The Enigma of the North Margin of the Amazon River: Proven *Lachesis* Bites in Brazil, Report of Two Cases, General Considerations about the Genus and Bibliographic Review

Rodrigo C. G. de Souza¹, Ana Paula Bhering Nogueira², Tiago Lima³ and João Luiz C. Cardoso⁴

Abstract

Confirmed snakebite accidents involving *Lachesis* vipers (bushmasters, or *surucucu*) are rare in the literature. We present two cases that occurred recently in the southern region of Bahia State, Brazil. These two cases were singled out of a series of nine accidents. Both presented intense local pain, edema, mild local ecchymosis, local hemorrhage and dramatic systemic alterations within the first 30 minutes after the bite: hypotension, vomiting and diarrhea, sinus bradycardia configuring a pre-shock state. Both patients were treated with antivenom within 60 minutes of the accident: one received 20 I.V. vials of Bothropic-Lachetic Antivenom (BLA—Butantan Institute) and the other received 10 I.V. vials of BLA. Both patients recovered fully. Few laboratory tests were made and both snakes were positively identified. Accidents in the north margin of the Amazon River seem to present different signs and symptoms. The objective of this case report is to contribute to a better understanding of these envenomings and of the genus as a whole, aiming at early diagnosis and treatment of *Lachesis* snakebites.

Keywords: Lachesis, bushmaster, snakebite, case report, poisoning.

Introduction

Proven Lachesis-inflicted accidents are rare in scientific literature while, on the other hand, the genus is given almost mythological status by common folk. According to the Villas-Boas brothers (indigenists and field men, who dedicated most of their lives to making first contact, in the late '40s, with previously unknown Indian tribes in the Amazon where the "white man" had never set foot before), "[Lachesis] is the only venomous snake of Brazil that might actually attack a human being" (Villas Boas and Villas Boas, 1994). In the ancient Tupi-Guarani Indian language, surucucu stands for "one who strikes repeatedly" (Silveira Bueno, 1982). Exploratory expeditions to South America such as those carried on by Von Spix and Von Martius (1817–1820) brought back to Europe weird, exaggerated accounts of huge snakes attacking campfires, for instance that by John Manley (1851), shown in Figure 1.

Those who actually deal with *Lachesis* on a daily basis, find it of "calm disposition and delicate constitution" (Boyer et al., 1989). However, when cornered, wounded, thermally disoriented or guarding eggs, the genus may react in a very particular way. In the words of the experienced Rob Carmichael (pers. com.):

As far as safety goes, I never work with these snakes unless I am 100% focused and alert. I keep many elapids (including king cobras), *Bothrops*, crotalines, etc. but nothing strikes more concern in me than these bushmasters. I fully know that a bite could end my life, which is why when I work with the bushmasters, I don't work with any other snake that day.... I want to make sure that I am ready, focused, relaxed and ready for anything. So far, I have found the bushmasters to be amazingly calm and wonderful ani-

mals; however, I also have experienced first hand the full wrath of this species. . . . Even a 16' king cobra coming full steam at me didn't scare me as much as an 8' bushmaster in full "I want to kill you" mode did a year ago. It made me completely rethink my strategies and safety procedures when working with them. But, for the most part, they have been very easygoing and I think staying calm, deliberate, keeping movements slow and always working on the bushmaster's terms is the best course of action.

This dauntless behavior, its almost mythical status and even

Snake's Antipathy to Fire. - There is in Brazil a very common poisonous snake, the Surucucu (Trigonocephalus rhombeatus), respecting which the Matutos and Sertanejos, the inhabitants of the interior, relate the following facts. They say that such is the antipathy of this reptile to fire, that when fires are made in the clearing away of woods, they rush into it, scattering it with their tails till it is extinguished, even becoming half roasted in the attempt; and that when an individual is passing at night with a torch, they pass and reposs him, lashing him with their tales till he drop it, and the snake is immediately found closely coiled round the extinguished torch. The greatest enemy of this snake is an immense Lacertian, five and six feet long, the Tiju-acu (the great lizard-its name in the Lingoa geral): it is said that when the snake succeeds in effecting a bite, the lizard rushes into the wood, eats some herb, and returns to the confliet, which almost invariably terminates in its JOHN MANLEY. favour.

Figure 1. Note published in London in 1851 reporting the alleged "Antipathy to fire" of *Lachesis*.

Pernambuco, June 30. 1851.

^{1.} Itacaré Medical Foundation, Itacaré, Bahia State, Brazil.

^{2.} Physician, Municipality of Itacaré, Bahia State, Brazil.

^{3.} Biologist, Belo Horizonte, Minas Gerais State, Brazil.

^{4.} Corresponding author: Hospital Vital Brazil—Butantan Institute, Av. Vital Brazil 1500, 05503.900, São Paulo / SP, Brazil. jlcardoso@butantan.gov.br

religious associations with "the evil one" fuel the ongoing slaughter of the species. In the case of the Atlantic bushmaster (*Lachesis muta rhombeata*), the destruction of 93% of its natural habitat makes it a highly endangered species, classified as "Vulnerable" by the International Union for the Conservation of Nature.

Case Reports

In six years in the region of Ilhéus, Bahia State, Brazil, we have positively identified eight accidents as caused by *Lachesis*, the most recent on 21 January 2007 and 28 February 2007. A ninth accident took place just before our arrival in the region and resulted in the almost instant death of J.A.D., a 7-year-old boy, who went out of his impoverished house at night to pee, stepped on an animal and was bitten more than once according to the family.

If there is venom inoculation, the first 60 minutes of these accidents are always dramatic and similar to the evolution of hypovolemic shock: severe hypotension may occur within 20 minutes, along with hypothermia as low as 35°C, vomiting, diarrhea, abdominal pain, difficulty swallowing, sensorial disorientation, sinus bradycardia, and eventually shock and cardiac arrest. Although these signs and symptoms are the norm in our experience, a literature review revealed no general agreement about them. This can be explained at least in part by the difficulty in determining what genus actually caused the accident (Hardy and Silva Haad, 1998), especially in the Amazon area where large Bothrops atrox (Linnaeus, 1758) are commonly confused with (small) Lachesis specimens. Of the eight above-mentioned cases, we chose to report only two, in which the animals are still alive, positively identified and photographed.

Case 1:

T.L., professional herpetologist and biologist, male, 23 years old, healthy, 140 pounds, was bitten on the top of his head by a 2.0 m male *Lachesis* at 11:40 on 27 May 2005 while working with de Souza in the Serra Grande Center:

Sequence of events from 27 May 2005, 11:40 A.M. on:

Time snce bite (hrs:mins)	Signs and symptoms	Medication
00:05	Severe local pain.	
00:10	Pain in the entire face, throat and neck.	
00:15	Profuse sweating; upper abdominal pain; vomiting.	

00:20	Hypotension; weak pulse; sinus bradycardia; pale; profuse sweating; pre-shock. Drowsy; vision, hearing and speech alterations; hypersalivation; great difficulty swallowing.	In the car, en route to hospital, began infusion of saline solution, atropine, metoclopramide and dopamine.
00:40	Not rousable, carried to the ICU of Regional Hospital, Ilháus, Bahia. Watery diarrhea. Blood pressure upon admission at 60 × 40 mm Hg.	Infusion of 1000 ml of saline solution up to this point.
00:45	Preparation for antivenom therapy. See Observation 1 below.	Promethazine, hydrocortisone.
00:55		12 I.V. vials of Bothropic-Lachet- ic Antivenom diluted in SGI 5% + another 500 ml of saline solution 0.9%.
01:00	Intense pain. Coagulation time > 30 min.	Meperidine 40 mg I.M. Check Ob- servation 2 below.
02:00	End of antivenom infusion. Drowsy. Profuse bleeding at the wound site. Figure 2b.	
02:06	Blood pressure at 100 × 60 mm Hg.	Fifth 500 ml of saline solution.
02:10	Local pain even with meperidine. Profuse bleeding at the inoculation site. Pain in knee joints.	

	1	T
02:20	Vagomimetic symptoms still present. Recovering consciousness.	
02:27	Intense diffuse head pain. Diarrhea, drowsiness, vomiting.	
03:12	Profuse local bleeding persists.	
03:25	Blood pressure at 90 × 40 mm Hg.	
03:36	Protection of gastric mucosa against bleeding (vomiting, stress).	Omeprazol
04:11	Blood pressure at 90 × 60 mm Hg	Sixth 500 ml saline solution I.V. infusion.
04:22	Urinary debt at zero ml.	
04:24	Coagulation of bleeding at the wound site. Figure 2c. (scale in cm)	
04:25	Urinary debt + (sui generis)	
12:20	Stable.	
	00:00 / 28 May 2005	
14:55	Blood pressure at 80 × 40 mm Hg.	
15:20	Blood pressure at 90 × 50 mm Hg.	
18:20	Blood pressure at 60 × 30 mm Hg.	Additional 8 I.V. vials of Bothropic- Lachetic Anti- venom (Butantan)
20:40	Normal renal function biochemistry.	

29:20	Edema extending from left eye to back portion of head and neck.	
	Figure 2d.	
31:20	Hemodynamically stable all day long; normal macroscopic aspect of urine. No bleeding at wound site. Mild local ecchymosis on face and right	
	arm.	
31:25	Gastrointestinal bleeding (melaena) without hemodynamic repercussion.	
36:20	Stable; vital signs within normal parameters.	
00:00 / 29 May 2005		
48:20	Hemodynamically stable with normal kidney function biochemistry.	
Hospital discharge		

Observations:

- "Preparation for antivenom therapy" according to Handbook for Diagnosis and Treatment of Accidents with Poisonous Animals [1998. Brasília: Health Ministry, National Health Foundation]. It should be stressed however, that Bucaretchi et al. (2002) have demonstrated that this routine is not only inefficient but potentially harmful.
- 2. The use of meperidine may aggravate the vagomimetic symptomatology and cause respiratory depression, requiring extra care if it is used for pain control.
- 3. Vomiting did not become a major problem/symptom due to early administration of metoclopramide, 10 minutes after the bite.

Late biochemistry (4-7 days after the accident, performed in Belo Horizonte, Minas Gerais State) indicated consumption of coagulation factors on the occasion of the accident and a slow recovery in the following days.

Ambulatory Follow-up for 21 days (D1-D21)

	1 1
D4 (1 June)	Blood urea 43 mg/dl; serum creatinine 1.0 mg/dl Total CK: 65 units/l C-reactive protein: 2.6 mg/dl Prothrombin time (quick): 18.6 seconds Prothrombin activity: 56%
D6 (3 June)	Platelet count: 251,000 / mm³ Prothrombin time: 15.4 seconds Prothrombin activity: 71%
D15-D21	"Serum disease": fever, dermatitis, painful knee/elbow joints, jaundice + + /4+ Stomach ache Fully recovered at D30

This is the only available blood chemistry. During this patient's treatment, only coagulation time (CT) tests were performed (> 30 min, always). Most Brazilian hospitals of the public health system (SUS) are poor and lack just about everything. However, whenever possible, one should rely on exams such as a complete hemogram (neutrophil leukocytosis, hematocrit may rise in the early stages due to hemoconcentration because of increased permeability of capillaries). Later on, the hematocrit falls due to bleeding in the interstitial space. Other essential exams are: INR, prothrombin time, FDP, renal function and continuous cardiac monitoring as well. As to late symptoms, articular pain was the most noticeable, along with great difficulty swallowing solid food due to gastritis.

Case 2:

Patient J.A.S., male, 49 years old, professional herp keeper at CEPLAC, a federal agency for cocoa research, was bitten in the medial third of the left forearm on 2 October 2006 at 8:30 A.M. by a two-meter male *Lachesis* fed 15 days before. Upon clinical examination, only one inoculation point was found.

J.A.S. suffers from high blood pressure and is under regular medication, but on that specific morning he reports to have forgotten to take his 25 mg of Captopril—this might have saved his life.

The first symptom was severe pain, and the patient immediately drove his car for 20 minutes to a nearby hospital, where he arrived "at the limit of his strength." Upon admission, systolic blood pressure was 70 mm Hg with no detectable diastolic blood pressure. The patient also presented intense sweating, diarrhea, upper abdominal pain and great difficulty swallowing.

Infusions of saline solution 0.9% + metoclopramide + 10 I.V. vials of Bothropic-Lachetic Antivenom (BLA — Butantan) were simultaneously administered. Coagulation time could not be measured (over 30 minutes) and remained like that for the next 24 hours, during which he had a compressive bandage around the wound site. The patient developed a moderate systemic reaction to the antivenom (see Figure 3). After 24 hours of hospitalization, blood pressure stabilized, bleeding at the inoculation point stopped, urinary debt was over 40 ml/hour

with normal macroscopic aspect. Therefore, after another two days under observation, he was discharged for an ambulatory follow-up. The left arm remained sore for two weeks.



Figure 3. J.A.S. back to work 14 days after the accident, handling the same animal involved in the accident.

Discussion

All confirmed accidents by Lachesis should be considered life-threatening since even mere scratches, one fang inoculations and accidents with babies or youngsters (Ripa, 2002), characterized by small amounts of poison delivered may still provoke early systemic symptoms, something we do not observe in the sympatric Bothrops genus, where the size of the animal is the most important prognostic factor: bigger animal = more venom = more damage (Ribeiro and Jorge, 1989). By saying this, we do not intend to affirm that the amount of venom delivered is unimportant for the clinical evolution, since in vitro, the neurotoxic action of the venom is dose-dependant. On the other hand, based on our experience, we infer the existence of a "Minimum Activating Dose" (M.A.D.) which triggers all symptomatology. It is worth noticing that this "M.A.D." is way below the 400 mg potentially delivered by adult bushmasters.

Regarding the biochemistry of *Lachesis* venom, the following activities have been described:

- Plasminogen activation, which increases the permeability of blood vessels, promoting edema and indirectly helping to lower blood pressure since large amounts of plasma may be lost from the vascular compartment (Sánchez et al., 2000; Hermogenes et al., 2006).
- Coagulant activity, where toxins such as the so-called "thrombin-like" enzymes act upon the fibrinogen, forming small clots that will be deposited in organs like kidneys and lungs, and eventually obstruct capillary blood flow (Magalhães and Diniz, 1979; Magalhães et al., 1973, 1981, 1997, 2003).

- Hemorrhagic activity, caused by metalloproteinases commonly called hemorrhagines, which directly damage capillary walls. The hemorrhagic and coagulant activities overlap each other and will trigger local and systemic hemorrhagic disorders (Rucavado et al., 1999; Estêvão-Costa, Diniz et al., 2000; Estêvão-Costa, Martins et al., 2000; Sánchez et al., 2003).
- Inflammatory action, mostly due to thrombin-like serine proteinases, phospholipase A₂ (PLA₂), metalloproteinases, histamine, serotonin, nitric oxide, by-products of the metabolism of the arachidonic acid, leukocyte recruitment and release of cytokines, and lymphoedema. Activities (A) and (C) are also important actors in this process. We believe that the immune system also plays a major part here, bringing to the wound site activated macrophages, oxygen radicals, gamma interferon, tumor necrosis factor among other "big guns" (Silva et al., 1985; Warrell, 1989; Soares et al., 2005).
- Proteolytic activivity, due to direct action of proteases (thrombins in particular), metalloproteinases, important myotoxic and cytolytic venom factors. Necrosis may be aggravated by ischemia due to thromboembolic alterations, by possible tourniquet use or by compartment syndrome (unlikely in *Lachesis* bites). Proteolytic action is seldom seen if specific antivenom is administrated within the third hour of the accident (Otero et al., 1998).
- Myotoxic action, due to the action of PLA₂s among other enzymes, generating an inflammatory infiltrate composed of polymorphonuclear leukocytes and macrophages, found around necrotic cells and in the interstitial space. Inexperienced surgeons may easily confuse the deposition of hemorrhagic debris over the muscle with direct myotoxic effects on the muscles (necrosis) but, given the chance to act due to delayed treatment or insufficient neutralization, the PLA₂s will induce necrosis of skeletal muscle fibers (Otero et al., 1998; Fuly et al., 2000; Damico et al., 2005).
- Defibrinating activity, resulting in incoagulability, a consumption coagulopathy (of factors II, VIII, IX and X, with normal platelet counts) that also occurs because of the direct action of thrombin on fibrinogen, and because several proteins with enzymatic activity such as PLA₂ and proteinases inhibit blood clotting (Yarlequé et al., 1989; Otero et al., 1998; Estêvão-Costa et al., 2000).
- Indirect hemolytic activity, thus called (indirect) because lectins mediate the process. Direct hemolysis is observed in some bee and elapid envenomings, with direct destruction of the cell wall (Otero et al., 1998; Silva Haad, 1982).
- "Kininogen-like" action, auto-pharmacological in nature since the venom will make the body release substances like bradykinin and kallikrein that will induce hypotension (Diniz and Oliveira, 1992; Giovanni-De-Simone et al., 1997, Felicori et al., 2003, 2005; Weinberg et al., 2004).
- Action of bradykinin-potentiating peptides that interfere with the metabolism of bradykinin, making it last longer in the blood, contributing to a longer lasting hypotension (Soares et al., 2005).
- · Neurotoxic action, recently described and based on the

isolation of the basic PLA_2 , since its purified form from *Lachesis* venom called LmTX-1 induced an irreversible block in neuromuscular transmission in vitro, in concentrations as low as 1 mg/ml (Damico et al., 2005, 2006)

We believe that the so-called "activation of the parasympathetic autonomous nervous system" can be considered partly neurotoxic in nature, with kinins (Silva Haad, 1982) and phospholipases playing a major role. Therefore, in *Lachesis*, the abnormally quick shock onset seems best explained by a synergy hypothesis, in which neurotoxicity, vasodilatation and leaks to interstitial space independently play a part.

One can only speculate as to the causative factors of specific clinical alterations such as dysphagia or the "vagal triad" (hypotension, diarrhea, vomiting—and why not, a fourth element: sinus bradycardia) or sensorial disorders (to colors, deafness, uncoordinated march) that will take place within 30–45 minutes after a bushmaster bite in Brazil, BUT it is not speculation to affirm that these clinical features can be considered pathognomonic of the genus that caused the accident, as noted by Jorge et al. (1997):

A review of reports of 20 cases of bites in humans reliably attributed to this snake [*Lachesis*] in Costa Rica, French Guyana, Brazil, Colombia and Venezuela confirms a syndrome of nausea, vomiting, abdominal colic, diarrhea, sweating, hypotension, bradycardia and shock, possibly auto-pharmacological or autonomic in origin, not seen in victims of other American crotaline snakes.

Bothropic accidents may lead to shock and hypotension and even death within one hour of inoculation, but such events are rare (Cardoso et al., 2003; Silva Haad, 1982). Statistics of a major ER (H.P.S João XXIII) in Belo Horizonte, Brazil, show that only 5% of all bothropic accidents present hemodynamic alterations such as blood pressure drops upon admission (Cecilia Haddad, pers. com.). A series of 29 accidents involving Bothrops jararacussu (Lacerda, 1884), normally the worst bothropic accident, presented two (6.8%) hemodynamically unstable patients (Milani et al., 1997). Therefore, hemodynamic repercussion as well as all morbidity in the bothropic accident is dose-dependent. It isn't so in Lachesis, probably due to the combination of factors described above. As long as at least the "M.A.D." is inoculated, the synergy of effects will produce major blood pressure drops in humans with unsurpassed speed.

Our observations about how dangerous these intoxications may be in humans are in agreement with recent accidents with North American herpetologists and also with a series presented by Bolaños et al. (1982) where three of four patients died, even with early (but insufficient) antivenom therapy (Ripa, 2002; Bolaños et al., 1982). Adult *Lachesis* may reach or exceed 3.40 m TL (Ditmars, 1933; Campbell and Lamar, 2004) and according to Bolaños (1972), can inoculate 333 mg or more of venom, but although there are usually great amounts of toxins to be neutralized, the severity of the symptoms is not necessarily related to the amount of venom injected. The unique, doseindependent body response to the overwhelming synergy, which includes direct actions of the poison, auto-pharmacological events and individual characteristics, something also noted by another author-victim (Ripa, 2002), can be taken as a stand-

point for further studies on the fundamentals of the "M.A.D." concept.

The present work diverges from that presented by Bührnheim, Souza and others (Sá Neto, 1995; Souza and Bührnheim, 1999), in which they report that only 15% of Lachesis accidents in the Manaus area (Amazonas State) present the "vagal triad" as a clinical feature. Their statistic may be due to: (1) inclusion of dry bites in their series ("only about 50% of people bitten by venomous snakes are actually envenomed" [Warrell, 1989]); (2) wrong information from patients (common) as to which animal caused the accident; (3) wrong classification by M.D.s (common) of the snake brought to the hospital; (4) mistakes in the application/interpretation of ELISA tests. Or maybe the clinical practice of the M.D.s working on the north margin of the Amazon river is revealing a totally different pattern of venom action when compared to the Atlantic coast and north of Mato Grosso State envenomings. Therein lies the enigma of the "north margin."

Only accidents by Lachesis acrochorda (Garcia, 1896) in Colombia should present low or no "vagal symptomatology" (Warrell, 2004), but Silva Haad (1982) and Hardy and Silva Haad (1998) presented three cases from Colombia in which the "triad" was observed. It has been experimentally proven that samples of venom from Brazil, Costa Rica, and Colombia did display toxic and enzymatic differences (Hardy and Silva Haad, 1998; Otero et al., 1998), but all induced a qualitatively similar pathophysiological profile in vitro (Otero et al., 1998). We will comment further down (see map below) on clinical variations in Lachesis accidents in humans as described by Warrell (2004), keeping Silva Haad and Hardy in mind: that "we are not mice." Maybe the observations (85% absence of "vagal symptoms") of our colleagues of the "north margin" will also fit in Warrell's observations, since the venom does present variations within populations, seasons, age of the animals (Gutiérrez et al., 1990), and that can also lead to wrong readings of ELISA tests. Coincidentally, Ripa in his latest work proposed the extension of the range distribution of Lachesis muta rhombeata to the entire forest south of the Amazon river, not just the Atlantic coast (Ripa, 2002).

Our position is clear: a snakebite in Brazil, or at least south of the Amazon river and in the Atlantic rainforest, without extreme and immediate local pain and edema and without early (20 minutes) gastrointestinal (diarrhea, vomiting) and cardio-vascular (hypotension) repercussion, is not a *Lachesis* bite. There is no such thing as "walk for two days for help," "deny local pain" or "refuse hospitalization" if you have been bitten by a *surucucu* (and had venom injected). In one accident in Serra Grande, Bahia, 21 January 2007, "N.R." was knocked out by hypotension and could not make the 40-minute walk to town to get help, being saved by his wife who rushed for an ambulance right after killing the snake, extracting its tongue and forcing the husband to swallow it as an "antidote."

Such "treatments" should be viewed as acts of despair due to the abandonment by the public health system (until very recently) of geographically isolated populations. However, we've also collected in the region ethnobotanic approaches, such as "graviola tea" (*Anonna muricatta*), which is now being

tested for possible anti-emetic and/or vasoactive properties.

In Serra Grande, we carry a kit of ampoules and syringes, ethylepinephrine cloridrate, adrenaline, atropine, meto-clopramide for I.M. use and also saline solution for I.V. use; working in pairs (at least) is essential. In Case 1, "T.L." was no longer capable of making a phone call within 15 minutes after the bite.

The field administration of antivenom must take into consideration the impossibility of quick rescue and the feasibility of controlling eventual reactions with limited resources. Alternating (12-20 vials of 10 ml ampoules) I.M. and I.V. administration to intentionally delay absorption for safety reasons (Pépin et al, 1995; Rivière et al., 1997) does not prevent the onset of complications such as major exanthema and bronchospasm, so it is wise to be ready for these medical emergencies. Allergy tests have been shown to be ineffective (Warrell, 1989). As soon as the patient makes it to the nearest hospital, signs and symptoms such as blood pressure drops, bleeding at the wound site, or the "triad" will reveal the need for more antivenom, "better late than sorry." If no such signs are present and the patient can be considered hemodynamically stable with proper urinary debt, it is time to face other complications, edema being one of them.

Fasciotomies seem to have no indication in *Lachesis* bites. In Brazil, the concept of Compartment Syndrome (CS), an event of the first 24 hours, is still plagued with empiricism. Statistics from Vital Brazil Hospital (França and Cardoso, 1989; Pereira, 1989) show that CS was observed in only 1.4% of all *Bothrops* accidents, locally more aggressive than *Lachesis*. Precise indication could avoid further exfoliation, blood loss, risk of infection, longer hospitalization time, and expenses. The "usually disappointing" (Warrell, 1989) results of fasciotomies can be explained, at least in part, by the lack of reliable parameters upon which the decision has to be made (compartmental pressure above 45 mm Hg and doppler revealing obstruction to blood flow), and to the fact that muscle swelling and necrosis can be attributed to direct action of venom injected in the area.

The possibility of late blood pressure drops, bleeding to the digestive system and reaction to antivenom therapy demands inhospital observation for 48–72 hours and ambulatory follow-up for the next 30 days. Infection in the wound site can turn into a major complication if deep fascial progression is undetected below normal looking skin. Common agents are: D group streptococcus, *Enterobacter* sp., *Providencia rettgeri*, *Providencia* sp., *Escherichia coli*, *Morganella morganii*, *Clostridium* sp., *Aeromonas hydrophila*, *Proteus mirabilis*, *Acinetobacter alcoaceticum*, *Pseudomonas aeruginosa* and *Klebsiela pneumonae* (Bolaños et al., 1982; de Andrade et al., 1989; Jorge et al., 1990).

Close attention also must be paid to "serum disease" around the 20th day (sore joints, fever, dermatitis), mesenteric thrombosis (Rosenthal et al., 2002) and intracranial bleeding (Eric Jennings, pers. com.) that can be of early (first 24 hours) or late (fifth day) onset (see Figures 4 and 5).

It is important to remember that the dosages of antivenom



Figure 4. Intracranial bleeding 24 hours after a *Lachesis* bite, causing the death of a 23-year-old man. Accident near Santarém, Pará State, in 2003. (Courtesy Dr. Eric Jennings)

are the same in children as in adults, and that antibothropic antivenom will not neutralize the coagulant factor of *Lachesis* venom, so its use is not recommended (Bard et al., 1994). Heparin has also no indication in *Lachesis* bites.

Conclusion

Lachesis bites should be considered medical emergencies, regardless of the size of the animal. In Brazil, they can happen anywhere in the Brazilian Atlantic rainforest remnants, from Rio de Janeiro State up to Rio Grande do Norte State, parts of Ceará State (Feitosa et al., 1997; Freitas and Silvia, 2005), possibly in "Parque do Rio Doce" or "Zona da Mata" in Minas Gerais State and in the Amazon region as a whole. The animal is highly dependent upon and adapted to unspoiled rainforest at medium altitude (high humidity and low temperatures).

From a medical standpoint, the academic discussion as to whether *Lachesis* should maintain its subspecific differentiation (Ripa, 2002) or should be considered as two populations of the same species (Fernandes et al., 2004) is irrelevant. The present edition of rules of the *International Code of Zoological Nomenclature* (Fourth Edition, ISBN 053301-006-4) maintains the trinominal status (subspecies), but it's true that the concept of subspecies in herpetology is highly questionable.

It is of great medical importance however, to keep in mind that the venoms of both populations (coastal and Amazonian) are similar (Otero et al., 1998) and the clinical features in intoxications should also be similar. However, important variations such as local effects and central nervous system activation have been described (Warrell, 2004). The venom of the Amazonian animal has greater hemorrhagic activity, whereas the venom of the Atlantic Rainforest animal has greater



Figure 5. Intracranial bleeding in a 57-year-old man 5 days after a *Lachesis* bite; the patient survived neurosurgery. We do not know of any other cases where the patient survived intracranial bleeding in ophidism, wordlwide. Great and historical job by Dr. Jennings, again near Santarém, Pará State in 2003. (Courtesy Dr. Eric Jennings)

coagulant activity (Otero et al., 1998). It is not clear at this point, how these differences fit in the puzzle of the "north margin" enigma.

Those who venture into *Lachesis* territory should recognize the risk, and work in pairs with a predetermined evacuation plan. In remote areas they should carry an emergency kit similar to the one used in Serra Grande, and know how to use it in to avoid early and severe hypotension and to allow oral intake of liquids or medication (blocking vomiting) while on the way to the nearest hospital.

Until a lyophilized version for human use reaches the Brazilian market, refrigeration at 3-8°C and respect to expiration dates insure antivenom effectiveness when needed. A well-planned distribution among major towns will help avoid the tragic costs of late treatment: death, suffering and monetary costs. In our series, efficient distribution meant eight lives saved without any permanent handicap. Expense considerations also lead us to affirm that tests such as ELISA are recommended but not necessary to differentiate *Lachesis* accidents from the others.

The statistical frequency of snakebite incidents in the Amazon region, 76% *Bothrops* and 17% *Lachesis* (Bard et al., 1994), indicates that the obvious antivenom to be distributed (and carried around) in these areas is the highly effective (Pardal et al., 2004) Bothropic-Lachetic Antivenom (BLA) but

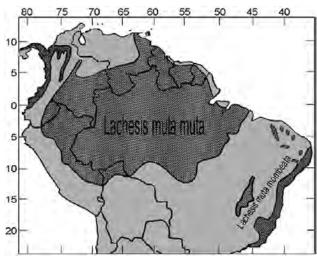


Figure 6. Dark areas denote Lachesis Territory.

attending physicians in ERs in the darker areas of the map above should keep in mind that *Crotalus* is also present in the Amazon and in some coastal biomes of Atlantic Rainforest ("restingas") in Piauí State (Freitas and Sylvia, 2005), and that *Micrurus* too (some without the red rings) share the well preserved forest with *Lachesis* and *Bothrops*.

Notification of snakebites is compulsory in Brazil, but most of our statistics remain unreliable due to undernotification, general ignorance about such accidents, and work overload in underequipped and understaffed ERs, all of which might contribute to poor planning in the distribution of BLA throughout the vast Brazilian territory. A good example of such unreliable statistics is an old review of medical records in the Ilhéus area that points to *Lachesis* bites as being about 0.5% of all venomous snakebites. *Lachesis* bites are uncommon due to the ecobiology of the animal and its usually calm disposition. Nevertheless, as noted by Bard et al. (1994) and in the present work, they are not so rare as 0.5%.



Figure 7. Baby Atlantic *surucucu*, Núcleo Serra Grande, in Itacaré, Bahia State, Brazil (see de Souza, 2007).

While we watch in real time the burning down of the Amazon and the progressive destruction of the remaining 7% of the Atlantic Rainforest, signaling a dire future of *Lachesis* in the wild, isolated actions such as the Serra Grande breeding center try to compensate the damage already done via programs that may generate animals for antivenom production, reintroduction of animals to their native habitat and advanced pharmacological research.

Acknowledgments

To Dr. Ronaldo Souza, our greatest inspiring and driving force in this article. To Drs. Daniela Damico from UNICAMP and Fatima Furtado from Butantan Institute, for the deep insights into the biochemistry of *Lachesis* venom. To Dr. Cecilia Haddad, for sharing her experience in the Toxinology Department of "H.P.S João XXIII-BH-MG," one of our major ERs. To Paulo de Tarso, director of YONIC, a non-governmental organization that has financed the Serra Grande Center.

Literature Cited

Bard, R., J. C. R. de Lima, R. P. de Sá Neto, S. G. de Oliveira and M. C. dos Santos. 1994. Ineficácia do antiveneno botrópico na neutralização da atividade coagulante do veneno de *Lachesis muta muta*. Relato de caso e comprovação experimental. Revista do Instituto de Medicina Tropical de São Paulo 36(1):77-81.

Bolaños, R. 1972. Toxicity of Costa Rican snake venoms for the white mouse. Amer. J. Trop. Med. Hyg. 21(3):360-363.

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. Revista de Biología Tropical 30(1):53-58.

Boyer, D. M., L. A. Mitchell and J. B. Murphy. 1989. Reproduction and husbandry of the bushmaster *Lachesis m. muta* at the Dallas Zoo. Int'l Zoo Yrbk. 28:190-194.

Bucaretchi, F., S. R. F. Herrera, S. Hyslop, E. C. E. Baracat and R. J. Vieira. 2002. Snakebites by *Crotalus durissus* ssp. in children in Campinas, São Paulo, Brazil. Revista do Instituto de Medicina Tropical de São Paulo 44(3):133-138.

Campbell, J. A., and W. W. Lamar. 2004. The venomous reptiles of the Western Hemisphere, Volume II. Ithaca, New York: Cornell University Press.

Cardoso, J. L. C., F. O. S. França, F. H. Wen, C. M. S. Málaque and V. Haddad, Jr. 2003. Animais peçonhentos no Brasil: Biologia, clínica e terapêutica dos acidentes. São Paulo: Servier / FAPESP.

- Damico, D. C., L. G. Bueno, L. Rodrigues-Simioni, S. Marangoni, M. A. da Cruz-Höfling and J. C. Novello. 2005. Neurotoxic and myotoxic actions from *Lachesis muta muta* (surucucu) whole venom on the mouse and chick nerve-muscle preparations. Toxicon 46(2):222-229, 2005.
- Damico, D. C., L. G. Bueno, L. Rodrigues-Simioni, S. Marangoni, M. A. da Cruz-Höfling and J. C. Novello. 2006. Functional characterization of a basic D49 phospholipase A₂ (LmTX-I) from the venom of the snake *Lachesis muta muta* (bushmaster). Toxicon 47(7):759-765.
- de Andrade, J. G., R. N. Pinto, A. L. de Andrade, C. M. Martelli and F. Zicker. 1989. Estudo bacteriológico de abscessos causados por picada de serpente do gênero *Bothrops*. Revista do Instituto de Medicina Tropical de São Paulo 31(6):363-367.
- de Souza, R. C. G. 2007. Reproduction of the Atlantic bushmaster (*Lachesis muta rhombeata*) for the first time in captivity. Bull. Chicago Herp. Soc. 42(3):41-43.
- Diniz, M. R. V., and E. B. Oliveira. 1992. Purification and properties of a kininogenin from the venon of *Lachesis muta* (bushmaster). Toxicon 30(3):247-258.
- Ditmars, R. L. 1933. Reptiles of the world (revised edition). New York: Macmillan Company.
- Estêvão-Costa, M. I., C. R. Diniz, A. Magalhães, F. S. Markland and E. F. Sánchez. 2000. Action of metalloproteinases mutalysin I and II on several components of the hemostatic and fibrinolytic systems. Thrombosis Research 99(4):363-376.
- Estêvão-Costa, M. I., M. S. Martins, E. F. Sánchez, C. R. Diniz and C. Chávez-Olórtegui. 2000. Neutralization of the hemorrhagic activity of *Bothrops* and *Lachesis* snake venoms by a monoclonal antibody against mutalysin-II. Toxicon 38(1):139-144.
- Feitosa, R. F. G., I. M. L. A. Melo and H. S. A. Monteiro. 1997. Epidemiologia dos acidentes por serpentes peçonhentas no estado do Ceará Brasil. Revista da Sociedade Brasileira de Medicina Tropical 30(4):295-301.
- Felicori, L. F., C. Chávez-Olórtegui and E. F. Sánchez. 2005. Specific identification of *Lachesis muta muta* snake venom using antibodies against the plasminogen activator enzyme, LV-PA. Toxicon 45(6):803-806.
- Felicori, L. F., C. T. Souza, D. T. Velarde, A. Magalhães, A. P. Almeida, S. Figueiredo, M. Richardson, C. R. Diniz, and E. F. Sánchez. 2003. Kallikrein-like proteinase from bushmaster snake venom. Protein Expression and Purification 30(1):32-42.
- Fernandes, D. S., F. L. Franco and R. Fernandes. 2004. Systematic revision of the Genus *Lachesis* Daudin, 1803 (Serpentes, Viperidae). Herpetologica 60(2):245-260.
- França, F. O. S., and J. L. C. Cardoso. 1989. Estudo retrospectivo da evolução dos acidentes botrópicos. Revista do Instituto de Medicina Tropical de São Paulo 31(2):84-90.
- Freitas, M. A. F., and T. F. S. Silvia. 2005. A herpetofauna da mata Atlântica nordestina (coleção Manuais de Campo USEB, vol. 6) Pelotas USEB.
- Fuly, A. L., S. Calil-Elias, R. B. Zingali, J. A. Guimarães and P. A. Melo. 2000. Myotoxic activities of an acidic phospholipoase A₂, isolated from *Lachesis muta* (bushmaster) snake venom. Toxicon 38(7):961-972.
- 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 a kallikrein-liks enzyme from the venom of *Lachesis muta rhombeata* (bushmaster). J. Protein Chem. 16(8):809-818.
- Gutiérrez, J. M., C. Avila, Z. Camacho and B. Lomonte. 1990. Ontogenetic changes in the venom of the snake *Lachesis muta stenophrys* (bushmaster) from Costa Rica. Toxicon 28(4):419-426.
- Hardy, D. L., Sr., and J. J. Silva Haad. 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.
- Hermogenes, A. L., M. Richardson, A. Magalhães, A. Yarlequé, E. Rodriguez and E. F. Sánchez. 2006. Interaction of a plasminogen activator proteinase, LV-PA with human α2-macroglobulin. Toxicon 47(4):490-494.
- Jorge, M. T., J. S. Mendonça, L. A. Ribeiro, M. L. R. Silva, E. J. U. Kusano and C. L. S. Cordeiro. 1990. Flora bacteriana da cavidade oral, presas e veneno de *Bothrops jararaca*: Possível fonte de infecção no local da picada. Revista do Instituto de Medicina Tropical de São Paulo 32(1):6-10.
- 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(4):545-554.
- Magalhães, 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.

- Magalhães, A., R. N. Ferreira, M. Richardson, S. Gontijo, A. Yarlequé, H. P. B. Magalhães, C. Bloch and E. F. Sánchez. 2003. Coagulant thrombin-like enzymes from the venoms of Brazilian and Peruvian bushmaster (*Lachesis muta muta*) snakes. Comp. Biochem. Physiol., Part B, Biochem. Mol. Biol. 136(2):255-266.
- Magalhães, A., M. R. Monteiro, H. P. B. Magalhães, M. Mares-Guia and E Rogana. 1997. Thrombin-like enzyme from *Lachesis muta muta* venom: Isolation and topographical analysis of its active site by means of binding of amidines an guanidines as competitive inhibitors. Toxicon 35(10):1549-1559.
- Magalhães, A., G. J. Oliveira and C. R. Diniz. 1973. Proteases de serpentes brasileiras. I—Separação da enzima coagulante (clotase) de veneno de *Lachesis muta*. Ciéncia e Cultura 25(9):872.
- Magalhães, A., G. J. Oliveira and C. R. Diniz. 1981. Purification and partial characterization of a thrombin-like enzyme from the venom of the bushmaster snake, *Lachesis muta noctivaga*. Toxicon 19(2):279-294.
- Manley, J. 1851. Snake's antipathy to fire. Notes and Queries: A Medium of Inter-communication for Literary Men, Artists, Antiquaries, Genealogists, etc. s1-IV(95):131.
- Milani, R., Jr., M. T. Jorge, F. P. Ferraz de Campos, F. P. Martins, A. Bousso, J. L. C. Cardoso, L. A. Ribeiro, F. H. Wen, F. O. S. França, I. S. Sano-Martins, D. Cardoso, I. de Cássia Oliveira Ferreira Fernandez, J. C. Fernandes, V. L. Aldred, M. P. Sandoval, G. Puorto, R. D. G. Theakston and D. A. Warrell. 1997. Snake bites by the jararacuçu (*Bothrops jararacussu*): Clinicopathological studies of 29 proven cases in São Paulo State, Brazil. Q J Med 90(5):323-34.
- Otero, R., M. de F. D. Furtado, L. R. C. Gonçalves, V. Núñez, M. E. García, R. G. Osorio, M. Romero and J. M. Gutiérrez. 1998. Comparative study of the venoms of three subspecies of *Lachesis muta* (bushmaster) from Brazil, Colombia and Costa Rica. Toxicon 36(12):2021-2027.
- Pardal, P. P. de O., S. M. Souza, M. R. de C. da C. Monteiro, F. H. Wen, J. L. C. Cardoso, F. O. S. França, S. C. Tomy, I. S. Sano-Martins, M. C. C. de Sousa-e-Silva, M. Colombini, N. F. Kodera, A. M. Moura-da-Silva, D. F. Cardoso, D. T. Velarde, A. S. Kamiguti, R. D. G. Theakston and D. A. Warrell. 2004. Clinical trial of two antivenoms for the treatment of *Bothrops* and *Lachesis* bites in the north eastern Amazon region of Brazil. Trans. R. Soc. Trop. Med. Hyg. 98(1):28-42.
- Pépin, S., C. Lutsch, M. Grandgeorge and J.-M. Scherrmann. 1995. Snake F (ab')₂ antivenom from hyperimmunized horse: Pharmacokinetics following intravenous and intramuscular administrations in rabbits. Pharm. Res. 12(10):1470-1473.
- Pereira, P. R. B. 1989. Aspectos da síndrome compartimental induzida no cão por veneno de *Bothrops jararaca*. Tese de doutorado, Universidade de São Paulo.
- Ripa, D. 2002. The bushmasters (genus *Lachesis* Daudin, 1803): Morphology in evolution and behavior. Wilmington, North Carolina: Ripa Ecologica. [CD-ROM].
- Ribeiro, L. A., and M. T. Jorge. 1989. Fatores prognósticos da evolução das manifestações locais em acidentes por serpentes do Gênero *Bothrops*. Revista da Sociedade Brasileira de Medicina Tropical 22 (supl.):68-69.
- Rivière, G., V. Choumet, F. Audebert, A. Sabourand, M. Debray, J.-M. Scherrmann and C. Bonn. 1997. Effect of antivenom on venom pharmacokinetics in experimentally envenomed rabbits: Toward an optimization of antivenom therapy. J. Pharmacology and Experimental Therapeutics 281(1):1-8.
- Rosenthal, R., J. Meier, A. Koelz, C. Müller, W. Wegmann and P. Vogelbach. 2002. Intestinal ischemia after bushmaster (*Lachesis muta*) snakebite a case report. Toxicon 40(2):217-220.
- Rucavado, A., E. F. Sánchez, A. Franceschi, A. Magalhães and J. M. Gutiérrez. 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(9):1297-1312.
- Sá Neto, R. P. de, and M. C. dos Santos. 1995. Aspectos clínicos comparativos dos acidentes botrópico e laquético. Revista da Sociedade Brasileira de Medicina Tropical 28 (supl. I):173.
- Sánchez, E. F., C. L. Santos, A. Magalhães, C. R. Diniz, S. Figueiredo, J. Gilroy and M. Richardson. 2000. Isolation of a proteinase with plasminogen-activating activity from *Lachesis muta muta* (bushmaster) snake venom. Archives of Biochemistry and Biophysics 378(1):131-141.
- Sánchez, E. F., C. T. Souza, C. A. Bello, M. Richardson, E. B. Oliveira and A. Magalhães. 2003. Resolution of isoforms of mutalysin II, the metalloproteinase from bushmaster snake venom; Toxicon 41(8):1021-1031.
- Silva, L. M., C. R. Diniz and A. Magalhães. 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.

- Silva Haad, J. 1982 (1980-81). Accidentes humanos por las serpientes de los géneros *Bothrops* y *Lachesis*. Mem. Inst. Butantan 44/45:403-423.
- Silveira Bueno, F. da. 1986. Vocabulário tupi-guarani Português (4a edição). São Paulo: Editora Brasilivros.
- Soares, M. R., A. L. Oliveira-Carvalho, L. S. Wermelinger, R. B. Zingali, P. L. Ho, I. de L. M. Junqueira-de-Azevedo and M. R. V. Diniz. 2005. Identification of novel bradykinin-potentiating peptides and C-type natriuretic peptide from *Lachesis muta* venom. Toxicon 46(1):31-38.
- Souza, A. R. B., and P. F. Bührnheim. 1999. Dez casos de acidente laquético atendidos no IMT-AM, de 1986 a 1996. Revista da Sociedade Brasileira de Medicina Tropical 32 (supl. I):388-389.
- Vanzolini, P. E. 1977. An annotated bibliography of the land and fresh-water reptiles of South America (1758–1975), Volume I (1758.–1900).
- Villas Bôas, O., and C. Villas Bôas. 1994. A marcha para oeste: A epopéia da Expedição Roncador-Xingú. São Paulo: Editora Globo.
- Warrell, D. A. 1989. Snake bite in five continents. Pp. 106-114. *In*: C. Bunch, editor, Horizons in medicine. London: Bailliere Tindall.
- ———. 2004. Snakebites in Central and South America: Epidemiology, clinical features, and clinical management. Pp. 709-761. In: J. A. Campbell and W. W. Lamar, editors, The venomous reptiles of the Western Hemisphere, Volume II. Ithaca, New York: Cornell University Press.
- Weinberg, M. L. D., L. F. Felicori, C. A. Bello, H. P. B. Magalhães, A. P. Almeida, A. Magalhães and E. F. Sánchez. 2004. Biochemical properties of a bushmaster snake venom serine proteinase (LV-Ka), and its kinin releasing activity evaluated in rat mesenteric arterial rings. J. Pharmacological Sciences 96(3):333-342.
- Yarlequé, 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.

Bull. Chicago Herp. Soc. 42(7):115-116, 2007

Book Reviews:

Alterna — The Gray-banded Kingsnake by Gerold Merker and Walter Merker 2005. 80 pp. LM Digital.

and

Zonata — The California Mountain Kingsnake by Mitchell Mulks and Gerold Merker 2004. 64 pp. LM Digital.

Gerry Salmon PO Box 823 Millbrook, NY 12545 gtsalmon@optonline.net

It seems fitting that I was asked to write a review on two new kingsnake picture books. Many years' worth of nights spent herping throughout the Big Bend region of West Texas involved endless hours of road-cruising. The daytime hours were for rest, relaxation, herp camaraderie, and catching up with old friends and their stories of collecting and breeding successes. Getting together over long lunches, occasionally leading well into cocktail hour, led to the development of larger and larger photo albums depicting the hard-to-believe variety of colors and patterns of gray-banded kingsnakes. The California boys would often blow us away with spectacular pictures of the western mountain kingsnakes (often attempting to teach us the nuances of regional variation). I was the compiler of one of the largest photo albums on gray-bands, which created "oohs" and "aahs" from many seasoned field herpers. Albums such as this whet the appetite for picture books that would show regional variation in polymorphic species. These two new books include informative but brief text (the text seems almost distracting from the great photos) as a narrative "to take you there," especially off-season when the fever sets in.

The two books are *Alterna — The Gray-banded Kingsnake* by Gerold and Walter Merker, and *Zonata — The California Mountain Kingsnake* by Mitchell Mulks and Gerold Merker. The Merkers are veteran field workers with both species and are excellent photographers as well. The Merkers have authored and co-authored over 60 articles for such magazines as *The Vivarium*, *Reptiles*, *Reptile and Amphibian Hobbyist* and *Ecology*.

Alterna — The Gray-banded Kingsnake is an 80-page, low-cost paperback, filled with wonderful images of Lampropeltis alterna specimens (arranged by locality), habitat shots and numerous other Big Bend and

