When a snake bites

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Primary care physicians may be required to treat snake-bitten patients and must differentiate between venomous and nonvenomous snakes. The chief distinguishing characteristics of venomous snakes are fangs and a single row of subcaudal anal plates. The physiologic effects of snake venom are on the cardiovascular, hematologic, and neurovascular systems. The snake-bitten patient first needs supportive treatment and stabilization. Then, the physician must establish whether envenomation has occurred, grade it, and monitor edema around the bite. Local treatment, broad-spectrum antibiotics, and tetanus prophylaxis should be used for all envenomation grades. The decision to administer antivenin therapy should be made on clinical grounds and the envenomation grade. Its use, however, can lead to anaphylaxis and anticomplement reactions.

(Key words: Snakebite, antivenin, envenomation)

Now the serpent was more subtle than any beast of the field which the Lord God had made. (Genesis 3:1)

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More than 3000 species of snakes exist throughout the world. They are found anywhere from below sea level to above timberline. Worldwide, 300,000 snakebites occur with 30,000 to 40,000 deaths per year.[1,2] In the United States, 45,000 snakebites occur with 12 to 15 deaths per year.[2] No clinician, whether practicing in a rural or a large, inner city hospital, is exempt from treating snakebites. This article reviews the characteristics of venomous snakes in the United States, the general management of snakebites, and complications associated with envenomation.

Two families of venomous snakes exist in the United States: Elapidae and Viperidae *(Table 1)*.[3] The Elapidae family consists of two genera of coral snakes, *Micrurus fulvius* and *Micruroides euryxanthus*. Crotalidae, a subfamily of Viperidae, consists of various species of the genera *Agkistrodon* (cottonmouths and copperheads), *Sistrurus* (pigmy and massasauga rattlesnakes), and *Crotalus*. The genus *Crotalus* consists of rattlesnakes including the eastern and western diamondbacks, mojave, sidewinder, timber, and prairie rattlesnakes. Venomous snakes exist in all states except Alaska, Hawaii, and Maine.[3] (*Figures 1* and *2* illustrate distributions of some common snakes in the United States.[4])

General characteristics

Primary care physicians should have a basic understanding of the general characteristics of snakes. Differentiating venomous from nonvenomous snakebites is a very important step in the management of the snake-bitten patient. Nonvenomous snakebites are benign and need only local wound care.

In contrast, venomous snakebites are frequently associated with complications. If patients or accompanying parties can describe the offending snake, they will provide information important in determining the course of treatment.

The two most constant factors differentiating

Table 1
Common Venomous Snakes in the United States

Family: Elapidae	
Micruroides euryxanthus	Arizona coral snake
Micrurus fulvius	American coral snake
Family: Viperidae	
Subfamily: Crotalidae	
Agkistrodon contortrix	American copperhead
Agkistrodon piscivorus	Cottonmouth
Crotalus adamanteus	Eastern diamondback rattlesnake
Crotalus atrox	Western diamondback rattlesnake
Crotalus cerastes	Sidewinder
Crotalus horridus	Timber rattlesnake
Crotalus scutulatus	Mojave rattlesnake
Crotalus viridis	Prairie rattlesnake
Sistrurus catenatus	Massasauga rattlesnake
Sistrurus miliarius	Pigmy rattlesnake

venomous from nonvenomous snakes are fangs and the presence of a single row of subcaudal anal plates (*Figures 3* and *4*). Nonvenomous snakes lack fangs and have a double row of subcaudal anal plates. With some exceptions, for example, the rat snake, venomous snakes generally have a triangular shaped head. Nonvenomous and the American and Arizona coral snakes (*M fulvius* and *M euryxanthus*) have a round head that is indistinct from the neck (*Figure 3*). Venomous snakes generally have elliptical pupils. Nonvenomous and coral snakes have round pupils. Coral snakes may be easily identified by their red-on-yellow-on-black circumferential markings. Snakes that display red-on-black-on-yellow markings, such as the king snake, are nonvenomous. One need only to remember the following:

Red-on-black; venom-lack.

Red-on-yellow; kill-a-fellow.

Characteristic of Crotalidae is a thermoreceptor "pit" located between the eyes and nose; hence, the term "pit viper." This pit allows the snake to sense gradations in temperature and locate prey. The thermoreceptor functions well with small prey but is overwhelmed by larger animals such as human beings. This feature may in part account for the defensive strike of the snake resulting in snakebite.

Venomous snakes have an elaborate envenomation apparatus, which consists of venom glands, ducts, and fangs. The venom gland is analogous to the human parotid gland. Venom is discharged via the actions of the external jaw muscle. The amount of venom discharged depends on the weight and size of the victim as determined by the thermoreceptors.[5] Because the comparatively large size of a human being overwhelms the snake's thermoreceptors, injection of a larger amount of venom may result. Most average-sized snakes discharge between 25% and 75% of their stored venom per strike.[6] The larger and older snake injects more, but less-concentrated, venom, whereas the younger and smaller snake injects less, but more-concentrated, venom.

Venom is delivered to the victim via fangs (*Figure 4*). All but the coral snakes have hinged fangs that fold posteriorly against the upper jaw. Coral snakes have a fixed pair of fangs that are shorter and fatter than those of Viperidae. Snakes shed their fangs as they do their skin. Reserve fangs may be in place at times resulting in one to four fang marks.

Rattlesnakes are named for their "rattle" located on the tail. The rattle is a group of interlocking segments formed on the tail each time the snake sheds. It is erroneous to determine the age of the snake by counting the number of rattles.[4] Snakes shed one to four times a year, the number depending on the temperature, climate, moisture, and the amount of food available.

Venom

Snake venom is a complex substance evolved for immobilizing, killing, and digesting the snake's prey. It is 90% water, 10% protein, and various trace elements. *Table 2* lists some components of venom.[5] The proteolytic enzymes in snake venom are capable of tissue necrosis; whereas hyaluronidase, "the tissue spreading enzyme," cleaves mucopolysaccharide bonds, allowing venom to travel through tissue. Thrombinlike esterases form unstable fibrin clots that are easily lysed by other enzymes in venom.[5]

The physiologic actions of snake venom are generally directed toward the hematologic, cardiovascular, and neuromuscular systems (*Figure 5*). The proteolytic action of snake venom wreaks

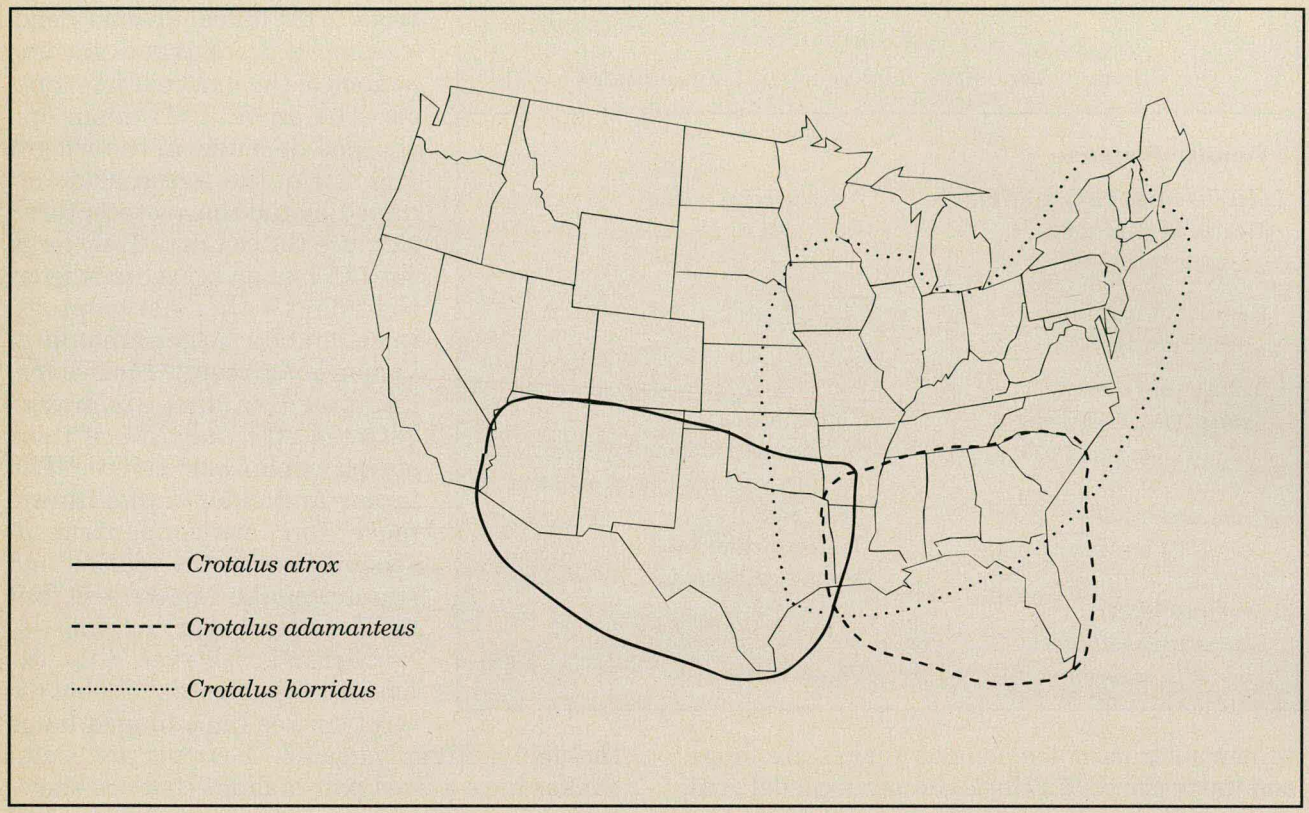

Figure 1. *Distribution of* Crotalus atrox, Crotalus adamanteus, *and* Crotalus horridus.

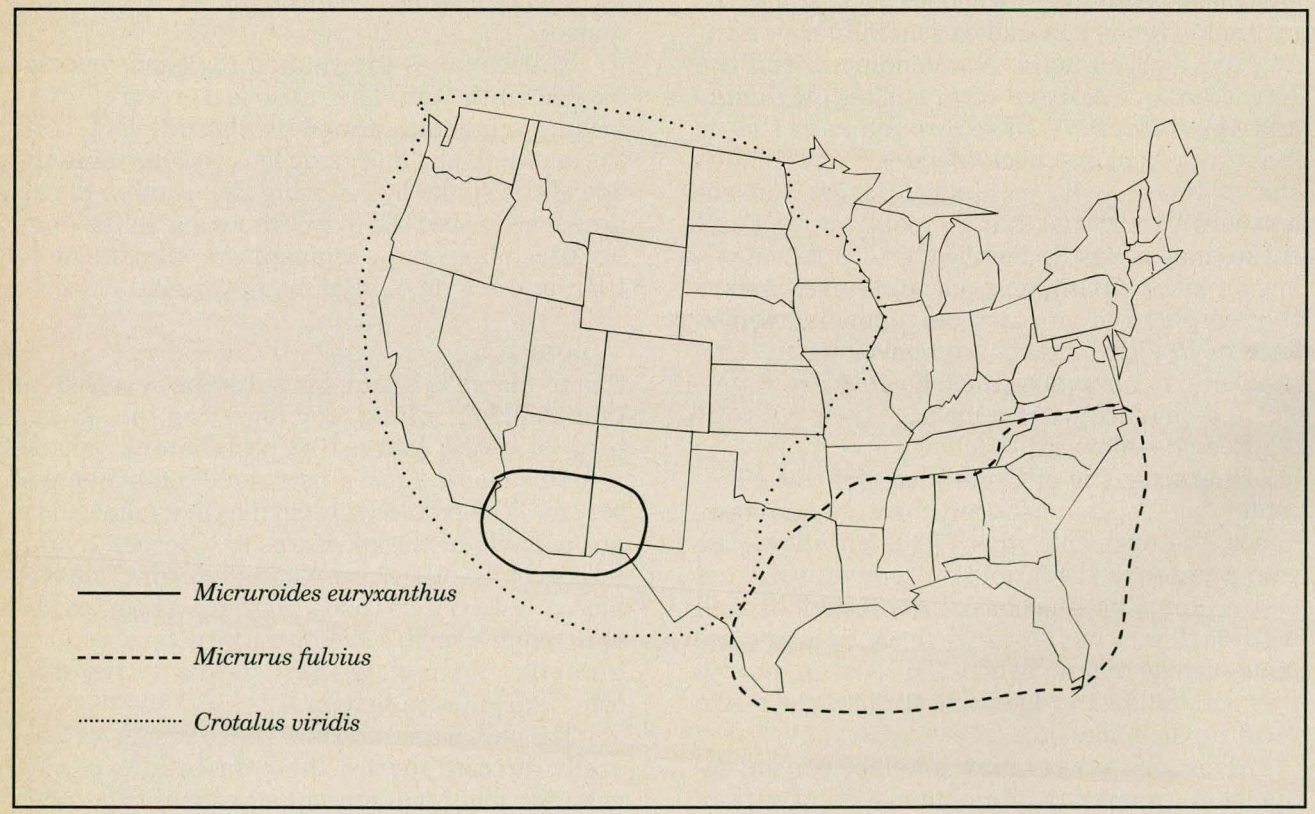

Figure 2. *Distribution of* Micruroides euryxanthus, Micrurus fulvius, *and* Crotalus viridis.

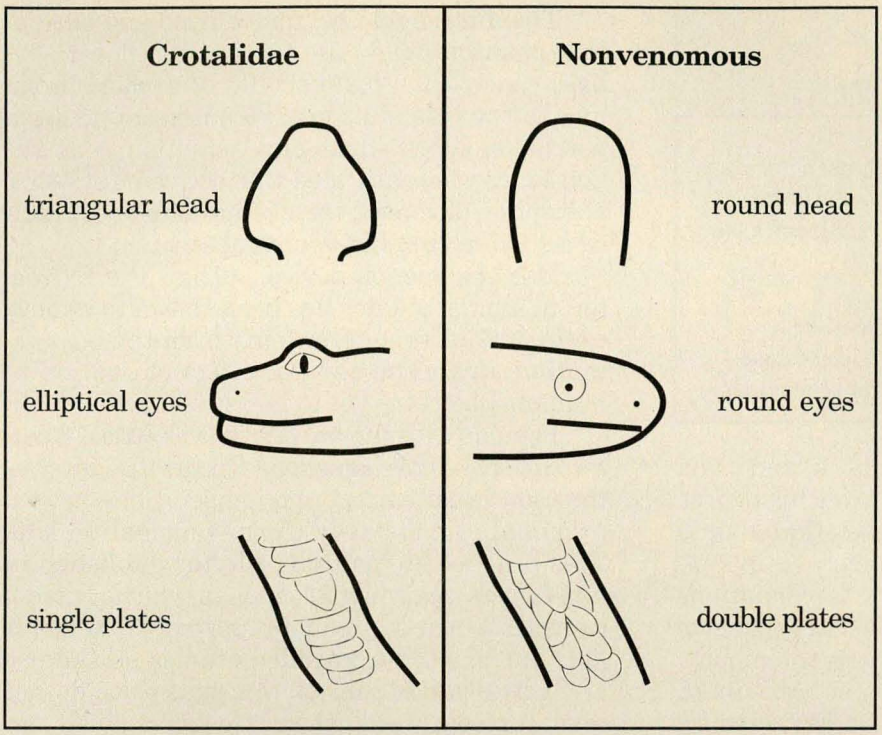

Figure 3. *General characteristics of Crotalidae versus nonvenomous snakes. (Adapted from Dowling and coauthors,[4] and Podgorny.[5])*

havoc on cell membranes throughout the body. Cells undergo lysis or become dysfunctional, vascular structures begin to leak, and microvascular thrombosis develops because of platelet aggregation. Disseminated intravascular coagulation may occur. Many of these effects are mediated by phospholipase A_2. Increased vascular permeability leads to hypotension, lactic acidemia, hemoconcentration, and hypoproteinemia. Venom may act at the site of the neuromuscular junction causing neuromuscular blockade, weakness, paralysis, and myonecrosis.

Clinical presentation

The clinical presentation of snake envenomation is dependent on several factors. Infants, children, and elderly or low-weight adults are more pregnable to snake envenomation and suffer more harm. Also important is the nature, location, depth, and number of bites. As a rule, the more superior the location of the bite on the body, the more serious the effects can be. The condition of the fangs and venom glands, the amount of venom injected, the amount and kind of clothing through which the fangs pass, and the length of time the snake holds on are also important factors. Greater complications occur with more venom injected. In the absence of symptoms, the physician should consider the possibility of a "dry bite": a bite without the injection of venom.[2] Also important is the species and size of the snake involved. Larger snakes inject more venom. The venom of the coral snakes is predominantly neurotoxic, whereas the venom of the rattlesnake generally causes hemorrhage and tissue necrosis.

Pathogens that are normal flora of the snake mouth, such as *Clostridium, Pseudomonas,* or *Staphylococcus* species, may complicate the wound site with infection. Although extremely rare, anaphylactic and anaphylactoid shock have also been reported to be a complication of snake envenomation.[7]

Common signs and symptoms of snake envenomation appear in *Table 3*. One or two fang marks approximately 0.5 cm to 4.0 cm apart is pathognomonic of a venomous snakebite.[3-6] After significant envenomation, victims notice pain, burning, and progressive swelling within 5 minutes which can be followed by edema and hemorrhage.

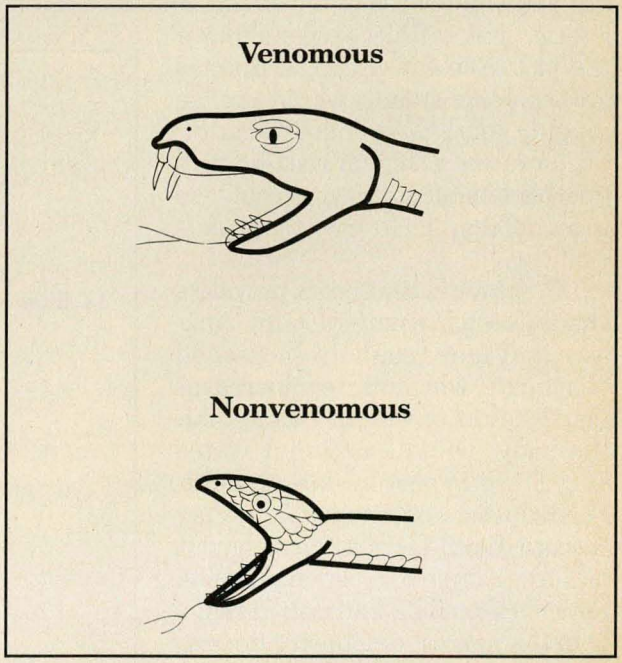

Figure 4. *Fangs and no fangs. (Adapted from Dowling and coauthors,[4] and Podgorny.[5])*

Table 2
Components of Venom[5]

Proteolytic enzymes	Phosphomonoesterase
Arginine ester hydrolase	Phosphodiesterase
Thrombinlike enzyme	Acetylcholinesterase
Collagenase	RNase
Hyaluronidase A_2(A)	DNase
Phospholipase B	5´-nucleotidase
Phospholipase C	NAD-nucleotidase
Lactate dehydrogenase	L-amino-acid oxidase

If they are severe, hypotension, shock, and coma may result. Swelling may occur to such a degree that compartment syndrome of the affected limb may develop. Paresthesia of the face, scalp, and lips along with periorbital muscle fasciculations suggest significant envenomation.[2,5,6] Some patients may complain of a metallic taste in the mouth, weakness, sweating, nausea, and light-headedness. Neuromuscular blockade may be heralded by hoarseness, dysphagia, and ptosis. Paralysis may progress to the diaphragm and cause respiratory arrest. Hemorrhage can occur within 6 hours of envenomation; its manifestations include epistaxis, hematemesis, petechiae, or hematochezia.

Management

The patient and prehospital personnel must leave the immediate area of the snake. Snakes are territorial and will not strike again if the victim is out of range. Snakes are capable of striking within a range roughly equal to their body length.[5] Children are at higher risk for multiple bites because they commonly are so fearful they fail to leave the snake's vicinity.

Prehospital healthcare providers should keep the patient calm. Anxiety and fear result in increased heart rate, which in turn increases distribution of venom throughout the body. These emotional states also cause hyperventilation, lightheadedness, and nausea, and may obscure the effects of a nonvenomous bite from those of a venomous bite. Patients should be transported rapidly to the nearest emergency department. Intravenous fluids and cardiac monitoring should be instituted.

The limb should be immobilized and be kept in a position below the level of the heart.[2,5] A light constriction band should be applied proximal to the bite site. In a recent study using a porcine model of snake envenomation, constriction bands were associated with decreased systemic absorption of venom; their removal did not result in a sudden surge in venom absorption.[8]

Use of a suction device, such as the Extractor, in animal studies has been shown to remove up to 30% of venom proteins from the envenomation site.[9] The clinical effect of suction in human subjects is yet to be established.

Popular with the lay public is electrical treatment of snake envenomation.[6] One method involves the use of a car battery and jumper cables hooked proximal and distal to the envenomation site. This practice stems from a letter published in *The Lancet* regarding 34 cases in which Equadorian tribesmen so treated reportedly had favorable outcomes.[10] Controlled studies on the use of electric shock therapy for snakebite do not exist. A recently published case report illustrates the failure and the complications of electrotherapy.[11] It is unclear at this time if electrotherapy has *any* role in the therapy of snakebite, and it *cannot* be recommended.

Cryotherapy at one time was recommended. However, it has been found ineffective and possibly deleterious.

Initial hospital management of the snake-envenomated patient is directed toward stabiliz-

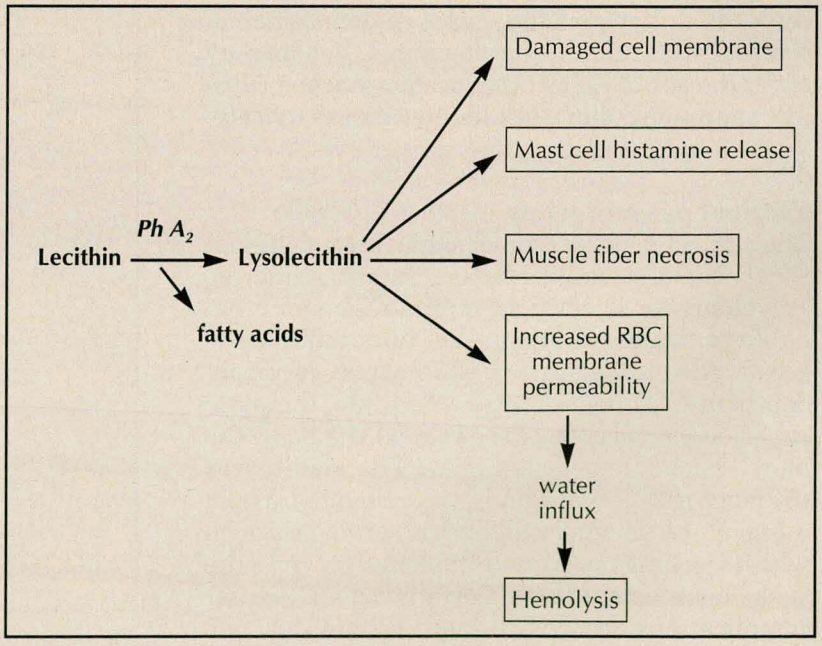

Figure 5. *The effects of phospholipase A_2.*

ing and supporting the patient. A "safety net" that generally includes supplemental oxygen, cardiac monitoring, and an intravenous line of normal saline or lactated Ringer's solution should be established for all patients.

Routine laboratory tests include complete blood cell count, urinalysis, prothrombin time/partial thromboplastin time, and electrolyte, creatinine, and blood urea nitrogen determination. Creatine phosphokinase levels may help to determine the degree of muscle necrosis. If the use of antivenin is anticipated, the patient's blood should be typed and crossmatched prior to administration. Antivenin may cause an antigen cross-reaction and interfere with the crossmatch procedure.

After completing primary and secondary surveys, the physician must establish whether envenomation has occurred. Up to 85% of snakebites result in insignificant or no envenomation.[12] Pain, erythema, edema, and ecchymosis in the bite region indicate deposition of venom. Systemic symptoms such as tingling, visual disturbances, altered sensorium, seizures, or shock indicate severe envenomation.

If envenomation is confirmed, it may be graded[5] (*Table 4*). Gradation schemes are useful in predicting the use of antivenin and the clinical course of the patient. The exact clinical findings should still be documented. Assigning only a number to the patient's envenomation is not helpful in following the clinical progress of the bite.

Table 3
Some Common Signs and Symptoms of Snake Envenomation*

Sign or symptom	Frequency (%)
Fang marks	100
Swelling and edema	74
Weakness	72
Pain	65
Diaphoresis or chills	64
Numbness or tingling not at affected part	63
Orthostatic symptoms	57
Ecchymosis	51
Nausea and vomiting	48
Numbness or tingling at affected part	42
Fasciculations	41
Vesiculations	40
Regional lymphadenopathy	40

*Adapted from Russell.[2]

Table 4
Grades of Envenomation

Grade	Signs and symptoms
1 (minimal)	Moderate pain, 22.5- to 15-cm edema, erythema, no systemic symptoms
2 (moderate)	Severe pain, tenderness, erythema, vomiting, petechiae, fever,weakness, 20- to 40-cm edema
3 (severe)	Widespread pain, tenderness, ecchymosis, systemic signs, vertigo, 40- to 50-cm edema
4 (very severe)	Rapid swelling, ecchymosis, CNS symptoms, visual disturbance, shock, and convulsions

Local wound treatment, broad-spectrum antibiotics, and tetanus prophylaxis should be administered to the patient with any grade of envenomation.

Monitoring the amount of edema around the bite is useful to follow the progression of local venom activity. The extremity circumference should be documented and reevaluated hourly. Increasing edema could result in compartment syndrome of the involved extremity. Relying on the classic signs and symptoms of compartment syndrome as an indication of its development in snake envenomation will underestimate the severity of compartment pressures. If compartment syndrome is suspected, compartment pressures should be monitored and kept below 30 mm Hg. Prompt surgical consultation is warranted if compartment syndrome develops.

Allergic reactions to snake venom is an uncommon but difficult situation.[13,14] Therapy involves a combined approach to envenomation and anaphylaxis.[7,15]

The technique of incision and suction first described by the Hindu is controversial.[6] Its effectiveness has never been proved in human beings. Also reported in the literature are excision and debridement. These procedures are no longer rec-

ommended because they increase morbidity.[16,17]

The use of antivenin is a controversial treatment modality for snake envenomation. Interestingly, the controversy exists almost exclusively in the United States; antivenin has long been the accepted treatment of snake envenomation elsewhere in the world. Antivenin, prepared from horse serum, contains antibodies directed against a particular snake's venom. Antivenin therapy is frequently associated with side effects, some of which are severe. The treating physician should obtain informed consent before its use.

In the United States, antivenins for Crotalidae and *M fulvius* are produced and marketed by Wyeth-Ayerst Laboratories. (Antivenin for *M euryxanthus* does not exist.) The antivenin kit contains one vial with 1.5 lyophilized horse serum, one 10-mL vial of bacteriostatic water, one vial of 1:10 dilution of horse serum used for skin testing, and the package insert. Antivenin is prepared by gently mixing lyophilized horse serum in 10 mL of bacteriostatic water (Package insert. Crotalidae antivenin, Wyeth Laboratories).

The decision to use antivenin must be made on a clinical basis, on the grade of the patient's envenomation, and after consultation with a local poison control center. It is best given within 12 hours, but its use after 72 hours has been successful.[6] The use of antivenin is associated with a high incidence of anaphylaxis and anticomplement reactions. Anaphylaxis, an IgE-mediated type I hypersensitivity reaction, may be precipitated by skin testing or antivenin administration. Common early manifestations are nausea, dyspnea, rash, and a hot, flushed feeling. Anticomplement reactions can also occur because of immunoglobulin and protein aggregates in antivenin.[18] This reaction often occurs when concentrated antivenin is administered rapidly.[6]

If antivenin is to be used, the patient must be scrutinized for history of horse serum sensitivity, asthma, and general allergic reactions, and should undergo skin testing. The latter is accomplished by intradermally injecting the patient with 0.01 mL to 0.3 mL of the 1:10 dilution of the horse serum provided in the antivenin kit. A positive reaction consists of erythema or pseudopodia (or both) at the site of injection. Skin testing with horse serum should never be done unless one fully intends to use antivenin, because it may sensitize the patient to additional equine-derived products.

Not all persons sensitive to horse serum will react to skin testing. It is our belief that if the decision has been made to use antivenin, it should be used regardless of the results of skin testing. The presence of a positive skin test allows the physician to prepare for potentially serious allergic reactions during antivenin administration. The patient should be pretreated with diphenhydramine hydrochloride, 50 mg to 100 mg (2 mg/kg in pediatric patients) administered intravenously followed by a slow intravenous infusion of one antivenin vial (10 mL) in a 1:20 dilution with 0.45 normal saline solution over 60 minutes. If the patient does not react to skin testing, antivenin is administered intravenously at a rate of 10 vials over 60 to 90 minutes. If anaphylaxis occurs during administration of antivenin, 0.3 mL to 0.5 mL of a 1:1000 solution of epinephrine administered subcutaneously may be all that is needed to treat the patient. One may also administer methylprednisolone, cimetidine, and an intravenous fluid bolus.[1,2,5-7,14]

Antivenin administration has been recommended during pregnancy. One case of abruptio placentae has been reported after snake envenomation.[19] Epinephrine should be avoided in pregnancy because it decreases uterine blood flow.[20] The intravenous use of 25 mg to 50 mg of ephedrine has proved to be an effective alternative if serious allergic reactions develop.[6]

Pediatric envenomation should be treated with the same antivenin dose used for the adult patient. Antivenin works on the snake venom on a molecule-per-molecule basis, so children should receive the same volume of antivenin as an adult.

Serum sickness is a common complication after the use of antivenin. It occurs 1 to 4 weeks after administration of antivenin, and is a type IV hypersensitivity reaction. Patients complain of urticaria, arthralgia, fever, myalgia, malaise, headache, wheezing, nausea, vomiting, and lightheadedness. A regimen of diphenhydramine hydrochloride, 50 mg every 4 hours; hydroxyzine, 10 mg every 4 hours; oxycodone/acetaminophen, one to two tablets every 4 hours as needed; cimetidine, 400 mg every 12 hours; and prednisone 80 mg every morning for 14 days without a tapering dose may be beneficial.

Comment

All physicians involved in primary care may be called on to treat snake-bitten patients. Evaluation for the presence and degree of envenomation is important in the decision to use antivenin. Medical management usually results in a successful outcome. The primary care physician

should be aware of the indications for surgical consultation.

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