Bites and Stings – Snakes, Spiders, and Scorpions in the United States

A 10-year-old boy is brought into an emergency department in San Diego, California after being bitten on the right hand by a rattlesnake. Although the envenomation occurred just one hour ago, there is swelling proceeding up the forearm. The patient is agitated and vomiting, and fine fasciculations of the face and upper extremities are present. The platelet count is 60,000/mm³, the fibrinogen is 90 mg/dL and the PT/PTT are elevated. The parents are frightened and want to know what you are going to do for their son.

A five-year-old girl in Jacksonville, Florida was bitten on the right ankle by a small snake that was red, yellow, and black in color. Her parents initially did not seek medical attention since she had no symptoms and seemed fine. Several hours later, she is brought by ambulance to your emergency department due to difficulty swallowing, paresthesia, generalized weakness, and shallow respirations. What snake is responsible for this patient’s symptoms and what are your priorities of treatment for this life-threatening envenomation?

A 13-year-old girl in Dallas, Texas was bitten on the left thigh by a black widow spider when she was looking for an old toy in the garage. On presentation to your emergency department, she is grimacing, restless, diaphoretic, and tachycardic, with severe pain and cramping of her left thigh and abdominal muscles. What is causing these impressive symptoms and what therapeutic measures should be implemented to treat this envenomation?

A two-year-old boy was stung on the left foot by a scorpion while he and his family were visiting Tucson, Arizona. He is brought to a local emergency department where he is noted to be agitated and drooling excessively with wandering eye movements. He has fine fasciculations of his tongue and intermittent shaking of his extremities. He is tachycardic with a heart rate of 190 beats per minute. His parents are very nervous and ask you if he is going to be okay.
Snakes, spiders, and scorpions are generally feared by the public because of the folklore that surrounds these animals and their potential to cause serious envenomation. These bites are rarely fatal in the United States but significant morbidity may result, especially when inappropriate treatment is administered. The lay public is often only aware of those treatments that they see and read in the media. These techniques may be antiquated and often cause more harm than good.

The unpredictable nature of these envenomations can make assessment and management difficult. The medical literature often consists of case reports and other anecdotal evidence, making evidence-based decisions tricky at best. Fortunately, there are some well-designed animal studies, large case series, and laboratory studies available to guide the clinician.

It is of the utmost importance that emergency physicians are up to date with currently accepted treatment of snake, spider, and scorpion envenomations. This issue of Pediatric Emergency Medicine Practice will focus on the evaluation and management of these bites and stings in the United States.

Critical Appraisal Of The Literature

The literature review for this article included Ovid MEDLINE® and PubMed searches for articles related to crotaline and elapid snakebites, black widow and brown recluse spider envenomations, and scorpion stings. Further manual literature searches of references from key publications and textbooks provided additional articles for review. The relevant literature cited in this article is provided for the reader in the reference section.

The major limitation of the literature for all of these envenomations is the lack of randomized, controlled human studies of therapeutic interventions, including the use of antivenom. Much of the literature consists of small animal studies or uncontrolled case series. The literature used for this review article consisted of 37 case reports/series, 22 review articles, 10 retrospective chart reviews, 10 in-vitro comparative studies, 5 prospective studies, 5 letters to the editors, and 2 textbooks. However, the use of published guidelines and grading systems should provide more consistency in the treatment of these envenomations and provide the basis for future study of outcomes for therapeutic interventions.

Although there are no universally accepted standards of care, we seek to provide an evidence-based approach to management while reminding the reader of the limitations of the literature.

Part I. Snakes

Epidemiology

We will discuss the main types of venomous snakes found in the United States, namely the crotalinae (pit viper) and elapidae (coral snake) species. Exotic snakes in the United States are usually restricted under the care of zoos and experienced handlers. Zoos are required to carry antivenoms for the exotic snakes and usually have contracts with specific hospitals to care for victims of these envenomations. Exotic snake envenomations will not be discussed in this issue.

Venomous snakes are found throughout the United States except in Maine, Alaska, and Hawaii. Most snakes hibernate in the winter and, as a result, the majority of bites in the United States occur between May and October. Most bites involve the extremities, although the occasional bite to the face and tongue may occur when the snake is held close to the body. In children, most bites occur to the lower extremities in contrast to adult patients who typically present with upper extremity injuries. Children, intoxicated individuals, snake handlers, and collectors are frequent victims.

It is important to note that some crotaline bites do not impart venom; these are known as “dry bites.” Dry bites are defined as bites that do not result in local tissue damage, hematological abnormalities, or regional lymph node pain; they have been reported in the medical literature to occur in approximately 25% of crotaline snakebites. The true incidence of dry bites may be much higher since they may not be seen in an emergency department and are not reported to the local poison center.

Though rarely fatal, snakebites do occur with significant frequency in the United States. In 2005, there were over 2900 reports to U.S. poison centers of people who were bitten by crotaline snakes, with 79% of these reports involving rattlesnakes and copperheads. 116 victims were less than six years of age and 542 patients were between 6 to 10 years of age. 1875 victims were evaluated at a health care facility. Six deaths were reported with rattlesnakes and unknown crotaline bites. 171 patients were reported...
to have life-threatening envenomations.5,6

Coral snake envenomations occur less frequently than crotaline bites. In 2005, 58 exposures were called to poison centers, of which, 14 victims were less than 19 years of age. Six victims had life-threatening envenomations, and there were no deaths.5

Etiology

Crotaline Snakes

Crotaline snakes are also known as pit vipers. They are identified by their triangular head, elliptical pupils, and fangs. The fangs are connected to venom sacs that inject venom. They can also retract on a hinge-like mechanism. The fangs have been reported to envenomate victims even after the snake’s death. In addition, the underside of the snake has a single row of caudal plates or scales, as opposed to the double row found on non-poisonous varieties.7,8

Crotaline snakes account for 99% of venomous snakebites in the United States. The remaining 1% result from bites of elapid (coral snake) and exotic species. Rattlesnakes account for 65% of crotaline snakebites while copperheads are responsible for 25%; the remaining 10% are from water moccasins.9,10 Rattlesnakes, in addition to having the longest fangs, have distinctive red, yellow, and black bands. There are many mimickers of the coral snake, including the California king snake. The misidentification of coral snakes is a common reason for envenomation.

In a study with 39 victims, nine patients were envenomated because they believed that they were dealing with the nonpoisonous scarlet king snake. The king and coral snake can be distinguished by the spacing of their colored rings and the color of their snouts. Coral snakes have black snouts and king snakes have red snouts. The red, yellow, and black rings are in different sequences. In the coral snake, the red and yellow rings touch while, in the king

| Table 1. Selected Venomous North American Snake Species |
|-----------------------------|-------------------|-----------------------|
| **Species (Common name, Scientific name)** | **Description** | **Geographic Location** |
| Crotaline Snakes | Length: 0.5 - 2 meters. Color: dark brown with large, dark diamond shapes edged in yellow trim, running down the length of its body. Vertical light stripes on snout. | Florida to north eastern North Carolina, west to southern Mississippi and eastern Louisiana. |
| Eastern Diamondback (C. adamanteus) | | |
| Western Diamondback (C. atrox) | Length: 1 - 1.2 meters. Color: gray-brown with dorsal dark grey to brown body blotches. Tail has 2 to 8 black and white bands. | Southeast California, Arizona, New Mexico, Texas, South Nevada, Oklahoma, Arkansas and Mexico. |
| Timber (C. horridus horridus) | Length: 0.9 - 1 meter Color: Varying colors with thick and wavy crossbands. | Southern Minnesota and southern New Hampshire, south to east Texas and north Florida. Found also in southern Canada. |
| Mojave (C. scutulatus scutulatus) | Length: 1 meter. Color: brown to pale green with dark diamond pattern down its back with white and black bands near its tail. | Southern California, southern Nevada, extreme southwestern Utah, most of Arizona, southern New Mexico and western Texas. Also in Mexico to southern Puebla. |
| Southern Pacific (C. viridis helleri) | Length: 0.7 - 1.1 meters. Color: brown to olive-brown with dark brown patches on back completely outlined by lighter pigment. Patches turn to bars near tail and are surrounded by dark rings. | Southern California to Mexico. |
| Canebrake (C. horridus atricaudatus) | Length: 0.9 - 1.5 meters. Color: dark-gold with brown stripe running down back. Tail end darkens to black. | Southern Virginia, south to Florida and west to Texas. |
| Other Crotaline Snakes | | |
| Copperhead (Agkistrodon contortrix) | Length: 0.5 - 1.2 meters. Color: light and dark brown or greenish banding that narrow dorsally giving the bands an hourglass shape. | East Coast from Massachusetts south to Florida and west to Oklahoma and Texas. Also found in Mexico. |
| Cottonmouth, Water Moccasin (Agkistrodon piscivorus) | Length: 0.5 - 1.2 meters. Color: dark in color, either black, dark brown, or a dark olive-green, with a muddy appearance. Occasionally, with muted banding. | East coast from Virginia to Florida. Through eastern Oklahoma and Missouri, north to southern Illinois, and east to Kentucky, Tennessee, and Alabama. |
| Elapid Snakes | | |
| Sonoran or Arizona Coral Snake (Micruroides euryxanthus) | Length: 0.3 - 0.5 meters. Color: red on yellow (or white) on black banding. Body: thin bodied, head and body are the same width, small round eyes and blunt snout. | Lowland regions from Arizona to Mexico. |
| Eastern Coral Snake (Micruirus fulvius fulvius) | Length: 0.5 - 0.8 meters. Color: Red on yellow on black banding. Body: thin-bodied, head and body are the same width, small round eyes and blunt snout. | Coastal plains of North Carolina to Louisiana, southeast to Florida. |
| Texas Coral Snake (Micruirus fulvius tenere) | | Texas and Louisiana south to Mexico. |

Elapid Snakes

The coral snakes (Micruroides and Micrurus spp.) have distinctive red, yellow, and black bands. There are many mimickers of the coral snake, including the California king snake. The misidentification of coral snakes is a common reason for envenomation.

In a study with 39 victims, nine patients were envenomated because they believed that they were dealing with the nonpoisonous scarlet king snake. The king and coral snake can be distinguished by the spacing of their colored rings and the color of their snouts. Coral snakes have black snouts and king snakes have red snouts. The red, yellow, and black rings are in different sequences. In the coral snake, the red and yellow rings touch while, in the king

Cottonmouth, Water Moccasin (Agkistrodon piscivorus) are semi-aquatic and have a distinctive white oral mucosa. They are reported to be aggressive and can bite underwater. Copperheads (Agkistrodon contortrix) are known for their coppery brown color and hourglass-shaped bands on their bodies.
snake, the red and black rings touch. This has lead to the common saying, “Red on yellow, kill a fellow; red on black, venom lack.”11,12

Envenomations by these snakes are not as frequent as crotaline bites because the venom apparatus is not as efficient for venom delivery and the snake’s small mouth size makes it difficult to maintain a large aperture. Coral snakes are a non-aggressive species of snake and live mostly underground. Most of the bites occur when the snakes are being handled.11,13

The coral snake relies on a chewing action to deliver its venom through hollow, short, anterior maxillary fangs which measure about 2 mm in length. It is generally thought that the snake must maintain its bite-hold for a prolonged period of time in order to administer a significant amount of venom. In most cases, fang marks will be evident at the site of injury, but there have been case reports of apparent coral snake envenomation where no marks were evident at the site of the bite. It has been estimated that envenomation occurs in less than 40% of coral snake bites.12,14

Pathophysiology

It is important to note that, since children have smaller limbs, less subcutaneous tissue, and smaller body mass, they can potentially receive more venom per kilogram of body weight and therefore have more clinical severity than adults.6

Venoms

Crotaline Venom

Crotaline venom is a complex solution of various proteins, peptides, lipids, carbohydrates, and enzymes, including ribonuclease, deoxyribonuclease, kinins, leukotrienes, histamine, phospholipase, serotonin, hyaluronidase, acetylcholinesterase, collagenase, and metallic ions.35,16 These components allow the snake to kill prey quickly and begin the process of digestion. Specific components cause direct tissue injury, capillary leakage, coagulopathy, and neurotoxicity. Crotaline bites usually cause severe pain from the time of envenomation and swelling that can progress at variable rates due to the lymphatic transport of venom.

Tissue damage at the site of the bite is the most common complication following envenomation by North American crotaline snakes. The etiology of this effect is only partially understood because snake venom varies with the different species of snakes, the individual members of the species, the season, and the nutritional status, location, and age of the snake. It is therefore difficult to predict the extent of local tissue damage that can develop following snakebites.2

After a bite, the area may become edematous and tense. Ecchymosis can be prominent. Fluid filled or hemorrhagic bullae can form at the site of the bite and necrosis may eventually become evident. Local reactions to envenomations are secondary to increased blood vessel permeability and direct tissue necrosis caused by the venom with additional tissue damage due to ischemia and swelling. Generalized rhabdomyolysis may occur in the absence of impressive muscular swelling in the case of envenomation by the canebrake rattlesnake (Crotalus horridus atrox).17

Venom metalloproteinases (VMPs) are important in the pathogenesis of tissue necrosis at the site of the bite because they cleave protumor necrosis factor alpha (pro-TNF alpha) and release activated TNF alpha, a mediator of the inflammatory response and inducer of macrophage differentiation. TNF alpha is also responsible for neutrophil degranulations, leukocyte migration, release of mediators of inflammation (i.e., interleukins), as well as its own synthesis and release by macrophages. It also stimulates the production of endogenous human metalloproteinases (HMPs). These HMPs subsequently cleave more pro-TNF alpha, further amplifying the inflammatory reaction. In addition, HMPs injure tissue directly by degrading extracellular matrix proteins. This self-inducing cycle causes an inflammatory response that is further augmented by other enzymes.2,18

Envenomation is a dynamic process which can progress unpredictably to serious local or systemic involvement. The full extent of symptoms may not be evident for hours. However, as a general rule, if there are no symptoms within six to eight hours, the patient can be considered medically cleared.6

Hematological abnormalities are common in crotaline envenomations. Coagulopathies were reported in over 40% of victims envenomated by all North American crotalines.19 In another series, coagulopathy was present in 60% of rattlesnake envenomation victims, hypofibrinogenemia was present in 49%, and thrombocytopenia was present in 33%.1

Hypofibrinogenemia results from fibrinolysins and thrombin-like enzymes in the crotaline venom. These specific components cause depletion of fibrinogen and elevation of fibrin and fibrinogen degradation products which cause elevation of prothrombin.
snake venom also contains nonspecific proteases that degrade clotting factors or activate the coagulation cascade, further prolonging clotting times.\textsuperscript{1,2}

There are different mechanisms responsible for the thrombocytopenia that results from crotaline envenomation. Platelet destruction may be mediated by the action of phospholipases which damage platelet membranes. In addition, the rapid rise in platelet count seen following administration of antivenom suggests that platelets are sequestered in the local microvasculature and subsequently released after antivenom treatment.\textsuperscript{1,2}

Thrombocytopenia is particularly common and often severe following the bite of the Timber Rattlesnake (\textit{Crotalus horridus horridus}). Timber Rattlesnake venom contains the protein crotalocytin which causes platelet aggregation and is thought to be partially responsible for thrombocytopenia.\textsuperscript{20}

The venom of water moccasins or cottonmouths produces less severe local and systemic pathology than rattlesnakes. Furthermore, copperhead envenomations tend to be less serious than water moccasins.\textsuperscript{3,11} Copperhead envenomations cause significant soft tissue edema but usually do not cause significant coagulopathy, systemic symptoms, or extensive tissue destruction; they usually require only conservative local treatment. However, with the availability of CroFab\textsuperscript{®} (Crotalidae Polyvalent Immune Fab), a sterile, nonpyrogenic, purified, lyophilized preparation of ovine Fab, more copperhead snakebites are being treated with antivenom.\textsuperscript{10,22}

An important exception to these general observations regarding crotaline envenomations is that of the Mojave Rattlesnake (\textit{Crotalus scutulatus scutulatus}), whose venom contains a potent neurotoxin. A patient bitten by a Mojave Rattlesnake can present with cranial nerve dysfunction, muscle fasciculations, and weakness, with delayed onset of paralysis and respiratory failure similar to coral snake envenomations.\textsuperscript{5,23}

In addition to the Mojave Rattlesnake, neurotoxic effects are described following Southern Pacific Rattlesnake (\textit{C. viridis helleri}), Western Diamondback Rattlesnake (\textit{C. atrox}), and Timber Rattlesnake (\textit{C. horridus horridus}) envenomations.\textsuperscript{24,25} Mojave toxin (venom A) may cause muscle paralysis by inhibition of acetylcholine release at the presynaptic neuromuscular junction, whereas muscle fasciculations may be caused by altered calcium binding on the nerve membrane. Successful treatment of fasciculations secondary to Mojave Rattlesnake and Western Diamondback Rattlesnake envenomations with CroFab\textsuperscript{®} has been reported.\textsuperscript{25} However, fasciculations secondary to Southern Pacific Rattlesnake envenomation may be refractory to CroFab\textsuperscript{®} treatment.\textsuperscript{26} Although CroFab\textsuperscript{®} incorporates Mojave Rattlesnake venom into its production process, the neurotoxic proteins in other North American rattlesnake venoms may not have sufficient immunogenic similarity to be neutralized by CroFab\textsuperscript{®}.\textsuperscript{26}

**Elapid Venom**

Coral snake venom has various toxins which produce systemic neurotoxicity, resulting in the loss of muscle strength and death by respiratory paralysis. Coral snake envenomations may present with serious systemic toxicity with little symptomatology at the actual site of the envenomation due to the venom’s lack of cytotoxicity.

\textit{M. fulvius} venom contains phospholipase A2 and alpha neurotoxin. The cardiotoxic or myotoxic phospholipase A2 has been theorized to depolarize the muscle fiber membrane. The alpha neurotoxins block motor endplate acetylcholine receptors, decreasing neuron activity. Onset of clinical effects following envenomation occurs between one and seven hours but can be delayed up to 18 hours. The neurological abnormalities may include slurred speech, paresthesias, ptosis, diplopia, dysphagia, stridor, muscle weakness, fasciculations, and respiratory paralysis. Coral snake envenomations have the potential to cause high morbidity with respiratory failure, neurological dysfunction, and cardiovascular collapse, requiring airway and respiratory management lasting several weeks.\textsuperscript{13,27}

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<th>Table 2. Clinical Effects Of North American Elapid Envenomation</th>
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<td><strong>Distribution and Timing of Toxicity</strong></td>
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<td>Early Systemic</td>
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Differential Diagnosis

In most cases, patients are aware that they have been bitten by a snake. However, in the rare cases where the bite is not immediately known, the differential diagnosis can be quite diverse. The initial symptoms of tissue edema and erythema can initially mimic urticaria and angioedema. However, when the ecchymosis, blistering, and signs of tissue necrosis become evident, disseminated intravascular coagulopathy, sepsis, and idiopathic thrombocytopenia can also be in the differential diagnosis.

In the case of elapid envenomations, it is important to recognize that the patient’s neuromuscular weakness is due to a coral snake bite rather than other etiologies, such as paralytic shellfish poisoning, tetrodotoxin poisoning, Guillain-Barré syndrome, botulism, myasthenia gravis, tick paralysis, periodic paralysis, and other forms of neuromuscular weakness. A detailed history, careful physical exam, and a working knowledge of the clinical presentation of such snakebites are of the utmost importance.3,28

Prehospital Care

Prehospital care of the snakebite victim centers on excellent supportive care. The airway should be maintained and secured, if necessary. Establish intravenous access in the unaffected extremity and administer intravenous fluids or pressors, as indicated. The affected extremity should be placed in a neutral position and pain control initiated. The patient should then be immediately transported to an emergency department.

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<th>Table 3. Prehospital Care Of The Envenomated Child</th>
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<td><strong>Intervention</strong></td>
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<td>Airway protection</td>
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<td>Ventilation assistance</td>
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<td>Circulation support</td>
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<td>Immobilization of affected limb</td>
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<td>Avoidance of physical activity</td>
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<tr>
<td>Transport to nearest healthcare facility</td>
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ED Evaluation

The initial evaluation in the emergency department for any North American envenomation discussed in this article should be no different than any other patient who presents for evaluation and management. After airway, breathing, and circulation have been evaluated and stabilized, a detailed history should be obtained for the following information: previous co-morbidities (i.e., bleeding dyscrasias), medications (i.e., warfarin), immunization status, allergies, type of animal which caused the envenomation, time and location of the bite, the progression of symptoms since envenomation, and the types of pre-hospital therapies performed. Tetanus status should be updated, if appropriate. The affected limb should be elevated and the area surrounding the bite and sting should be marked for progression of symptoms.5,7,20,29,34

Diagnostic Studies

In cases of crotaline envenomation, baseline studies should be obtained upon the patient’s arrival to the emergency department. A complete blood count with platelets, PT, PTT, INR, and fibrinogen, electrolytes with glucose, BUN, creatinine, and urinalysis should all be obtained and repeated in four to eight hours. The creatine phosphokinase should be checked in cases of extensive myonecrosis or fasciculations. It is important to monitor for recurrence phenomena and rebound coagulopathy following treatment with crotaline Fab antivenom (CroFab®). This phenomenon may be due to the rapid clearance of the Fab fragments compared to retained venom at the envenomation site; therefore, recommendations have been made to closely monitor patients after CroFab® therapy.20,28,35

Treatment

Crotaline Snakes

Supportive Care

After the initial assessment of the patient’s airway, breathing, and circulation, adequate pain control is a high priority. Generous use of opioids may be necessary in order to effectively control the patient’s pain. Tetanus prophylaxis should be administered if primary immunization is inadequate. Antibiotics are usually not necessary as crotaline venom is bacteriostatic.36

Antivenoms

Antivenoms are helpful in that they can correct systemic dysfunction and coagulopathy. They can also
Rattlesnake), *C. durissus terrificus* (Cascabel) and *Bothrops atrox* (Fer-de-Lance), had a high incidence of acute and delayed hypersensitivity reactions.37

Production of the Antivenin (*Crotalidae*) polyvalent® ceased in 2002 but it is important to note that supplies may still be stocked in hospital pharmacies. Vials should be carefully inspected prior to mixing and administration in order to prevent unexpected adverse reactions.

In 2000, Crotaline Fab (CroFab®) was introduced to the market. This antivenom is extracted from pooled serum of sheep inoculated with venom from the following four North American crotaline species: *C. atrox*, *C. adamanteus*, *C. scutulatus scutulatus* (Mojave Rattlesnake) and *Agkistrodon piscivorus* (water moccasin). Antibodies produced against these venoms are extracted and subjected to papain which cleaves the larger and more antigenic Fc fragments, enabling their removal. The remaining Fab fragments with their specific antigen-binding sites are affinity purified through a column before lyophilization. This new preparation is a less antigenic antidote. Although there are case reports of delayed allergic reactions to CroFab®, the incidence of serum sickness is still considerably lower compared to the previously available antivenom.38

Issues unique to pediatric patients should be considered prior to the administration of CroFab® to children. Usually, CroFab® dosages are not adjusted based on the child’s weight or age because the antivenom dosage should reflect venom load rather than patient size. The dose is based on the severity of the signs and symptoms of envenomation. The CroFab® package insert recommends dilution in 250 cc normal saline and administration over one hour. Fluid adjustments may be necessary for children less than 10 kilograms.35

Local and coagulopathic recurrences have been observed during clinical trials with CroFab®. The cause of this phenomenon appears to be the difference between the kinetics and the dynamics of the Fab immunoglobulin and its target antigens in the venom. CroFab® has a faster clearance than some of the venom’s components, allowing signs and symptoms to recur. It is due to this recurrence phenomenon that the manufacturers of CroFab® recommend a treatment protocol of two vials every six hours for three doses total (and possibly more, if necessary) after the initial bolus of four to six vials.39,40 If control of swelling or coagulopathy is not gained after the initial four to six vials, more needs to be given. This

| Table 4. Grading And Treatment Of Crotaline Snake Envenomation |
|-------------------|-------------------|-------------------|
| Grade 0 | No envenomation. Fang marks and minimal pain. | Observe for progression of signs and symptoms for six to eight hours. |
| Grade I | Minimal envenomation. Fang marks, pain, 1 to 5 inches of edema and erythema during the first 12 hours. No systemic symptoms. | If no progression, patient may be discharged home. |
| Grade II | Moderate envenomation. Fang marks, pain, 6-12 inches of edema and erythema in first 12 hours. Systemic symptoms may present along with rapid progression of signs from Grade I. May have bleeding from envenomation site. | Consider CroFab® administration per protocol. Admit patient for observation. |
| Grade III | Severe envenomation. Fang marks, pain, edema greater than 12 inches in first 12 hours. Systemic symptoms, including coagulation defects. Signs of Grade I and II envenomation appear in rapid progression. | Administer CroFab® per protocol. Admit patient to intensive care unit for further management. |
| Grade IV | Very severe envenomation. Local reaction develops rapidly. Edema may involve ipsilateral trunk; ecchymoses, necrosis and blebs develop. Potential development of compartment syndrome in areas with tightly restrictive fascial planes. | Halt progression of further local edema, hemorrhage, and soft tissue swelling if these conditions are treated early. If these conditions are already present, then antivenom will not be able to reverse pathology at the site of envenomation. In spite of antivenom treatment, digit loss as well as severe tissue necrosis requiring debridement may occur. Plastic surgery or hand surgery consults may be necessary for these patients. |


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Prior to December 2000, the only crotaline antivenom preparation commercially available in the United States was Antivenin (*Crotalidae*) polyvalent®, a whole IgG horse serum derivative produced by Wyeth-Ayerst Pharmaceuticals. Antivenin (*Crotalidae*) polyvalent®, a preparation of whole equine IgG molecules purified by ammonium sulphate precipitation from hyperimmune plasma of horses immunized with venoms of *C. atrox* (Eastern Diamondback Rattlesnake), *C. adamanteus* (Western Diamondback
may occur during the maintenance phase as well. Another concern is that CroFab® contains thimerosal as a preservative. Although the long term health risks of this mercury containing preservative are debated, current evidence suggest that the risks of untreated rattlesnake envenomation far outweigh the risks associated with thimerosal.41

Elapid Snakes
Antivenin (Micrurus fulvius)® is manufactured by Wyeth-Ayerst Laboratories and approved by the Food and Drug Administration. It has been used in treating coral snake envenomations and is effective at preventing lethality and limiting morbidity from most coral snake envenomations. The exception is that Antivenin (Micrurus fulvius)® has not been shown to be effective in treating Arizona coral snake (Micruroides) envenomations. Fortunately, this venom is much less toxic than that of the Micrurus species and there has not been a reported fatality caused by the Arizona coral snake. Antivenin (Micrurus fulvius)®, like the Antivenin (Crotalidae) polyvalent®, is also produced by Wyeth-Ayerst Laboratories and is a preparation of whole equine IgG molecules purified by ammonium sulphate precipitation from hyperimmune plasma of horses immunized with the venom of M. fulvius. As with the Antivenin (Crotalidae) polyvalent®, this antivenom is associated with a relatively high incidence of adverse reactions. Wyeth-Ayerst discontinued production of this product in 2001. Once remaining stocks of Antivenin (Micrurus fulvius)® are used, supportive treatment will be the only available treatment.14,27,37

Two nondomestic antivenoms may soon prove to be effective treatment for Micrurus envenomations in the United States. Coralmyn®, made by Instituto Bioclon in Mexico, has been used to treat Micrurus envenomation for several years. Also, Tiger Snake Antivenom (Notechis scutatus), produced by CSL Limited in Australia, has been shown to have cross reactivity with many elapid species and was potentially capable of preventing lethality from M. fulvius venom in a mouse model. However, no human clinical trials have been performed to assess if these antivenoms will be effective in M. fulvius envenomated humans.13,27

Special Circumstances

First Aid For Snakebites
Availability of prompt medical care is usually not an issue for victims of snake envenomation. However, in cases of snakebites occurring in isolated areas, first aid treatment can help prolong survival. If a snakebite victim is unable to get help within 30 minutes, a loose bandage wrapped two to four inches above the bite may slow the venom’s lymphatic spread. The bandage should be loose enough for a finger to slip between the bandage and the extremity. Another possibility is using a commercially available suction device to attempt to remove any venom that is pooled underneath the subcutaneous tissue. Unfortunately, studies have not proven that these extractors are effective in treating snake envenomations in humans.42

A possible option for treatment of crotaline snakebites in isolated areas is to carry unconstituted lyophilized CroFab®. CroFab® is heat and motion stable and can be easily transported. It could possibly be reconstituted in the field and administered to a snakebite victim.

Pregnancy
Crotaline envenomations have been reported to cause sequelae to both mother and fetus. In one case review, crotaline envenomations caused a 43% rate of fetal demise and a 10% maternal mortality rate.43 In another series of pregnant women suffering snake envenomation, the abortion rate was 30% compared to a baseline 7.7% abortion rate in the population. The authors of this series suggest a significantly increased risk of poor fetal outcome if envenomated earlier in the pregnancy.44

The use of CroFab® in pregnancy has not been evaluated because pregnant patients were excluded from the pre-marketing studies. There have been case reports documenting treatment with CroFab® in the third trimester of pregnancy, but no definite recommendations can be made from these cases.22

Controversies

Fasciotomy
Fasciotomy of the affected limb for suspected compartment syndrome has been a controversial aspect of treatment for crotaline envenomation. Sub-fascial envenomation is unusual and true compartment syndrome is usually not present when intracompartmental pressures are invasively monitored. In addition, a recent porcine study supports previous clinical experience that fasciotomy is unlikely to be beneficial for the treatment of crotaline bites and may
actually worsen outcome. Based on this evidence, fasciotomy cannot be routinely recommended. Rapid administration of CroFab® antivenom and elevation of the involved extremity is more likely to improve the local swelling. Fasciotomy should not be undertaken unless intracompartmental pressures are invasively monitored and documented to be persistently elevated despite antivenom treatment, and myonecrosis is considered imminent.45

Electroshock Therapy
Electroshock therapy has been proposed in a case report to prevent further toxicity resulting from rattlesnake envenomation. There are no human trials to support this modality of treatment. It was theorized that proteins in the venom would be denatured and inactivated by the electricity. However, this treatment would likely injure the patient’s tissues as well. This dangerous therapy cannot be recommended.6

Hyperbaric Oxygen Therapy
Hyperbaric oxygen therapy has been proposed to limit rattlesnake venom-induced myonecrosis and to promote healing in mouse models. In one case report, antivenom, mannitol, and hyperbaric oxygen were used in treating compartment syndrome and were deemed effective because they prevented fasciotomy. It is difficult to ascertain whether the hyperbaric oxygen therapy alone or the combination of therapies prevented the compartment syndrome from worsening. There have been no human trials demonstrating significant improvement in outcome with this treatment.46,47

Pressure Immobilization
Pressure immobilization has been used in Australia in the prehospital treatment of snakebites. The technique involves wrapping the entire extremity, starting at the bite site with an elastic or compressive bandage and immobilizing it with a splint in order to slow the systemic spread of the venom. For North American snake envenomations, two porcine model studies of this treatment have shown promise in increasing survival after envenomation. One study involving subcutaneous injection of Eastern Coral Snake venom showed significantly prolonged survival times with pressure immobilization. This is not surprising since the pressure immobilization technique originated in Australia where most venomous snake species are elapids. The other study involving intramuscular injection of Eastern Diamondback Rattlesnake venom demonstrated that the pressure immobilization group had longer survival times and decreased local swelling. However, higher intracompartmental pressures were documented. There have been no human data confirming these animal findings and, at this time, there are no official recommendations regarding the use of pressure immobilization for the prehospital treatment of crotaline snakebites.48-50

Disposition
Crotaline Envenomation
Disposition of crotaline snakebite patients depends on the severity of the bite. If the patient displays no signs and symptoms of a bite, it is likely that a dry bite has occurred and no venom was injected. It is prudent to observe these patients for six to eight hours in order to identify any delayed onset of symptoms. If significant toxicity occurs that requires treatment with antivenom, the patient should be admitted for further evaluation and treatment. The patient may be discharged home when antivenom treatment is complete, all of the systemic signs have resolved, swelling has peaked, and pain is well-controlled with oral analgesics. It is important to inform the patient that it may take several weeks to regain full use of the affected extremity and that frequent follow-up is necessary.6

Elapid Envenomation
Patients with known or suspected elapid envenomation should be admitted to the hospital for observation. Some experts recommend empiric treatment

Key Points

- Coral snake envenomations present with delayed neurotoxicity
- Rattlesnakes are the most venomous of the three groups of crotaline snakes
- CroFab® may require repeat doses due to recurrence phenomenon
- CroFab® can still cause hypersensitivity reactions
- Prehospital care of crotaline snakebites should be confined to immobilization of the affected limb and neutral positioning
- Fasciotomy is rarely indicated for crotaline snakebite
- Adequate analgesia and anxiolysis are important aspects of care for envenomations
- Antibiotics are not indicated prophylactically for snakebites
- The risks and benefits of antivenom therapy must be carefully considered prior to treatment
- Consult your local poison center early for advice in the course of treatment
Clinical Pathway: CroFab® Administration

Crotaline bite meeting criteria for antivenom? (See Table 4 on page 7) (Class II)

- NO
  - Observe for 6 - 8 hours. If patient is asymptomatic, discharge home.

- YES
  - Administer CroFab® 4 to 6 vials

- NO
  - Swelling, coagulation, hematologic, and systemic manifestations controlled?
    - YES
      - Start maintenance CroFab® infusions of 2 vials q6 hours x 3 doses total (continue assessing for recurrent local tissue injury)
      - No recurrent local tissue injury - Maintenance completed
      - Recheck physical exam, PT/PTT/INR, CBC, and fibrinogen (check daily)
      - Bleeding or significant coagulopathy?
        - YES
          - Consider additional antivenom
        - NO
    - NO
      - Recurrent local tissue injury

The evidence for recommendations is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient’s individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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with elapid antivenom even if the patient is asymptomatic due to the risk of delayed onset of paralysis and respiratory failure. Another approach is to admit the patient for 24 hours of careful monitoring and treat with antivenom only if neurological symptoms develop.

Part II. Spiders

Epidemiology, Etiology, And Pathophysiology

Epidemiology
The two main species of spiders that account for virtually all of the medically significant spider bites in the United States are the Black Widow Spider (*Latrodectus* spp.) and the Brown Recluse Spider (*Loxosceles* spp.).

*Loxosceles*
The brown recluse spider, as its name implies, is known to be reclusive. Most species of *Loxosceles* reside in the southern and western United States. The bites have the capacity to be significantly harmful, but life-threatening envenomation is rare. Other recluse spider species are distributed further to the southwest. However, these species cause less necrotizing wounds. In 2005, there were 2236 brown recluse spider exposures called in to U.S. poison centers, with 464 victims being less than 19 years of age. 1016 victims were evaluated at a health care facility, and 14 envenomations were considered life-threatening. No deaths from *Loxosceles* envenomations were reported. Brown recluse spider bites are most prevalent during the summer time but may occur from spring to autumn.

*Latrodectus*
In the past 20 years, more than 40,000 presumed black widow spider bites have been reported to the American Association of Poison Control Centers. Death is rarely reported. Most of the fatality reports are from Africa and Europe, and even these are unusual.

Etiology
*Latrodectus*
Black widow spiders are found throughout most of North America. They prefer warm, dark, and dry places – either outdoors (such as woodpiles), or indoors (such as basements and garages). People are usually bitten when they disturb the spider, often when they approach the web or otherwise encroach

Table 5. Selected North American Spiders Of Medical Importance

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Common Name</th>
<th>Description</th>
<th>Geographic Location</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Latrodectus</em> spp. - The Widow Spiders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>L. mactans</em></td>
<td>Southern Black Widow Spider</td>
<td>Adult female: black, shiny body with red hourglass shape on ventral abdomen. Total length: 38 mm, including leg span.</td>
<td>New England to Southern United States</td>
</tr>
<tr>
<td><em>L. varius</em></td>
<td>Northern Black Widow Spider</td>
<td></td>
<td>Eastern Texas to the East Coast of United States</td>
</tr>
<tr>
<td><em>L. hesperus</em></td>
<td>Western Black Widow Spider</td>
<td></td>
<td>Midwest and Southwestern United States</td>
</tr>
<tr>
<td><em>L. bishopi</em></td>
<td>Red Widow Spider</td>
<td>Red-orange cephalothorax. Abdomen is black with yellow rings outlining rows of red spots. Small red bar in place of hourglass.</td>
<td>Florida</td>
</tr>
<tr>
<td><em>L. geometricus</em></td>
<td>Brown Widow Spider</td>
<td>Tan to dark brown. Prominent hourglass marking of yellow or orange color.</td>
<td>Florida, Mississippi, Georgia, Texas</td>
</tr>
<tr>
<td><em>Loxosceles</em> spp. - The Recluse Spiders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>L. reclusa</em></td>
<td>Brown recluse spider</td>
<td>Tan to brown, violin-shaped mark on dorsal cephalothorax. Long legs, short body hair. 8-9 mm with leg span of 50 mm.</td>
<td>Arkansas, Missouri, Oklahoma, Tennessee and surrounding areas</td>
</tr>
<tr>
<td><em>L. desertota, L. arizonica</em></td>
<td>Desert Recluse Spider</td>
<td></td>
<td>Arizona, Nevada, New Mexico, Utah, and Southern California</td>
</tr>
<tr>
<td><em>L. rufescens</em></td>
<td>Mediterranean Recluse Spider</td>
<td></td>
<td>Arkansas and along Gulf of Mexico coast</td>
</tr>
</tbody>
</table>
on the spider. The female black widow spider is larger (8-10 mm) than the male and has a characteristic red hourglass-shaped mark on the undersurface of the abdomen. The male black widow spider is smaller, does not have the hourglass mark, and is not capable of envenomating humans due to its inability to penetrate the skin.33,53

**Loxosceles**

Brown recluse spiders are often found in the house because they thrive in the dark environments of attics, basements, and boxes. The spider has a brown violin shaped mark on the dorsum of the cephalothorax (hence the common nickname “fiddle-back spider”), three pairs of eyes arranged in a semi-circle on top of the head, and legs that are five times as long as the body. Brown recluse spiders are 6 - 20 mm long and usually gray to reddish brown.30,34

**Pathophysiology**

**Latrodectus**

Black widow spider venom is a complex mixture of six recognized toxins which induce symptoms by stimulating the release of peripheral and central nervous system neurotransmitters.54

The venom lacks cytotoxic agents so there is little to no local tissue injury and tenderness. The most important human neurotoxin, α-latrotoxin, acts at the pre-synaptic membrane of the neuromuscular junction, opening cation channels, and decreasing reuptake of acetylcholine which results in severe muscle cramping. It can also trigger release of dopamine, norepinephrine, glutamate, γ-aminobutyric acid, and other neuropeptides.6

Latrodectism has been recognized as a clinical syndrome for the last two centuries. The syndrome consists of abdominal pain and spasms with lesser involvement of the muscles of the flank, thighs, and chest. Other less common findings include intercostal muscle pain and spasm producing dyspnea, hypertension, hyperreflexia, fever, diaphoresis, headache, anxiety, nausea, vomiting, urinary retention, and priapism. This clinical syndrome has also been referred to as the hypertoxic myopathic syndrome of latrodectism. Death is fortunately rare and occurs as a sequel to cardiovascular failure, especially in children.54

**Loxosceles**

*Loxosceles* venom contains many cytotoxic enzymes which aid the brown recluse spider in the capture and digestion of its prey. The enzymes include alkaline phosphatase, 5-ribonucleotide phosphohydrolase, esterase, hyaluronidase, and, most importantly, sphingomyelinase D. Sphingomyelinase D interacts with plasma membranes of cells, leading to hemolysis, platelet aggregation, and thrombosis. Other inflammatory mediators are released, such as prostaglandins, leukotrienes, and thromboxanes, resulting in further tissue injury and dermatonecrosis.30

Cutaneous lesions caused by *Loxosceles* species vary from mild erythema to extensive dermatonecrosis. The initial bite may be painless and early vesicle or bullae formation may occur up to three hours after the bite. The wound increases in size over the next 12 - 24 hours and develops central hemorrhagic vesicles and violaceous necrosis. The surrounding skin can display blanching and ischemia, with a surrounding rim of erythema and induration often described as “red, white, and blue.” Eschar formation continues until complete necrosis occurs, which takes 3 to 7 days post bite. Ulceration may continue to increase in size. Gradual healing occurs.

### Table 6. Clinical Effects Of Latrodectus Bites

<table>
<thead>
<tr>
<th>System Involved</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous</td>
<td>Initial (5 min-1 hr after bite): local pain 1-2 hours: Puncture marks More than 2 hours: Regional lymphadenopathy, central blanching at bite site with surrounding erythema</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Initial tachycardia followed by bradycardia, dysrhythmias, initial hypotension followed by hypertension</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Leukocytosis</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Transient hyperglycemia</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Hypertonia, abdominal rigidity, &quot;facies luctrotoxism&quot;</td>
</tr>
<tr>
<td>Neurologic</td>
<td>CNS: Psychosis, hallucination, visual disturbance, seizure PNS: Local pain ANS: Increase in all secretions: diaphoresis, salivation, diarrhea, laccimation, bronchorrhea, mydriasis, miosis, priapism, ejaculation</td>
</tr>
<tr>
<td>Renal</td>
<td>Glomerulonephritis, oliguria, anuria</td>
</tr>
</tbody>
</table>


### Table 7. Cutaneous Presentation Of Loxosceles spp. Bites

<table>
<thead>
<tr>
<th>Time from Bite</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>At time of bite</td>
<td>Painless to mild stinging sensation.</td>
</tr>
<tr>
<td>1 to 3 hours post bite</td>
<td>Vesicles, erythema, pruritus.</td>
</tr>
<tr>
<td>2 to 6 hours post bite</td>
<td>Burning pain at bite site with localized erythema, pruritis, and swelling. Ulceration may occur.</td>
</tr>
<tr>
<td>12 hours to 1 day post bite</td>
<td>Bullae, &quot;red, white and blue sign&quot; (surrounding erythema around area of ischemic blanching with central violaceous necrosis).</td>
</tr>
<tr>
<td>1 to 3 days post bite</td>
<td>Further necrosis of central ulcer, spreading edema.</td>
</tr>
<tr>
<td>3 to 7 days post bite</td>
<td>Eschar formation. Erythema regression.</td>
</tr>
<tr>
<td>7+ days up to several weeks post bite</td>
<td>Ulcer may continue to increase in size. Gradual healing occurs.</td>
</tr>
</tbody>
</table>
tion follows necrosis and occurs five to seven days after the bite. The ulcer can continue to expand for up to six weeks, with the eschar eventually falling off after 7 - 14 days. The resulting denuded area heals by secondary intention. Fatty areas of the body, such as thighs and buttocks, are more susceptible to the necrosis caused by Loxosceles venom. The size of the dermatonecrosis can be quite large, up to 30 centimeters in diameter.55-57

Systemic loxoscelism is rare but occurs with a higher incidence and mortality in pediatric and immunocompromised patients.57,58 Systemic symptoms begin 24 - 72 hours after envenomation, and range from mild flu-like symptoms of fever, chills, arthralgias, malaise, vomiting, and a generalized pruritic rash to severe symptoms of hemolytic anemia, thrombocytopenia, leukocytosis, disseminated intravascular coagulation, renal failure, pulmonary edema, shock, convulsions, and possibly death. A purpuric morbilliform eruption lasting 24 - 48 hours may occur, often on the trunk and extremities. Systemic toxicity is unlikely to develop if it has not occurred within 72 hours of envenomation. 55,57

Systemic loxoscelism may be caused by distribution of venom away from the local site of envenomation. Systemic effects have been attributed to the capacity of sphingomyelinase D to alter the plasma membranes of red blood cells, platelets, and endothelial cells resulting in hemolysis, platelet aggregation, and thrombosis. It is also postulated that the venom itself may set into motion a cascade of effects which lead to systemic loxoscelism via the release of interleukins and other mediators. 57

**Differential Diagnosis**

### Loxosceles

The diagnosis of brown recluse spider envenomation can be difficult if the spider is not positively identified or if the envenomation is not suspected after either the history or physical examination are obtained. The clinician may have a tendency to assume any dermatonecrotic lesion is a brown recluse spider envenomation. Other etiologic possibilities include bacterial infection, fungal infection, pyoderma gangrenosum, viruses, adverse drug reactions, other arthropod bites, thromboembolic phenomenon, Lyme disease, neoplasms, chemical burns, and necrotizing fasciitis. The differential diagnosis for systemic loxoscelism includes Toxic Shock Syndrome, sepsis with disseminated intravascular coagulation, hemolytic-uremic syndrome, and other causes of extensive hemolysis. Also, airway compromise may occur if the patient develops significant airway swelling in reaction to the bite.32,36,59,60

Making the correct initial diagnosis is important and requires the diagnostician to take a careful history and be aware of the typical presentation of Loxosceles envenomation, including dermatonecrosis and systemic toxicity.

### Prehospital Care

As with snakebites, initial treatment of these envenomated patients begins with excellent supportive care. Support the airway as necessary, obtain intravenous access, control pain, and transport the patient quickly to an emergency department. If possible, safely bring the spider in for identification.6,34

### ED Evaluation

The initial evaluation of spider bites is no different than the other envenomations discussed in this issue. For Loxosceles bites, the bite site itself may have no local swelling or ecchymosis but a complete physical exam with emphasis on the vital signs, cardiovascular, and neurological status of the victim is essential. Loxosceles victims can have severe autonomic dysfunction that needs to be immediately addressed. In Loxosceles victims, dermal changes around the bite...
site should be documented and marked for progression. Systemic symptoms of loxoscelism require aggressive supportive therapy.6,7,20,29-34

Diagnostic Studies

Latrodectus

Laboratory data are not helpful in diagnosing or managing patients who have been bitten by a black widow spider. There is no specific laboratory assay to definitively diagnose a black widow spider bite. The most common laboratory findings are leukocytosis and increased creatine phosphokinase and lactate dehydrogenase concentrations.29

Loxosceles

Definitive diagnosis is possible only when the spider that inflicted the bite is positively identified. There are no diagnostic tests commercially available for brown recluse envenomations. Basic laboratories may reveal hemolysis, hemoglobinuria, hematuria, coagulopathy, and abnormal liver and renal function and will aid the clinician in the management of these complications.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Mild Envenomation</td>
<td>• Local pain at envenomation site  • Normal vital signs</td>
</tr>
<tr>
<td>Grade II</td>
<td>Moderate Envenomation</td>
<td>• Muscular pain in the envenomated extremity  • Extension of muscular pain to the abdomen if bitten on a lower extremity or to the chest if envenomated on an upper extremity  • Local diaphoresis of envenomation site or involved extremity  • Normal vital signs</td>
</tr>
<tr>
<td>Grade III</td>
<td>Severe Envenomation</td>
<td>• Generalized muscular pain in the back, abdomen, and chest  • Diaphoresis remote from envenomation site  • Abnormal vital signs (blood pressure greater than 140/90 mm Hg, pulse greater than 100 in adults)  • Nausea and vomiting  • Headache</td>
</tr>
</tbody>
</table>

Treatment

Latrodectus

After routine wound care and support of respiratory and cardiovascular function, control of pain and muscle cramping is the usual priority. A combination of intravenous opioids and benzodiazepines provides analgesia, anxiolysis, sedation, and muscle relaxation.29 Tetanus status should be updated.

Indications For The Use Of Latrodectus Antivenin®

Latrodectus Antivenin® is a whole IgG antibody produced by Merck Pharmaceuticals. The administration of Latrodectus Antivenin® may be complicated by hypersensitivity reactions and serum sickness.54 Controversy exists in treating patients with the antivenom because, although morbidity is high (pain, cramping, and autonomic dysfunction), mortality is low. There are case series supporting the efficacy and safety of this product in decreasing duration of illness.61,62 The antivenom can be considered in high risk patients and those with severe toxicity, such as extreme muscle pain and cramping, hypertension, respiratory distress, and priapism, that is unresponsive to other therapy.29,61,63 It is important to note that Latrodectus Antivenin® carries risk for serum sickness and needs careful consideration prior to administration to patients. Many experts believe that the antivenom has too high of a risk-benefit ratio to justify its use, since the mortality of Latrodectus bites is so low. Therefore, the indications for possible use of antivenom include severe muscle cramping, hypertension, diaphoresis, nausea, vomiting, and respiratory difficulty that is unresponsive to other therapy.29,61 There is a Fab antivenom product which is currently being studied but is not yet available on the market.

Loxoceles

Most brown recluse spider bites are mild and require no specific treatment. Appropriate treatment for dermal lesions includes rest and elevation to minimize inflammation and venom spread. Antihistamines can minimize pruritis, and analgesics are frequently required for pain control.56 Tetanus status should be updated. Treatment for systemic symptoms is supportive and vigorous hydration should be maintained.

In the past, treatment of L. reclusa bites has included steroids, antibiotics, dapsone, and hyperbaric oxygen therapy. However, none of these treatments have been proven to be effective in human tri-
als. Thus, most therapy remains supportive, including adequate pain control and wound debridement, if necessary.

**Special Circumstances**

**Pregnancy**
The pain and severe muscle cramping associated with black widow spider bites in the pregnant patient can be quite concerning. Not much is known about black widow bites in pregnancy and there are few reports regarding the effects of envenomation in this situation. However, there are some theoretical effects of envenomation which can be dangerous to the fetus. These include hypertension, shock, and convulsions. There are insufficient data to determine if spontaneous abortion or preterm labor is caused by black widow spider envenomation during pregnancy. Nonetheless, pregnancy has been suggested as a possible indication for *Latrodectus* antivenom administration.

**Controversies: Latrodectus**

**Calcium Gluconate**
In the past, intravenous administration of calcium gluconate was advocated because it was purported to decrease the muscle cramping due to black widow spider envenomation. Current evidence indicates that calcium gluconate is of no benefit and may actually worsen the venom’s toxic effects.

**Controversies: Loxosceles**

Brown recluse spider bites are characterized by polymorphonuclear leukocyte infiltration at the site of the lesion. The optimal treatment is controversial. Diverse treatments have been advocated, including steroids, antibiotics, surgical excision, antihistamines, colchicine, hyperbaric oxygen therapy, antivenom, electroshock therapy, and observation.

**Dapsone**
Dapsone is the therapy most frequently recommended by authorities secondary to its leukocyte-inhibiting properties, but scientific evidence supporting the efficacy of dapsone for the treatment of brown recluse bites is scarce. In one study involving guinea pig models, there was some evidence that the lesions healed better with dapsone. However, in these studies, the dapsone was either given prior to or at the same time as the injection of the venom.

This approach is clearly not possible from a clinical standpoint. To date, no double blind, randomized trial has been conducted to compare dapsone and placebo in human beings for the treatment of brown recluse spider envenomations.

Furthermore, dapsone has many potential side effects. Reported complications from the treatment of brown recluse bites and other medical conditions with dapsone include hemolysis, agranulocytosis, aplastic anemia, methemoglobinemia, hypersensitivity reactions, rashes, and toxic epidermal necrolysis. Dapsone-related fatal reactions have also been reported.

**Local Treatment**

**Aggressive Excision**
Aggressive early surgical excision has been anecdotally advocated to limit the extent of dermatonecrosis caused by brown recluse spider envenomation, but controlled trials have found that early surgical intervention should be avoided. Surgery appears to increase local inflammation resulting in chronicity of the wound, repeated graft rejection, and pyoderma granuloma. Sharp debridement or excision of spider bite lesions should be discouraged.

**Corticosteroids**
Steroids are commonly recommended for the treatment of brown recluse bites. However, systemic and intralesional steroids have not been observed to alter lesion size or progression in animal models or human studies and should not be routinely used. Likewise, the use of corticosteroids for severe systemic complications has been recommended without strong evidence-based support.

**Anti-Loxosceles Fab Fragments**
Intradermal injection of rabbit-derived anti-Loxosceles Fab fragments has only been studied in animal models. Although early injection (less than four hours) was shown to attenuate dermatonecrotic lesion size, the following two factors make this therapy impractical: 1) the anti-Loxosceles Fab fragments are not available commercially, and 2) the typical delay in presentation of dermatonecrosis makes early treatment virtually impossible.

**Hyperbaric Oxygen**
The use of hyperbaric oxygen therapy to treat brown recluse bites has been proposed. Two studies of this modality have been conducted in small animals and
both found no benefit of hyperbaric oxygen therapy in the treatment of brown recluse spider bites.\textsuperscript{34,72,85,86}

**Electroshock Therapy**

Though electroshock therapy has been reported in case reports as a possible therapy for the treatment of brown recluse bites, it is not accepted as standard treatment of these envenomations and may be harmful.\textsuperscript{87}

**Prophylactic Antibiotics**

As with the other envenomations discussed in this article, prophylactic antibiotics are not of proven benefit and should be used only if secondary bacterial infection occurs.\textsuperscript{55}

**Cyproheptadine And Colchicine**

Cyproheptadine (a serotonin antagonist) and colchicine (a leukocyte inhibitor) are of unproven utility in the treatment of dermatonecrosis and are not recommended due to the potential for serious side-effects.\textsuperscript{55}

**Disposition**

**Latrodectus**

Patients who present to the emergency department with a black widow spider bite may be observed for four to six hours for development of symptoms. Asymptomatic patients may then be discharged for further observation at home. Patients with muscle pain and cramping should not be sent home until their pain is controlled. Some patients will require hospital admission for continued treatment with intravenous opioids and benzodiazepines. It should be noted that these patients will often complain of malaise or other vague complaints for the next two to four weeks.\textsuperscript{6}

**Loxocelae**

Most patients with brown recluse spider bites can be discharged home from the emergency department with adequate pain control and good follow-up for wound care. In the rare occasion of systemic toxicity, the patient should be hospitalized for intensive supportive care until their symptoms of nausea, vomiting, malaise, rash, fever, arthralgias, thrombocytopenia, and hemolysis have been treated and resolved.\textsuperscript{6}

**Part III. Scorpions**

**Epidemiology, Etiology, And Pathophysiology**

**Epidemiology**

*Centruroides exilicauda* is found throughout Arizona and other adjacent areas in the Southwestern United States. Parts of Texas, northern Mexico, and small areas of California also have *C. exilicauda* populations. Scorpion envenomations are relatively common occurrence in the southwestern United States. In 2005, the American Association of Poison Control Centers reported 14,521 nationwide reports of scorpion envenomations, with 4074 occurrences in patients less than 19 years of age. Twenty patients were considered to have “major” or life-threatening outcomes, but no deaths were reported.\textsuperscript{5,88,89}

**Etiology**

*Centruroides exilicauda* (previously known as *Centruroides sculpturatus*) or bark scorpion is the only scorpion in the United States of medical importance with venom potent enough to produce a potentially life threatening illness. It ranges in size from 13 - 75 mm, depending on maturity. *Centruroides exilicauda*
has slender pincers which are about six times as long as the broadest part of the arthropod. It also has a small tubercle located at the base of the stinging apparatus and the proximal tail segment is rectangular rather than square-shaped. Its five segmented tail contains a bulbous end segment called the telson that contains the venom apparatus which stings rather than bites. The venom apparatus contains a pair of venom glands and a stinger. *Centruroides exilicauda* is unique in that it is a climbing species and never burrows. As the common name “bark scorpion” describes, this scorpion prefers to live in or near trees. They are not aggressive and usually only sting when handled or threatened. *Centruroides exilicauda*

**Ten Pitfalls To Avoid**

1. “I thought that fasciotomy was indicated for rattlesnake bites.”

   Fasciotomy is not indicated for the majority of snakebites, since true compartment syndrome is rare. Unnecessary fasciotomy worsens outcome and results in a disfiguring scar and, possibly, loss of function.

2. “I thought a two hour observation period was long enough for an elapid snakebite.”

   The neuromuscular weakness resulting from coral snakebites is typically delayed by several hours. An inadequate observation period can result in disastrous consequences, including death by respiratory failure.

3. “I thought the new CroFab® antivenom didn’t cause any hypersensitivity reactions.”

   Although the newer CroFab® antivenom has been documented to result in fewer hypersensitivity reactions than the older product, the potential for life threatening reactions and serum sickness is still present. Patients must be adequately monitored for these reactions.

4. “I thought one dose of CroFab® was all that was needed to treat rattlesnake bites.”

   Because of the more rapid clearance of the smaller Fab fragments when patients are treated with CroFab®, recurrence of crotaline toxicity often occurs. Repeat dosing of CroFab® is therefore required in many cases.

5. “Don’t all rattlesnake bites need antivenom?”

   Up to 25% of crotaline snakebites result in no toxicity (so-called “dry bites”). No antivenom is required for such asymptomatic bites, or for those with minimal local swelling with no progression and no systemic toxicity.

6. “I didn’t know that scorpion stings could be so severe in kids.”

   The severity of *Centruroides exilicauda* scorpion envenomations is greatest in small children who receive a larger dose of venom per kilogram than an adult. Small children therefore require more vigilant monitoring and treatment.

7. “I was so busy treating the other aspects of the envenomation that I forgot the tetanus prophylaxis.”

   Although it is easy to focus on treating the more impressive toxicities of these envenomations, it is important not to forget important basic principles of wound care, such as tetanus prophylaxis.

8. “Isn’t *Latrodectus* antivenom the first line of therapy for black widow spider envenomations?”

   Many patients with black widow spider bites who are experiencing muscle pain and cramping can be adequately managed with intravenous opioids and benzodiazepines. Although *Latrodectus* antivenom is effective in reversing toxicity, it exposes the patient to the risk of hypersensitivity reactions.

9. “Aren’t dapsone, aggressive surgical excision, and electrotherapy accepted therapies for brown recluse spider bites?”

   These therapies are of unproven benefit for brown recluse spider envenomation and may actually worsen outcome. Good basic wound care is the most important aspect of treatment.

10. “I didn’t think that brown recluse spider bites were that big of a deal.”

   It is important to be aware that brown recluse spider bites can result in severe systemic toxicity and significant delayed dermatonecrosis. The patient must be advised that close follow-up of the wound is mandatory to monitor for complications and the possible need for plastic surgery referral.
sting by grasping the victim’s flesh with their pincers and repeatedly thrusting their tail over their bodies into their victim.6,31,88,90

Pathophysiology

Centruroides exilicauda venom contains two groups of neurotoxins which are heat stable low molecular weight proteins that bind to sodium channels. One group, termed “stabilizers,” causes incomplete sodium channel inactivation, resulting in a prolongation of the action potential. A second group induces a slowly developing inward sodium current after membrane repolarization which results in sodium channel activation and cell membrane depolarization. These toxins prolong the action potential and enhance membrane depolarization by producing inward sodium currents at more negative membrane potentials, causing repetitive firing of neuronal axons. This results in over-stimulation of sympathetic and parasympathetic nervous systems, resulting in excessive acetylcholine and catecholamine release. Ultimately, catecholamine-induced myocarditis, dysrhythmias, myocardial ischemia, and myocardial infarction may occur.31,88,91

As in the case of the black widow spider venom, there are no local cytotoxins so there is usually no erythema, swelling, or blanching at the site of the sting. Peripheral motor neuron and cranial nerve manifestations may appear in small children, including uncontrolled jerking movements of the extremities, peripheral muscle and tongue fasciculation, roving eye movements, and facial twitching. Severely affected infants may be misdiagnosed as experiencing seizures and respiratory distress.6,88

Symptoms develop rapidly after envenomation, peak after several hours, and may persist for one to two days.92

Differential Diagnosis

Scorpion envenomation bears some clinical resemblance to black widow spider envenomation. However, unlike black widow spider bites, scorpion stings often cause intense local pain at the site of the envenomation. Additionally, black widow spider bites result in local sweating and possibly lymphangitis, unlike scorpion stings. Cardiac manifestations of myocarditis and dysrhythmias suggest consideration of myocardial infarction, infectious myocarditis, and other cardiac diseases. The neurological irritability, including rotatory eye movements, muscle fasciculations, and myoclonus, may suggest the possibility of seizures. Intoxication with cocaine, amphetamines, and other stimulants should be considered.31,90,93

1. Prescribe antibiotics for envenomations only when secondary bacterial infection occurs.

Empiric antibiotic prophylaxis is not indicated because most of these envenomations do not become secondarily infected. The immediate local swelling, erythema, warmth and pain are due to venom effects and should not be mistaken for infection.

2. Reserve antivenom therapy for the indications discussed in this article.

Antivenom is expensive. Excessive use not only increases cost but also exposes the patient to complications, such as hypersensitivity reactions. Following the clinical pathway for CroFab® administration provided on page 10 will help the clinician to utilize CroFab® appropriately.

3. Not all envenomations require hospital admission. Selected “dry” bites and minor envenomations may be safely discharged from the emergency department after an adequate observation period.

Hospital admission will be reserved for those envenomations with significant clinical toxicity or certain high risk situations (such as delayed neurotoxicity with coral snake envenomation).

4. Avoid the use of expensive and unproven therapies.

For example, hyperbaric oxygen therapy has been recommended for brown recluse spider bites but has not been of proven benefit in animal studies. In addition, the patient is exposed to potential complications of hyperbaric oxygen therapy.
Prehospital Care

As with snakebites, initial treatment of envenomated patients begins with excellent supportive care. Support the airway as necessary, obtain intravenous access, control pain, and transport the patient quickly to an emergency department. If possible, safely bring the scorpion in for identification.6,34

ED Evaluation

The initial evaluation of scorpion envenomations is as described for the other envenomations discussed in this article. On physical exam, the sting area needs to be examined because there is usually no significant local swelling and bruising around the site due to the lack of cytotoxins in the scorpion venom. The bite site, however, may have a positive “tap test” (severe pain and paresthesias when the sting site is tapped by a finger). A neurological exam will demonstrate clinical signs of envenomation, including roving eye movements and tongue fasciculations. In severe envenomations, patients will have uncontrolled limb movements. Vital signs need to be monitored for signs of autonomic dysfunction.6,20,29,34

Diagnostic Studies

As with spider bites, there is no single diagnostic test that is helpful in the diagnosis of scorpion envenomations.

Treatment

Most victims of C. exilicauda scorpion bites can be managed solely with supportive care, such as local wound care, tetanus prophylaxis, opioids, benzodiazepines, airway support, ventilation, and supplemental oxygen administration. Due to hypersalivation and autonomic dysfunction, patients may suffer aspiration pneumonia. Airway support is critical. Antivenom should only be considered when there is severe somatic or cranial nerve dysfunction which is not well controlled by supportive measures. Fortunately, symptoms usually resolve in 12-48 hours. The utility of the antivenom in reversing the neurological symptoms must be weighed against the high incidence of delayed rash or serum sickness (58% in one series).6,34

Antivenom for C. exilicauda envenomation is produced from goat serum at Arizona State University and approved by the Arizona State Board of Pharmacy. The antivenom was prepared by lyophilizing, micron-filtered, hypersensitized goat serum and was produced every two to three years, as needed. This antivenom is not approved by the Federal Drug Administration and should not be transported across state lines. Its approved use has been limited to patients within the state of Arizona. However, as of November 2004, all production of the antivenom has stopped and all stockpiles have expired.60

Special Circumstances

Cholinergic Crisis

In certain scorpion envenomations, patients can present with cholinergic symptoms, especially excessive oral secretions. In such cases, atropine has been reported to be helpful in managing such symptoms. Atropine, however, should not be routinely used and should only be administered to patients who are stung by scorpions that cause significant cholinergic crisis (i.e., Parabuthus transvaalicus scorpion found in North Africa). The benefits of atropine must be weighed against the risk for tachycardia and dysrhythmias.45

Controversies

Foreign Antivenoms

Due to the expired stockpiles of the C. exilicauda goat derived antivenom, there has been a search for other antivenoms which could potentially treat severe C. exilicauda stings. In Mexico, two antivenoms have been used to treat Centruroides stings. The Mexico-Pharma Polyvalent Scorpion Antivenom may be effective against North American Centruroides stings, though no reliable repository of this antivenom exists in the United States. In June 2000, Silanes Laboratory received orphan drug status for Alacramyn, which is an equine-derived Fab antivenom specific for Centruroides limpidus, C. noxius, C. suffuses, and C. mei-sei. Clinical trials in envenomated children are currently in progress in the United States due to the unavailability of the Arizona State University antivenom.86

The incidence of allergic reactions to Alacramyn is reported to be 2.7%, which is similar to the Arizona State University goat-derived antivenom. If the current clinical trials demonstrate that Alacramyn is safe and effective and the FDA approval is granted, the antivenom may become widely available for treatment of severe Centruroides envenomation.84 Alacramyn may be marketed under the name Anascorp in the United States.
**Disposition**

Most adult victims of scorpion envenomation do not manifest severe toxicity requiring hospital admission. Such victims may be managed solely with supportive care and may be safely discharged from the emergency department with careful follow-up. Patients with severe envenomation should be admitted for intensive supportive care and treatment with antivenom, if available. Small children are more likely to suffer from severe envenomation with somatic or cranial neuromuscular dysfunction and are more likely to require treatment with antivenom and hospitalization.

**Case Conclusions**

The snake responsible for this envenomation was a Southern Pacific Rattlesnake (Crotalus viridis helleri). You controled the patient’s pain with opioids and began treatment with CroFab®. After the initial dose of antivenom, the child’s thrombocytopenia improved and the swelling stopped progressing. He was admitted to the hospital for further observation and continuing antivenom therapy. The fasciculations gradually resolved and the child was kept comfortable with opioids and benzodiazepines. The next day, after finishing the antivenom protocol, the patient’s pain was well controlled with opioids and the swelling improved. There were no further changes on his morning laboratory values. The patient was discharged home on oral pain medications, with a warning that the swelling may take several weeks to completely resolve. You told his parents to follow-up with his pediatrician for re-examination and recheck of his blood counts and coagulation studies.

The implicated snake in this vignette is the coral snake, an elapid. The venom in coral snakes is a neurotoxin causing respiratory failure. In this case, the child was immediately intubated, placed on ventilatory support, and transferred to the intensive care unit. Attempts were made by the physicians to locate Antivenin (Micrurus fulvius) without success and the decision was made to manage the child with supportive care and antivenom therapy was not pursued further. After two days, the effects of the neurotoxic venom began to wear off and the patient started to have spontaneous respirations. By day four, the patient was extubated and maintained her own respirations, though she had some residual generalized weakness. She was discharged home by day five of hospitalization with instructions to her parents to follow-up with her general physician.

The patient’s symptoms are caused by α-latrotoxin, a potent neurotoxin. You immediately began treating this patient with opioids and benzodiazepines in order to control her pain and anxiety. Your hospital pharmacy had latroductus antivenom available. However, after discussing the risks and benefits of the treatment options, the family declined antivenom therapy. You admitted the child to the observation unit on opioids and benzodiazepines. In the morning, her pain was much improved and she was discharged home on oral pain medications.

Based on the patient’s presentation, he was likely stung by Centruroides exilicauda, the bark scorpion. As you were speaking with the family, your staff members called the Arizona State University to inquire if there were any units of the scorpion antivenom still available. They were told that the antivenom stores are now expired and can not be used. You started the patients on opioids and benzodiazepines in order to control his pain and anxiety as well as other supportive measures, such as intravenous fluids. He responded to the treatment by becoming less anxious and less tachycardic. You admitted him to the pediatric ward where, over the next two days, he continued to require opioids and benzodiazepines. His fasciculations and drooling gradually improved. On day three, the patient’s pain had greatly diminished and he was discharged home on oral pain medications with instructions to the parents to follow up with his pediatrician.

**Summary**

Envenomation by snakes, spiders, and scorpions in the United States results in significant morbidity and mortality each year. It is therefore necessary for the emergency physician to be well-versed in the appropriate evaluation and management of these serious bites and stings. Proper treatment and avoidance of unproven and potentially harmful interventions will optimize outcome for the patient. Envenomations by snakes, spiders, and scorpions invariably result in significant fear and anxiety for patients and their families. Understanding the principles discussed in this article will enable the physician to treat envenomated children with confidence.

**References**

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each ref-
ence, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.


25. Clark RF, Williams SR, Nordt SP, Boyer-Hassen LV. Successful treat-
35. Which of the following is a common finding following black widow spider envenomation?
   a. Severe local tissue damage at the site of the bite
   b. Muscle pain and cramping
   c. Respiratory failure
   d. Thrombocytopenia

36. What is one of the most common toxicities following brown recluse spider envenomation?
   a. Dermatonecrosis
   b. Neuromuscular weakness
   c. Respiratory failure

37. What is the most appropriate treatment for rapidly progressing local tissue swelling and hemotoxicity following crotaline envenomation?
   a. Fasciotomy
   b. Corticosteroids
   c. Constrictive tourniquet of affected extremity
   d. CroFab® antivenom administration

38. Which toxic species and matching distinguishing physical characteristic is correct?
   a. Eastern coral snake: red on black on yellow bands
   b. Crotaline snake: triangular head, elliptical pupils
   c. Brown recluse spider: red hourglass-shaped mark on ventral abdomen
   d. Black widow spider: violin-shaped mark on dorsal thorax

39. Which of the following statements regarding Centruroides exilicauda scorpion stings is correct?
   a. Local pain and paresthesias are decreased by percussion over the affected area
   b. Young children are least severely affected
   c. Severe cases include fasciculations, uncontrolled muscle movements, and cranial nerve dysfunction

40. Which of the following statements regarding CroFab® therapy for crotaline envenomation is correct?
   a. Recurrence phenomena do not occur due to decreased clearance of Fab fragments
   b. CroFab® can ameliorate both tissue and hematological toxicity
   c. CroFab® causes more hypersensitivity reactions than the previously available Wyeth-Ayerst antivenom product
   d. Repeat dosing of CroFab® is unnecessary for severe envenomations
   e. CroFab® can ameliorate both tissue and hematological toxicity
   f. CroFab® causes more hypersensitivity reactions than the previously available Wyeth-Ayerst antivenom product
   g. Repeat dosing of CroFab® is unnecessary for severe envenomations

41. Which of the following is the best treatment modality for dermatonecrosis caused by brown recluse spider envenomations?
   a. Good local wound care, analgesia, and tetanus prophylaxis
   b. Hyperbaric oxygen therapy
   c. Electric shock therapy
   d. Dapsone or colchicine

42. Which of the following statements is true regarding coral snake envenomations?
   a. Local tissue effects are typically severe
   b. Neurological symptoms are characteristically delayed for several hours
   c. Cranial nerve dysfunction, paralysis, and respiratory failure do not occur
   d. Hemotoxicity is common

43. Which of the following snakes causes the most severe envenomation?
   a. Western Diamondback Rattlesnake (Crotalus atrox)
   b. Cottonmouth (Agkistrodon piscivorus)
   c. Southern Copperhead (Agkistrodon contortrix contortrix)
   d. Northern Copperhead (Agkistrodon contortrix mokason)

44. Which of the following is the most appropriate initial treatment for severe muscle pain and cramping due to black widow envenomation?
   a. Opioids and benzodiazepines
   b. Antibiotics
   c. Latrodectus antivenom
   d. Calcium gluconate

45. Which of the following are important aspects for treatment for coral snake envenomation?
   a. Careful monitoring and support of respiratory function
   b. Repeated monitoring of coagulation profiles
   c. Careful monitoring of the site of envenomation for severe tissue damage.

46. What is the most important initial treatment for the coagulopathy caused by crotaline envenomation?
   a. CroFab® antivenom
   b. Fresh frozen plasma
   c. Platelet transfusion
   d. Vitamin K

47. Which of the following should be the initial treatment of crotaline snakebites?
   a. Incision and Suction
   b. Cryotherapy
   c. Immobilization and neutral positioning
   d. Electroshock therapy
48. Which of the following is true regarding “dry” crotailine snakebites?

a. Empiric CroFab® antivenom treatment is indicated
b. Empiric antibiotic treatment is indicated
c. Patients should be monitored for six hours for development of symptoms
d. Local wound care and tetanus prophylaxis are not indicated

Class Of Evidence Definitions

Each action in the clinical pathways section of Pediatric Emergency Medicine Practice receives a score based on the following definitions.

Class I
• Always acceptable, safe
• Definitely useful
• Proven in both efficacy and effectiveness

Level of Evidence:
• One or more large prospective studies are present (with rare exceptions)
• High-quality meta-analyses
• Study results consistently positive and compelling

Class II
• Safe, acceptable
• Possibly useful

Level of Evidence:
• Generally higher levels of evidence
• Non-randomized or retrospective studies: historic, cohort, or case-control studies
• Less robust RCTs
• Results consistently positive

Class III
• May be acceptable
• Possibly useful
• Considered optional or alternative treatments

Level of Evidence:
• Generally lower or intermediate

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Target Audience: This enduring material is designed for emergency medicine physicians.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of mortality and morbidity data from nationally recognized NCHS, and AACEP; and evaluation of prior activities for emergency physicians.

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