CHAPTER 117

Snakes and Other Reptiles

Bradley D. Riley • Anthony F. Pizon • Anne-Michelle Ruha
James R. Roberts • Edward J. Otten

Case 1 A 25-year-old man exploring the mountains of Virginia was bitten on the toe by an unidentified snake when he was rock climbing in bare feet. He did not hear a rattle and only caught a glimpse of a copper-colored snake as it crawled away. Within 10 minutes he noted mild swelling and discomfort around a single puncture wound on the top of the fourth toe.

Within 1 hour the man developed moderate throbbing pain in the entire foot, associated with paresthesias. At 2 hours a hemorrhagic blister developed at the bite site. The swelling had progressed to the dorsum of the ankle, but he had no systemic symptoms. A friend drove him to a local hospital. No specific first aid was administered. The swelling did not progress past the ankle, and the patient did not report nausea, vomiting, diaphoresis, dizziness, or systemic weakness. The vital signs, complete blood cell count, and coagulation profile were normal. The patient reported only mild pain of the foot.

Because of progression of local symptoms and lack of definitive identification of the snake, the patient was admitted to the hospital. Antivenom was obtained but not administered. The patient had moderate pain and stiffness of his foot. Edema reached the lower leg at 24 hours but did not progress further. No systemic symptoms developed, and the laboratory profile remained normal. Minor surgical debridement of a small area of skin slough on the toe was required. The patient was discharged after 48 hours to continue extremity elevation, and outpatient physical therapy was arranged. After 10 days of a progressive decrease in swelling, the patient had full use of the foot with only minor stiffness. Within 3 weeks, the stiffness had disappeared completely.

Case 2 A 40-year-old utility worker was bitten on the right hand by a snake while he was working on an electrical box. He had immediate onset of pain at the bite site. Coworkers who were familiar with snakes native to the area identified the snake as a western diamondback rattlesnake (*Crotalus atrox*). An intravenous line was established and fluids administered en route to the hospital.

The patient arrived to the emergency department approximately 45 minutes after the bite. He complained of worsening pain in his right arm, nausea, and dizziness. His presenting vital signs were: blood pressure, 90/45 mm Hg; pulse, 118 beats/min; respiratory rate, 24 breaths/min; temperature 97°F (36.1°C). Two puncture wounds were identified on his right thumb, as were surrounding ecchymosis and a small amount of blood oozing from the wounds. Swelling extended from his right hand to just beyond his elbow, and his forearm compartments were soft. No other bleeding was noted, and the remainder of the physical examination was unremarkable.

A second large-bore intravenous line was placed, and 0.9% sodium chloride solution administered while the patient's blood was sent for analysis. The pharmacy was asked to prepare 6 vials of crotalidae polyvalent immune Fab (ovine) in 250 mL 0.9% sodium chloride solution. In the meantime, the patient's right arm was splinted in near-complete extension and elevated above the level of his heart. While awaiting the reconstituted antivenom, the patient's blood work returned: hemoglobin, 15.1 mg/dL; platelets 90,000/mm^3; prothrombin time, >100 seconds; fibrinogen, 55 μg/mL. Following administration of 3 L 0.9% NaCl, the patient's systolic blood pressure increased to 110 mm Hg and his pulse decreased to 95 beats/min. Intravenous fentanyl was given for pain as infusion of 6 vials of crotalidae polyvalent immune Fab (ovine) was initiated.

After a dose of 6 vials of antivenom was administered, local tissue injury was reassessed and repeat laboratory studies obtained. Despite elevation of the arm, the patient developed increased swelling in his hand that progressed to his shoulder. Repeat blood work demonstrated hemoglobin, 13.2 mg/dL; platelets, 76,000/mm^3; prothrombin time, >100 seconds; fibrinogen, 55 μg/mL. Another dose of 6 vials of antivenom was administered based on worsening laboratory results and local swelling. At the conclusion of the second dose of antivenom, the upper extremity swelling, while not resolved, did not appear to be progressing further. Results of hematologic studies performed at the conclusion of the second antivenom dose were improved from the previous results: platelets, 100,000/mm^3; prothrombin time, 45 seconds; fibrinogen, 105 μg/mL.

The patient was admitted to the intensive care unit, where maintenance infusions of crotalidae polyvalent immune Fab (ovine) were initiated at 2 vials every 6 hours for a total of 3 additional doses. Hourly measurements of hand, forearm, and arm circumferences during crotalidae polyvalent immune Fab (ovine) maintenance infusions were unchanged. After all antivenom doses were administered, the patient's pain was controlled with oral analgesics. His final laboratory findings were hemoglobin, 13.5 mg/dL; platelets, 175,000/mm^3; prothrombin time, 12 seconds; fibrinogen 240 μg/mL. After a 48-hour hospital stay, he was discharged home with analgesics and strict instructions to avoid any activity that could result in trauma for 3 weeks. He was informed that his coagulopathy and thrombocytopenia could recur despite the treatment with antivenom.

At follow-up examination 48 hours after hospital discharge, the patient's hand swelling had increased slightly, but he stated that he had not kept the hand adequately elevated. He was feeling well but had not returned to work because of the inability to use his dominant hand. Repeat blood work demonstrated platelet count, 100,000/mm^3; prothrombin time, 25.2 seconds; fibrinogen concentration, 75 μg/mL. He was reminded that he was at risk for bleeding and told to return for repeat laboratory studies in 48 hours.

The patient was reevaluated every 2–3 days with repeat hematologic studies. Multiple laboratory studies over the subsequent week demonstrated a stable thrombocytopenia and coagulopathy. Tissue swelling continued to decrease. His hematologic parameters normalized 2 weeks after the envenomation. The patient had no bleeding episodes or other ill effects.

EPIDEMIOLOGY

Incidence of Venomous Snakebites in the United States

Venomous snakes are found throughout the United States, except Maine, Alaska, and Hawaii. They are common in the Appalachian states, the south, and the west; they are rare in New England and the northern states. Approximately 6000 to 8000 venomous snakebites occur per year, and many thousands more snakebites occur from nonvenomous species. Mortality from snakebites is considered rare in the United States; estimates range from 5–15 deaths per year.[32,51] Exact statistics are lacking, but mortality rates can be significantly higher in other countries. As many as 27,000 rattlesnake bites and 100 fatalities occur per year in Mexico,[15] and thousands of deaths per year occur in some developing countries in Asia and Africa.

Because snakes hibernate in the winter, most bites in the United States occur between May and October. Snakes may bite at night, but the most common time for envenomation is between 2 and 6 PM.[81] Coral snakes are particularly known for their nocturnal habits. The majority of bites occur to the extremities, but bites to the face and tongue occur when snakes are purposefully held near the body. The striking range of a snake is approximately half its length.

Children, intoxicated individuals (mostly men), snake handlers, and collectors are frequent victims. More than half of the reported bites occur while the individual is purposely handling a known venomous snake. There is a significant market for many illegal and dangerous reptiles, and a surprising number of individuals keep and sell venomous snakes as pets. Many specimens are exotic and highly toxic species from other countries. Some religious groups in the mid- and southeastern states handle poisonous snakes (usually rattlesnakes) as a routine ceremonial practice, and envenomation is common.

Identification of a Venomous Snake

There are 120 species of snakes native to North America, including approximately 30 venomous species (Table 117–1). Most of these venomous snakes are members of the family Viperidae (subfamily Crotalinae), which include the rattlesnakes (*Crotalus and Sistrurus*) and the copperheads and water moccasins (*Agkistrodon*) (see ILAGKISTRODONCONTOTRIX1 and ILCROTALUSATROX in the Image Library at goldfrankstoxicology.com). Snakes of the subfamily Crotalinae are also called *pit vipers* because of the presence of a pitlike depression of the skin behind the nostril that contains a heat-sensing organ. The other family of venomous snakes native to the United States is the Elapidae, which includes the coral snakes. The vast majority of venomous snakebites in the United States are from pit vipers, with approximately 60% of bites from rattlesnakes and the remainder from copperheads and water moccasins.[74] Fewer than 1% of venomous bites are from the docile coral snake.[61,69]

TABLE 117–1. Scientific and Common Names of Medically Important Venomous Snakes of North America

Scientific Name	Common Name
Crotalinae (Pit Vipers)	
Rattlesnakes	
Crotalus adamanteus	Eastern diamondback
Crotalus atrox	Western diamondback
Crotalus cerastes cerastes	Mojave Desert sidewinder
Crotalus cerastes cercobombus	Sonoran Desert sidewinder
Crotalus horridus horridus	Timber
Crotalus horridus atricaudatus	Canebrake
Crotalus molossus molossus	Northern blacktail
Crotalus ruber ruber	Red diamond
Crotalus scutulatus scutulatus	Mojave
Crotalus viridis cerberus	Arizona black
Crotalus viridis helleri	Southern Pacific
Crotalus viridis lutosus	Great Basin
Crotalus viridis oreganus	Northern Pacific
Crotalus viridis viridis	Prairie
Sistrurus catenatus catenatus	Eastern massasauga
Sistrurus catenatus edwardsi	Desert massasauga
Sistrurus catenatus tergeminus	Western massasauga
Sistrurus millarius millarius	Carolina pigmy
Other Pit Vipers	
Agkistrodon contortrix contortrix	Southern copperhead
Agkistrodon contortrix laticinctus	Broad-banded copperhead
Agkistrodon contortrix mokason	Northern copperhead
Agkistrodon piscivorus conanti	Florida cottonmouth
Agkistrodon piscivorus piscivorus	Eastern cottonmouth
Agkistrodon piscivorus leucostoma	Western cottonmouth
Bothrops lanceolatus	Fer-de-lance
Elapidae (Coral Snakes)	
Micruroides euryxanthus	Sonoran coral snake
Micrurus fulvius fulvius	Eastern coral snake
Micrurus fulvius tenere	Texas coral snake

Pit Vipers

The venomous Crotalinae in the United States have a triangular-shaped head, vertically elliptical pupils, and easily identifiable fangs (Figure 117–1). The fangs are paired, needlelike structures that inject venom and can retract on a hingelike mechanism into the roof of the mouth. Rattlesnakes have the longest fangs, reaching 3 to 4 cm. In addition to fangs, venomous snakes have rows of small teeth. An adult snake usually has 2 fangs, but the fangs may be single or multiple. The undersurface of pit vipers has a single row of plates or scales, as opposed to the double row found on nonvenomous varieties. Depending on maturity, rattlesnakes may or may not have rattles, which occasionally are heard before a strike. Water moccasins are semiaquatic and have a distinct white mouth suggesting their common name (cottonmouths). They reportedly are quite aggressive and capable of underwater bites. Copperheads are known for their reddish-brown (copper) heads and hourglass markings on their bodies.

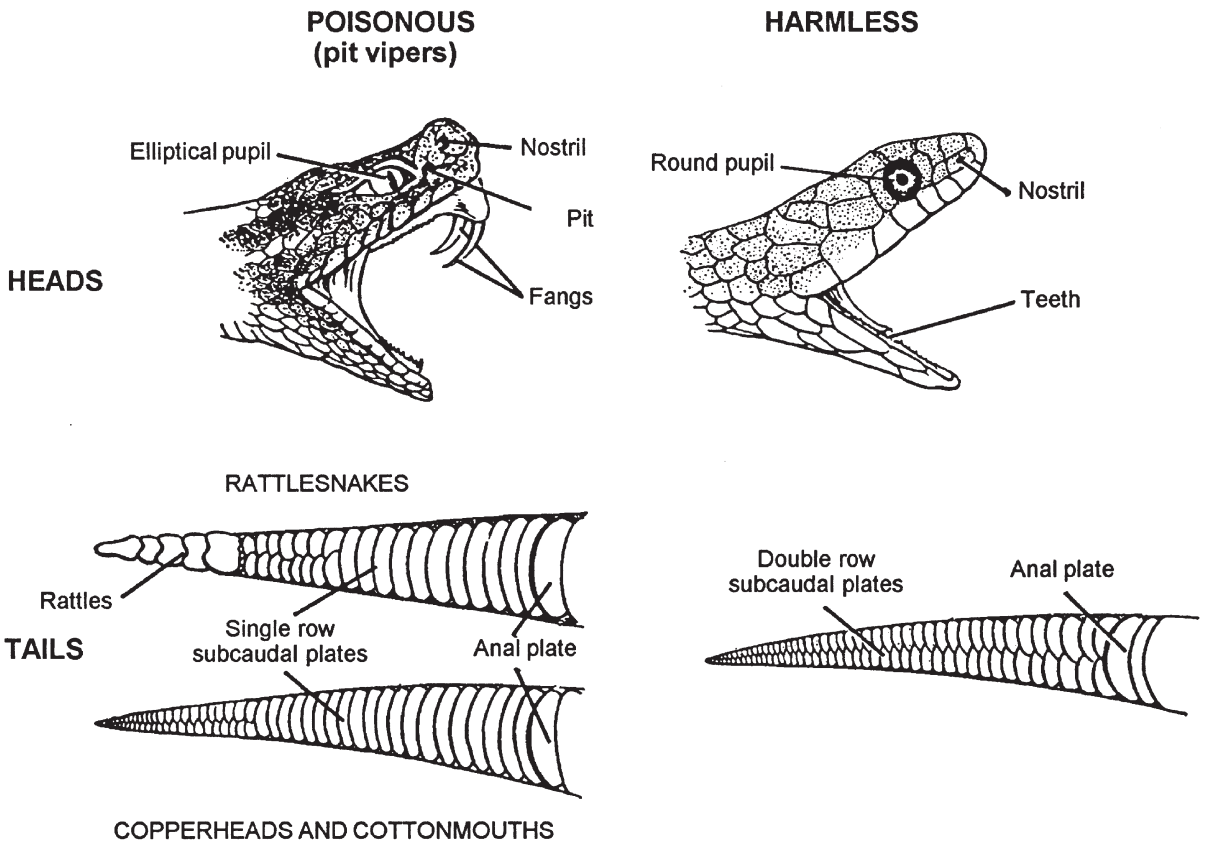

Figure 117–1. Features of pit vipers and harmless snakes. (Modified and reprinted with permission from Parrish HM, Carr CA: Bites by copperheads in the United States. JAMA 1967;8:201:927.)

Elapidae

The coral snakes (*Micruroides* and *Micrurus* spp) are the brightly colored Elapids, which have easily identifiable red, yellow, and black bands along the length of their body. Coral snakes and the similarly colored nonpoisonous scarlet king snake often are confused. In a report of 39 victims of coral snake bites, 9 patients were envenomated because they erroneously believed they were dealing with the nonpoisonous scarlet king snake.[48] The coral and king snakes can be distinguished by the spacing of their colored rings and the color of the head. Coral snakes have black snouts, whereas king snakes have red snouts. Both species have red, yellow, and black rings, but in different sequences. The red and yellow rings touch in the coral snake but are separated by black rings in king snakes ("Red on yellow kills a fellow, red on black, venom lack").

The fangs of coral snakes are much smaller (1–3 mm) than those of the rattlesnakes, and discrete fang marks may not be obvious after envenomation. Coral snakes appear to have the curious propensity of hanging onto a victim or "chewing" for a few seconds, and a history of this activity may help identify a coral snakebite when the offending reptile cannot be located. Removing a coral snake from the skin has been likened to separating pieces of hook and loop closure (Velcro).

Exact identification of a snake often is not possible unless the victim brings the offending reptile to the hospital. This usually is impossible and poses an additional threat to the victim or prehospital personnel and is discouraged. Because of the excitement generated by the bite, the victim's identification of the snake may not be accurate. Identifying a snake by its color or markings is difficult for the novice. Knowledge of the indigenous venomous snakes often is helpful to medical personnel. Snake handlers and owners of pet snakes usually know the exact species responsible for their bite, but some are reluctant to offer specific information out of fear of prosecution or confiscation of the illegal snake by authorities.

Characteristics of a Venomous Snakebite

The severity and clinical manifestations of envenomation depend on a number of factors, including number of strikes, depth of envenomation, size of the snake, potency and amount of venom injected, size and underlying health of the victim, and location of the bite (Figure 117–2).[52,64] Larger snakes generally inject more venom, but the potency is species variable. Children and small adults, as well as those with underlying medical conditions (diabetes, cardiovascular disease) may be more seriously affected by envenomation.[62] Envenomation usually occurs in subcutaneous tissues and less commonly in muscle. Systemic absorption occurs via lymphatic and venous drainage of the envenomated sites. Intravenous envenomation may occur and result in the rapid development of life-threatening complications.[22] Airway obstruction necessitating tracheal intubation has been reported after a rattlesnake bite to the face and tongue.[28] Individuals may be envenomated by rattlesnakes thought to be dead, even up to

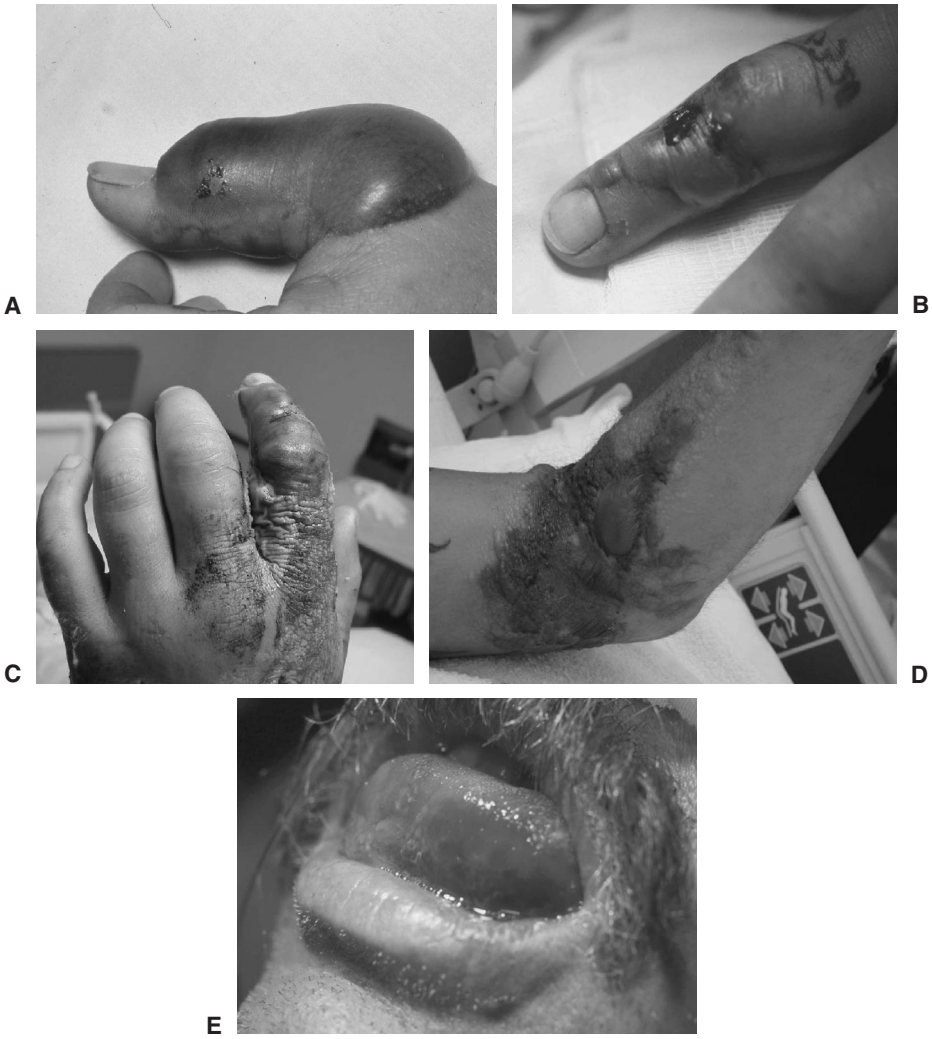

Figure 117–2. **A, B:** Hemorrhagic bullae approximately 24 hours following bite by *Crotalus atrox.* **C:** Swelling and hemorrhagic bullae 36 hours following bite by unknown rattlesnake. **D:** Antecubital hemorrhagic bullae and skin necrosis following bite by unknown rattlesnake. **E:** Tongue swelling 24 hours following bite to tongue by *Crotalus atrox.* (Copyright © 2002, Department of Toxicology. Good Samaritan Regional Medical Center.)

60 minutes after decapitation, because of persistent reflexes in the venom apparatus.[75]

Pit vipers produce a characteristic bite when they strike, and distinct fang marks usually can be identified (see ILDIAMONDBACK1 in the Image Library at goldfrankstoxicology.com). The small delicate fangs of coral snakes may not produce easily identifiable fang marks. Fang marks may be single, double, and occasionally multiple. Although most snakes have two fangs, the exact number of fang marks may vary because of glancing blows and/or multiple strikes. Protection by clothing or shoes can alter these findings. The bites of rodents, lizards, and even thorn or cactus injuries can be misdiagnosed as poisonous snakebites.

PHARMACOLOGY OF VENOM

It is difficult to attribute specific pathology or pathophysiology to particular components of snake venom. Crotaline venom is a complex heterogeneous solution and suspension of various proteins, peptides, lipids, carbohydrates, and enzymes, including ribonuclease and deoxyribonuclease, kinins, leukotrienes, histamine, phospholipase, serotonin, hyaluronidase, acetylcholinesterase, collagenase, and metallic ions.[44,45] It has been referred to as a "mosaic of antigens." Numerous unidentified proteolytic enzymes, procoagulants and anticoagulants, cardiotoxins, hemotoxins, and neurotoxins abound in crotaline venom, making it very complex to analyze.

Crotalinae venom can simultaneously damage tissue directly, affect blood vessels and cellular elements of blood, and alter the myoneural junction and nerve transmission. Toxic components of snake venom exhibit their pathology at varying times, and some of the variation in clinical manifestations of envenomation result not only from the specific properties of the venom but from differences in absorption rates and ability to permeate membranes and tissues. In addition, the content and potency of venom in any given snake vary with size, age, diet, climate, time of year, and possible cross-breeding among different species. Venom is present in the circulation and fixed to tissues. Circulating venom is more readily neutralized by antivenom, whereas the effects of tissue-fixed venom are more difficult to counteract. This may partly explain the clinical observation that antivenom corrects systemic dysfunction and coagulopathy but does little to reverse local pathology. Antivenom may halt progression of further edema, hemorrhage, and soft-tissue swelling, but once these conditions are present, antivenom likely will not rapidly reverse pathology at the site of envenomation.

Coral snake venom consists of a number of unidentified neurotoxins with curarelike effects that produce systemic neurotoxicity, as opposed to local tissue injury.

PATHOPHYSIOLOGY AND CLINICAL MANIFESTATIONS

Crotaline Envenomation

Local Reactions. Crotaline (pit viper) venom usually is injected only into the subcutaneous tissue, although deeper, intramuscular (subfascial) envenomation rarely occur. Not every bite from a venomous snake results in release of venom into the victim; so-called "dry bites" occur in up to 20% of strikes.[49] Repeat strikes may result in additional envenomation because the snake's entire supply of venom usually was not exhausted with the first attack. Approximately 25–75% of stored venom is discharged following a rattlesnake bite, and the entire supply is replenished in 3–4 weeks.[69]

Symptoms may range from mild to severe, but the initial benign presentation of a pit viper bite may be very misleading[43] (Table 117–2). Generally, within minutes after significant envenomation from a pit viper, the area around the bite becomes swollen and painful. Within minutes to hours, ecchymosis, blistering, and signs of tissue necrosis may be evident both proximal and distal to the bite. The patient may describe paresthesias or other neurologic symptoms around the bite. Edema may progress to involve an entire extremity within a few hours, and systemic symptoms may develop. The local reaction to pit viper envenomation results from altered blood vessel permeability and direct necrosis of the tissue caused by the venom. Additional tissue damage can result from the effects of ischemia, swelling, and rarely secondary infection. In addition to local myonecrosis, generalized severe rhabdomyolysis may occur in the absence of impressive muscular swelling. This finding is considered characteristic following envenomation of the canebrake rattlesnake (*Crotalus horridus atricaudatus*) found in the Gulf Atlantic states.[12] (See ILMASSASAUGA1, ILMASSASAUGA2, and ILRATTLER1 in the Image Library).

Compared with the venom of rattlesnakes, the venom of water moccasins (cottonmouths) produces less severe local and systemic pathology, and envenomation from copperheads tends to be less severe than that of either rattlesnakes or water moccasins. Although the soft-tissue swelling from a copperhead bite may be significant, envenomation from this snake usually does not cause coagulopathy, systemic symptoms, or extensive tissue destruction. Copperhead envenomation often results in only minimal edema and pain and usually requires only conservative local treatment.[80] (See ILCOPPERHEADHAND and ILCOPPERHEADTOE in the Image Library). Lethality is so rare that it is considered reportable.

Envenomation is a dynamic and ever-changing process that can rapidly or unpredictably progress to serious local or systemic involvement. The full extent of envenomation may not become evident for a number of hours. On rare occasions symptoms appear to be resolving, only to return minutes to hours later with greater intensity. If local symptomatology initially is ameliorated or arrested by antivenom therapy, the swelling may recur when antivenom concentrations drop hours later. As a general rule, however, it may be assumed that envenomation from a North American pit viper has not occurred (dry bite) if no symptoms develop within 8–12 hours from the time of the bite.

Systemic Signs. Most bites from pit vipers that occur on the extremities are limited to local or regional pathology; however, systemic symptoms and life-threatening toxicity may develop. When venom is injected subcutaneously, it travels by lymphatic and superficial venous channels and spreads slowly to the general circulation. Generally, subcutaneous envenomation produces systemic symptoms within a number of hours, but this timetable is variable. Occasionally, symptoms occur rapidly even with subcutaneous envenomation. Intravascular envenomation produces significant systemic symptoms in minutes.[22] Direct intravenous envenomation probably is rare, but this occurrence, in addition to the unusual case of overt anaphylaxis, may account for the majority of fatalities. Rarely, respiratory compromise from airway obstruction or bronchospasm is a direct consequence of crotaline envenomation.[28]

Systemic signs of pit viper envenomation vary, and some symptoms result from fear, pain, or anxiety alone. In mild cases, the patient may manifest nonspecific weakness, malaise, nausea, and restlessness. More severe envenomation produces confusion, abdominal pain, vomiting, diarrhea, sweating, dyspnea, tachycardia, hypotension, blurred vision, salivation, and a metallic taste in the

TABLE 117–2. Evaluation and Treatment of Crotaline Envenomation

Extent of Envenomation	Clinical Observations	Antivenom Recommendation[a]	Other Treatment	Disposition
None ("dry bite")	Fang marks may be seen, but no local or systemic symptoms after 8–12 hours	None	Local wound care Tetanus prophylaxis	Discharge after 8–12 hours of observation
Minimal	Minor local swelling and discomfort only, with no systemic symptoms or hematologic abnormalities	None	Local wound care Tetanus prophylaxis	Admit to monitored unit for 24-hour observation
Moderate	Progression of swelling beyond area of bite, with local tissue destruction, hematologic abnormalities, or systemic symptoms	Yes	IV fluids Cardiac monitoring Analgesics Follow laboratory values Tetanus prophylaxis	Admit to ICU
Severe	Marked progressive swelling and pain, with blisters, bruising, and necrosis; systemic symptoms such as vomiting, fasciculations, weakness, tachycardia, hypotension, and severe coagulopathy	Yes	IV fluids Cardiac monitoring Analgesics Follow laboratory values Oxygen Vasopressors PRN Tetanus prophylaxis	Admit to ICU

[a] See Antidotes in Depth: Crotaline and Elapid Antivenoms, for dosing recommendations.

mouth. Rarely, patients exhibit disseminated intravascular coagulation (DIC) with spontaneous bleeding, significant hypotension, and multiorgan system failure.[18,29] Although crotaline venom may be directly nephrotoxic, renal failure probably is secondary to hemoglobinuria, myoglobinuria, or cardiovascular collapse.

Local tissue destruction dominates Crotalinae envenomations, but neurotoxic effects also occur with certain species of snakes. The Mojave rattlesnake (*Crotalus scutulatus scutulatus*) produces the neurotoxic Mojave toxin, which can cause lethargy, cranial nerve dysfunction, and respiratory paralysis.[46] It acts at presynaptic terminals of the neuromuscular junction by inhibiting acetylcholine release. Mojave toxin is formed by a heterodimer protein composed of an acidic subunit and a basic subunit, both of which are required for a functional neurotoxin. Interestingly, production of Mojave toxin appears to be geographically distributed. A western population in California produces functional Mojave toxin A with neurotoxic effects, but little or no tissue destruction. More eastern populations lack the acidic subunit and do not make functional Mojave toxin, but do express metalloproteases that lead to tissue necrosis. Mojave rattlesnakes in an intergrade zone (Arizona and New Mexico) between these two populations produce both neurotoxic and tissue destructive toxins.[30,83] Bites from Mojave rattlesnakes in this zone often look identical to bites from other local rattlesnake species, with local tissue effects and hematologic toxicity, but an absence of clinical neurotoxicity. Mojave toxin has also been found in the venom of the Southern Pacific rattlesnake (*Crotalus halleri*) found in southern California, with envenomations leading to neurologic symptoms.[13,26] The Timber rattlesnake (*Crotalus horridus horridus*) commonly causes myokymia, particularly of the facial muscles.[7,53] Crotamine, a neurotoxic protein found in the venom of the South American rattlesnake (*Crotalus durissus terrificus*), typically produces analgesia at the bite location and possesses potent opioid activity.[6]

Hematologic. Significant crotaline envenomation may produce complex and dramatic hematologic abnormalities secondary to the effects of the venom on the blood coagulation pathways, endothelial cells, and platelets[3,9,68,73] (Figure 117–3). An initial drop in fibrinogen concentrations (to near zero) and platelet count (in the 10,000–50,000/mm^3 range), in addition to immeasurably high prothrombin time (PT) and partial thromboplastin time (PTT), frequently occur after moderate-to-severe crotaline envenomation. Regardless of which snake caused the envenomation, the majority of patients have no clinical bleeding, even with severe coagulopathies and thrombocytopenias. A routine coagulation profile and platelet count should be obtained following envenomation by a crotaline and repeated in 4–6 hours. Significant coagulopathy and/or thrombocytopenia may be present, but other systemic effects may be sparse. Coagulopathy is attributed to a complex variety of anticoagulants, procoagulants, fibrinolysin, and hemorrhagins in crotaline venom (Table 117–3). Some portions of snake venom may actually have therapeutic uses as anticoagulants or platelet receptor (GPIIb-IIIa) antagonists. Overall, crotaline venom has a thrombinlike effect, but specific hematologic effects are species dependent. No single venom contains all of the identified hemostatically active components. Thrombocytopenia ($<$150,000/mm^3) is a common finding following envenomation from most species of rattlesnakes and can occur in the absence of elevated PT or PTT.[3] Thrombocytopenia appears to be especially common, and often severe, following the bite of the timber rattlesnake (*Crotalus horridus horridus*), which inhabits the Appalachian mountains of the eastern United States.[3] The protein crotalocytin, which is found in timber rattlesnake venom, causes platelet aggregation and is thought to be at least partially responsible for thrombocytopenia. Following the trends in laboratory parameters is an important way to assess the progression or reversal of envenomation.

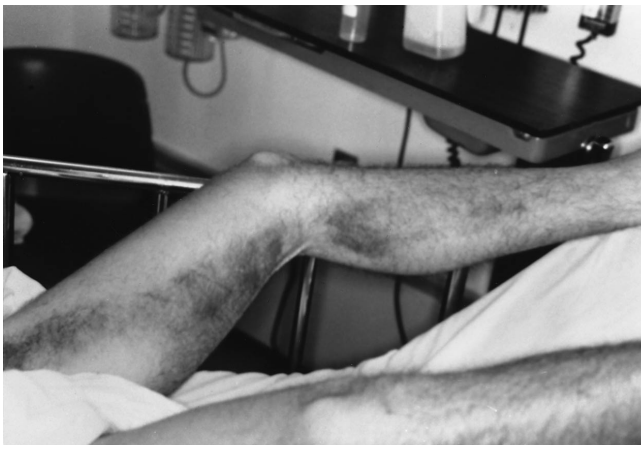

Figure 117–3. Ascending subcutaneous hemorrhagic ecchymosis developed within 8 hours of a copperhead bite to the foot. The ecchymosis follows the course of lymphatic or venous drainage. Only minor discomfort was noted. There was no systemic coagulopathy. The actual cause is unknown, but this case is an example of the hemorrhagic diatheses produced by crotaline envenomation. (Reproduced with permission from Roberts JR, Greenberg MI: Ascending hemorrhagic signs after a bite from a copperhead. N Engl J Med 1997;336:1262–1263.)

A major difficulty in objectively grading the severity of crotaline envenomation and following its progress is that no scoring system readily fits the vagaries of envenomation. Most patients exhibit only a subset of all of the possible consequences, so all, some, or none of the anticipated signs and symptoms may develop in any given individual. In addition, some of the characteristics of envenomation (nausea, tachycardia, restlessness, and tachypnea) may be related to fear and not to envenomation. A validated severity score for objective assessment of crotaline envenomation has

TABLE 117–3. General Hemostatic Characteristics of Snake Venom

Enzymes that clot fibrinogen
Enzymes that degrade fibrinogen
Plasminogen activators
Prothrombin activators
Factor V activators
Factor X activators
Anticoagulant activities including inhibitors of prothrombinase complex formation, inhibitors of thrombin, phospholipases, and protein C activators
Enzymes with hemorrhagic activity
Enzymes that degrade plasma serine proteinase inhibitors
Platelet aggregation inducers including direct-acting enzymes, direct-acting nonenzymatic components, and agents that require a cofactor
Platelet aggregation inhibitors including α-fibrinogenases, 5′-nucleotidases, phospholipases, and disintegrins

From Markland FS: Snake venoms and the hemostatic system. Toxicon 1998;36:1749–1800.

been developed for research purposes and holds promise as a standardization tool for clinical evaluation.[21]

Anaphylaxis. Rarely, patients bitten by crotalines experience classic anaphylaxis from the venom itself. This reaction can complicate evaluation, or mimic a severe systemic reaction to venom. In one report, a man developed pruritus and shortness of breath accompanied by hypotension, generalized urticaria, and wheezing immediately following a rattlesnake bite.[40] The symptoms quickly responded to standard treatment for anaphylaxis (epinephrine, antihistamines, and corticosteroids). The patient was bitten previously and may have been sensitized at that time. Snake handlers may be sensitized through inhalation or skin contact and develop IgE antibodies to venom. Antivenom is not indicated for treatment of anaphylaxis, but differentiating anaphylaxis from envenomation often is clinically difficult. The presence of pruritus and urticaria or wheezing, which is uncommon with envenomation, suggests anaphylaxis.[12]

Elapid Envenomation

The severe local reaction to crotaline envenomation contrasts with the usually minor pain and clinically unimpressive local reactions that occur with a coral snake bite. However, lack of local symptoms does not signify that serious envenomation has not occurred. Initially judging which patients bitten by coral snakes will develop symptoms is difficult. In general, less than 40% of patients bitten by a coral snake are subsequently determined to have been envenomated; rates for envenomations from the eastern coral snake species possibly are higher.[48] Coral snake envenomation may be manifested by serious systemic reactions with little symptomatology at the actual site of envenomation, even after an asymptomatic period of up to 12 hours. The venom of the eastern coral snake (*Micrurus fulvius*) and Texas coral snake (*Micrurus tenere*) are more potent than that of the Sonoran coral snake (*Micruroides euryoxanthus*). In fact, no cases are reported of serious toxicity following the bite of the Sonoran coral snake, which is found primarily in Arizona and western New Mexico.

Systemic Effects. The systemic effects of elapid envenomation (Table 117–4) are characteristically delayed for a number of hours.

TABLE 117–4. Signs and Symptoms of Envenomation by the Eastern Coral Snake (*Micrurus Fulvius*) (N = 20)

Sign or Symptom	Percent
Fang marks	85
Local swelling	40
Paresthesias	35
Nausea	30
Vomiting	25
Euphoria	15
Weakness	15
Dizziness	10
Diplopia	10
Dyspnea	10
Diaphoresis	10
Muscle tenderness	10
Fasciculations	5
Confusion	5

Reprinted, with permission, from Kitchens CS, Van Mierop LHS: Envenomation by the eastern coral snake (Micrurus fulvius): A study of 39 victims. JAMA 1987;258:1615.

One report described a patient who had an asymptomatic period of 13 hours followed by a sudden and precipitous deterioration severe enough to require ventilatory support.[49] The neurologic abnormalities noted included slurred speech, paresthesias, ptosis, diplopia, dysphagia, stridor, muscle weakness, fasciculations, and respiratory paralysis.[49] The major immediate cause of death from coral snake envenomations is respiratory arrest secondary to neuromuscular weakness; cardiovascular effects are less common than in crotaline envenomation. Patients can develop total-body paralysis that may last 3–5 days and take weeks to resolve completely. With respiratory support, however, the paralysis is completely reversible. Pulmonary aspiration is a common sequela in the subacute phase.

MANAGEMENT

Objectives for Treatment

The specific treatment of a patient with a snakebite is controversial, and the literature contains confusing and contradictory recommendations. Folklore and home remedies abound. The benign natural history of many bites undoubtedly has accounted for many apparent cures from "therapeutic" interventions such as ethanol, electric shocks, carbolic acid, strychnine, cauterization, and cryotherapy. Many accepted treatment plans are based on anecdotal or biased information, with conclusions drawn from animal studies or uncontrolled case reports. There are no universally accepted standards of care for many aspects of treatment.[81] Many authors tend to be staunch advocates of their particular regimens and are unwilling to accept a less rigid approach. The initial objectives are to determine the presence or absence of envenomation, to provide basic supportive therapy, to treat the local and systemic effects of envenomation, and to limit or repair tissue loss and/or functional disability (Table 117–2).

A combination of medical therapy including supportive care, antivenom when warranted, and conservative surgical treatment using debridement of devitalized tissue when indicated, individualized for each patient, likely will provide appropriate results. In general, the more rapidly treatment is instituted, the better the final outcome.

Observation of Asymptomatic Patients

All patients who report a history of snakebite from North American crotalines should be observed for 8–12 hours after the bite, if the skin is broken and the offending snake cannot be positively identified as nonpoisonous. The initial presentation of pit viper bites may be misleading. Significant worsening of a seemingly benign bite may occur as long as 24 hours after presentation,[43] but such cases are unusual. Restlessness, anxiety, abdominal pain, nausea, and tachycardia are nonspecific symptoms, but could signal systemic envenomation, and they should not be routinely dismissed as resulting from fear or anxiety. Fang marks may be subtle and easily mistaken for scratches or teeth marks. A prudent approach is to observe all victims of possible crotaline bites for at least 8–12 hours after the bite, and admit patients with any evidence of envenomation. If the patient was bitten by an exotic or nonnative snake, the period of observation should be extended to 12–24 hours.

Eastern coral snake bites can be misleading because of the absence of early symptomatology. Serious delayed neurologic and respiratory symptoms have been specifically noted, so patients bitten by these snakes should be observed for 24 hours regardless of initial presenting symptoms and treatment.

Initial Treatment

No first aid measures or specific field treatment is proven to positively affect the outcome of a crotaline envenomation. Undue importance is placed on the immediate prehospital care of patients with snakebites, and some therapies could be detrimental. When the patient is not in extremis and medical attention is available within a few hours, the prudent approach is a conservative one. The excitement or hysteria generated by a possible poisonous snakebite compels some caregivers to intervene quickly, often irrationally, and with unproven or harmful procedures. It is common to confuse treatment priorities and create additional morbidity with hurried or ill-conceived attempts to stop or limit "certain death" or subsequent amputation. In reality, both death and amputation are rare if proper medical attention is available within a few hours. Most morbidity stems from delayed treatment, either because of inaction of the patient, often related to alcohol intoxication, or because of inaccessibility to medical care. Prehospital care generally should be limited to immobilization of the patient's affected limb and rapid transport to a medical facility. Physical activity, such as walking, should be avoided because this action may hasten systemic absorption of venom. Prehospital personnel should follow standard advanced cardiac life support protocols for the rare unstable snakebite victim.

Pressure Immobilization

In the past, various methods have been advocated to prevent systemic absorption of venom following snakebites. The traditional tourniquet that occludes venous and arterial flow is contraindicated and may compound the initial insult by increasing edema and aggravating ischemia. (See ILTOURINQUET in the Image Library). Evidence indicates that a broad, firm, constrictive wrap (elastic bandage) placed over the bitten area and encircling the entire immobilized limb will slow the systemic absorption of venom. In a human volunteer study simulating intradermal and subcutaneous envenomation using labeled radiotracer, immediately wrapping an entire extremity with a rolled elastic bandage to a pressure of 50–70 mm Hg significantly delayed transit time from periphery to the systemic circulation.[42] This wrapping procedure (the Sutherland wrap) is intended to collapse lymphatics and superficial veins to retard venom uptake. A reasonable guide is to wrap the bandage as tightly as a compression bandage would be applied for a sprained ankle. A constriction band is not a true tourniquet. When a constriction bandage is applied properly, a finger can be easily placed between the band and the skin.

The pressure immobilization technique has been used for treatment of nonnecrotizing elapid snakebites in Australia where systemic toxicity is the major concern and transit times can be prolonged.[82] The benefit of this technique for the more necrotizing bite of North American pit vipers is less clear. A randomized controlled study using a porcine model with intramuscular injection of a lethal dose of *C. atrox* (western diamondback) venom followed by pressure immobilization versus observation was performed. The results demonstrated prolonged time to death in the pressure immobilization group but also markedly increased compartment pressures. With local tissue necrosis, not death, the major morbidity associated with North American pit viper envenomations, the authors concluded that pressure immobilization with a compression bandage cannot be suggested as a routine field procedure.[10] We do not recommend pressure immobilization for management of North American pit viper envenomations.

Venom Removal

Incision and suction, whether by mouth or a commercially available device, cannot be recommended as standard first aid in the field. Incision may lead to damage of underlying structures such as nerves and tendons, and mouth suction is unproven and can introduce bacteria into the wound. A commercially available plunger-type suction device (The Extractor, Sawyer Products, Long Beach, CA) can generate up to 1 ATA negative pressure when placed over nonincised puncture wounds for extraction of venom.[4] Animal models addressing this intervention give conflicting results. In human models, no benefit of negative-pressure venom extraction was found, and additional injury resulting from use of the device was possible. Venom extractors currently are unproved therapy and are not recommended.[1,11,27] Simple suction cups supplied in first aid kits are worthless.

It should be stressed that compression dressings and vacuum extraction should not be considered if the patient can rapidly reach a hospital. Minor pain or swelling is not an indication for aggressive field treatment. Furthermore, these treatments are never a substitute for rapid transport, in-hospital evaluation, or antivenom therapy. The bitten area should not be placed in ice, because cryotherapy is not effective in neutralizing venom, and may compound the initial injury.[56]

Immediate In-Hospital Therapy

The initial in-hospital approach to a victim of a poisonous snakebite follows standard accepted guidelines for stabilization and assessment of any patient with a potentially serious medical problem.[57] A complete medical history, including current tetanus immunization status and known allergies, should be obtained. A careful description of the bite and the extent of the local pathology should be documented, including measuring the diameter of the extremity and noting the extent of edema by marking the skin with a pen to help recognize progression of the envenomation. This evaluation should be repeated as required by the clinical condition. A comprehensive physical examination should be performed, with emphasis on vital signs, cardiorespiratory and neurologic status, neurovascular status of the extremity, and evaluation for evidence of melena, hematuria, and gingival bleeding. A baseline complete blood count (CBC and platelet count), electrolytes, urinalysis, blood urea nitrogen (BUN), glucose, PT, PTT, and fibrinogen concentration should be obtained initially and repeated in 4 to 6 hours.

Pain and anxiety should be treated with analgesics and anxiolytics as clinically warranted. Tetanus prophylaxis should be addressed. The extremity should be immobilized in a well-padded splint in near-full extension and elevated to prevent dependent edema. The patient should be reassessed frequently with serial vital signs and repeat physical examinations, specifically noting any progression of swelling. This can be accomplished by taking measurements of the circumference of the involved extremity at multiple points proximal to the wound.

Victims of proven copperhead bites should be observed for 8 hours and evaluated for signs of systemic involvement, development of coagulation abnormalities, or progression of local pathology. In many instances, the entire care of a patient with a minimal copperhead envenomation can be accomplished in the emergency department, but a conservative approach is advised. Hospital admission for further observation is warranted if follow up cannot be assured or if the identification of the snake or progression of symptoms is questionable.

Antivenom Therapy

For Crotaline envenomations, antivenom should be considered as first-line therapy for patients with moderate-to-severe envenomations (Table 117–2). Each clinical case must be individualized, but in the vast majority of patients who have a significant envenomation, the benefits of antivenom therapy outweigh the risks. Antivenom given in a timely manner can reverse the coagulopathy and halt progression of local symptoms.

The most common currently available antivenom for treatment of North American pit viper envenomation is Crotalidae polyvalent immune Fab CroFab, Protherics, Savage Laboratories). It is an ovine-derived Fab fragment antivenom developed from commonly encountered North American pit vipers. It has largely replaced the traditional Antivenin Crotalidae Polyvalent (Wyeth-Ayerst). Its use has produced far fewer hypersensitivity reactions than reported with administration of the equine-derived whole immunoglobulin product. It is infused intravenously in 4–6 vials doses reconstituted in 0.9% sodium chloride solution. The infusions are initiated at a slow rate. If no signs of anaphylactoid reaction develop (hives, wheezing), the rate is increased to complete the infusion over 1 hour. The patient is reassessed at the end of the infusion for evidence of progressive swelling or worsening thrombocytopenia or coagulopathy. If these conditions are present, a repeat dose of 4–6 vials is infused. This process is repeated until symptoms are controlled. Once control has been gained, maintenance doses are given as 2 vials every 6 hours for a total of 3 maintenance doses. Antivenom therapy is discussed in detail in Antidotes in Depth: Antivenom (Crotaline and Elapid).

Surgical Therapy

Envenomation may mimic a compartment syndrome by producing distal paresthesias, tense soft-tissue swelling, pain on passive stretch of muscles within a compartment, and muscular weakness. However, because subfascial envenomation is uncommon, much of the impressive edema produced by envenomation does not occur in compartmentalized areas. Using noninvasive vascular arterial studies and skin temperature determinations in patients with rattlesnake envenomation, a report demonstrated that pulsatile arterial blood flow to an envenomated extremity actually increased after envenomation, even distal to the site of envenomation.[17] A compartment syndrome cannot be reliably diagnosed in envenomated extremities without directly measuring compartment pressures. Although there is little doubt that some crotaline bites eventually may require some surgical debridement or even skin grafting, the initial routine use of tissue excision, fasciotomy, or "exploration and debridement" is not recommended.[36,76] Excising tissue likely will not significantly halt the envenomation process. Indications for fasciotomy are rare and only based on objective data of measured compartment pressures. Following crotaline envenomation, successful treatment of documented elevated compartment pressure with antivenom and mannitol alone is reported. [33] (See ILCOMPARTMENT1 and ILCOMPARTMENT2 in the Image Library).

Surgical debridement of necrotic tissue and hemorrhagic blebs and blisters usually is performed between 3 and 6 days after envenomation. Physical therapy should be instituted early to ameliorate joint stiffness and decrease swelling.

Surgery is not a concern in the treatment of coral snakebites. Similarly, copperhead and water moccasin bites rarely require surgical intervention, except for delayed local debridement.

Blood Products

Alterations in platelet count, PT/PTT, fibrin split products, and fibrinogen concentration are commonly encountered with crotaline envenomations. All such victims should be evaluated for a coagulopathy, even in the absence of symptoms.[22,62] Surprisingly abnormal laboratory results, such as immeasurably low fibrinogen concentrations, PT $>$100 seconds, and platelet count $<$20,000 are routinely encountered, and such abnormal laboratory results alone should not prompt the clinician to treat with blood products in the absence of major clinical bleeding. The circulating crotaline venom responsible for the initial hematologic changes still is present and likely will inactivate any component transfusions. For this reason, the mainstay of treatment for crotaline envenomation-induced coagulopathy is antivenom, not blood products. Correction of laboratory coagulation abnormalities and bleeding frequently can be achieved with antivenom. Monitoring trends in the coagulation profile is an objective way to assess the seriousness of envenomation and the response to antivenom therapy.

Rarely, antivenom alone does not correct a significant coagulopathy, in which case fresh-frozen plasma, cryoprecipitate, packed red blood cells, or platelet transfusions are required. The criteria for use of blood products appears to be arbitrary in clinical practice, but in general, blood products should be administered along with antivenom only if the patient is actively bleeding.

Thrombocytopenia following rattlesnake envenomation may be difficult, or impossible, to totally correct with platelet transfusions or large amounts of antivenom. The initial elevation of platelet counts following platelet transfusion or antivenom administration tends to be transient (lasting only 12–24 hours), and thrombocytopenia may persist for days to weeks after normalization of other coagulation parameters. The significance of prolonged thrombocytopenia in the absence of bleeding complications is uncertain. In the absence of bleeding, thrombocytopenia may be a benign self-limiting disorder that is best tolerated and closely followed in lieu of repeated platelet transfusions or additional antivenom administration.[67] Persistent thrombocytopenia, as an isolated finding, does not require aggressive threatment.[67] Hypofibrinogenemia alone generally is not associated with clinically significant bleeding and may not require correction. Coral snake venom does not alter coagulation, so no bleeding diathesis is expected.

Treatment of Coral Snake Envenomation

The benign local effects of coral snake envenomation can be misleading and mistakenly equated with a dry bite.[60] Because initially judging which patients are envenomated is impossible, any patient with confirmed coral snake exposure who have fang marks or other evidence of skin penetration should receive antivenom therapy, even in the absence of symptoms. A more conservative approach in the patient with a less likely coral snake envenomation still requires at least 24 hours of observation. Clinical deterioration may be totally unexpected and progress rapidly. Eastern coral snake envenomation can be fatal, but patients usually recover completely with supportive care and antivenom therapy. In one series, 6 of 39 patients required intubation and ventilation, but none died or suffered tissue loss or permanent neurologic sequelae.[49]

Other Considerations

Tetanus prophylaxis should be administered and hyperimmune tetanus antitoxin given if primary immunization is inadequate or the history is uncertain.

Prophylactic antibiotics are not indicated, as studies show extremely low (0–3%) rates of wound infections.[54] There is no rationale for use of corticosteroids or antihistamines in the routine treatment of patients with snakebites, but they are used to combat the rare cases of anaphylaxis from exposure to venom or the more common acute and delayed allergic reactions to antivenom. Corticosteroids may be detrimental to local tissue in the early stages of envenomation.[16] Cardiovascular collapse is a life-threatening consequence of severe systemic envenomation and should be treated aggressively with large amounts of antivenom, invasive monitoring, and standard intensive care techniques.[18] Vasopressors may be required, and respiratory compromise should be anticipated in severe cases. Because of sudden and unpredictable respiratory paralysis associated with coral snake envenomation, tracheal intubation should be considered at the first sign of bulbar paralysis. Any patient given antivenom or who has significant envenomation should be observed in an intensive care unit.

Multiple treatments with hyperbaric oxygen suggest that enhanced healing of myonecrosis may occur in mice injected with *C. atrox* venom. No effect on the edema associated with envenomation was observed in one study, and the beneficial effect was dose dependent, with up to 10 treatments (1–1.5 hours at 2–2.75 ATA) given.[47] The mechanism of action is not known but is speculated to be related to enhanced tissue oxygenation. The effects of hyperbaric oxygen therapy for poisonous snakebites in humans is unknown; its use should be considered experimental at this time.

Recurrence Phenomena of Crotaline Envenomation

Data detailing the natural history of crotaline envenomation following initial treatment with traditional Antivenin Crotalidae Polyvalent are sparse. However, studies assessing the efficacy and safety of ovine Fab antivenom have shed interesting light on the clinical course of victims of crotaline envenomation treated with this newer antivenom. Definite recurrent local and coagulopathic effects, in the form of worsening of symptoms after initial clinical improvement, are described following antivenom.[5,72] Recurrence phenomena are attributed to the interrelated kinetics and dynamics of venom and antivenom. Simply stated, Fab antivenom has a clinical half-life shorter than that of venom. Once tissue injury and coagulation deficits have been halted or corrected, tissue injury and coagulopathies may worsen, unless additional antivenom is administered. This may result in greater tissue injury and a risk of hemorrhage. Complicating matters, recurrence of coagulopathy may manifest days after hospital discharge. The exact clinical significance of this observation and need for clinical intervention are uncertain and may be predominately theoretical. Currently, the most reasonable way to address possible delayed recurrent effects of crotaline envenomation, especially coagulopathy, is careful followup after hospital discharge. This concern has not been extended to coral snake envenomation [see discussion in Antidotes in Depth: Antivenom (Crotalid and Elapid)].

Nonvenomous Snakebites

Approximately 50,000 snakebites occur annually in the United States, and most (90–95%) are from nonvenomous snakes.[32] Most snakes in the United States are nonvenomous, and the majority are of the Colubrid family, which are generally considered harmless to humans. However, several authors have reported toxic secretions from Duverney glands in many common species, including the hognose snake, garter snake, parrot snake, banded water snake, and ringneck snake.[35,58,78] Although no deaths have been reported, some victims developed coagulopathies and local edema and hemorrhage that could be confused with early crotaline envenomation.[56] No antivenom is available for treatment of bites from these snakes, and serious complications from nonvenomous snakebites are extremely rare.

Although Colubrids do not possess true fangs, some species, such as the common wandering garter snake (*Thamnophis* spp), have elongated and grooved posterior maxillary teeth (a primitive rear fang) that can penetrate the skin and deliver irritating saliva into the victim via a chewing motion. Some clinicians believe that the presence of teeth marks at the bite excludes the possibility that the bite was made by a venomous snake. Although it is true that fang marks are absent following nonvenomous snakebites, venomous snakes do have teeth, and abrasions or teeth marks may occur in conjunction with a venomous bite. This fact, along with the possibility that snakes heretofore considered nonvenomous may be dangerous, should make the clinician more cautious in diagnosing a nonvenomous bite based entirely on the presence of teeth marks.

When no sign of envenomation is present after an appropriate period of observation following a suspected nonpoisonous snakebite, attention should be focused on the basic principles of wound care. The wound should be cleansed, any foreign material removed, and an appropriate dressing applied. Certain large snakes of the Boidae family (not seen in the United States, except as pets or in zoologic gardens), including boas, pythons, and anacondas, may present a special problem because the force of contraction of their jaws may be great enough to cause severe tissue contusion or fractures and retained teeth (Figure 117–4). These reptiles also have numerous large, brittle teeth that commonly break off and lodge in the wound when the bitten part is forcibly extricated from the snake's mouth.

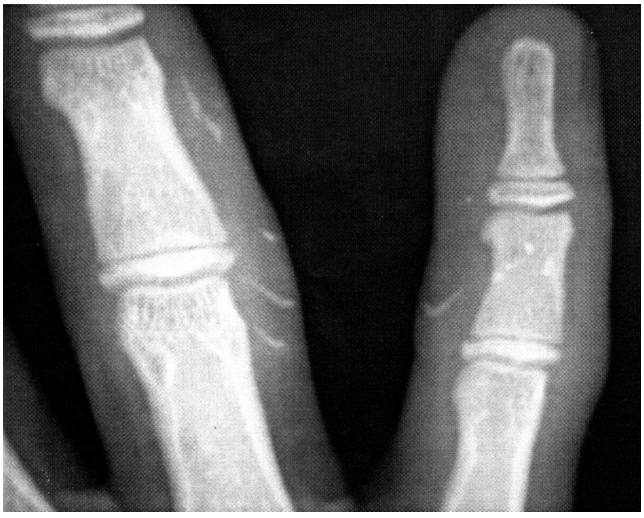

Figure 117–4. Significant local morbidity can result from the bite of nonvenomous snakes. This 10-year-old boy was bitten on the hand by a large albino python. After the snake was removed, the boy complained of persistent pain, redness, and swelling. The radiograph shows retained teeth in the soft tissues. Following a short hospitalization for intravenous antibiotics, the child recovered without sequelae. (Courtesy of the Toxicology Fellowship of the New York City Poison Center.

Usually radiographs of the bitten area are required to exclude fracture or foreign body.

The morbidity associated with a nonvenomous snakebite results from the rare case of bony injury and wound infection. Some authors recommend antibiotics for nonvenomous snakebites, but their routine use cannot be supported. In one report, no infections followed nonpoisonous snakebites in 72 patients bitten by a variety of nonpoisonous snakes indigenous to New England and imported boa constrictors and pythons.[79] Although *Clostridium tetani* has not been isolated from the mouths of snakes, the ubiquitous nature of this organism requires prophylaxis following the recommended approach for a contaminated wound. A cogent argument can be made for administering prophylactic antibiotics in nonvenomous snakebites if tooth fragments are retained or soft-tissue contusion is significant. A first-generation cephalosporin or antistaphylococcal penicillin given for 7–10 days should be adequate. Outpatient therapy is appropriate; the patient should be instructed on wound care and told to seek medical care if signs of infection occur. Minor abrasions from nonvenomous snakes require only local wound care and tetanus prophylaxis. Delayed infection should prompt an investigation for a retained foreign body, especially a tooth fragment.[38]

Special Considerations for Management of Pregnant Patients with Snakebites

Scant information on the effects of poisonous snakebites during pregnancy is available. Case series show that maternal death is rare, but fetal loss may be as high as 43%.[24] The mechanism of injury to the fetus from envenomation includes uterine artery hypotension and subsequent hypoxia, hemorrhagic complications such as abruptio placentae, or uterine contractions initiated by venom.[63]

Intracranial hemorrhage and death in an infant born at 34 weeks of gestation was reported in a woman envenomated by a copperhead during week 28 week of pregnancy.[25] At the time of the bite, she was given antivenom and developed anaphylaxis and hypotension, which was treated with large doses of epinephrine. It is suggested that the α-adrenergic effects of epinephrine on the uterine artery, coupled with maternal hypotension, contributed more to the fetal demise than the direct effects of venom. As in each case of snakebite, it is prudent to evaluate the need for antivenom carefully during pregnancy and to administer antivenom only when envenomation is significant and the benefits of antivenom outweigh the possible risks from allergic reactions. Fetal monitoring should be routine following poisonous snakebite.

Repeated Exposure to Snake Venom

Handlers and collectors are at risk for multiple bites over their careers, and questions have been raised about possible immunity. In a report of 14 patients with two or more bites, evidence that immunity develops as a result of repeated envenomation was not established.[64] Victims of repeat bites actually may be at greater risk for anaphylaxis because of a prior sensitization and the development of IgE antibodies to venom.

EXOTIC SNAKEBITES (See ILNAGANAGA2 in the Image Library)

Approximately 3% of poisonous snakebites in the United States are from nonnative species.[2,8,34] Many such snakes are owned by collectors, illegally imported, or stolen from zoos or pet stores. However, private individuals can easily purchase a plethora of vipers, cobras, and adders by mail or at reptile shows. There is surprisingly little regulation of the sale or ownership of exotic snakes in the United States. Exotic venomous snakes pose a particularly difficult problem for both diagnosis and management. Many victims are collectors or researchers who can identify the offending snake. However, because of fear of legal retribution, some owners of exotic snakes can be quite vague about the circumstances or origin of their envenomation. If they cannot provide identification, the local zoo, regional poison center, or herpetology society may be helpful. Once the snake is identified, the antivenom must be obtained. This is always a formidable task and often impossible, but local zoos, poison centers, or collectors may have the antivenom. Some poison centers, some zoos, and the American Association of Zoological Parks and Aquariums (301-562-0777) maintain the Antivenom Index, a listing of available antivenoms for exotic snakes, but these resources have limited ability to deliver many antivenoms. Bites from many nonnative Elapidae snakes, such as mambas, kraits, cobras, and several Australian species, are associated with high morbidity and mortality rates. Approximately one-third of bites from the king cobra are fatal.[34] Bites from these snakes may not display early local or systemic signs (Table 117–2); therefore, the grading system developed for North American pit vipers is not helpful. Although local tissue destruction and edema may develop, classically the neurologic signs, such as ptosis, dysphagia, muscular weakness, paresis, ophthalmoplegia, and respiratory failure, are noted, often at a delayed or advanced stage. Cobra envenomation usually produces significant local toxicity, and these snakes are the only elapids whose venom possesses hemorrhagic activity. Enzyme-linked immunosorbent assay techniques can be used to identify specific venom antigens in suspected exotic snakebites. This technique currently is not available in the United States but is used in Africa, Asia, and Australia. (See ILMALAYSIANCOBRA1 in the Image Library).

Guidelines for the administration of antivenom for exotic snakes are vague and empiric. In addition, there is little standardization of the antivenoms for the same snake among the different manufacturers. Exotic snakes generally are quite poisonous, so if fang marks are present, envenomation is strongly suspected, the snake is identified, and the specific antivenom is obtained, many physicians believe it is logical to proceed with antivenom administration empirically. Antivenom is administered according to the package insert. Generally, 4–5 vials are administered under the same guidelines given for crotaline antivenom. If the antivenom cannot be obtained, then supportive care and close in-hospital observation may be all that is possible. Local incision and suction are best avoided. Compression immobilization of an entire extremity with an elastic bandage (the Sutherland wrap) for the bite of some elapids (eg, sea snakes, kraits, cobras, and brown snakes) experimentally decreases the movement of elapid snake venom from the bite site to the systemic circulation and may be useful when antivenom is not available. This intervention, when it does not delay transport to medical care, has been recommended for bites from exotic elapids.[82] Crotalinae Polyvalent Antivenom (Wyeth) is ineffective for the bites of elapid snakes, but is active against venom of South American pit vipers, such as the bushmaster (*Lachesis muta*) and fer-de-lance (*Bothrops*). Whether Crotalidae polyvalent immune Fab (Protherics) is effective for South American pit viper envenomations is unknown. Coral snake antivenom is active only against the North American eastern coral snake and is not effective

against the western, Mexican, or South American species. It is prudent, but often difficult, to obtain expert assistance with managing any exotic snakebite.

One report documents dramatic reversal of the neurotoxic effects of a monocellate cobra (*Naja kaouthia*) bite following intravenous administration of the anticholinesterase neostigmine methyl sulfate (0.5 mg every 20 minutes for 4 doses).[31] The major neurotoxin from this snake is believed to resemble curare, causing a postsynaptic blockade of nicotinic neuromuscular receptor sites. The neurotoxicity from sea snakes and other elapids has also been experimentally reversed with neostigmine.[71] Edrophonium chloride (10 mg administered intravenously with 0.5 mg of atropine) has also been suggested.

Other Poisonous Reptiles in the United States

In North America there are 2 indigenous species of venomous lizards that belong to the order Squamata, the same order as venomous snakes: the Gila monster (*Heloderma suspectum*) and the beaded lizard (*Heloderma horridum*). These lizards are found primarily in the desert areas of Arizona, southwestern Utah, southern Nevada, New Mexico, California, and Mexico. They are large, slow-moving, nocturnal thick-bodied lizards that are prized by collectors and hobbyists. Adults are 30–40 cm long. In general, they are shy creatures, so bites are relatively rare, usually unintentional or secondary to handling. Gila monsters are known for their forceful bite. They have a propensity to hang on tenaciously during a bite and may be difficult to disengage. Some rather innovative anecdotal techniques have been developed to remove a Gila monster from an extremity, including the use of chisels, screwdrivers, and crowbars, pouring gasoline or ammonia into the lizard's mouth, or holding a flame to the animals jaw. Teeth may break off in the wound.

Gila monster venom is complex, containing components similar to those of snake venoms, including numerous enzymes, hyaluronidase, phospholipase A, kallikrein, and serotonin.[37,70,77] Helothermine is the suspected toxin. Their venom delivery systems are not as efficient as those of poisonous snakes and consist of venom glands and grooved teeth rather than fangs. Dry bites often occur because of the ineffective mechanism of delivery. Following skin puncture and venom release, the victim experiences local tenderness and soft tissue swelling, pain, and edema. Anaphylactoid reactions, hypotension, angioedema of lip, tongue, and throat, respiratory depression, coagulopathy, and myocardial infarction are reported occasionally.[65,66] Significant tissue destruction is unusual, but maceration may occur, and a cyanosis or blue discoloration is noted about the wound. No antivenom against lizard venom is available. Treatment consists of avoiding overaggressive local treatment and providing supportive care and wound care. Serious morbidity from lizard bites is unusual. The characteristics of the beaded lizard are similar, but their bites are less commonly confronted clinically.

Other Venomous or Poisonous Animals

It was generally believed that there are poisonous or venomous members of all classes of animals except birds. However, discoveries in New Guinea have added birds to the list.[23,41] Three avian Pitohui species have been found to contain homobatrachotoxin, a poison very similar to that in poison dart frogs of South America. Like the frogs, the Pitohui birds are conspicuous and brightly colored. Little information on the toxicity of these birds is available.

Several species of mammals contain venomous members. For example, the male Australian duckbilled platypus (*Ornithorhynchus anatinus*) has a hollow spur that can inject venom. The Cuban insectivore (*Solendon paradoxes*) and North American short-tailed shrew both secrete venom from the maxillary glands and bite with the lower incisors. Envenomations from mammals are rare, and little is known about the specific clinical toxicity from these creatures.

Several species of amphibians, frogs, toads (*Anura*), newts, and salamanders (*Urodela*) can secrete toxins through their skins, which may be a defensive repellant or alarm mechanism.[6,14,19,20,39] These creatures are not truly venomous because they have no specific mechanism for delivering the xenobiotic. Most cases of toxicity involve children or pets ingesting the animals. The best-known examples are the Colombian poison dart frogs (*Phyllobates* and *Atelopus*), which secrete the toxins zetekitoxin, tetrodotoxin, and batrachotoxin.[59] Batrachotoxin irreversibly activates (depolarizes) the sodium channel and is 250 times more toxic than curare in mice. Newts of the genus *Taricha* contain the irreversible sodium channel-blocking agent tetrodotoxin in their skin and internal organs. Their toxicity is expected to be similar to that occurring with puffer fish (fugu) poisoning (Chap. 45). Ingestion of a newt has potential adverse consequences. Treatment is supportive. The East Coast species is less toxic than the West Coast variety, the Oregon rough-skinned newt (*Taricha granulosa*). Salamanders of the genus *Salamandra* contain the very potent CNS toxin salamanderin. Large exposures theoretically could produce neurotoxicity.

Toad species of the genus *Bufo* have been abused by a curious technique of licking their skin, which contains a number of toxic substances, including biogenic amines (serotonin), steroids, and polypeptides. A lysergic acid diethylamide (LSD)-like high is reported, but there is considerable folklore and confusion on the exact effects.[55] Toxicity is reported following toad licking, toad mouthing, toad ingestion, and toad soup consumption. Salivation, seizures, and cardiac dysrhythmias have been reported with ingestion of toxin from *Bufo alvarius,* the Colorado River toad. The cane toad (*Bufo marinus*) is less toxic. Bufotalin, a cardioactive steroid toxin (bufadienolide) derived from this toad, has a chemical structure very similar to that of digoxin[50] (further details in Chap. 62).

SUMMARY

The physician faces numerous critical decisions when treating a patient who possibly has been bitten by a poisonous snake. The most basic questions to address are whether or not the patient actually was bitten by a snake and, if so, whether envenomation has occurred. Careful history and examination, along with judicious use of laboratory data and observation, should answer these questions. For patients with significant envenomations, supportive care and early use of antivenom are the mainstays of treatment.

REFERENCES

1. Alberts BM, Shalit M, LoGalbo F: Suction for venomous snakebite: A study of "mock venom" extraction in a human model. Ann Emerg Med 2004;43:181–186.
2. Bey TA, Boyer L, Walter FG, et al: Exotic snakebite: Envenomation by an African puff adder. J Emerg Med 1997;15:827–831.
3. Bond GR, Burkhart KK: Thrombocytopenia following timber rattlesnake envenomation. Ann Emerg Med 1997;30:40–44.

4. Bornstein AD, Russell FE, Sullivan JB: Negative pressure suction in field treatment of rattlesnake bite. Vet Hum Toxicol 1985;25:297–299.
5. Boyer LV, Seifert SA, Cain JS: Recurrence phenomena after immunoglobulin therapy for snake envenomations: Part 2. Guidelines for clinical management with Crotaline Fab antivenom. Ann Emerg Med 2001;37:196–210.
6. Bradley SG, Klika LJ: A fatal poisoning from the Oregon rough skinned newt *(Taricha granulosa*). JAMA 1981;246:247.
7. Brick JF, Gutmann L, Brick J, et al: Timber rattlesnake venom-induced myokymia: Evidence of peripheral nerve origin. Neurology 1987;37:1545–1546.
8. Britt A, Burkhart KK: *Naja naja* cobra bite. Am J Emerg Med 1997; 15:529–531.
9. Burgess JL, Dart RC: Snake venom coagulopathy: Use and abuse of blood products in the treatment of pit viper envenomation. Ann Emerg Med 1991;20:795–780.
10. Bush SP, Green SM, Laack TA, et al: Pressure immobilization delays mortality and increases intracompartmental pressure after artificial intramuscular rattlesnake envenomation in a porcine model. Ann Emerg Med 2004;44:599–604.
11. Bush SP, Hegewald KG, Green SM, et al: Effects of a negative pressure venom extraction device (Extractor) on local tissue injury after artificial rattlesnake envenomation in a porcine model. Wild Environ Med 2000;11:180–188.
12. Bush SP, Jansen PW: Severe rattlesnake envenomation with anaphylaxis and rhabdomyolysis. Ann Emerg Med;1995;25:845–848.
13. Bush SP, Siedenburg E: Neurotoxicity associated with suspected Southern Pacific rattlesnake envenomation. Wild Environ Med 1999; 10:247–249.
14. Chadwick JB: New England's venomous mammals. N Engl J Med 1969;281:274.
15. Cruz NS, Alvarez RG: Rattlesnake bite complications in 19 children. Pediatr Emerg Care 1994;10:30–33.
16. Cunningham ER, Sabback MS, Smith RM, et al: Snakebite: Role of corticosteroids as immediate therapy in an animal model. Am Surg 1979;45:757–759.
17. Curry SC, Kraner JC, Kunkel DB, et al: Noninvasive vascular studies in management of rattlesnake envenomation to extremities. Ann Emerg Med 1985;4:1081–1084.
18. Curry SC, Kunkel DB: Death from a rattlesnake bite. Am J Emerg Med 1985;3:227–235.
19. Daly JW: Biologically active alkaloids from poison frogs (Denodrobatidae). Toxin Rev 1982;1:33.
20. Daly JW, Myers CW, Whittaker N: Further classification of skin alkaloids from neotropical poison from Denodrobatidae, with a general survey of toxic/noxious substances in the amphibia. Toxicon 1987;25: 1023–1095.
21. Dart RC, Hurlbut KM, Garcia R, Bkoren J: Validation of severity score for the assessment of crotaline snakebite. Ann Emerg Med 1996;27:321–326.
22. Davidson TM: Intravenous rattlesnake envenomation. West J Med 1988; 148:45–47.
23. Dumbacher JP, Beehler BM, Spande TF, et al: Homobatrachotoxin in the genus *Pitohui*: Chemical defense in birds? Science 1992;258: 799–801.
24. Dunnihoo DR, Rush BM, Wise RB, et al: Snakebite poisoning in pregnancy: a review of the literature. J Reprod Med 1992;37:653–658.
25. Entman SS, Moise KJ: Anaphylaxis in pregnancy. South Med J 1984; 77:402.
26. French WJ, Hayes WK, Bush SP, et al: Mojave toxin in venom of *Crotalus halleri* (Southern Pacific rattlesnake): Molecular and geographic characterization. Toxicon 2004;44:781–99.
27. Gellert GA: Snake-venom and insect-venom extractors: An unproved therapy. N Engl J Med 1992;327:1322.
28. Gerkin R, Sergent K, Curry SC: Life-threatening airway obstruction from rattlesnake bite to the tongue. Ann Emerg Med 1987;16: 813–816.
29. Gibly RL, Nowlin SW, Berg RA: Intravascular hemolysis associated with North American crotaline envenomation. J Toxicol Clin Toxicol 1998;36:337–343.
30. Glenn JL, Straight RC, Wolfe MC, Hardy DL: Geographical variation in *Crotalus scutulatus scutulatus* (Mojave rattlesnake) venom properties. Toxicon 1983;21:119–130.
31. Gold BS: Neostigmine for the treatment of neurotoxicity following envenomation by the Asiatic cobra. Ann Emerg Med 1996;28:87–89.
32. Gold BS, Barish RA: Venomous snakebites: Current concepts in diagnosis, treatment and management. Emerg Med Clin North Am 1992;10: 249–267.
33. Gold BS, Barish RA, Dart RC, et al: Resolution of compartment syndrome after rattlesnake envenomation utilizing non-invasive measures. J Emerg Med 2003;24:285–288.
34. Gold BS, Pyle P: Successful treatment of neurotoxic king cobra envenomation in Myrtle Beach, South Carolina. Ann Emerg Med 1998;32: 736–738.
35. Gomez HF, Davis M, Phillips S, et al: Human envenomation from a wandering garter snake. Ann Emerg Med 1994;23:1117–1118.
36. Hall EL: Role of surgical intervention in the management of crotaline snake envenomation. Ann Emerg Med 2001;37:175–180.
37. Hendon RA, Tu AT: Biochemical characterization of the lizard toxin gilatoxin. Biochemistry 1981;20:3517–3522.
38. Herman RS: Nonvenomous snakebite. Ann Emerg Med 1988;17: 1262–1263.
39. Hitt M, Ettinger DD: Toad toxicity. N Engl J Med 1986;314:1517–1518.
40. Hogan DE, Dire DJ: Anaphylactic shock secondary to rattlesnake bite. Ann Emerg Med 1990;19:814–816.
41. Holloway M: Pitohui: The colorful bird that looks better than it tastes. Sci Am 1993;258:20–22.
42. Howarth DA, Southee AE, Whyte IM: Lymphatic flow rates and first-aid in simulated peripheral snake or spider envenomation. Med J Aust 1994;161:695–699.
43. Hurlbut KM, Dart RC, Spaite D: Reliability of clinical presentation for predicting significant pit viper envenomation. Ann Emerg Med 1988;12:438.
44. Iyaniwura TT: Snake venom constituents: Biochemistry and toxicology, Part 1. Vet Hum Toxicol 1991;33:468–474.
45. Iyaniwura TT: Snake venom constituents: Biochemistry and toxicology, Part 2. Vet Hum Toxicol 1991;33:475–480.
46. Jansen PW, Perkin RM, VanStralen D: Mojave rattlesnake envenomation: Prolonged neurotoxicity and rhabdomyolysis. Ann Emerg Med 1992;21:322–325.
47. Kelly JJ, Sadeghani K, Gottlieb SF, et al: Reduction of rattlesnake-venom-induced myonecrosis in mice by hyperbaric oxygen therapy. J Emerg Med 1991;9:1–7.
48. Kitchens CS, Van Mierop LHS: Envenomation by the eastern coral snake (*Micrurus fulvius fulvius*). JAMA 1987;258:1615–1618.
49. Kunkel DB, Curry SC, Vance MV, Ryan PJ: Reptile envenomations. J Toxicol Clin Toxicol 1983–1984;21:503–526.
50. Kwan T, Paiusco AD, Kohl L: Digitalis toxicity caused by toad venom. Chest 1992;102:949–950.
51. Langley RL, Morrow WE: Deaths resulting from animal attacks in the United States. Wild Environ Med 1997;8:8–16.
52. Lewis JV, Portera CA: Rattlesnake bite of the face: Case report and review of the literature. Am Surg 1994;60:681–682.
53. Lewis RL, Gutmann L: Snake venoms and the neuromuscular junction. Semin Neurol 2004;24175–179.
54. LoVecchio F, Klemens J, Welch S, Rodriguez R: Antibiotics after rattlesnake envenomation. J Emerg Med 2002;23:327–328.
55. Lyttly T, Goldstein D, Gartz J: Bufo toads and bufotenine: Fact and fiction surrounding an alleged psychedelic. J Psychoactive Drugs 1996; 28:267–281.
56. McCollough N, Gennaro J: Evaluation of venomous snakebite in the southern United States. J Fla Med Assoc 1963;49:959–967.
57. McKinney PE: Out-of-hospital and interhospital management of Crotaline snakebite. Ann Emerg Med 2000;37:168–174.

58. McKinstry DM: Evidence of toxic saliva in some colubrid snakes of the United States. Toxicon 1978;16:523–534.
59. Myers CW, Daly JW: Dart-poison frogs. Sci Am 1983;248:96–105.
60. Norris RL, Dart RC: Apparent coral snake envenomation in a patient without visible fang marks. Am J Emerg Med 1989;7: 402–405.
61. Parrish HM: Incidence of treated snakebites in the United States. Public Health Rep 1966;81:269–276.
62. Parrish HM, Goldner JC, Silbert SL: Comparison between snakebites in children and adults. Pediatrics 1965;36:251.
63. Parrish HM, Khan MS: Snakebite during pregnancy. Report of four cases. Obstet Gynecol 1966;27:468–471.
64. Parrish HM, Pollard CB: Effects of repeated poisonous snakebites in man. Am J Med Sci 1959;237: 277–286.
65. Placentine J, Curry SC, Ryan PJ: Life-threatening anaphylaxis following Gila monster bite. Ann Emerg Med 1986;15:147–149.
66. Preston CA: Hypotension, myocardial infarction, and coagulopathy following Gila monster bite. J Emerg Med 1989;7:38–40.
67. Rao RB, Palmer M, Touger M: Thrombocytopenia after rattlesnake envenomation. Ann Emerg Med 1998;31:139–141.
68. Roberts JR, Greenberg JI: Ascending hemorrhagic signs after a bite from a copperhead. N Engl J Med 1997;336:1262–1263.
69. Russell FE: Snake Venom Poisoning. Philadelphia, JB Lippincott, 1980.
70. Russell FE, Bogert CM: Gila monster: Its biology, venom and bite—A review. Toxicon 1981;19:341–359.
71. Sakai A, Junsuke T, Mamoru V: Efficacy of anticholinesterase against paralysis caused by postsynaptic neurotoxic snake venom [abstract]. Ann Emerg Med 1995;26:712–713.
72. Seifert SA, Boyer LV: Recurrence phenomena after immunoglobulin therapy for snake envenomations: Part 1. Pharmacokinetics and pharmacodynamics of immunoglobulin antivenoms and related antibodies. Ann Emerg Med 2001;37:189–195.
73. Simon TL, Grace TG: Envenomation coagulopathy in wounds from pit vipers. N Engl J Med 1981;305:443–447.
74. Spaite D, Dart R, Sullivan JB: Skin testing in cases of possible crotaline envenomations. Ann Emerg Med 1988;7:105–106.
75. Suchard JR, LoVecchio F: Envenomations by rattlesnakes thought to be dead. N Engl J Med 1999;340:1930.
76. Tanen DA, Danish DC, Grice GA, et al: Fasciotomy worsens the amount of myonecrosis in a porcine model of crotaline envenomation. Ann Emerg Med 2004;44:99–104.
77. Tu AT: Handbook of Natural Toxins, Vol. 5. New York, Marcel Dekker, 1991, pp. 755–776.
78. Vest DK: Toxic Duvernoy's secretions of the wandering garter snake *Thaminophis elegans vagrans*. Toxicon 1981;19:831–839.
79. Weed HG: Nonvenomous snakebite in Massachusetts: Prophylactic antibiotics are unnecessary. Ann Emerg Med 1993;22:220–224.
80. Whitley RE: Conservative treatment of copperhead snakebites without antivenom. J Trauma 1996;41:219–221.
81. Wingert WA, Chan L: Rattlesnake bites in southern California and rationale for recommended treatment. West J Med 1988;148:37–43.
82. Winkel KD, Hawdon GM, Levick N: Pressure immobilization for neurotoxic snake bites. Ann Emerg Med 1999;34:294–295.
83. Wooldridge BJ, Pineda G, Banuelas-Ornelas JJ, et al: Mojave rattlesnakes (*crotalus scutulatus scutulatus*) lacking the acidic subunit DNA sequence lack Mojave toxin in their venom. Comp Biochem Physiol B Biochem Mol Biol 2001;130:169–179.