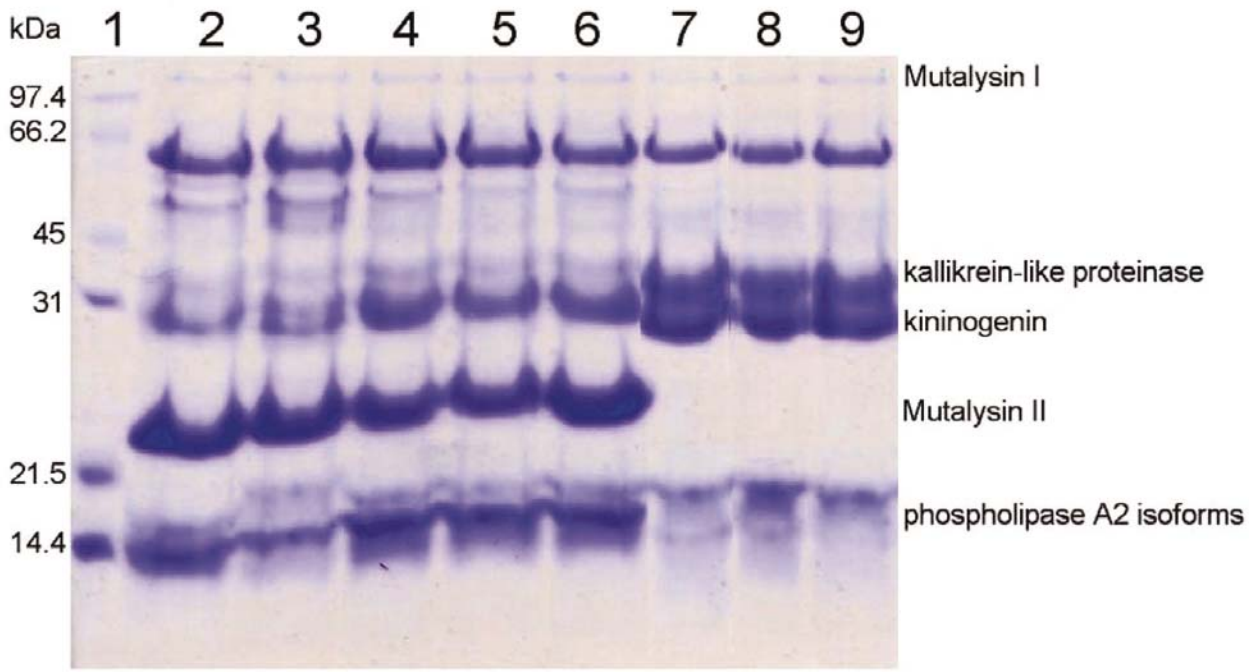



**Figure 6. Illus. 5.** SDS-polyacrylamide gel electrophoresis (15%) of venoms obtained from specimens of bushmaster snakes of different species and different ages. (1) Molecular weight standards: a, 97,400; b, 66,200; c, 45,000; d, 31,000; e, 21,500; f, 14,400. (2) Venom from adult *Lachesis stenophrys* specimen. (3) Venom from adult *Lachesis muta muta* specimen. (4) Venom from adult *Lachesis melanocephala* specimen #1. (5) Venom from adult *Lachesis melanocephala* specimen #2. (6) Venom from adult *Lachesis melanocephala* specimen #3. (7) Venom from two-week old *Lachesis melanocephala* specimen. (8) Venom from four-week old *Lachesis melanocephala* specimen. (9) Venom from three-month old *Lachesis melanocephala* specimen. For each sample, 45 mcg of venom was loaded. All samples were reduced with 2-mercaptoethanol. The identity of the proteins is indicated on the right. From Ripa, Boomershine and Ripa (in prep); electrophoresis by Will Boomershine.

**Phospholipase $A_2$** – are calcium dependent enzymes that hydrolyze the two-ester bonds of 1,2-diacyl-3*sn*-phosphoglycerides. They display a wide variety of activities including presynaptic/postsynaptic, neurotoxicity, myotoxicity, cardiotoxicity, anticoagulant, antiplatelet, convulsant, hypotensive, haemolytic, hemorrhagic and edema-inducing effects (Huang et al., 1997). These belong to group II secretory phospholipase $A_2$s, formed by venoms from Crotalidae and Viperidae families.

**Mutalysin I & II** – are hemorrhagic metalloproteinases that are thought to cause local and systemic hemorrhage (Estevao-Costa et al., 2000). Mutalysis I (100 kDa) is a member of the class P-IV reprolysins (Bjarnason and Fox, 1994; Kini and Evans, 1992). Mutalysin II (22.5 kDa) is a member of the class P-I reprolysins (Bjarnason and Fox, 1994; Kini and Evans, 1992). Mutalysin I has 35X higher hemorrhagic activity than mutalysin II while mutalysin II has 27X higher proteolytic activity towards dimethylcasein than mutalysin I (Estevao-Costa et al., 2000). Both mutalysin I & II degrade the á-chain of fibrinogen over the â-chain (Estevao-Costa et al., 2000). Mutalysin II will also degrade the â- and ã-ã-chains of fibrin (Estevao-Costa et al., 2000). Mutalysin II interacts with the human plasma glycoprotein á2-M (725 kDa) in a 1:1 ratio (Estevao-Costa et al., 2000). Binding of á2-M to mutalysin II inhibits proteinase activity (Estevao-Costa et al., 2000; Starkey and Barrett, 1982). Mutalysin I is unaffected by á2-M binding indicating that it may be involved in systemic bleeding (Estevao-Costa et al., 2000). Mutalysin I also inhibits collagen induced, but not ADP induced, platelet aggregation (Estevao-Costa et al., 2000).

**Kininogenin** – is a serine protease (28 kDa) that releases bradykinin from kininogen (Diniz and Oliveira, 1992). It also induces a hypotensive effect (Diniz and Oliveira, 1992).

**Kallikrein-like proteinase** – is a 33 kDa glycoprotein that has considerable homology to serine proteases from other snake venoms (Felicori et al., 2003). It too releases bradykinin from kininogen and induces hypotensive effects (Felicori et al., 2003). This protease also activates plasminogen (Felicori et al., 2003).

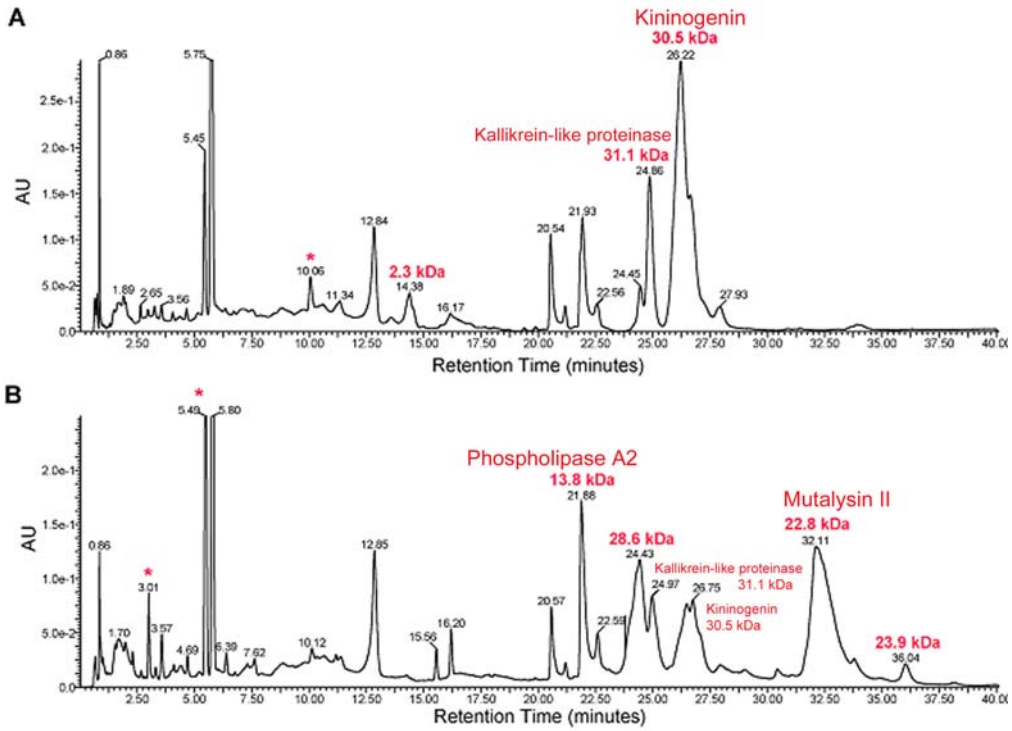



**Figure 7. Illus. 6.** UPLC chromatograms of venom from *L. stenophrys* of various ages. A is neonate (2- weeks-old) and B is adult. Small black numbers indicate retention time in minutes. Red labels indicate the molecular weight of protein in that peak as determined by electrospray-time-of-flight (ToF) mass spectrometry. Peaks labeled in red indicate that this age of snake contains more of this component of venom then other ages. The * indicates peaks with different intensities between ages but no molecular weight was determined. Again, as in *L. melanocephala* neonates, note dramatic increase of "K-complex" and deficit of typical proteolytic factors (PLA2 and Mutalysin 2) in the neonate. The venom is shifting from direct lethality to delayed lethality with exodigestive effects. From Ripa. Boomershine, and Ripa (in prep); UPLC by Will Boomershine.

teolytic agents, such as those that demolish and "digest" tissue, while surely toxic, are not the actions that kill the prey that bushmasters eat. They are not "first-kill" toxins in this sense, but secondary ones: their usefully digestive effects do not have time to develop before the prey is already dead. This is evidenced by the very low concentrations of these agents in the neonate venom (illus. 1 - 8 provide an overview of these proportions). Rather, the prey is immobilized swiftly—by a catastrophic shock effect. Other agents may go to work on the prey's system both during and after this process, but this is not what brings about immobilization. Thus we must rate the toxicity of bushmaster venom according to the disproportion of its shock-producing agents and temporarily forget its proteolytic effects if we are to predict its first-lethal effects in man. It should be mentioned before we go further that the Gutiérrez et al. (1990) analysis was limited to the blood-tissue destructive elements of the venom, and at no point were the kallikrein/kininogenin complex (here called "K-complex") of fractions described or even mentioned. The concept of what bushmaster *should be*, according to contemporary knowledge of other venoms, dominated their model for lethality. In Gutiérrez et al. (1990), the expectations are of a viper that kills by the conventional processes, and these processes all leave a visible fingerprint upon the cells. What the Gutiérrez et al. (1990) analysis told us then, was that these conventionally understood processes were very low in the venoms of neonates and juveniles, compared to the venoms of adult specimens.

Figure 6 (Illustration 5) shows an electrophoresis of three species of bushmaster venom, at early and mature stages of the snake's lives. Abundant components are seen at some ages and conspicuous absences in others. For example, in three samples of neonate venom from *Lachesis melanocephala*, taken at 2 weeks of age, 4 weeks of age, and 12 weeks of age, we see a preponderance of kallikrein-like proteinase and kininogenin. These are both bradykinin releasers, powerful vasodilators whose principle job in venom is to produce hypotension. These proportions are significantly higher than in adults. As Chippaux (2002) notes of bradykinin and prostaglandins in other kinds of snakebite: "The consequence of these mechanisms is a severe drop of peripheral resistance causing the arterial pressure to drop as well. This drop is early on (a few minutes after the inoculation of the venom), fast and severe. The heart rhythm is not modified and this ex-

cludes a direct cardiac toxicity." In a few words the dynamic systemic changes seen in the bushmaster bites recorded in Chapter 22.

Whether or to what extent the "K-complex" also participates in the enzymatic or proteolytic digestion of the prey is not essential to this discussion. Death will be brought about by the shock-activators long before these actions can be appreciated, in an animal that will have already expired several minutes before it is swallowed, and more than 24 hours before it is gastrally digested.

The K-complex of bradykinin-releasers is in relatively much greater proportion in the venom of baby and young bushmasters than in the venom of adults (Illus. 1 - 8). The shock effects observed in Bites 3 and 4 (Chapter 22), involving 1 year old and 2 month old bushmasters, are thus explainable. There is simply much more "shock-agent" in the neonate venom than any other component, so we should expect these agents, both known to be fast acting, to strike first before the typically slower blood derangements are appreciated as local tissue damage.

For example, neonate venom showed only traces of phospholipase $A_2$ isoforms and were completely lacking in (Illus. 4). The former enzyme is credited with a wide variety of actions, ranging from neurotoxicity to hemolysis, so it is too early to predict symptomatology here; however, Mutalysin 2, a metalloproteinase, appears to be a definite hemorrhagin. The dearth of both components could account for the low hemolytic and hemorrhagic effects seen in Bites 1, 2, 3, 4 and 5.

While Mutalysin 2 is completely absent in the neonate venom, Mutalysin 1 is amply represented, just as in adults. Clinical edema and inflammation in the neonate bite seems no less great than in the adult, so at least in Mutalysin 1 we have a probable culprit. Mutalysin 1 is then a powerful producer of edema and inflammation, but its role in hemorrhage is much less significant. The effects seen in Bites 1, 3, and 4, all from young snakes, confirm this idea.

Phospholipase $A_2$ is found in so many disparate snake venoms that it is difficult to pinpoint its meaning in bush-

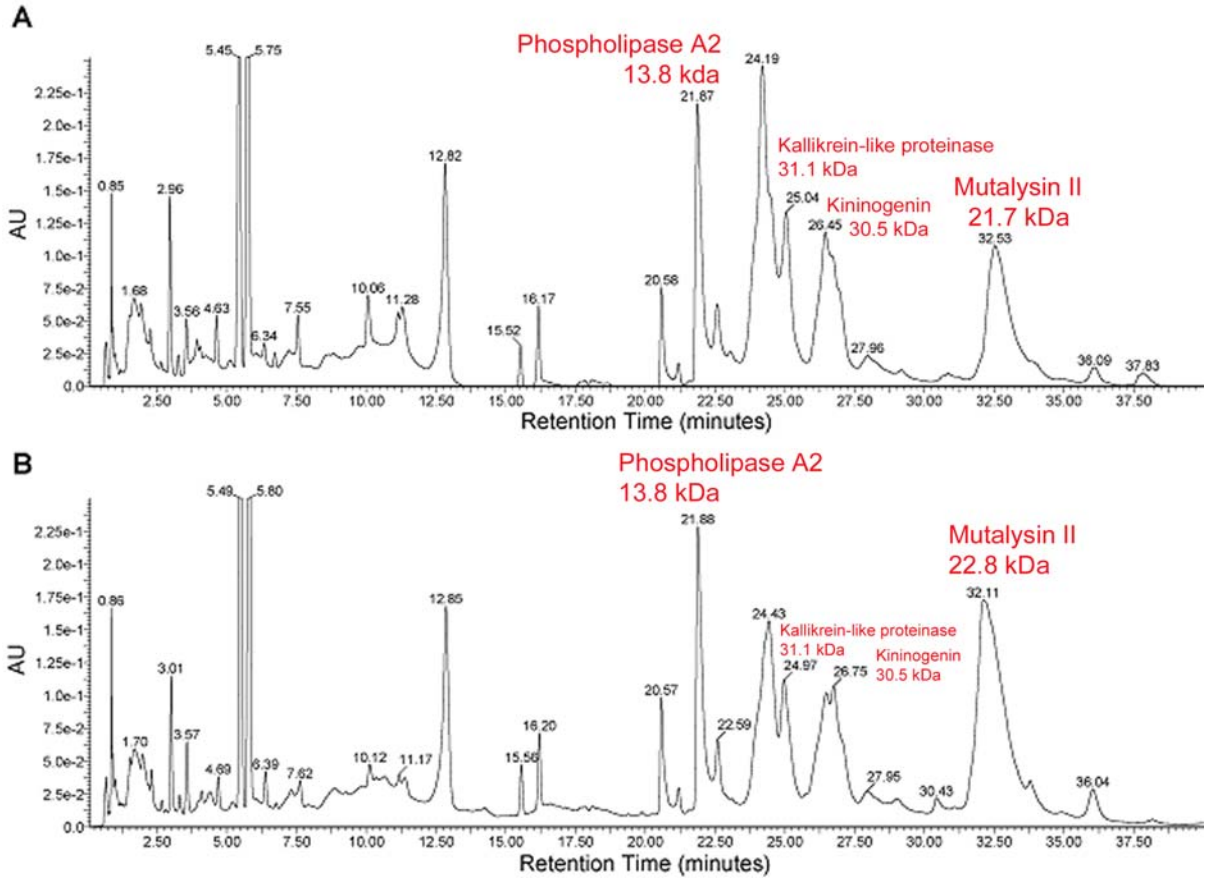



**Figure 8. Illus. 7.** UPLC chromatograms of venom from neonate *L. melanocephala* (A) and *L. stenophrys* (B). In the neonate stages these two venoms are much the same, showing the same inequalities compared to adult snakes. From Ripa, Boomershine and Ripa (in prep); UPLC by Will Boomershine.

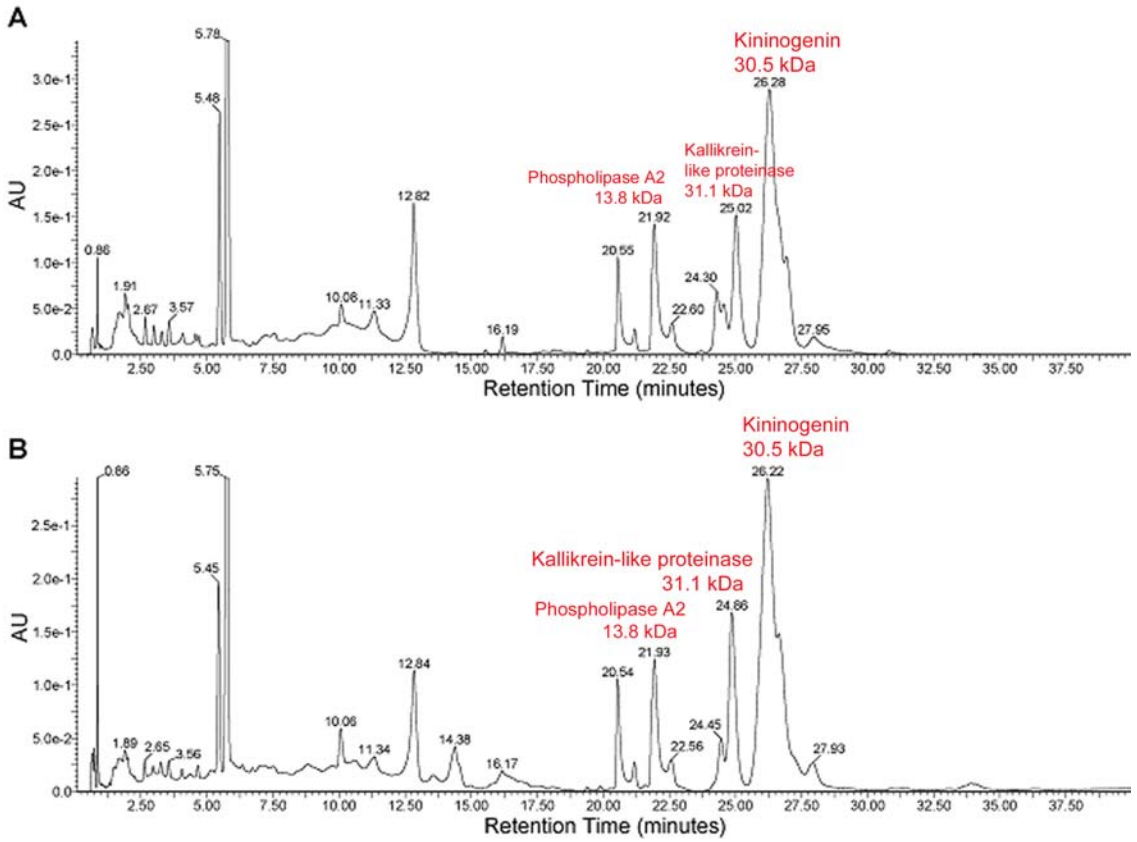



**Figure 9. Illus. 8.** UPLC chromatograms of venom from adult snake of *L melanocephala* (A) and *L. stenophrys* (B). Note greater PLA2 in *L. melanocephala* and somewhat greater "K-complex," with greater Mutalysin 2 in *L. stenophrys*. From Ripa, Boomershine and Ripa (in prep); UPLC by Will Boomershine.

masters. This, nevertheless, deadly enzyme is most abundant in adult *L. melanocephala*. $PLA_2$ may produce structural changes in the central nervous system (Russell, 1983), increasing presynaptic density, widening of the extracellular spaces, distension of nerve terminals and mitochondria, decreased numbers of synaptic vesicles, and rupture of the plasma membrane (Cedergren et al, 1973).

The rapid dynamics of the L-syndrome have been observed repeatedly. Jorge et al. (1997) recorded some 20 cases, and more have appeared since then. To date, however, only the shock-effect (with its severe hypotensive action) has proved significant in loss of human life in bushmaster envenoming. This does not exclude sequelae similar to other Crotaline envenomings, involving a slower degradation of the cardiovascular system that could invite a second fatal shock later on. But we have no way to measure this, since all known fatalities have involved shock, even when death was delayed by several days. Without doubt, systemic degradations through hemostatic alterations, including hemorrhage and necrosis inviting secondary infection, could also enhance or alter (to sepsis) the shock-producing pharmacology, clinically appreciated as a second kind of shock (e.g., septic shock). And yet this is not a necessary hypothesis. The K-complex is present in enough quantity in all bushmaster venoms, whether adult or neonate, to produce shock without resorting to a theory of a secondary reaction (e.g., shock from bacterial infection). Further study as new bite cases come in will no doubt determine this feature more exactingly.

Neonate bushmasters kill their prey very rapidly, whether performing strike-hold or strike-release tactics (Chapter 21). There is no appreciable deficit, vis-à-vis adults, in their ability to kill prey. If anything, the smaller food animal dies more quickly than the adult's larger prey. The disproportion of kallikrein-like proteinase and kininogenin in the neonate venom, and the lack of other hemostatic agents, suggests that the neonate venom kills the prey by inducing a shock effect. The hemorrhage producing enzymes and proteins in the venom have a long-term digestive purpose, but perhaps they could not kill the prey quickly enough for the snake to be able to recover it if strike-released. Hence, rating the venom of neonates according to classic proteolytic-type properties alone (as did Gutiérrez et al., 1990) will always pro-

duce a misleading picture of "low toxicity." The digestive components are not the explicitly lethal properties to begin with. They are in too short a supply. In the neonate venom we have a pharmacology almost entirely predicated on the use of shock as a quick-kill strategy. This bradykinin-releasing K-complex is a necessary component for an otherwise slow acting venom, benefiting neonates by making sure they get their vital first meals in life. While the K-complex is retained in the adult, it is not retained in such disproportion, being replaced by greater concentrations of Mutalysin 2 and $PLA_2$. The venom becomes more proteolytic in the larger, more difficult to digest prey of adult snakes.

While in adult snakes we find less concentration of the shock-producing agents, the lack is certainly compensated by the greater amount of venom these larger snakes can deliver. In the adult snakes, uniformly, the shift appears toward the hemorrhagic productions of Mutalysin 2 and Phospholipase $A_2$; that is, the venom is becoming more blood and tissue destructive. At some point in the snakes' lives a shift occurs toward greater proteolytic activity and less directly lethal action, proportionate to the available K-complex. This change does not occur early on. At 10 months the venom is still relatively similar to the neonate's. Further analysis should tell us as what age this change occurs (e.g., and whether it corresponds with size, prey-size shifts [to relatively smaller prey], or sexual maturity). Perhaps the proportion of the K-complex is balanced toward the critical minimum necessary to insure that shock-instigators will always be in enough supply to do their job.

This study brings an unexpected new insight into the effects of bushmaster venom in prey and in human beings. Contrary to previous assertion, juvenile bushmasters are formidably armed. Drop for drop, their venom is significantly more dangerous to man that the venom of adults. Based on the effects seen in Bites 3 and 4 in Chapter 22, and the proportions of venom injected by other neonates of similar size when strike-holding prey (Chapter 21), I propose that as little as 20 - 25 mg (dry weight) of the neonate venom injected intramuscularly could be the relative lethal dose for an adult human being. This potency will be less in the mature snake, where the K-complex is almost halved (although surely made up for by the greater venom delivery possible in the adult snake). Nevertheless, the shift toward greater proteolytic action, as Mutalysin 2 and $PLA_2$, may to some extent provide the needed synergy to compensate for the deficit.

The agonizing abdominal seizures experienced in consort to the sudden loss of blood pressure (and rapid heart rate accompanying this, being a good indicator of the onset of shock) can be explained at least partially by the effects of bradykinin on the smooth muscles of the abdomen and intestines, which cause spasmodic contractions in test animals (sensu Feres et al., 1994). These symptoms, along with dysphagia, dysphonia, numbness of the lips and face, etc., have probably been confused with an apparent neurotoxicity.[2] As these data show, the expected instigator of neurotoxic action ($PLA_2$) is very low in the venom of the neonate and sub-1-year-old juvenile; the phospholipase $A_2$ isoforms usually associated with neurotoxic action are but spottily represented. They are far outweighed by the K-complex, which, indeed, but for the presence of Mutalysin 1, we might say is really almost all the juvenile venom is composed of. The clinical data provided by Bites 3 and 4 in this book (Chapter 22) strongly suggest that the L-syndrome is alive and well in the juvenile snake, and is not dependent on $PLA_2$.

There is more good evidence against neurotoxicity. Signs of neurotoxicity, even in strongly neurotoxic envenomings such as those of cobras and kraits, usually do not appear earlier than several hours; while in the bushmaster, dysphagia, convulsive pain of the abdominal muscles (probably from contractions of the smooth muscles), projectile vomiting and diarrhea are experienced within 20 minutes of the envenoming; in other words, at the very start of the hypotensive crisis. From this I infer that true neurotoxicity (e.g., Vagal stimulation) is not respon-

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[2] Damico et al. (2005b) attempt to show neurotoxicity in *L. muta muta* venom in vitro, in mouse phrenic nerve diaphragm and chick bicenter cervicis preparations; however, the massive quantities they used (20 µg/ml, 50 µg/ml and 100 µg/ml, &c.), injected into the tiny mouse and chick parts, equivalent to as many as 100 lethal doses for an adult human being, would rather disprove an argument, than otherwise, that bushmaster venom inspires a significant neurotoxicity in man. No bushmaster can administer this much venom: 2 - 6 grams required to produce a neurotoxic effect in an animal weighing as much as the average adult person! The total yield for most bushmasters is not more than 333 mg and the amount injected in a bite is typically much smaller, in the range of 50 - 120 mg. Short of being bitten by more than a dozen bushmasters at once, we should detect no such effect in human beings; nor should we assume such an effect to be fatal, in any case. Even granting that, at these massive dosages, certain neurotoxic effects can be detected in mice and poultry, such results cannot be applied across species. To date, no human fatality from a bushmaster bite can be attributed to neurotoxicity, and such effects as have been portrayed as nerve-affecting (e.g., oropharyngeal dysphagia, often mistaken for paralysis) are rather symptoms of the onset of the bushmaster shock-syndrome, than any true neurotoxic presence in the venom.

sible for these most conspicuous alterations seen in the L-syndrome (but this deserves further study). Bushmaster venom kills by producing a swift autopharmocological reaction due to a preponderance of kininogen-like substances that release bradykinin and kallikrein, in effect triggering the body to kill itself. The onslaught is more sudden than that seen in typical "neurotoxic" snakebite, and in a venom that is not, or should not, be more than mildly neurotoxic, it is difficult to implicate nerve poisoning in this effect. The sudden death syndrome (< 45 minutes) in bushmaster bite can be directly attributed to the abundance of K-complex in the venom. If these effects are not completely neutralized, the L-syndrome, although managed initially, can return and become irreversible within 1 - 4 days, advancing on the victim in combination with other proteolytic effects in an already weakened patient. While this progressive sequence is surely exacerbated by the proteolytic degradations of blood and tissue, one wonders if these are really so essential to the formula. After all, neonate venom lacks almost all the major cell-destructive agents and is still capable of producing a significant shock-effect in man.

The till-now unexplained syndrome of "bushmaster bite death despite immunotherapy" can probably be blamed on the failure of treatment to control the activating factors of K-complex poisoning.

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**Materials and methods for HPLC**

***High performance liquid chromatography***

The venom was analyzed using $C_{18}$ reversed-phase high performance liquid chromatography (HPLC) on a Vydac 218TP510 column (10 x 250 mm). Components were resolved using a 120 mL linear gradient from 5% to 75% acetonitrile, 3% isopropanol, 0.1% trifluoroacetic acid (TFA) over 40 minutes. The absorbance was monitored at 215 nm.

***Electrophoresis***

Sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed in a 15% gel (Laemmli, 1970). Samples were reduced with 2-mercaptoethanol. The gel was run at 150 volts for approximately 1.5 hours with 45 mg of each sample. Gels were stained with Coomassie Brilliant blue. The number and approximate molecular weight of the bands were estimated for comparative analysis.

**Methods and materials for UPLC**

Ultra Performance Liquid Chromatography (UPLC) –the snake venom was analyzed by UPLC. Approximately 5 mg of lyophilized snake venom was dissolved in enough mobile phase A to bring the concentration to 5 mg/mL. 50 µg of venom was placed onto an Acquity UPLC BEH C18 1.7 µm 2.1 mm X 100 mm column and eluted with a linear gradient from 10 % mobile phase B to 50 % mobile phase B over 40 minutes at 0.2 mL/minute. Mobile phase compositions were as follows: mobile phase A, 0.1 % formic acid, 0.01 % trifluoroacetic acid, 2 % acetonitrile, 98 % water; mobile phase B, 0.1 % formic acid, 0.01 % trifluoroacetic acid, 2 % water, 98 % acetonitrile. Proteins were monitored by UV absorbance at 280 nm and analyzed by mass spectrometry using a Waters MALDI Q-ToF Premier mass spectrometer using electrospray ionization.

**Results**

Comparison of venom from *L. melanocephala* of various ages (Figure 5, Illus. 4): The venom of adult and baby snakes is very similar in protein composition. However, there are some dramatic differences in the amounts of individual proteins between the two age groups. Baby snakes lack the 21.7 kDa protein with a retention time of 32.5 minutes. Adult snakes also appear to have a greater quantity of the 28.6 kDa protein with a retention time of 24.19 minutes. While baby snakes lack a major component of the venom, they do have higher quantities of several other proteins including the 13.5 kDa protein at retention time 20.55 minutes, the 31.1 kDa protein at retention time 25.02 minutes and the 30.5 kDa protein at retention time 26.28 minutes. The venom from a juvenile snake appears to fall in between baby and adult venom in terms of composition. The juvenile venom has increased amounts of the proteins at 24.27 minutes and 32.70 minutes versus the baby venom, while having decreased amounts of the proteins at 26.40 minutes, 25.04 minutes and 20.56 minutes. The peak at 19.83 minutes (13.9 kDa) could be a protein that only appears during this time of development or is due to individual variation, since this peak is not present in either the baby or adult venom samples.

Composition of venom from *L. stenophrys* of various ages (Figure 7; Illus. 6). The venom of adult and baby snakes is very similar in protein composition. However, there are some dramatic differences in the amounts of individual proteins between the two age groups. Baby snakes lack the 22.8 kDa protein with a retention time of

32.11 minutes. Adult snakes also appear to have a greater quantity of the 28.6 kDa protein with a retention time of 24.43 minutes, the 13.8 kDa protein with retention time of 21.88 minutes and the 23.9 kDa protein with a retention time of 36.04 minutes. While baby snakes lack a major component of the venom, they do have higher quantities of several other proteins including the 2.3 kDa protein at retention time 14.38 minutes, the 31.1 kDa protein at retention time 24.86 minutes and the 30.5 kDa protein at retention time 26.22 minutes. The differences in venom between adult and baby snakes for both *L. melanocephala* and *L. stenophrys* were very similar.

Comparison of venom between baby *L. melanocephala* and *L. stenophrys* (Figure 8; Illus. 7): The venoms from baby snakes from different species are quite similar in both the quantity of proteins present and the identity of proteins present. There are some minor differences in retention times between peaks. However, these differences are probably due to sequence differences within the same functional protein rather than two different functional proteins.

Comparison of venom from adult *L. melanocephala* and *L. stenophrys* (Figure 9; Illus. 8): The venoms from adult snakes from different species are quite similar in both the quantity of proteins present and the identity of proteins present. There are some minor differences in retention times between peaks (such as 32.53 minutes for *L. melanocephala* and 32.11 minutes for *L. stenophrys*). These differences, however, are probably due to sequence differences within the same functional protein rather than two different functional proteins.

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**Literature Cited and Related Reading**


Abe, A. S., and M. C. Crupi. 1993. Variação sazonal da taxa metabólica na cascavel, *Crotalus durissus* (Serpentes, Viperidae). Mem. Inst. Butantan 55:47-53.

Ananjeva N. B., Dihnuchamedov M. E., and Matveyeva T. N. (1991), The skin sense organs of some Iguanian lizards. I. Herpetol.,2 5(2), 186- 199. Honda M., Ota H., Kobayashi M., Nabhitabhata

Andrade, D. V., A. P. Cruz-Neto, and A. S. Abe. 1997. Meal size and specific dynamic action in the rattlesnake *Crotalus durissus* (Serpentes: Viperidae). Herpetologica 53(4):485-493.

Andrén, C. 1982. The role of the vomeronasal organs in the reproductive behaviour of the adder *Vipera berus*. Copeia 1982: 148-157.

Andren, C. 1986. Courtship, mating and agonistic behavior in a free-living population of adders, *Vipera berus*. Amphibia-Reptilia 7:353-383.

Andren, C., and G. Nilson. 1981. Reproductive success and risk of predation in normal and melanistic color morphs of the adder, *Vipera berus*, Biol. J. Linn. Soc. 15:235-246.

Andrusiak. L. E. Walters. E. Terry and K. Simpson. 1998. Wildlife radiotelemetry. In: *Standards for components of British Colombia's biodiversity No. 5*. Ed. J. Quayle, and L. Westereng. Ministry of Environment, Lands and Parks, Resources Inventory Branch for the Terrestrial Ecosystems Task Force, Resources Inventory Committee. Vancouver, BC.

Argôlo, A.J. S. 2003. *Lachesis muta rhombeata* Wied, 1825 (Serpentes, Viperidae): defense behavior and snakebite risk. Herpetological Review, USA, v. 34, n. 3, p. 210-211.

Argôlo, A.J. S. 2004. As serpentes dos Cacauais do Sudeste da Bahia. Editora da UESC, Ilheus, Brazil.

Arnold, S. J. 1983. Morphology, performance and fitness. Am. Zool. 23:347-361.

Arnold, S. J. 1993. Foraging theory and prey-size predator-size relations in snakes. In: R. A. Seigel and J. T. Collins (eds.), Snakes: ecology and behavior. MacGraw-Hill, New York, N.Y.

Barbour, T. 1914. A contribution to the zoogeography of the West Indies, with especial reference to amphibians and reptiles. Mem. Mus. Comp. Zool. 44:209-359.

Barker, D. G. 1992. Variation, infraspecific relationships, and biogeography of the ridgenosed rattlesnake, *Crotalus willardi*. In Biology of the pitviper, ed J. A. Cambell and E. D. Brodie Jr., 89-106. Tyler, Tex.: Selva.

Barnett, K. E., R. B. Cocroft, and L. J. Fleishman. 1999. Possible communication by substrate vibration in a chameleon. Copeia 1999:1:225-228.

Barrett, R., Maderson, P. F. A., and Meszler, R. M. 1970. The pit organs of snakes. In: C. Gans, and T. S. Parsons (eds.), Biology of the Reptilia. New York, Academic Press, 1970.

Bateson, W. 1885. The later stages in the development of *B. kowalevskyi*, with a suggestion as to the affinities of the Enteropneusta. Q. J. Microsc. Sci. **25**:81–122.

Bauchot, R. 1994. Snakes: A Natural History. Sterling; New York, N.Y.

Beebe, W. 1916. Noosing a bushmaster. Bull. New York Zool. Soc. 4:1372-75.

Beebe, W. 1946. Field notes on the snakes of Kartabo, British Guiana, and Caripito, Venezuela. Zoologica 31: 11-52

Behura, B. K. 1962. On the vocal sounds of snakes. J. Utkal Univ. Bhubaneswar 2:40-42.Bolaños, R. 1971. Nuevos recursos contra el ofidismo en Centroamérica. 2 Edicion. Ciudad Universitaria: Universidad de Costa Rica.

Bjarnason, J. B., and J. W. Fox. 1994. Hemorrhagic metalloproteinases from snake venoms. Pharmacol Ther 62, 325-372.

Blaylock, R.S. 2000. Antibacterial properties of KwaZulu Natal snake venom. Toxicon. 38:1529-34.

Bogert, C. M. 1943. Dentitional phenomena in cobras and other elapids, with notes on adaptive modifications. Bull. Am. Mus. Nat. Hist. 81: 285-360.

Bogert, C. M. 1954. Amphibians and repitles of the world, Book 3. In: *The Animal Kingdom*, vol. 2, ed. F. Drimmer. Garden City, N.Y; Garden City Books, Doubleday.

Bolaños, R. 1972. Toxicity of Costa Rican snake venoms for the white mouse. Amer. Jour. Trop. Med. Hyg. 21:360-363.

Bolaños, R. 1982. Las serpientes venenosas de Centroamérica y el problema del ofidismo. Primera parte. Aspectos zoológicos, epidemiológicos y biomédicos. Rev. Costarr. Cienc. Méd. 3:165-184.

Bolaños, R. 1984. Serpientes, venenos y ofidismo en Centroamérica. Editorial Universidad de Costa Rica.

Bolaños, R., G. Muñoz and L. Cerdas. 1978. Toxicidad, neutralización e immunoelectroforesis de los venenos de Lachesis muta de Costa Rica y Colombia. Toxicon 16:295-300.

Bolaños, R., O. Rojas and C. E. Ulloa Flores. 1982. Aspectos biomédicos de cuatro casos de mordedura de serpiente por *Lachesis muta* (Ophidia: Viperidae) en Costa Rica. Rev. Biol. Trop. 30:53-58.

Boos, Hans E. A., 2001. The snakes of Trinidad and Tobago. W. L. Moody, Jr., Natural History Series. Texas A&M University Press.

Boulenger, G. A. 1896. Catalogue of the snakes in the British Museum (Natural History). London, British Museum of Natural History.

Boyer, D. M., C. M. Garrett, J. B. Murphy, H. M. Smith and D. Chiszar. 1995. In the footsteps of Charles C. Carpenter: Facultative strike-induced chemosensory searching and trail-following behavior of bushmasters (*Lachesis muta*) at Dallas Zoo. Herpetological Monographs 9:161-168.

Boyer, D. M., L. A. Mitchell, and J. B. Murphy. 1989. Reproduction and husbandry of the bushmaster (*Lachesis muta muta*) at the Dallas Zoo. International Zoo Yearbook 28:190-194.

Brock, O. G. 1980. Predatory behavior of eastern diamondback rattlesnakes (*Crotalus adamanteus*): Field enclosure and Y-maze laboratory studies, emphasizing prey trailing behavior. Unpubl. Ph.D. dissert, Florida State University, Tallahassee, FL.

Bullock, T. H., and R. B. Cowles. 1952. Physiology of an infrared receptor: The facial pit of pit vipers. Science 115:541.

Burchfield, P. 1975. The bushmaster *Lachesis muta* in captivity. International Zoo Yearbook 15:175-177.

Burroughs, W. S. 1953. The Yage Letters. New York; Grove Press.

Burroughs, W. S. 1957. Naked Lunch. New York; Grove Press.

Burroughs, W. S. 1978. The Third Mind. New York; Viking.

Burroughs, W. S. 1989. The Western Lands. New York; Viking.

Cadle, J. E. 1987. Geographic distribution: problems in phylogeny and zoogeography. Pp. 77-105. In: R. A. Seigel, J. T. Collins and S. S. Novak (eds.), Snakes: Ecology and evolutionary biology. New York: Macmillan Publ. Co.

Cadle, J. E. 1988. Phylogenetic relationships among advanced snakes. Univ. Calif. Publ. Zool. 119:1-77.

Calder, W. A. III. 1984. Size, function, and life history. Harvard Univ. Press. Cambridge, Mass.

Campbell, J. A. and E. D. Brodie, Jr. (eds.) 1992. Biology of the pitvipers. Tyler, Tex: Selva.

Campbell, J. A. and W. W. Lamar. 1989. The venomous reptiles of Latin America. Ithaca, NY: Cornell University Press.

Campbell JA, A Solorzano. 1992. The distribution, variation,and natural history of the middle American montane pitviper, *Porthidium godmani*. *In* JA Campbell, ED Brodie Jr, eds. Biology of the pitvipers. Tyler, TX: Selva Press,pp. 223-250.

Cansdale, G. S. 1961. West African Snakes. Longman Group UK Ltd., Essex, U.K.

Carpenter, C. C. 1977a. Communication and displays in snakes. Amer. Zool. 17:217-23.

Carpenter, C.C. 1986. An inventory of combat rituals in snakes. Smithsonian Herp. Inf. Serv. 69:1-18.

Carpenter, C.C., and J. C. Gillingham. 1975. Postural responses to kingsnakes by crotaline snakes. Herpetologica. 31:293-302.

Carpenter, G. 1977b. Variation and evolution of stereotyped behaviour in reptiles. In: *Biology of the Reptilia, Vol.* 7 (Ed. by C. Gans & D. Tinkle), pp.353-554. London: Academic Press.

Carthew, P. and J. Gannon. 1981. Secondary infection of rat lungs with *Pasteurella pneumotropica* after Kilham rat virus infection. Laboratory Animals. 15, 219-221.

Cavalier-Smith T. 1983. A 6-kingdom classification and a unified phylogeny. In: Schenk HEA, Schwemmler W, editors. Endocytobiology II: intracellular space as oligogenetic ecosystem. Berlin (Germany): Walter de Gruyter; p. 1027-1034.

Cavalier-Smith T. 1998. A revised six-kingdom system of life. Biol Rev Camb Philos Soc. 73:203-266.

Cedergren, E, Johansson, B., Heilbronn, E., and Widlund, L. 1973. Ultrastructural analysis of phospholipase A induced changes in membranes of synaptic regions in rat motor cortex. Ex. Brain Res., 16:400.

Chippaux, Jean-Philippe. 2002. Venins de serpent et envenimations. IRD editions.

Chiszar, D., C. Andren, G. Nilson, B. O'Connell, J. S. Mestas Jr. and H. M. Smith. 1982. Strike-induced chemosensory searching in Old World vipers and New World vipers. Anim. Learn. Behav. 10:121-125.

Chiszar, D., D. Boyer, R. Lee, J. B. Murphy, and C. W. Radcliffe. 1990. Caudal luring in the southern death adder, *Acanthophis antarcticus*. J. Herpetol. 24:253-260.

Chiszar, D., R. K. K. Lee, C. W. Radcliffe and H. M. Smith. 1993. Searching behaviors by rattlesnakes following predatory strikes. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. Tyler, Tex.: Selva.

Chiszar, D., J. B. Murphy, C. W. Radcliffe and H. M. Smith. 1989. Bushmaster (*Lachesis muta*) predatory behavior at Dallas Zoo and San Diego Zoo. Bull. Psychon. Soc. 27:459-461.

Chiszar , D., & Radcliffe, D. (1976). Rate of tongue flicking by rattlesnakes during successive stages of feeding on rodent prey. *Bulletin of the Psychonomic Society, 7*(5), 485–486.

Chiszar, D. and C. W. Radcliffe. 1989. The predatory strike of the jumping viper (*Porthidium nummifer*). Copeia 1989(4):1037-1039.

Chiszar, D., C. W. Radcliffe and K. M. Scudder. 1977. Analysis of the behavioral sequence emitted by rattlesnakes during feeding episodes. I. Striking and chemosensory searching. Behav. Biol. 21:418-425.

Chiszar, D., K. Skudder, H.M. Smith and C.W. Radcliffe. 1976. Observations of courtship in the western massasauga (*Sistrurus catenatus tergeminus*). Herpetologica 32:337-338.

Chiszar, D., and H. M. Smith. 1999. The Null Hypothesis and the Croaking Anurans of Cyrene. Bull. Chicago Herp. Soc. 34(8):192-193.

Coates, A. G. and J. A. Obando. 1996. The geologic evolution of the Central American Isthmus. Pp. 21-56. In: J. B. C. Jackson, A. F. Budd and A. G. Coates, (eds.) Evolution and environment in tropical America. Chicago: University of Chicago Press.

Conant, R.C. and J.T. Collins. 1991. A Field Guide to Reptiles and Amphibians: Eastern and Central North America. Peterson Field Guide Series. Houghton Mifflin Co. Boston, Massachusetts. 450 pp.

Cope, E. D. 1876. On the Batrachia and Reptilia of Costa Rica, with notes on the herpetology and ichthyology of Nicaragua and Peru. Journal of the Academy of Natural Sciences, Philadelphia, ser. 2, 8:93-157.

Cox, M. J. 1991. The Snakes of Thailand and Their Husbandry. Krieger, Florida, USA.

Crother, B. I. and C. Guyer. 1996. Caribbean historical biogeography: Was the dispersal–vicariance debate eliminated by an extraterrestrial bolide? Herpetologica 52(3):440-465.

Crouch, M.F., M. L. Roberts and K. A. Tennes (1981). Mepacrine inhibition of bradykinin-induced contractions of the rabbit ear vein. Agents and Actions. Vol. 11; 4.

Cundall, D. 1983. Activity of head muscles during feeding by snakes: a comparative study. Am Zool 23:383–396.

Cundall, D. 2002. Envenomation strategies, head form and feeding ecology in vipers. Pp. 149–161 *in* G.W. Schuett, M. Hoggren, M.E. Douglas, and H.W. Greene, eds. Biology of the Vipers.

Curtis, L. 1949. The Snakes of Dallas County, Texas. Field and Laboratory. 18:1:13.

Cuvier, G.F. 1812 "Sur un nouveau rapprochement à établir entre les classes qui composent le règne animal." *Annales du muséum d'Histoire Naturelle*, 1812, vol. 19.

Damico, D.C., L. G. F. Bueno. L. Rodrigues-Simioni. S. Marangoni, M. A. da Cruz-Hofling, J. C. Novello. (2005a.) Neurotoxic and myotoxic actions from *Lachesis muta muta* whole venom on the mouse and chick-nerve muscle preparations. Toxicon 46: 222-229.

Damico, D. C., S. Lilla, G. de Nucci, L. A. Ponce-Soto, F. V. Winck, J. C. Novello, and S. Marangoni. (2005b). Biochemical and enzymatic characterization of two basic Asp49 phospholipase A2 isoforms from *Lachesis muta muta* (Surucucu) venom. Biochim Biophys Acta 1726, 75-86.

Danch, J. M., 1997. The South American bushmaster. Reptiles Magazine. 5(7): 10-12, 14, 16, 18 20, 20. Mission Viejo, Calif.

Dart, R. 1999. Int J Med Toxicol 1999; 2(1):1, Hall EL. Ann Emerg Med 2001;37:175-80).

Dart, R. C., J. T. McNally, D. W. Spaite and R. Gustafson. 1992. The sequellae of pitviper poisoning in the United States. In: Biology of the Pitvipers, (eds.) J. A. Campbell and E.D. Brodie Jr. Tyler, Tex.: Selva.

Darwin, C. R. 1859. On the Origin of Species by Means of Natural Selection. John Murray, London. (Facsimile reprint: Harvard University Press, Cambridge, Mass. 1964).

Darwin, C.R. 1871. The descent of man and selection in relation to sex. 2nd ed., John Murray, London.

Darwin, C. R. 1890. Journal of researches into the natural history and geology of the various countries visited by H.M.S. Beagle.

DaSilva, N. J., S. D. Aird, C. Seebart and I. I. Kaiser. 1989. A gyroxin analog from the venom of the bushmaster (*Lachesis muta muta*). Toxicon 27:763-771.

Daudin, F. M. 1803. Histoire naturelle generale et particuliere des reptiles. Vol. 8. Paris, F. Dufort.

Denardo, D. 1996. Reproductive biology in amphibians and reptiles. In: D, Mader, Reptile Medicine and Surgery. Elsevier, Inc.

Dessauer, H. C., J. E. Cadle and R. Lawson. 1987. Patterns of snake evolution suggested by their proteins. Fieldiana (Zoology) 34:1-34.

De Souza, R., R. DeSouza and D. Ripa. Delayed-type hypersensitivity necrosis in snakebite. In prep.

Deuve, J. 1970. Serpents du Laos. Office de la Recherche Sco. Tech. Outre-Mer. Mem. 39:1-251.

Devine, M. C. 1975. Copulatory plugs, restricted mating opportunities and reproductive competition among male garter snakes. Nature 267:345-346.

Devine, M. C. 1984. Potential for sperm competition in reptiles: Behavioral and physiological consequences, in R. L. Smith, ed. Sperm competition and the evolution of animal mating systems. Academic, New York. 509-521.

Dilmuchamedov, M. E. and T. N. Matveyeva. 1991. The skin sense organs of some iguana lizards. Ananjeva N.B. Zool. Inst., Acad. Sci., Leningrad, USSR. Journal of Herpetology 25(2):186-199 1991. WR 225.

Diniz, M. R., and E. B. Oliveira. (1992). Purification and properties of a kininogenin from the venom of *Lachesis muta* (bushmaster). Toxicon 30, 247-258.

Ditmars, R. L. 1910. Reptiles of the world: Tortoises and turtles, crocodilians, lizards and snakes of the eastern and western hemispheres. NY: Sturgis and Walton Co.

Ditmars, R. L. 1931. Snakes of the world. N.Y. MacMillan.

Ditmars, R. L. 1932. Thrills of a Naturalist's Quest. N.Y. Halcyon House

Ditmars, R. L. 1937. The making of a scientist. N.Y. MacMillan.

Dixon, J. R. 1979. Origin and distribution of reptiles in lowland tropical rainforests of South America. In: The South American herpetofauna: its origin, evolution and dispersal. W. E. Duellman, (ed.), Lawrence, Kansas: Mus. Nat. Hist.

Dorcas, M. E. 1990. Relationships among montane populations of *Crotalus lepidus* and *Crotalus triseriatus*. M.S. Thesis, The University of Texas at Arlington.

Dorcas, M. E. 1992. Relationships among montane populations of *Crotalus lepidus* and *Crotalus triseriatus*. pp. 71-87. *In* Biology of the Pitvipers. (J.A. Campbell and E.D. Brodie, Jr., eds.) Selva Publ., Tyler, Texas.

Dorcas, M. E. 1999. A study of the defense behavior of cottonmouths (*Agkistrodon piscivorus*) in South Carolina. N.C. Herp. Soc. Newsletter No. 22:2.

Dorcas, M. E, C. R. Peterson, and M. E. T. Flint. 1997. The thermal biology of digestion in Rubber Boas (*Charina bottae*): physiology, behavior and environmental constraints. Physiol. Zool. 70:292–300.

Dowling, H. G. 1960. A bushmaster in the zoo again. Animal Kingdom, Zool. Soc. Bull. 63(3): 109-11.

Dowling, H. G. 1961. Our air-conditioned bushmaster. Animal Kingdom, Zool. Soc. Bull. 64(5): 155-56.

Duellman, W.E. 1978. The biology of an Equatorial herpetofauna in Amazonian Ecuador. Misc. Publ. Mus. Nat. Hist. Univ. Kansas, 65: 1-352.

Duellman, W. E. and A. W. Salas. 1991. Annotated checklist of the amphibians and reptiles of Cuzco Amazonico, Peru. Univ. Kansas Mus. Nat. Hist. Occ. Pap. No.143.

Duvall. D., S. J. Arnold, and G. W. Schuett. 1992. Pitviper mating systems: ecological potential, sexual selection, and microevolution. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. Tyler, Tex.: Selva.

Duvall, D., G. W. Schuett, and S. J. Arnold. 1993. Ecology and evolution of snake mating systems. In: R. A. Seigel and J. T. Collins (eds.), Snakes: ecology and behavior. MacGraw-Hill, New York, N.Y.

Esquerre, C. 1976. The minimum lethal dose (MLD) of venoms from Peruvian Crotalidae Snakes. San José, Costa Rica: Fifth international symposium on animal, plant, and microbial toxins abstracts.

Estep, K., T. Poole, C. W. Radcliffe, B. O'Connell and D. Chiszar. 1981. Distance traveled by mice (*Mus musculus*) after envenomation by prairie rattlesnakes (*Crotalus viridis*). Bull. Psychon. Soc. 18:108-110.

Estevao-Costa, M. I., Diniz, C. R., Magalhaes, A., Markland, F. S., and Sanchez, E. F. 2000. Action of metalloproteinases mutalysin I and II on several components of the hemostatic and fibrinolytic systems. Thromb Res 99, 363-376.

Fan, H. W., and J. L. Cardoso. 1995. Clinical toxicology of snake bites in South America. In: J. Meier and J. White, (eds.) Handbook of clinical toxicology and animal venoms and poisons. New York: CRC press.

Faraci, F. M., M. A. Klotz, H. W. Shirer, A. Orr and J. W. Trank. 1980. Characteristics of bulbus cordis mechanoreceptors in the pond turtle *Pseudemys scripta elegans*. Trans. Kansas Academy of Sciences 83(1):132 1980.

Farmer, S.G., R.M. Burch, C.J. Dehaas, J. Togo and L.R. Steranka. (1989) [Arg1-Phe7]-substituted bradykinin analogs inhibit bradykinin- and vasopressin-induced contractions of the uterine smooth muscle. JPET Vol. 248. No. 2. 677-681.

Fawcett, P. H. 1953. *Exploration Fawcett*. Essex, U.K.: Arrow Books. Anchor Press.

Feder, M. E., S. J. Arnold, 1982. Anaerobic metabolism and behavior during predatory encounters between snakes (*Thamnophis elegans*) and salamanders (*Plethodon jordani*). Oecologia 53: 93-97.

Felicori, L. F., C. T. Souza, D. T. Velarde, A. Magalhaes, A. P. Almeida, S. Figueiredo, M. Richardson, C. R. Diniz, and E. F. Sanchez. 2003. Kallikrein-like proteinase from bushmaster snake venom. Protein Expr Purif 30; 32-42.

Feres, T., E. Frediani-Neto, TB Paiva. 1994. Mechanism of smooth muscle contraction and relaxation mediated by kinin receptor. Braz J Med Biol Res 27:1911-6.

Field, J.L., S.K. Butt, I.K. Morton, and J.M. Hall. (1994). Bradykinin B2 receptors and coupling mechanisms in the smooth muscle of the guinea-pig tanenia caeci. Br. J. Pharmacol. 113(2): 607-13.

Fitch, H. S. 1981. Sexual size differences in reptiles. Miscellaneous Publications of the Museum of Natural History, University of Kansas 70:1-72.

Ford, N. B. and G. M. Burghardt. 1993. In: R. A. Seigel and J. T. Collins (eds.) Snakes: ecology and behavior. MacGraw-Hill, New York, N.Y.

Frost, D. R., and D. M. Hillis. 1990. Species in concept and practice: herpetological applications. Herpetologica. 46(1). 87-104.

Fuly A.L., S. C. Elias, R.B. Zingali, J. A. Guimarães, and P. A. Melo. Myotoxic activity of an acid phospholipase A2 isolated from *Lachesis muta* (Bushmaster) snake venom Toxicon 2000; 38: 961–72

Gaede, B. 2008. Why god doesn't exist. VINI

Gans, C. 1983. Snake feeding strategies and adaptations - conclusions and prognosis. Amer. Zool. 23:455-460.

Gans, C. 1985. Limbless locomotion, a current overview. *In* Functional Morphology of Vertebrates. Eds. G. F. Verlag, Stuttgart-New York.

Gans, C. and P. F. A. Maderson. 1973. Sound producing mechanisms in recent reptiles: review and comment. Am. Zool. 13:1195-1203.

Garcia,E. 1896. Los Ofidios Venenosos del Cauca. Métodos empíricos y racionales empleados contra los accidentes producidos por la mordedura de esos reptiles. Cali: Librería Colombiana.

Garman, S. 1883. The Reptiles and Batrachians of North America. Memoirs of the Museum of Comparative Zoology 8(3). Frankfurt, KY: Yeoman Press.

Gennaro, J. F., R. S. Leopold, and T. W. Merriam. 1961. Observations on the actual quantity of venom introduced by several species of crotalid snakes in their bite. Anat. Rec. 139:303.

Gentry, A. H. 1982. Neotropical floristic diversity: Phytogeographical connections between Central and South America, Pleistocene climatic fluctuations, or an accident of the Andean orogeny? Annals of the Missouri Botanical Garden 69:557-593.

Geoghegan, W. H. 1976, Polytypy in Folk Biological Taxonomies. *American Ethnologist*, Vol. 3, No. 3, Folk Biology, pp. 469-480

Gibbons, J. W. 1972. Reproduction, growth and sexual dimorphism in the canebrake rattlesnake (*Crotalus horridus atricaudatus*). Copeia:222-227.

Gillingham, J. C. 1987. Social behavior. In: R. A. Seigel, J. T. Collins, and S. S. Novak (eds.), Snakes: ecology and evolutionary biology. MacGraw-Hill, New York, N.Y., pp. 184-209.

Giovanni-De-Simone, S., A. S. Aguiar, A. R. Gimenez, K. Novellino and R. S. de Moura. 1997. Purification, properties and N-terminal amino acid sequence of kallikrein-like enzymes from the venom of *Lachesis muta rhombeata*. J. Protein Chem. 16(8):809-818.

Gloyd, H. K., and R. Conant. 1990. Snakes of the *Agkistrodon* Complex. A Monographic Review. Society for the Study of Amphibians and Reptiles, Oxford, Ohio. 614. pp.

Gmelin, J.F. 1789. Caroli a Linné Systema naturae. 13. ed., Tom 1 Pars 3. G. E. Beer, Lipsiae.

Good, D. A. 1994. Species limits in the genus Gerrhonotus (Squamata: *Anguidae*). Herpetological Monographs. 8:180-202.

Goodrich, E. S. (1930). Studies on the Structure and Development of Vertebrates. London: Macmillan.

Gould, S. J. 1978. Morton's ranking of races by cranial capacity. Science, Vol. 200.

Gray, J.E. 1825. A synopsis of the genera of reptiles and Amphibia, with a description of some new species. Annals of Philosophy, 10:193—217.

Gray, J. E. 1826. Reptilia. Appendix in: King, P. P. Narrative of a survey of the Intertropical and Western Coasts of Australia performed between the years 1818 and 1822. London: John Murray 2: 424-434.

Greene, G. 1936. Journey Without Maps. Garden City, NY: Doubleday, Doran & Company, Inc.

Greene, H. W. 1983. Dietary correlates of the origin and radiation of snakes. Amer. Zool. 23:431-441.

Greene, H. W. 1986. Natural History and evolutionary biology. Pp. 99-108. In: M. E. Feder and G. B. Lauder (eds.), Predator-prey relationships: Perspectives and approaches from the study of lower vertebrates. Chicago: University of Chicago Press.

Greene, H. W. 1988. Antipredator mechanisms in reptiles. In: C. Gans and R. B. Huey (eds.), Biology of the reptilia. Vol. 16, Ecology B: Defense and Life History, 1-152. New York: Alan R. Liss.

Greene, H. W. 1992. The ecological and behavioral context for pitviper evolution. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. Tyler, Tex.: Selva.

Greene, H. W. 1997. Snakes, the evolution of mystery in nature. Berkeley and Los Angeles: University of California Press.

Greene, H. W. and D. L. Hardy. 1989. Natural death associated with skeletal injury in the terciopelo, Bothrops asper (Viperidae). Copeia 1989(4): 1036-1037.

Greene, H. W. and M. A. Santana. 1983. Field studies of hunting behavior by bushmasters. Am. Zool. 23:897.

Greene, H. W., May, P. G., Hardy, D. L., Sciturro, J. M. & Farrell, T. M. 2002. Parental behavior in vipers. In *Biology of the pitvipers* (ed. G. W. Schuett, M. Hoggren, M. E. Douglas & H. W. Greene), pp. 179–205. Eagle Mountain, UT: Eagle Mountain Publishing.

Greenwald, O. E. and M. E. Kanter. 1974. The effects of temperature and behavioral thermoregulation on digestive efficiency and rate in corn snakes (*Elaphe guttata guttata*). Physiol. Zool. 52:398-408.

Greenwood, P. J. and J. Adams. 1987. Sexual selection, sexual dimorphism and a fallacy. Oikos, 48:106-108.

Griffin, D. R. 1991. Cognitive ethology: the minds of other animals: essays in honor of Donald R. Griffin. (ed.) C. A. Ristau. Lawrence Erlbaum Assoc. Inc.

Grobben, K. (1908): Die systematische Einteilung des Tierreichs– Verhandlungen der Kaiserlich-Königlichen Zoologisch-Botanischen Gesellschaft in Wien, **58**: 491–511.

Gutiérrez, J. M. 1995. Clinical toxicology of snakebite in Central America. In: J. Meier and J. White, (eds.), Handbook of clinical toxicology of animal venoms and poisons. New York: CRC Press.

Gutiérrez, J. M. and F. Chaves. 1980. Efectos proteolítico, hemorrágico, y mionecrótico de los venenos de serpientes costarricenses de los géneros *Bothrops*, *Crotalus* y *Lachesis*. Toxicon 18:315-321.

Gutiérrez, J. M., F. Chaves and R. Bolaños. 1980. Estudio comparativo de venenos de ejemplares recién nacidos y adultos de Bothrops asper. Rev. Biol. Trop. 28:341-351.

Gutiérrez, J. M., F. Chaves and R. Bolaños. 1990. Ontogenetic changes in the venom of the snake *Lachesis muta stenophrys* (bushmaster) from Costa Rica. Toxicon 28:419-426.

Gutiérrez, J. M., G. Rojas and L. Cerdas. 1987. Ability of a polyvalent antivenom to neutralize the venom of *Lachesis muta melanocephala*, a new Costa Rican subspecies of the bushmaster. Toxicon 25:713-720.

Hardy, D. L., Sr. 1992. A review of first aid measures for pitviper bite in North America, with an appraisal of the Extractor (TM) and stun gun electroshock. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. 405 - 14 Tyler. Tex.: Selva.

Hardy, D. L., Sr. 1998. Male-male copulation in captive Mojave rattlesnakes (*Crotalus scutulatus*). Bull. Chicago Herp. Soc. 33(12):258-262.

Hardy, D. L., Sr. and J. Silva. 1998. A review of venom toxinology and epidemiology of envenoming of the bushmaster (*Lachesis*) with report of a fatal bite. Bull. Chicago Herp. Soc. 33(6):113-123.

Harrington, H. J. 1962. Paleogeographic development of South America. Bull. American Assoc. Petrol. Geol. 46(10):1773-1814.

Hatschek, B. 1888: Lehrbuch der Zoologie, 1. Lieferung (pp. 1–144); Jena (Gustav Fischer).

Hayes, W. K. 1991. Ontogeny of striking, prey-handling and envenomation behavior of Prairie Rattlesnakes (*Crotalus v. viridis*). Toxicon 29:867-875.

Hayes, W. K. and J. G. Galusha. 1984. Effects of rattlesnake envenomation upon mobility of male wild and laboratory mice. Bull. Maryland Herp. Soc. 20:135-144.

Hayes, W. K., S. S. Herbert, G. C. Rehling, and J. F. Gennaro. 2002a. Factors that influence venom expenditure by viperid and other snakes during predatory and defensive contexts. Pp. 207-233 *in*: G. W. Schuett, M. Hoggren, M. E. Douglas, and H. W. Greene (eds), *Biology of the Vipers*. Eagle Mountain Publ., Eagle Mountain, Utah.

Hayes T. B., A.Collins, M. Lee, M. Mendoza, N. Noriega, and A.A. Stuart. 2002b. Hermaphroditic, demasculinized frogs after exposure to the herbicide atrazine at low ecologically relevant doses. Proc Natl Acad Sci USA 99:5476–5480.

Henderson, R. W. and S. B. Hedges. 1995. Origin of West Indian populations of the geographically widespread boa *Corallus enydris* inferred from mitochondrial DNA sequences. Molecular Phylogenetics and Evolution. 4:88-92.

Hering, C 1879. The Guiding Symptoms of our Materia Medica. Edited by C.G. Raue, C.B. Knerr and C. Mohr. Vols. 5-10. Estate of Constantine Hering.

Hoge, A. R. 1966 (dated, 1965). Preliminary account on neotropical crotalinae (Serpentes: Viperidae). Mem. Inst. Butantan 32:109-184.

Hoge, A. R. and A. R. Lancini. 1962. Sinopsis de las serpientes venenosas de Venezuela. Pub. Ocas. del Museo de Cien. Naturales. Caracas, Venezuela.

Hoge, A. R. and S.A.R.W.D.L. Romano. 1976/77. *Lachesis muta rhombeata* (Serpentes, Viperidae, Crotalinae). Mem. Inst. Butantan, 40/41:53-54.

Hoge, A. R. and S.A.R.W.D.L. Romano-Hoge. 1981 (1978/79). Poisonous snakes of the world. Part 1: Check list of the pitvipers: Viperoidea, Viperidae, Crotalinae. Mem. Inst. Butantan. 42/43:179-310.

Hoge, A.R.; S.A.R.W.L. Romano, & C. L. Cordeiro. 1978. [1976-1977.] Contribuicão ao conhecimento das serpentes do Maranhao, Brasil. Serpentes, Boidae, Colubridae, e Viperidae. Mem. Inst. Butantan 40/41: 37-52

Holdridge, L. R. 1964. Life zone ecology. Trop. Sci. Center. San José, Costa Rica.

Hoorne, C. 1994. An environmental reconstruction of the paleo-Amazon River system (middle-late Miocene, NW Amazonia). Palaeogeography, Palaeoclimatology, Palaeoecology 112:187-238.

Horne, E, A., and R. G. Jaeger. 1988. Territorial pheromones of female red-backed salamanders. Ethology, 78:143-152.

Hudson, W. H. 1904. Green Mansion: A Romance of the Tropical Forest. London: Duckworth & Co.

Huang, M. Z., P. Gopalakrishnakone, M. C. Chung, and R. M. Kini. 1997. Complete amino acid sequence of an acidic, cardiotoxic phospholipase A2 from the venom of Ophiophagus hannah (King Cobra): a novel cobra venom enzyme with "pancreatic loop". Arch Biochem Biophys 338, 150-156.

Hulin., A., Ochoa and J. M. Desbordes. 1982. Envenimations par des crotalides en Guyane Francaise. Med. D'Afrique Noire 29:249- 225.

Jackson, M. K. and M. Sharawy. 1980. Scanning electron microscopy and distribution of specialized mechanoreceptors in the Texas rat snake, *Elaphe obsoleta* lindheimeri. Journal of Morphology 163(1):59-67 Jan. 1980 WR 177.

Jacobs, C., H. Burgt and D. L. Conley. 1963. Backbone of Colombia. Pp. 62-72. In: O. E. Childs and B. W. Beebe (eds.), Backbone of the Americas: tectonic history from pole to pole. Tulsa, OK: Am. Assoc. Petrol. Geol. Mem. 2.

Jacobson, E. R. 1983. Parasitic diseases of reptiles. In: R. W. Kirk (ed.), Current veterinary therapy. Vol. 8., W. B. Saunders, Philadelphia.

Jaeger, R.G., and W.F. Gergits. 1979. Intra- and interspecific communication in salamanders through chemical signals on the substrate. Animal Behaviour 27:150–156.

Jaeger, R.G., D. Kalvarsky, and N. Shimizu. 1982. Territorial behavior of the Red-backed Salamander: Expulsion of intruders. Animal Behaviour 30:490–496.

Jaeger, R.G., J.A. Wicknick, M.R. Griffis, and C.D. Anthony. 1995. Socioecology of a terrestrial salamander: Juveniles enter adult territories during stressful foraging periods. Ecology 76:533–543.

Jaynes, J. 1976. The origin of consciousness in the breakdown of the bicameral mind. Boston: Houghton Mifflin.

Johnson, R. N. 1972. Aggression in man and animals. W. B. Saunders, Philadelphia.

Jorge, M.T.; S.D. Nishioka; R. B. de Oliveira, L.A.. Ribeiro, & P. V. Silveira. 1998. *Aeromonas hydrophyla* soft-tissue infection as complication of snake bite: report of three cases. Ann. trop. Med. Parasit., 92: 213-217.

Jorge, M.T.; L. A. Ribeiro & J. L. O'Connnell. 1999. Prognostic factors for amputation in the case of envenoming by snakes of the *Bothrops* genus (Viperidae**).** Ann. trop. Med. Parasit., 93: 401-408.

Jorge, M.T. L.A. Ribeiro, M.L.R Silva, E.J. Kusano, & J.S. Mendonca. 1994. Microbiological studies of abscesses complicating *Bothrops* snakebite in humans: a prospective study. Toxicon, 32: 743-748

Jorge, M.T., I. S. Sano-Martins, S. C. Tomy, S.C.B Castro, R. A. Ferrari, L. A. Ribeiro and D. A. Warrell. 1997. Snakebite by the bushmaster (*Lachesis muta*) in Brazil: Case report and review of the literature. Toxicon 35: 545-554.

Jorge da Silva, N., and J.W. Sites, Jr. 1995. Patterns of diversity of Neotropical squamate reptile species, with emphasis on the Brazilian Amazon and the conservation potential of indigenous reserves. Conservation Biology 9:873-901.

Kardong, K. V. 1982. Comparative study of changes in prey capture behavior of the cottonmouth (*Agkistrodon piscivorus*) and Egyptian cobra (*Naja haje*). Copia 1982:337-343.

Kardong, K. V. 1986. Predatory strike behavior of the rattlesnake, Crotalus viridis oreganus, J. Comp. Psychol. 100:304-314.

Kardong, K. V. and P. R. Smith. 1991. The role of sensory receptors in the predatory behavior of the brown tree snake, Boiga irregularis (Squamata: Colubridae). Dep. Zool. Washington State University, Pullman 99164-4236. Journal of Herpetology 25(2):229-231 1991 WR 225.

Kinghorn, J. R. 1929. The snakes of australia. London; Angus and Robertson.

Kini, R. M., and Evans, H. J. (1992). Structural domains in venom proteins: evidence that metalloproteinases and non-enzymatic platelet aggregation inhibitors (disintegrins) from snake venoms are derived by proteolysis from a common precursor. Toxicon 30, 265-293.

Klauber, L. M. 1956. Rattlesnakes: Their Habits, life Histories, and Influence on Mankind, 2 Vols. University of California Press, Berkeley and Los Angeles.

Klauber, L. M. 1972. Rattlesnakes: their habits, life histories and influence on mankind. 2nd. ed., 2 vols. Berkeley and Los Angeles: Univ. California Press.

Kleiber M. 1932. Body size and metabolism. Hilgardia 6:3125-3153.

Klingenberg, R. J. 1993. Understanding reptile parasites. Advanced Vivarium Systems, Lakeside, California.

Kohler, G. 1996. Krankheiten der Amphibien und Reptilien. Eugen Ulmer GmbH & Co., Stuttgart, Germany.

Kondo, H., S. Kondo, S. Sadahiro, K. Yamauchi, A. Ohsaka, R. Murata. 1972. Estimation by a new method of the amount of venom ejected by a single bite of *Trimeresurus* species. Japan. J. Med. Sci. Biol. 25:123-131.

Korzybski, A. H. S. 1933. Science and sanity: an introduction to non-Aristotelian systems and general semantics. Lancaster, Pa.: International Non-Aristotelian Publishing Co.

Kraus, F., D. G. Mink and W. M. Brown. 1996. Crotaline intergenetic relationships based on mitochondrial DNA sequence data. Copeia 1996(4):763-773.

Krysko, K. L. 2003. Reproduction in the Madegascar leaf-nosed snake, *Langaha madagascariensis*. Afr. J. Herpetol. 52(1): 61-68.

Laemmli, U. K. 1970. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227, 680-685.

Lakatos, I. 1978. The methodology of scientific research programs. Cambridge: Cambridge University Press.

Latreille, P.A. 1802. In: C.N.S. Sonnini de Manoncourt and P.A. Latreille. Histoire Naturelle des Reptiles, avec Figures Déssinnées d'après Nature. Vol. 1. Détérville, Paris, xx + 280 p. [1802]

Leslie, F. 1888. The Kingdom of Nature.Thompson & Thomas, Chicago.

Liais. 1872. Clim. Géol. Faune Géogr. Brésil.

Lillywhite, H. B., 1989. Temperature, energetics, and physiological ecology. In: R. A. Seigel, J. T. Collins and S. S. Novak (eds.), Snakes: ecology and evolutionary biology. New York: Macmillan Publ. Co.

Linnaeus, C. 1758. Tomus I. Systema naturae per regna tria naturae, secundum classes, ordines, genera, species, cum

characteribus, differentiis, synonymis, locis. Editio decima, reformata. Holmiae. (Laurentii Salvii).: [1-4], 1-824.

Linnaeus C. 1766. Syst. Nat. 12th ed., p.373.

Lloyd, J. J. 1963. Tectonic history of the south Central American orogen. Pp. 88-100. In: O. E. Childs and B. W. Beebe (eds.), Backbone of the Americas: tectonic history from pole to pole. Tulsa, OK: Am. Assoc. Petrol. Geol. Mem. 2.

Lucus, S. M., and Jurg Meier. 1995. The biology and distribution of spiders of medical importance. In: J. Meier and J. White, (eds.), Handbook of clinical toxicology of animal venoms and poisons. New York: CRC Press.

Madsen, T. and R. Shine. 1992. A rapid, sexually-selected shift in mean body size in a population of snakes. Evolution. 46:1220-1224.

Madsen, T., R. Shine, J. Loman and T. Hakansson. 1993. Determinants of mating success in male adders, *Vipera berus*, Anim. Behav.

MacLean, P. D. 1973. A triune concept of the brain and behavior. Univ. of Toronto Press: Toronto.

Maclean, S. 1980. Ultrastructure of epidermal sensory receptors in *Amphibolurus barbatus* (Lacertilia: Agamidae). Cell Tissue Research 210(3):435-445 Sept. 1980 WR 179.

Maclean, W. P. 1968. A case of intersexuality in *Bothrops moojeni.* Copeia 1968:1:170.

Magalhaes, A. and C.R. Diniz. 1979. Purification and partial characterization of the thrombin-like enzyme from the venom of *Lachesis muta noctivaga*. Toxicon 17, Suppl. No. 1:112.

Magalhaes, A., R. N. Ferreira, M. Richardson, S. Gontijo, A. Yarleque, H. P. B. Magalhaes, C. Bloch, E. F. Sanchez. 2003. Coagulant thrombin-like enzymes from the venoms of Brazilian and Peruvian bushmaster (*Lachesis muta muta*) snakes. Comparative Biochemistry and Physiology Part B 136:255-266.

Mallow, D. D. Ludwig, and G. Nilson. 2003. True vipers: natural history and toxinology of Old World vipers. Kreiger.

Manthey, U., and W. Grossman. 1997 Amphibien & Reptilien Suedostasiens. Natur und Tier Verlag, Muenster.

Marsh, N.E., B. C. Whaler. 1984. The Gaboon viper (*Bitis gabonica*); its biology, venom components and toxinology. Toxicon 22 (5):669-94

Marshall, L. G., S. D. Webb, J. J. Sepkoski and D. M. Raup. 1982. Mammalian evolution and the great American interchange. Science 215:1351-1357.

Martin, W. F. and R. B. Huey. 1971. The function of the epiglottis in sound production (hissing) of *Pituophis melanoleucus.* Copeia 1971:752-754.

Martínez, V. and R. Bolaños. 1982. The bushmaster, *Lachesis muta muta* (Linnaeus) (Ophidia: Viperidae) in Panamá. Rev. Biol. Trop. 30:100-101.

Matthew, W. D. 1915. Climate and evolution. Ann. New York Acad. Sci. 24:171-318.

Mayr. E. 1940. Speciation phenomenon in birds. American naturalist. 72: 752

Mayr, E. 2001. What evolution Is. New York: Basic Books.

Mayr, E. and P. D. Ashcock. 1991. Principles of Systematic Zoology. New York: McGraw-Hill.

McDiarmid, R. W., J. A. Campbell, and T. A. Touré. 1999. Snake Species of the World, A Taxonomic and Geographic Reference. Vol. 1. The Herpetologists League, Washington, D. C.

Means, D.B. 2008. Stalking the plumed serpent and other adventures in herpetology. Pineapple press, Sarasota,Florida

Mehta, R. and N. B. Ford. 2001. Courtship in the Madagascar cat-eyed snake, Madagascarophis colubrina (Boignae). African L. Herpetol. 50:115-120.q

Mellor, N. H. and J. C. Arvin. 1996. Case report. A bushmaster bite during a birding expedition in lowland southeastern Peru. Wildn. Environmental. Med. 3:236-240.

The Merck manual of diagnosis and therapy. Ed. M. H. Beer and R. Berkow. 1999. Merck Research Laboratories. Whitehouse Station, N.J.

Merrem, B. 1820. Versuch eines Systems der Amphibien I (Tentamen Systematis Amphibiorum). J. C. Kriegeri, Marburg, 191 pp.

Milani Junior R, MT Jorge, FP de Campos, FP Martins, A Bousso, JL Cardoso, LA Ribeiro, HW Fan, FO Franca, IS Sano-Martins, D Cardoso, C Ide Fernandez, JC Fernandes, VL Aldred, MP Sandoval, G Puorto, RD Theakston and DA Warrell. 1997. Snake bites by the jararacucu (*Bothrops jararacussu*): clinicopathological studies of 29 proven cases in Sao Paulo State, Brazil. QJM, Vol 90, Issue 5 323-334, Oxford University Press.

Ministerio de Obras Publicas Panamá. 1993. Sintesis geografica de Panamá; Edicion 2; Instituto Geographico Nacional “Tommy Guardia”; Universidad de Panamá.

Minton, S. A. Jr. and M. R. Minton. 1969. Venomous reptiles. New York: Scribner.

Mitchell, S. W. 1860. Researches upon the venom of the rattlesnake. Smithson. Contrib. Knowledge 1860:1-139.

Mole, R.R. 1895a. A visit to the highwoods of Caparo. Journal of the Trinidad Field Naturalists’ Club 2(2):147-61.

Mole, R.R., 1895b. The dimensions of animals. Journal of the Trinidad Field Naturalists Club. 2(8): 191-94.

Mole, R.R., 1917. Letter to G. A. Boulenger, British Museum (Natural History), June 22.

Mole, R. R. 1924. The Trinidad Snakes. Proc. Zool. Soc. London 1924:235-78.

Mole, R. R. and E. W. Urich. 1894. Biological notes upon some of the ophidia of Trinidad. Proceedings of the Zoological Society of London, 499 - 518.

Morgan, K. R. 1988a. Body temperature, energy metabolism, and stamina in two neotropical forest lizards (*Ameiva*, Teiidae). Journal of Herpetology, 22:236–241.

Morgan, T. 1988b. Literary Outlaw: The Life and Times of William S. Burroughs. Avon Books, New York.

Morrison, J. J., N. T. Charles, J. H. Pearn. 1983a. The use of experimental models to study the biting habits of Australian snakes in both "defensive" and "hunting" bites. Toxicon Suppl. 3:305-308.

Morrison, J. J., J. H. Pearn, N. T. Charles, A. R. Coulter. 1983b. Further studies on the mass of venom injected by Elapid snakes. Toxicon 21:279-284.

Morton, S. G. 1849. Observations on the size of the brain in various races and families of man. Proc. Acad. Nat. Sci. Phila. 4, 221.

Murphy, J. C. and R. W. Henderson. 1997. Tales of Giant Snakes. Malabar, Florida; Krieger Pub. Co.

Myers, C. W. 1969. The ecological geography of cloud forest in Panamá. Am. Mus. Novitates 2396.

Myers C. W., J. W. Daly and B. Malkin. 1978. A dangerously toxic new frog (*Phyllobates*) used by Emberá indians of western Colombia, with discussion of blowgun fabrication and dart poisoning. Bull. American Mus. Nat. Hist.161(2):307-366.

Neill, W. T. Size and habits of the cottonmouth moccasin. 1947. *Herpetologica*, Vol. 3, No. 6: 203-205

Noble, G. K. and A. Schmidt. 1937. The structure and function of the facial and labial scales of snakes. Proc. Am. Phil. Soc. 77:263.

Nowak, R. M. 1991. Walker's mammals of the world. 5th ed. Baltimore and London: The Johns Hopkins University Press.

Nygren, W. E. 1950. Bolivar geosyncline of northwestern South America. Bull. Am. Assoc. Petrol. Geol. Soc. Am. 34(10): 1998-2006.

Oliver, J. A. 1956. Reproduction in the king cobra. *Ophiophagus hannah* . Cantor. Zoologica 41:145-52.

Oliver, J. A. 1957. Is temperature the secret? How to feed a bushmaster. Animal Kingdom, Zool. Soc. Bull. 40(6): 175-77

Oliver, J. A. 1958. Snakes in Fact and Fiction. Macmillan, New York.

Oliver, J. A. 1959. Snakes in fact and fiction. New York; H M. Parrish

Oppel, M. 1811. Die Ordnungen, Familien und Gattungen der Reptilien als Prodom einer Naturgeschichte derselben. Joseph Lindauer Verlag, München.

Otero, R., M. de F. D. Furtado, L. R. C. Goncalves, V. Nunez, M. D. Garcia, R. G. Osorio, M. Romero, J. M. Gutierrez. 1998. Comparative study of the venoms of three subspecies of *Lachesis muta* (bushmaster) from Brazil, Colombia and Costa Rica. Toxicon Vol. 36, No. 12:2021-2027.

Oxford Dictionary of Zoology. 1999. Ed. Michael Allaby. Oxford University Press. Oxford, New York.

Peters, J. A. and B. Orejas-Miranda. 1970. Catalogue of the neotropical squamata. Part 1. Snakes. Bull. U.S. Natl. Mus. 297:1-347.

People (Trinidad). 1935. Crocodile Tears. October, 19 6-7.

Phelps, T. 1981. Poisonous snakes. Blanford Press Ltd. Poole, Dorset, UK.

Picado T. C. 1931. Obras completas. Editorial Technogica de Costa Rica.

Pindell, J. L. and S. F. Barrett. 1990. Geological evolution of the Caribbean region; a plate tectonic perspective. Pp. 405-432. In: G. Dengo and J. E. Case (eds.), The geology of North America. Vol. H. The Caribbean region. Boulder: The Geological Society of America.

Piso, W. and G. Marcgrave. 1648. Historia Naturalis Brasiliae. Leiden: Fransciscus Hack. Amsterdam, Ludovicus Elzevier

Pitman, C. R. S. 1974. A guide to the snakes of Uganda. Rev. ed. Codicote, England: Wheldon and Wesley.

Pope, C. H. 1961. The Giant Snakes. Alfred A. Knopf, New York.

Potts, R. and A. K. Behrensmeyer. 1992. Late Cenozoic terrestrial ecosystems. Pp. 419-541. In: A. K. Behrensmeyer, J. D. Damuth, W. A. DiMichele, R. Potts, HD Sues & SL Wing (eds) Terrestrial ecosystems through time: evolutionary paleoecology of terrestrial plants and animals: 419-541. University of Chicago Press, Chicago, Illinois.

Potts, H. D. Sues and S. L. Wing (eds.) Terrestrial ecosystems through time - evolutionary paleoecology of terrestrial plants and animals. Chicago: University of Chicago Press.

Pough, F. H. and J. D. Groves. 1983. Specialization of the body form and food habits of snakes. Am. Zool. 23:443-454.

Pough, F. H., G. Kwieciniski and W. Bemis. 1978. Melanin deposits associated with the venom glands of snakes. J. Morph. 155:63-72.

Radcliffe, C. W., D. Chiszar and B. O'Connell. 1980. Effects of prey size on post-strike behavior in rattlesnakes (*Crotalus durissus*, *C. enyo*, and *C. viridis*). Bull. Psychon. Soc. 16:449-450.

Redi, F. 1664. *Osservazioni intorno alle vipere*. In: Francesco Redi on vipers. 1988. ed. E.J. Brill. Knoefel.

Reid, H. A. 1976. Venoms and Antivenoms. (Review on Glass, T. G. Jr. Early debridement in pitviper bites. J.A.M.A., 235:2513, 1976). Abstracts on Hygiene 51:1139.

Reinert, H. K. 1992. Radiotelemetric field studies of pitvipers: data acquisition and analysis. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. Tyler, Tex.: Selva.

Ripa, D. 1994. Reproduction of the Central American bushmaster (*Lachesis muta stenophrys*) and the black-headed bushmaster (*Lachesis muta melanocephala*) for the first time in captivity. Bull. Chicago Herp. Soc. 29(8):165-183.

Ripa, D. 1997. Range extension for *Bothrops leucurus*. Bull. Chicago Herp. Soc. 32(2):25-26.

Ripa, D. 1998 (unpubl.) A new "old" species of *Lachesis* (Serpentes: Viperidae) from southeastern Panamá, Pacific Colombia and Ecuador, and the inter-Andean valleys of Colombia.

Ripa, D. 1999. Keys to understanding the bushmasters (Genus *Lachesis Daudin*, 1803). Bull. Chicago Herp. Soc. 34(3):45-92.

Ripa, D. 2000 a. The bushmasters (Genus *Lachesis* Daudin 1803); morphology in evolution and behavior. CD-Rom.

Ripa, D. 2000 b. Degenerated Science. Bull. Chicago Herp. Soc. 35(5): 93-134.

Ripa, D. 2003. Six New Cases of Bushmaster Envenoming. *In* The Bushmasters (Genus *Lachesis* Daudin, 1803) Morphology in Evolution and Behavior; 3rd Edition. Electronic book. Cape Fear Serpentarium. Wilmington, NC.

Ripa, D. 2007. Ontogeny of the Shock Death in Human Beings. *In* The Bushmasters (Genus *Lachesis* Daudin, 1803) Morphology in Evolution and Behavior; 5th Edition. Electronic book. Cape Fear Serpentarium. Wilmington, NC.

Roberts, J. B., and H. B. Lillywhite. 1980. Lipid barrier to water exchange in reptile epidermis. Science 207:1077-1079.

Rogers, R. T., J. C. Anderson, C.A. Palmer, W. G. Henderson. (1973). Septicaemia due to Pasteurella pneumotropica. Journal of Clinical Pathology. 26(6):396-8.

Rose, J. 1970. (ed.) Progress of Cybernetics: Proceedings of the International Congress of Cybernetics, London, 1969. Gordon and Breach, 1970.

Rose, S. 1973. The conscious brain. New York: Knopf.

Rosenfeld, G. 1971. Symptomatology, pathology, and treatment of snake bite in South America. Pp. 345-383. In: W. Bucherl and E. E. Buckley, (eds.), Venomous animals and their venoms. Vol. 2. New York: Academic Press.

Rosenthal, R., J. Meier, A. Koelz, C. Muller, W. Wegmann, and P. Vogelbach. 2002. Intestinal ischemia after bushmaster (*Lachesis muta*) snakebite. Toxicon. 40(2):217-220.

Roze, J. A. 1966. La Taxonomia y Zoolgeographia de los Ophidios en Venezuela. Caracas: Univ. Cent. de Venezuela.

Rucavado, A., E. Flores Sanchez, A. Franceschi, A. Magalhaes, J. M. Gutierrez. 1999. Characterization of the local tissue damage induced by LHF-II, a metalloproteinase with weak hemorrhagic activity isolated from *Lachesis muta muta* snake venom. Toxicon 37:1297-1312.

Russell, F. E. 1983. Snake venom poisoning. Greatneck, NY: Scholium International.

Salomão, M.G., W. Wüster, R.S. Thorpe & BBBSP 1997. DNA evolution of South American pitvipers of the genus Bothrops. In R.S. Thorpe, W. Wüster & A. Malhotra (Eds.), Venomous Snakes: Ecology, Evolution and Snakebite. Symposia of the Zoological Society of London, No. 70, Pp. 89-98. Clarendon Press, Oxford.

Salomão, M.G., W. Wüster, R.S. Thorpe, & BBBSP. 1999. MtDNA evolution in Neotropical pitvipers of the genus *Bothrops* (Squamata: Serpentes: Viperidae). Kaupia, 8: 127-134.

Sanchez, E. F., T. V. Freitas, D. L. Ferreira-Alve, D. T. Valverde, M. R. Diniz, M. N. Cordeiro, G. Agostini-Cotta, C. R. Diniz. 1992. Biological activities of venoms from South American snakes. Toxicon 30:95-103.

Sanchez, E. F., C. I, Santos, A. Magalhaes, C. R. Diniz, S. Figueiredo, J. Gilroy, M. Richardson. 2000. Isolation of Proteinase with Plasminogen-Activating Activity from *Lachesis muta muta* (Bushmaster) Snake Venom. Archives of Biochemistry and Biophysics. Vol. 378, No. 1: 131-141

Sanchez, E. F., C. T. Souza, C. A. Bello, M. Richardson, E. B. Oliveira, A. Magalhaes. 2003. Resolution of isoforms of mutalysin II, the metlloproteinase from bushmaster snake venom. Toxicon 41:1021-1031.

Savage, J. M. 1966. The origins and history of the Central American herpetofauna. Copeia 1966:(4):719-766.

Savage, J. M. 1982. The enigma of the Central American herpetofauna: Dispersals or vicariance? Annals of the Missouri Botanical Gardens. 69:464-547.

Savitsky, B. C. 1992. Laboratory studies of piscivory in an opportunistic pitviper, the cottonmouth, *Agkistrodon piscivorus*. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. 347-68. Tyler, Tex.: Selva.

Sazima, I. 1992. Natural history of the jararaca pitviper, *Bothrops jararaca* , in southeastern Brazil. Pp. 199-216 In J. A. Campbell and E. D. Brodie, Jr. (Eds), Biology of the Pitvipers, Selva, Tyler, Texas.

Schinz, H. R. 1822. Das Thierreich eingetheilt nach dem Bau der Thiere als Grundlage ihrer Naturgeschichte und der vergleichenden Anatomie von dem Herrn Ritter von Cuvier. Vol. 2. J. G. Cotta, Stuttgart.

Schmidt-Nielsen, K. 1984. Scaling: why is animal size so important? New York. Cambridge University Press

Schöttler, W. H. A. 1951. Toxicity of the principle snake venoms of Brazil. Am. Journ. Trop. Med. Hyg. 31:489-500.

Schuett, G.W., S.L. Carlisle, A.T. Holycross, J.K. O´Leile, D.L. Hardy, Sr., E.A. Van Kirk, and W.J. Murdoch. 2002. The breeding system of male Mojave Rattlesnakes (*Crotalus scutulatus*) in Arizona: Seasonal timing of mating, male aggression, plasma sex steroids, spermatogenesis, and sexual segment of the kidney. *In* Schuett, G.W., M. Höggren, M.E. Douglas

and H.W. Greene (eds.), Biology of the Vipers, Eagle Mountain Publishing, Eagle Mountain, Utah.

Schuett, G. W. and J. C. Gillingham. 1986. Sperm storage and multiple paternity in the copperhead, *Agkistrodon contortrix*. Copeia 1986:807-811.

Schuett, G. W. and J. C. Gillingham. 1988. Courtship and mating of the copperhead, Agkistrodon contortrix. Copeia 1988:374-381.

Schuett, G. W. and J. C. Gillingham. 1989. Male-male agonistic behavior of the copperhead, *Agkistrodon contortrix*. Amphibia-Reptilia, 10:243-266.

Schuett, G. W., Hoggren, M., Douglas, M.E., and Green, H.W. 2002, Biology of the Vipers, Eagle Mountain Publishing,LC, Utah

Seymour, R. S. 1982. Physiological adaptations to aquatic life. Pp. 1– 51 in C. Gans and F.H. Pough, eds. Biology of the Reptilia. Physiology D: Physiological Ecology. Academic Press, New York.

Seymour, R. S. 1987. Scaling of cardiovascular physiology in snakes. Am Zool 27:97–109.

Shaw, C. E. 1968. The male combat dance of some crotalid snakes. Herpetologica 4:137-145.

Shaw, George. 1802. General Zoology or Systematic Natural History. Volume III. Amphibians and Reptiles. G. Kearsley, London.

Sherbrooke, W. C. and R. B. Nagle. 1996. *B. phrynosoma* intraepidermal receptor; a dorsal intraepidermal mechanoreceptor in horned lizards (Phrynosoma; Phrynosomatidae; Reptilia). Journal of Morphology 1996 228(2):145-154.

Shine R. 1978. Sexual size dimorphism and male combat in snakes. *Oecologia* 33: 269–277.

Shine, R. 1991. Why do larger snakes eat larger prey? Funct. Ecol. 5:493-502.

Shine, R. 1994. Sexual size dimorphism in snakes revisited. Copeia 1994:2:326-346.

Shine, R., G. C. Grigg, T. G. Shine, and P. Harlow. 1981. Mating and male combat in the Australian blacksnake. *Pseudechis prophyriacus* (Serpentes: Elapidae). J. Herpetol., 15:101-107.

Silva Haad, J. L. 1980/1981. Accidentes humanos por las serpientes de los generos Bothrops y Lachesis. Mem. Inst. Butantan 44/45:403-423.

Silva, L. M., C. R. Diniz and A. Magalhaes. 1985. Purification and partial characterization of an arginine ester hydrolase from the venom of the bushmaster snake, *Lachesis muta noctivaga*. Toxicon 23(4): 707 - 718.

Silveira Bueno, F. da. 1986. Vocabulario tupi-guarani Portugues. Sao Paulo: Editora Brasilivros.

Simhony, M. 1999. The story of matter and space. World Scientific Publishing Co. Hebrew University. Jerusalem, Israel.

Simpson, G. G. 1961. Principals of animal taxonomy. New York: Colombia University Press.

Smith, H. M. 1968. Heterecious sexual behavior versus homosexuality in snakes. J. Herpetology 2 (3-4):162-163.

Solórzano, A. and L. Cerdas. 1986. A new subspecies of the bushmaster, *Lachesis muta*, from southeastern Costa Rica. J. Herpetology 20(3):463-466.

Solórzano, A. and L. Cerdas. 1989. Reproductive biology and distribution of the terciopelo, *Bothrops asper* Garman (Serpentes: Viperidae) in Costa Rica. Herpetologica. 45(4):444-450.

Solórzano-López, A., M. Santana and H. W. Greene. 1987. Reproductive biology of *Lachesis muta stenophrys* (Serpentes: Viperidae) in Costa Rica. Abst. Jt. Ann. Mtg. SSAR Herpet. League :146.

Somma, L. A., 2003. Parental Behavior in lepidosaurian and testudinian reptiles: a literature survey. Krieger.

Somma, L. A. and J. D. Fawcett. 1989. Brooding behavior of the prairie skink (Eumeces septentrionalis), and its relationship to the hydric environment of the nest. Zool. J. Linnean Society 95:245-256.

Souza, Alcídea R.B, and P. F. Buhrnheim. 1995. Dez casos de acidente laquético atendidos no IMT-AM, de 1986 a 1996. Rev. Soc. Bras. Med. Tropical, n. 32, Sup.I, 388-89.

Sprawls, S. and B. Branch. 1996. A Guide to the Poisonous Snakes of Africa. Cape Town (South Africa): Struik.

Starkey, P. M., and J. A. Barrett. 1982. Evolution of alpha 2-macroglobulin. The structure of a protein homologous with human alpha 2-macroglobulin from plaice Pleuronectes platessa L.) plasma. Biochem J 205, 105-115.

Stevenson, R. D., C. R. Peterson and J. S. Tsuji. 1985. The thermal dependence of locomotion, tongue flicking, digestion, and oxygen consumption of the wandering garter snake. Physiol. Zoo., 58:46-57.

Stewart, H., H. Fowler, and W. K. Honig. 1978. Cognitive processes in animal behavior. Hillsdale, N. J., Lawrence Erlbaum & Assoc.

Stuart, L. C. 1966. The environment of the Central American cold-blooded vertebrate fauna. Copeia 1966:684-699.

Sutherland, S. K. andTibballs J. 2001. Australian Animal Toxins (2nd ed.) Oxford University Press, Melbourne, Australia.

Swanson, P. L. 1946. "X". Natural History Magazine. Am. Mus. Nat. History. Vol. LV. No. 10.

Taylor, E. H. 1951. A brief review of the snakes of Costa Rica. Univ. Kansas Sci. Bull. 34:1-188.

Taylor, R., A. Flores, G. Flores and R. Bolaños. 1974. Geographical distribution of Viperid*ae,* Elapidae and Hydrophiidae in Costa Rica. Rev. Biol. Trop. 21:383-397.

Theakston, R.D.G., R. E. Phillips, and D. A. Warrell, D.A. 1988. Envenoming by the common krait (*Bungarus caeruleus*) and the Sri Lankan cobra (*Naja naja naja*): efficacy and complications of therapy with Haffkine antivenom. Trans R Soc Trop Med Hyg. 84 (2):301-308.

Thomas, R. G. and F. H. Pough. 1979. The effect of rattlesnake venom on digestion of prey. Toxicon 17:221-228.

Timmerman, W.W. and W.H. Martin. 2003. Conservation guide to the Eastern Diamondback Rattlesnake (*Crotalus adamanteus*), John Moriarity, editor. Society for the Study of Amphibians and Reptiles Circular No. 32. 55 pp.

Torres, J. R., M. A. Torres and M. A. Arroyo-Parejo. 1995. Coagulation disorders in bushmaster envenomation. [Letter] Lancet 346:449-450.

Tosi, J. A., Jr. 1969. Republica de Costa Rica, Mapa Ecologico. Instituto Geographico Nacional. San José. Costa Rica.

Tosi, J. A., Jr. 1971. Inventariacion y demostraciones forestales. Panamá. Zonas de vida. FO:SF/PANAG. Informe tecnico 2. PNUD. FAO.

Tryon, B. 1975. How to incubate reptile eggs; a proven technique. Bull. New York Herp. Soc. 11:33-37.

Van der Hammen, T. 1961. Late Cretaceous and Tertiary stratigraphy and tectogenesis of the Colombian Andes. Geologie en Mijnbouw 51:181-188.

Van der Hammen, T. and M. L. Absy. 1994. Amazonia during the last glacial. Palaeogeography, Palaeoclimatology, Palaeoecology 109:247-261.

Vanzolini, P. E., 1977. An annotated bibliography of the land and fresh-water reptiles of South America (1758-1975); Vol 1; Univ. de San Paulo.

Vial, J. L. and J. M. Jiménez-Porras. 1967. The ecogeography of the bushmaster, *Lachesis muta*, in Central America. American Midland Naturalist. 78:182-187.

Vidal N., G. Lecointre, J. C. Vie and J. Gasc. 1997. Molecular systematics of pitvipers: paraphyly of the *Bothrops* complex. Comptes Rendu de l'Academie des Sciences, Serie III, Sciences de al Vie 320:95-101.

Wagler, J. 1824. Serpentum Brasiliensium species novae….In J. de Spix. Animalia nova sive species novae. Monaco, Typis Franc. Seraph. Hubschmanni.

Wallace, A. R. 1876. The geographic distribution of animals. 2 vols. London: MacMillan and Co.

Warwick, K. 1997. March of the machines; why the new race of robots will rule the world. London: Century.

Watt, G. 1989. Snakebite treatment and first aid. In: J. Campbell and W. W. Lamar (eds.), The venomous reptiles of Latin America. Ithaca NY: Cornell University Press.

Weldon, P. J., R. Ortiz and T. R. Sharp. 1992. The chemical ecology of crotaline snakes. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. 347-68. Tyler, Tex.: Selva.

Werman, S. D. 1992. Phylogenetic relationships of Central and South American pitvipers of the genus Bothrops (Sensu Lato): cladistic analysis of biochemical and anatomical characters. In: J. A. Campbell and E. D. Brodie Jr. (eds.), Biology of the pitvipers. Tyler, Tex.: Selva.

Wever, E. G., and J. A. Vernon. 1960. The problem of hearing in snakes. J. Auditory Res.

Whaler, B.C. 1971. Venom yields from captive Gaboon vipers (Bitis gabonica). Uganda J. 35(2): 195-206.

Whaler, B. C. 1972. Gaboon viper venom and its effects. J. Physiol 222:61-2.

White, J. 1995. Clinical toxicology of snake bite in Australia and New Guinea. In: J. Meier and J. White, (eds.) Handbook of clinical toxicology and animal venoms and poisons. New York: CRC press.

Whittaker RH, Margulis L. 1978. Protist classification and the kingdoms of organisms. BioSystems 10: 3–18.

Wied-Neuwied, Maximilian, Prinz zu. 1822. Abbildung zur Naturgeschichte Brasiliens. Weimar. (1822-1831).

Wied-Neuwied, M. 1824. Verzeichniss der Amphibien, welche im zweyten Bande der Naturgeschichte Brasiliens vom Prinz Max von Neuwied werden beschrieben werden. Isis von Oken 14: 661—673

Wiley, E. O. 1978. The evolutionary species concept reconsidered. Syst. Zool. 27:17-26.

Williams, D. and B. Bal. 2003. Papuan Taipan envenomation in rural Papua New Guinea. Annals of ACTM 4:1:6-9

Williams, E. E. 1989. Old problems and new opportunities in West Indian biogeography. Pp. 1-46. In: C. A. Woods (ed.), Biogeography of the West Indies, past, present and future. Gainesville, FL. Sandhill Crane Press.

Worrell,E. 1970. Reptiles of Australia, 2nd ed. Angus & Robertson, Sydney: xv + 169 pp.

Yarleque, A. S. Campos, E. Escobar, F. Lazo, N. Sanchez, S. Hyslop, N. A. Marsh, P. J. Butterworth and R. G. Price. 1989. Isolation and characterization of a fibrinogen-clotting enzyme from venom of the snake Lachesis muta muta (Peruvian bushmaster). Toxicon 27(11):1189-1197.

Young, B. A. 1991. Morphological basis of "growling" in the king cobra, *Ophiophagus hannah*. J. Exp. Zool. 260:275-87.

Zamudio, K. R. and H. W. Greene. 1997. Phylogeography of the bushmaster (Lachesis muta: Viperidae): Implications for neotropical biogeography, systematics, and conservation. Biol. J. of Linnean Soc. 62:421-44.

Zamudio, K. R., D. L. Hardy, Sr., M. Martins, and H. W. Greene. 2000. Fang tip spread, puncture distance, and suction for snake bite. Toxicon 38: 723-728.