Venomous Animal Injuries
Edward J. Otten

PERSPECTIVE

Epidemiology
Venomous animals account for considerable morbidity and mortality worldwide. Snakes alone are estimated to inflict 2.5 million venomous bites annually, with approximately 125,000 deaths. The actual numbers may be much larger. Southeast Asia, India, Brazil, and areas of Africa lead the world in snakebite mortality. It is impossible to estimate the worldwide morbidity and mortality resulting from other venomous animals such as bees, wasps, ants, and spiders.

Approximately 45,000 snakebites occur annually in the United States; 7000 to 8000 are inflicted by venomous snakes, and 5 to 10 result in death. Insects are responsible for 52% of deaths, snakes for 30%, and spiders for 13%. Specifically, bees are responsible for the most fatalities, followed by rattlesnakes, wasps, and spiders. Historically, most of the recorded deaths from spider bites were caused by the black widow, although the brown recluse spider has been implicated in an increasing number of deaths.

The American Association of Poison Control Centers began collecting data in 1983 on deaths caused by venomous animals. Their 25-year experience shows a significant number of exposures by bite or sting but relatively few deaths (Table 62-1). Although these data include most of the United States, there is no requirement that hospitals, emergency departments, coroners, or public health agencies report deaths or exposures to regional drug and poison information centers. This decline in deaths may be caused by an actual decrease in mortality or may be a result of inadequate reporting. Meaningful morbidity data, such as the number of amputations, hospitalizations, and disabilities, do not exist. The number of exposures and deaths from exotic snakes seems to be increasing, possibly because of interest in collecting so-called “hot” or venomous varieties such as cobras, mambas, and vipers.

Venom Delivery
Animals that have developed specific venom glands and venom delivery systems can be found in every class, including birds. The toxin and toxic apparatus vary from class to class. For example, the rattlesnake has modified salivary glands and maxillary teeth and uses this system primarily to obtain food. The bee has a modified ovipositor that is used mainly for defense. Poisonous and venomous animals are not the same and should be differentiated. Animals can be considered poisonous because of various toxins distributed in their tissues. For example, certain shellfish, toads, and barracuda have been known to cause death after ingestion. However, only animals with specific glands for producing venom connected to an apparatus for delivering that venom to another animal can be considered venomous.

VENOMOUS REPTILES

Snakes
Of the 3000 species of snakes, approximately 10 to 15% are venomous. Of the 14 families of snakes, four contain venomous species. Snakes are distributed throughout most of the earth’s surface, including fresh and salt water. The major exceptions are the Arctic and Antarctic zones, New Zealand, Malagasy, and many small islands. Most snakebites occur in tropical and subtropical climates, especially in agricultural settings where the inhabitants go barefoot. Sea snakes are found only in the Pacific and Indian Oceans. Snakes are poikilotherms, which accounts for their distribution and activity. Their inability to raise their body temperature above ambient levels restricts their activity to a fairly narrow temperature range, approximately 25 to 35° C. All snakes are carnivorous, and their venom apparatus evolved for the purpose of obtaining food.

Epidemiology
The incidence of reported venomous snakebites in the United States is greatest in the South. States having the highest death rates are North Carolina, Arkansas, Texas, and Georgia. Of all snakebites, 97% occur on the extremities, with two thirds on the upper extremities and one third on the lower extremities. This reversal of historical distribution may reflect bites being provoked rather than accidental. Bites that occur accidentally are considered “legitimate,” whereas bites that occur during attempts to handle or disturb a snake are considered “illegitimate.” Men are bitten nine times more frequently than women.
Imported venomous snakes have recently been an increasing problem throughout the United States. In the past, only zoos, research centers, and herpetologists kept exotic venomous snakes. Today, however, hundreds of people are raising deadly venomous snakes without the necessary precautions, such as specialized cages, safe handling techniques, and rapid access to specific antivenin. They place not only themselves, but also their families and the general public, in danger.

Classification and Characteristics

The four venomous families of snakes are the Colubridae, Elapidae, Viperidae, and Atractaspididae. The Colubridae, although representing 70% of all species of snakes, have very few venomous members dangerous to humans; these include the boas and the vipers. The Viperidae are the more common and include the cobras, kraits, mambas, and coral snakes. The Hydrophiidae are sea snakes that are often confused with the elapid sea snakes. The colubrid species found in the United States that were previously thought to be harmless may indeed be venomous. Examples are the copperhead, the hognose snake, and the viper. Pit vipers account for 98% of all venomous snakebites in the United States.

The Colubridae and Hydrophiidae have few venomous encounters with humans and are responsible for even fewer injuries. Some colubrid species found in the United States that were previously thought to be harmless may indeed be venomous. Examples are the copperhead, the hognose snake, and the wandering garter snake. No deaths have been reported, but the problem has generated much interest among herpetologists and toxicologists. The yellow-bellied sea snake (Pelamis platurus; subfamily Hydrophiidae) has been found off the coast of southern California and western Mexico, but bites by this snake are rare.

The other major group of venomous snakes in the United States is the coral snakes. The eastern coral snake (Micrurus fulvius) is found in North Carolina, South Carolina, Florida, Louisiana, Mississippi, Georgia, and Texas. There are two subspecies that have similar clinical presentations and will be discussed together. The western or Sonoran (Micrurus euryxanthus) coral snake is native to Arizona and New Mexico. Although both species are generally quite shy unless handled, the eastern coral snake is considered deadly. There are no records of fatalities caused by the western species.

Coral snakes can be readily identified by their color pattern. At first glance, they resemble one of several varieties of king snake found in the southern United States. The coral snake can be differentiated from the king snake by two characteristics: The nose of the coral snake is black, and the red and yellow bands are adjacent on the coral snake but separated by a black band on the king snake. The popular rhyme is as follows:

Red next to yellow, kill a fellow.
Red next to black, venom lack.

This rhyme can be used only in the United States; Brazilian coral snakes have red next to black bands, and some coral snakes have no red bands.

Identification

There are two key principles for identifying venomous snakes: Only experts should handle live snakes, and even dead snakes can envenomate careless handlers. It is not difficult to differentiate between pit vipers and harmless snakes found in the United States (Fig. 62-1). Pit vipers, as their name implies, have a characteristic pit midway between the eye and the nostril on both sides of the head. This pit is a heat-sensitive organ that enables the snake to locate warm-blooded prey. Pit vipers may be identified through other methods, but this characteristic is 100% consistent. The triangular shape of the head, the presence of an elliptical pupil, the tail structure, and the presence of fangs are useful characteristics but are inconsistent. The arrangement of subcaudal plates may be used for Crotalinae if the head has been damaged or is unavailable. An individual specimen may not fit the classic description, depending on the age of the snake, the time of the year, and the condition of the tail and mouthparts. Neither color nor skin pattern is a reliable method of identifying pit vipers.

Size is not an important factor in identifying various reptiles. Venomous snakes range in length from several inches to several feet. Although a 6-foot eastern diamondback rattlesnake is much more dangerous than a 10-inch copperhead, all venomous snakes are able to envenomate from birth and should be treated as though they are dangerous.

Exotic snakes that are not pit vipers are not as easily identified. If possible, they should be safely transported to an expert for positive identification. Local zoos, herpetology groups, and colleges often have individuals who can identify unknown snakes.

Table 62-1  Venomous Animal Injuries and Deaths, 1983-2009

<table>
<thead>
<tr>
<th>ANIMAL</th>
<th>ENVENOMATIONS</th>
<th>DEATHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coelenterates</td>
<td>16,019</td>
<td>1</td>
</tr>
<tr>
<td>Fish</td>
<td>26,960</td>
<td>0</td>
</tr>
<tr>
<td>Ants</td>
<td>49,793</td>
<td>0</td>
</tr>
<tr>
<td>Bees, wasps, hornets</td>
<td>351,204</td>
<td>23</td>
</tr>
<tr>
<td>Caterpillars, centipedes</td>
<td>49,237</td>
<td>0</td>
</tr>
<tr>
<td>Other arthropods</td>
<td>265,557</td>
<td>3</td>
</tr>
<tr>
<td>Copperheads</td>
<td>14,580</td>
<td>1</td>
</tr>
<tr>
<td>Rattlesnakes</td>
<td>21,122</td>
<td>28</td>
</tr>
<tr>
<td>Water moccasins</td>
<td>2,467</td>
<td>0</td>
</tr>
<tr>
<td>Coral snakes</td>
<td>1,337</td>
<td>0</td>
</tr>
<tr>
<td>Exotic snakes</td>
<td>2,196</td>
<td>3</td>
</tr>
<tr>
<td>Nonvenomous snakes</td>
<td>37,001</td>
<td>0</td>
</tr>
<tr>
<td>Unknown snakes</td>
<td>41,758</td>
<td>4</td>
</tr>
<tr>
<td>Black widow spiders</td>
<td>58,304</td>
<td>0</td>
</tr>
<tr>
<td>Brown recluse spiders</td>
<td>42,544</td>
<td>7</td>
</tr>
<tr>
<td>Other or unknown spiders</td>
<td>261,769</td>
<td>1</td>
</tr>
<tr>
<td>Scorpions</td>
<td>260,288</td>
<td>4</td>
</tr>
</tbody>
</table>

Principles of Disease

Toxins

The two main factors influencing the pathophysiology of any venomous animal injury are the toxic properties of the venom and the victim's response to these toxins. In the past, snake venoms were classified as either neurotoxic or hematotoxic, depending on the observed response of the victim to the various venoms. Modern toxicologic investigation has shown that this classification is inadequate because most snake venoms studied contain compounds that have many toxic properties. It is true, however, that the venom of a particular species of snake may cause a clinical response that is predominantly neurotoxic or hematotoxic.

The toxic components of snake venom can be classified into four broad categories: enzymes, polypeptides, glycoproteins, and low-molecular-weight compounds. They can also be classified as protein and nonprotein compounds. Proteins, which account for most of the toxic manifestations, make up 90 to 95% of venom. Symptoms can generally be classified as local or systemic. Local effects are usually caused by enzymatic action on the various cellular and noncellular structures in the victim's tissues. These enzymes can cause coagulation, anticoagulation, cell lysis, hemorrhage, hemolysis, and the destruction of nucleic acid, mitochondria, and other organelles.

Polypeptides are structurally smaller and more rapidly absorbed than proteins and may account for the venom's effects on presynaptic and postsynaptic membranes and other organ systems. Phospholipase A can inhibit electron transfer at the level of cytochrome c and render mitochondrial-bound enzymes soluble. It can hydrolyze phospholipids in nerve axons, break down acetylcholine vesicles at the myoneuronal junction, cause myonecrosis, and induce lysis of red cell membranes. This single enzyme has been identified in all venoms of Hydrophiidae, Elapidae, Viperidae, and Crotalinae thus far investigated.

Elapidae and Hydrophiidae venoms have predominantly systemic effects, whereas Colubridae, Viperidae, and Crotalinae venoms have mainly local effects. There are many exceptions to this general division. For example, the venom of the Mojave rattlesnake (Crotalus scutulatus) may show minimal local effects and significant systemic effects, whereas the venom of the cobra (Naja naja) may cause extensive local tissue destruction.

Venom Delivery

The mechanism for delivering venom is fairly standard among snakes. It consists of two venom glands, hollow or grooved fangs, and ducts connecting the glands to the fangs. The glands, which evolved from salivary glands, are located on each side of the head above the maxillae and behind the eyes. Each gland has an individual muscle and a separate nerve supply that allow the snake to vary the amount of venom injected. The venom duct leads from the anterior portion of the gland along the maxilla to the fangs. Pit vipers have fangs that are large anterior maxillary teeth. These teeth are hollow and rotate outward from a resting position to a striking position. The coral snake has fixed, hollow maxillary teeth that are much smaller than those of pit vipers. The fangs in most snakes are shed and replaced regularly, and it is not unusual to see a snake with double fangs on one or both sides of its mouth.

The snake can control the amount of venom injected. In biting a human, a prey much too large to swallow, the snake may inject little or no venom (a "dry" bite), especially if injured or surprised.
However, the snake may inject more than 90% of the contents of the gland for the same reasons.

**Clinical Features**

The signs and symptoms of a venomous snakebite vary considerably and depend on many factors. From 30 to 50% of venomous snakebites result in little or no envenomation. A person with impaired cardiovascular, renal, or pulmonary function is less able to cope with even a moderately severe envenomation. Because of these multiple variables, the individual clinical response is the only way to judge the severity of a venomous snakebite. Factors that influence the effects of a snakebite are the age, health, and size of the snake; the relative toxicity of the venom; the condition of the fangs; whether the snake has recently fed or is injured; the size, age, and medical problems of the victim; and the anatomic location of the bite.

Local envenomation, if left untreated, can cause serious systemic problems (e.g., disseminated intravascular coagulation, pulmonary edema, and shock) as the toxic products are absorbed. The victim’s autopharmacologic response to the envenomation must also be taken into account. An immunoglobulin E (IgE)—mediated anaphylactic-type reaction may develop in victims of a previous snakebite when reexposed to the venom. Many venoms contain enzymes that trigger the release of bradykinin, histamine, and serotonin from the patient’s cells, which may cause fatal anaphylactoid reactions. A wave of effects ranging from minimal pain to multisystem failure and death can occur over a period of several days.

**Pit Vipers**

The most consistent symptom associated with pit viper bites is immediate burning pain in the area of the bite, whereas pain may be minimal with bites of Elapidae and other exotic snakes. With pit vipers, the severity of pain is probably related to the amount of venom injected or the degree of swelling. Edema surrounding the bite that gradually spreads proximally is a common finding. This edema is usually subcutaneous, begins early, and may involve the entire extremity. Compartment syndrome has been described; however, it is unusual even with severe edema. It has been reported more frequently in models involving intracompartmental venom injection. Most fangs do not penetrate into the fascial compartments, although muscle destruction may result from direct toxicity. Mortality is less frequent with distal bites to the toe and may be minimal with bites of Elapidae and other exotic snakes. With pit vipers, the relative toxicity of the venom; the condition of the fangs; whether the snake has recently fed or is injured; the size, age, and medical problems of the victim; and the anatomic location of the bite.

Local envenomation, if left untreated, can cause serious systemic problems (e.g., disseminated intravascular coagulation, pulmonary edema, and shock) as the toxic products are absorbed. The victim’s autopharmacologic response to the envenomation must also be taken into account. An immunoglobulin E (IgE)—mediated anaphylactic-type reaction may develop in victims of a previous snakebite when reexposed to the venom. Many venoms contain enzymes that trigger the release of bradykinin, histamine, and serotonin from the patient’s cells, which may cause fatal anaphylactoid reactions. A wave of effects ranging from minimal pain to multisystem failure and death can occur over a period of several days.

**Coral Snakes**

Signs and symptoms can vary considerably with bites of coral snakes, Mojave rattlesnakes, and many exotic snakes, especially cobras and Australian elapids. Little pain and swelling may occur. Many of these species’ venoms contain compounds that block neuromuscular transmission at acetylcholine receptor sites and have direct inhibitory effects on cardiac and skeletal muscle. Ptosis is common and often the first outward sign of envenomation. Other signs and symptoms include vertigo, paresthesias, fasciculations, slurred speech, drowsiness, dysphagia, restlessness, increased salivation, nausea, and proximal muscle weakness. The usual cause of death is respiratory failure.

**Gila Monster**

Gila monster bites are generally associated with pain, edema, and weakness. Hypotension is common with severe bites. Envenomation involves secretion of the venom from glands along the lower jaws. The venom is introduced into the victim through grooved teeth and a chewing mechanism. There are no reported deaths from Gila monster bites.

**Infection**

Although snakebite envenomation has been stressed here, any bite or puncture wound carries a risk for bacterial contamination. Gram-negative organisms predominate when snake venom and mouthparts are cultured. Although several studies have shown that prophylactic antibiotics are not indicated for snakebite, tetanus, osteomyelitis, cellulitis, or gas gangrene may occur in cases of snakebite with or without envenomation. This is especially true when a large amount of local tissue destruction has occurred, treatment has been delayed, or inappropriate first aid was attempted.

**Management**

**Out-of-Hospital Care**

All snakebites are considered an emergency, and any victim should be medically evaluated. The initial 6- to 8-hour period after a snakebite is critical. During this time, medical therapy can help prevent the morbidity associated with severe envenomation. Effective out-of-hospital care can be important.

Out-of-hospital care is relatively simple if guided by four basic concepts. First, the estimated time until arrival at a medical facility, as well as the skill of the on-scene assistants, must be considered when first aid is instituted. Separate the victim from the snake if possible to prevent further bites. A stick, pole, or other object longer than the snake can be used to move the snake away from the victim or, if necessary, to kill the snake by striking it behind the head. Rapid transportation to a medical facility is the best first aid for a snakebite. Any constricting jewelry or clothing should be removed from an extremity to prevent a tourniquet effect proximal to the swelling.

Second, spread of the venom should be slowed if possible; several methods are known. The patient’s excitement and physical activity, movement of the bitten area, alcohol consumption, and greater depth of the bite may increase the spread of venom. Except for the last factor, these issues can be addressed by calming the victim, immobilizing the bitten area with a sling or splint, and not giving anything by mouth. A method of first aid for venomous snakebites that was developed in Australia—the immobilization and compression technique (also called the Commonwealth Serum Laboratory technique)—slows uptake of Elapidae venom and mock venom in humans. The bitten extremity is either wrapped in an elastic bandage or placed in an air splint. In another technique from Australia called the Monash method, a thick pad and bandage are placed over the bite wound and extremity. Both these techniques have similar postulated mechanisms of action: The
lymphatic vessels and superficial veins are collapsed, and the proximal spread of venom is slowed. Although this method is successful as first-aid therapy for Elapidae bites, its use for pit vipers has not been demonstrated. If less than 30 minutes has elapsed since the bite, a constricting band applied tightly enough to impede superficial venous and lymph flow, but not arterial blood flow, may be used. The band is applied loosely enough to admit a finger between the band and the skin after application. It is used with caution to prevent the development of a tourniquet effect under swollen tissue, which may cause more destruction than the snakebite. Incision of bite wounds has no proven efficacy and poses potential danger to underlying structures and therefore is not recommended. The use of ice is not helpful in slowing the spread of venom, but an ice bag wrapped in a towel and applied to the bite area helps relieve pain. Ice water immersion and packing of the extremity in ice are dangerous and only contribute to tissue destruction. The use of suction devices has not been shown to be beneficial.

Third, when feasible, the snake should be identified or brought to the treating facility with the victim, though this should not delay transport of the patient to definitive medical care. Identification of the snake must be done safely—usually only by someone expert in handling snakes. A photo may be useful in identifying the snake if a close-up of the head and tail are included. Dead snakes can be placed in a hard container, such as a bucket or ice chest. Care should be taken to not touch the head of the snake because envenomation can occur even after death.

Fourth, additional medical interventions, if available, should be initiated, including cardiac monitoring, intravenous fluids, and analgesics.

Emergency Department Care

Many snakes do not envenomate the victim when they bite, which has provided false support for the historical use of whisky, clam juice, or split chickens in the treatment of snakebite. The only proven therapy is antivenin. Emergency department care of a snakebite focuses on supportive care and rapid treatment with the appropriate antivenin. Rapid decision-making is required to determine the optimal type, amount, and route of administration of the antivenin. By the time the emergency physician examines a snakebite victim, the venom may have already caused much damage, both locally and systemically. In this case, the emergency physician must be prepared to support the victim’s cardiovascular and respiratory systems.

Patient History. Specific historical information includes time elapsed since the bite, the number of bites, whether first aid was administered and what type, location of the bite, and symptoms (e.g., pain, numbness, nausea, tingling around the mouth, metallic taste in the mouth, muscle cramps, dyspnea, and dizziness). A brief medical history includes the last tetanus immunization, medications, and cardiovascular, hematologic, renal, and respiratory problems. An allergy history with emphasis on symptoms after exposure to horse or sheep products, previous injection of horse or sheep serum, and a history of asthma, hay fever, urticaria, or allergy to wool, papain, chymopapain, papaya, or pineapple should be obtained if antivenin treatment is being considered.

Patient Examination. The bite area is examined for signs of fang marks or scratches and local envenomation (e.g., edema, petechiae, ecchymosis, and bullae). The area distal to the bite is checked for pulses. A general physical examination is performed, with emphasis on the cardiorespiratory system and the neurologic examination, especially if a Mojave rattlesnake, coral snake, or exotic snake is suspected. If the bite involves an extremity, the circumference of the extremity at the site of the bite and approximately 5 inches proximal to the bite should be measured and recorded. These data aid in objectively estimating both spread of the venom and the effect of antivenin (Fig. 62-3).

Initial Medical Care. If the bite occurred less than 30 minutes before arrival in the emergency department, first-aid measures can be instituted, including a constricting band until antivenin, can be obtained. Snakebite victims with clinical evidence of envenomation should have an intravenous line with normal saline placed in an unaffected extremity. An electrocardiogram, complete blood count, urinalysis, protime, and levels of fibrinogen, fibrin split products, electrolytes, blood urea nitrogen, and creatinine are recommended; blood should be typed and crossmatched for 4 units of packed red blood cells.

The patient’s vital signs are monitored closely. Snakebite victims may be hypotensive because of third-space losses and hemorrhage. In an edematous extremity, the distal pulse may have to be examined with a Doppler instrument. If a compartment syndrome is suspected, insert a pressure monitor and obtain surgical consultation. If signs and symptoms of compartment syndrome are present, pressure greater than 30 mm Hg may necessitate fasciotomy, although there is evidence that administration of antivenin may lower compartment pressures.

Antivenin. The emergency physician must determine the type of antivenin to administer, how much, and over what period. If the bite is from a pit viper, the problem is not too difficult. Bites from copperheads usually cause a moderate amount of edema but generally do not require antivenin, although it may be indicated in selected cases. Envenomation may be classified according to severity into five grades, from grade 0 (no sign of envenomation) to grade IV (very severe envenomation). The amount of antivenin to be given is correlated with the grade of envenomation:

- Grade 0 (minimal). There is no evidence of envenomation, but snakebite is suspected. A fang wound may be present. Pain is minimal, with less than 1 inch of surrounding edema and erythema. No systemic manifestations are present during the first 12 hours after the bite. No laboratory changes occur.
• **Grade I (minimal).** There is minimal envenomation, and snakebite is suspected. A fang wound is usually present. Pain is moderate or throbbing and localized to the fang wound, surrounded by 1 to 5 inches of edema and erythema. No evidence of systemic involvement is present after 12 hours of observation. No laboratory changes occur.

• **Grade II (moderate).** There is moderate envenomation, more severe and widely distributed pain, edema spreading toward the trunk, and petechiae and ecchymoses limited to the area of edema. Nausea, vomiting, and a mild elevation in temperature are usually present.

• **Grade III (severe).** The envenomation is severe. The case may initially resemble a grade I or II envenomation, but the course is rapidly progressive. Within 12 hours, edema spreads up the extremity and may involve part of the trunk. Petechiae and ecchymoses may be generalized. Systemic manifestations may include tachycardia and hypotension. Laboratory abnormalities may include an elevated white blood cell count, creatine phosphokinase, prothrombin time, and partial thromboplastin time, as well as elevated fibrin degradation products and D-dimer. Decreased platelets and fibrinogen are common. Hematuria, myoglobinuria, increased bleeding time, and renal or hepatic abnormalities may also occur.

• **Grade IV (very severe).** The envenomation is very severe and is seen most frequently after the bite of a large rattlesnake. It is characterized by sudden pain, rapidly progressive swelling that may reach and involve the trunk within a few hours, ecchymoses, bleb formation, and necrosis. Systemic manifestations, often commencing within 15 minutes of the bite, usually include weakness, nausea, vomiting, vertigo, and numbness or tingling of the lips or face. Muscle fasciculations, painful muscular cramping, pallor, sweating, cold and clammy skin, rapid and weak pulse, incontinence, convulsions, and coma may also be observed. An intravenous bite may result in cardiopulmonary arrest soon after the bite.

Dart and colleagues have advocated slightly different grading systems and higher doses of antivenin: Grades 0 and I correspond to minimal envenomation, grade II represents moderate envenomation, and grades III and IV correspond to severe envenomation.

Either system can be used interchangeably.

Onset of symptoms after a pit viper bite may be delayed and may involve a variety of neurologic symptoms, including weakness, paresthesia, stupor, bulbar paralysis, and other cranial nerve dysfunction, as well as nausea, abdominal pain, and headache.

**Administration of Antivenin.** Any victim of a venomous snakebite with moderate or severe envenomation is a candidate for antivenin. The choice of antivenin depends on the species of snake, and the antivenin may be horse serum- or sheep-derived Fab fragments. Wyeth Laboratories, producer of the polyvalent horse serum–derived antivenin for Western Hemisphere pit vipers, has not been clinically studied for envenomation caused by four species of U.S. pit vipers and has not been clinically studied for envenomation caused by four species of U.S. pit vipers. CroFab has been shown to be as effective as the Wyeth antivenin, with fewer allergic reactions. Because of more rapid clearance of smaller Fab fragments by the kidney, however, a repeat-dose regimen must be used to prevent the recurrence of coagulopathy. The duration of action of the venom may be longer than the therapeutic effect of the antivenin. Initial studies have shown promise for a new affinity-purified, mixed monospecific ovine Fab antivenin that has been tested with favorable results in humans after minimal to moderate crotalid envenomation. Its efficacy in pit vipers from South America or Asia has not been proved. Purification of antivenin by separation of active fractions may lead to safer administration of horse serum–derived antivenin rather than the horse serum product. This is designed to limit the allergic reactions associated with horse serum antivenin by use of antigen-binding fragments (Fabs) of sheep (ovine) immunized against four species of venomous snake found in the United States. CroFab has been shown to be as effective as the Wyeth antivenin, with fewer allergic reactions. Because of more rapid clearance of smaller Fab fragments by the kidney, however, a repeat-dose regimen must be used to prevent the recurrence of coagulopathy. The duration of action of the venom may be longer than the therapeutic effect of the antivenin. Initial studies have shown promise for a new affinity-purified, mixed monospecific ovine Fab antivenin that has been tested with favorable results in humans after minimal to moderate crotalid envenomation. Its efficacy in pit vipers from South America or Asia has not been proved. Purification of antivenin by separation of active fractions may lead to safer administration of horse serum–derived antivenin. An algorithm has been developed that can aid in decision-making after a crotalid bite (Table 62-2 and Fig. 62-4). In the next decade, snakebite management will probably change radically throughout the world. Phytotherapy (botanical therapy) and other nonantivenin drug therapies for snakebite have shown promise in experimental animal studies, and some centers have successfully treated snakebite with medical support only. Hyperbaric oxygen therapy has also been used as an adjunct to antivenin in the treatment of venomous snakebite; however, there is insufficient evidence to recommend its use.

The following are general guidelines to maximize patient care when antivenin is used:

1. Because anaphylaxis may occur whenever antivenin is administered, appropriate therapeutic agents (e.g., oxygen supply, airway support, epinephrine, and other pressors) must be ready for immediate use. Any patient requiring antivenin should have two intravenous lines inserted. If an allergic reaction occurs, the line with the antivenin can be clamped and the other line used for resuscitation. Administration of 0.3 mg of 1:1000 epinephrine subcutaneously before administration of antivenin may

<table>
<thead>
<tr>
<th>ENVENOMINATION</th>
<th>INITIAL DOSE TOTAL</th>
<th>MAINTENANCE DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>4-6 vials</td>
<td>2 vials</td>
</tr>
<tr>
<td>Severe</td>
<td>8-12 vials</td>
<td>2-4 vials</td>
</tr>
<tr>
<td>Very severe</td>
<td>12-18 vials</td>
<td>4-10 vials</td>
</tr>
</tbody>
</table>

FabAV, Fab antivenin.

*Dosage based on initial findings and clinical response to antivenin. (See also Fig. 62-4.)

†If this dose elicits a clinical response, it is recommended that an additional two vials be given at 6, 12, and 18 hours. The patient’s coagulation studies should be followed to determine additional amounts.

Moreover, testing with normal horse serum may precipitate an allergic reaction, and even a positive test result may not preclude treatment if a patient has sustained severe envenomation. The incidence of allergic reactions with Fab antivenins has been much less than previously seen with whole IgG. The incidence of allergic reactions was 17% for early reactions and 12% for late reactions in postmarketing analysis. This was thought to be a result of incomplete purification of one lot contaminated by Fc fragments. Most of these reactions were minor and did not require stopping the infusion of the antivenin. The true incidence is unknown.

**Dosage and Precautions.** Current treatment of pit viper envenomation in the United States is to use a FabAV polyvalent antivenin rather than the horse serum product. This is designed to limit the allergic reactions associated with horse serum antivenin by use of antigen-binding fragments (Fabs) of sheep (ovine) immunized against four species of venomous snake found in the United States. CroFab has been shown to be as effective as the Wyeth antivenin, with fewer allergic reactions. Because of more rapid clearance of smaller Fab fragments by the kidney, however, a repeat-dose regimen must be used to prevent the recurrence of coagulopathy. The duration of action of the venom may be longer than the therapeutic effect of the antivenin. Initial studies have shown promise for a new affinity-purified, mixed monospecific ovine Fab antivenin that has been tested with favorable results in humans after minimal to moderate crotalid envenomation. Its efficacy in pit vipers from South America or Asia has not been proved. Purification of antivenin by separation of active fractions may lead to safer administration of horse serum–derived antivenin. An algorithm has been developed that can aid in decision-making after a crotalid bite (Table 62-2 and Fig. 62-4). In the next decade, snakebite management will probably change radically throughout the world. Phytotherapy (botanical therapy) and other nonantivenin drug therapies for snakebite have shown promise in experimental animal studies, and some centers have successfully treated snakebite with medical support only. Hyperbaric oxygen therapy has also been used as an adjunct to antivenin in the treatment of venomous snakebite; however, there is insufficient evidence to recommend its use.
Figure 62-4. Algorithm for use of FabAV (antivenin).

1. Monitor for progression

- **Minimal**
  - No FabAV
  - Yes (move to moderate)

- **Moderate**
  - No FabAV
  - Yes (move to severe)

- **Severe**
  - No FabAV
  - Yes (move to severe)

**Initial FabAV 4 vials over 60 min**

- Control

**Maintenance**

- 2 vials every 6 hours × 3
  - Yes (move to severe)
  - No (move to moderate)

- Repeat FabAV 4-6 vials
  - Yes
  - No (move to severe)

**Repeat FabAV until control then maintenance doses**

Coral and Exotic Snakes. It is recommended that all victims of bites by the eastern coral snake (*Micrurus fulvius*) be given antivenin even before any symptoms develop. Unfortunately, this antivenin is no longer manufactured by Wyeth, and existing stocks are slowly being depleted. The toxicity of this venom has a rapid onset, and once symptoms develop, it may be too late to reverse the effects with antivenin. The recommended dose is three to five vials in 300 to 500 mL of normal saline. Antivenin is given based on the clinical response. If no antivenin is available, management is based on meticulous supportive care emphasizing the respiratory and neurologic status. No antivenin exists for the venom of the Arizona (Sonoran) coral snake, which fortunately is less dangerous. Treatment of this type of snakebite is supportive.

The problems with bites of exotic snakes are threefold: Positive identification of the specimen is sometimes difficult, even for experts; specific antivenin is not always readily available; and even if the antivenin is available, the instructions for reconstitution and dosage may not be written in English. Many zoos maintain a supply of antivenin for their venomous snakes, and this may be the best source of antivenin for an exotic species. Some collectors keep appropriate antivenin on hand for the species that they collect. The Antivenin Index at the Arizona Poison Center (602-626-6016) can assist in identifying sources of exotic antivenin or in obtaining more pit viper antivenin. As with coral snakes, many patients do not show any early signs after envenomation by exotic snakes. The antivenin should be administered before neurologic symptoms develop.

Wound Care. The snakebite wound is cleaned and examined for foreign bodies, such as retained fangs or teeth, the area is immobilized, and analgesia is addressed. Elevation at or above heart level may relieve some of the pain. Some authors have previously advised excision of the bitten area, but such management is no longer recommended. As with any puncture wound, one should ensure that tetanus immunization is up-to-date. Broad-spectrum antibiotics have not been shown to be useful in uncomplicated snakebites. If signs of secondary infection develop, ampicillin-clavulanate is recommended.

Patients admitted to the hospital require serial determinations of platelets, fibrinogen, prothrombin time, and urinalysis every 4 hours to check for myoglobin and hemoglobin. Blood products,
including packed red blood cells, fresh frozen plasma, and other coagulation factors, are administered as needed. Usually, it is best to wait until antivenin therapy has been started, or the use of the blood products may be futile. Awake patients who have no nausea or abdominal pain can be given oral fluids. Local wound care includes daily cleansing with soap and water and the application of a sterile dressing to open wounds.

Surgical consultation is recommended for debridement or skin grafting. Debridement should probably not be performed earlier than 3 days after the bite, until the coagulopathy has resolved. Surgical exploration of the bite wound is not necessary and may be harmful. Skin grafts are occasionally necessary after bites by pit vipers that produce large necrotic areas. Fasciotomy is not usually indicated unless compartment pressures are elevated above 30 mm Hg and signs of compartment syndrome are present. Physical therapy is often needed and should begin soon after the acute phase of the envenomation is complete.

**Serum Sickness.** In most patients who receive more than 10 vials of horse serum–derived antivenin and in approximately 15% of those who receive FabAV, serum sickness develops up to a week later. The administration of diphenhydramine plus cimetidine, and in severe cases a tapering dose of steroids, can be used to treat this problem. Serum sickness is the only indication for the use of steroids with snakebite.34

**Other Envenomation.** Gila monster and Mexican beaded lizard bites are treated similarly to pit viper bites with regard to first aid. No definitive medical treatment exists. Antivenin is currently not available. Local wound care, tetanus prophylaxis, the use of antibiotics and analgesics, and supportive care are the extent of emergency department treatment available for this type of envenomation.

Envenomation by the yellow-bellied sea snake causes severe muscle necrosis with the release of large amounts of myoglobin and neurologic symptoms. Although a polyvalent antivenin is available from Australia, maintenance of adequate urine output, alkalization of urine, and general supportive care are usually sufficient.

**Disposition**

If no envenomation is evident after clinical examination and the snake was either nonvenomous or a pit viper, the victim can be observed for 6 to 8 hours. With some snakebites, however, toxicity may be delayed by up to 8 hours. If no sign of envenomation is seen after 8 hours, the patient may be discharged. These patients require tetanus immunization when indicated, wound care instructions, and referral for follow-up within 24 to 48 hours. They require instructions on the types of delayed symptoms that may occur and when to return to the emergency department.

If only local pain and minimal edema have occurred, the patient is closely watched for 12 hours in the emergency department. If the pain and swelling decrease and no systemic symptoms or laboratory abnormalities develop, the patient may be treated with the same precautions as a patient with no signs of envenomation. Any patient with moderate or severe envenomation should be admitted to an intensive care unit for monitoring during antivenin therapy. Depending on the severity of the bite, blood products, vasopressors, and invasive monitoring may be necessary.

Any patient bitten by a coral snake, a Mojave rattlesnake, or an exotic snake is at risk for severe neurologic sequelae that may not become evident for many hours. As a result, these patients require hospital admission, preferably to an intensive care unit where they can be monitored closely. Arrangements should be made to have a ventilator, invasive monitoring, and dialysis equipment available if necessary. Appropriate antivenin should be obtained and treatment initiated at the earliest onset of symptoms. Some experienced clinicians may wait until symptoms develop before administering antivenin. All patients receiving antivenin require close monitoring for recurrence of coagulopathy, which may occur several days after initial envenomation.35

**VENOMOUS ARTHROPODS**

Arthropods are animals with segmented bodies and jointed appendages. This phylum (Arthropoda) contains approximately 80% of all known animals. The living members of this phylum are categorized into 12 classes. Two classes, the Insecta and the Arachnida, are of particular interest because numerous venomous species have evolved that are harmful to humans. Many species have developed venom glands and an apparatus for delivering the venom to obtain food. Others have developed venom delivery systems used solely for defense; most of these species are found in the orders Hymenoptera and Lepidoptera.

Arthropods account for a higher percentage of deaths from envenomation than do snakes. They are found inside dwellings, as well as in deserts, forests, and lakes. Although most arthropods are more active during the warmer months, many are active throughout the winter. Arthropods are also active 24 hours a day, and many can fly, thus increasing their range. This high level of contact results in millions of cases of envenomation annually. Most fatalities result from an autopharmacologic response by the victim rather than the toxicity of the venom. An individual stung by a bee may have a small amount of pain and local swelling or, in severe cases, an anaphylactic reaction and death.

Arthropods use three main methods of delivering venom: stinging, biting, and secreting venom through pores or hairs. Some arthropods combine two systems, one for offense and the other for defense. In general, venom systems found on the oral pole of an animal are used for offensive purposes or food acquisition, whereas systems found on the caudal pole are used for defense. Humans are not considered prey for any venomous arthropod, and therefore bites from them are defensive, accidental, or reflexive. Many venomous arthropods are omitted from this discussion because of their infrequent contact with humans or the relative impotence of their venom.36

**Hymenoptera**

Hymenoptera is a familiar order of arthropods that is composed of the families of bees, wasps, hornets, yellow jackets, and ants. Many of these species are social insects, and their defense response is related to protection of the group rather than the individual organism. Although most members of this order are stinging insects, several species of ant can bite and sting simultaneously.

Bees and wasps have similar mechanisms of delivering venom. Female insects of this type have modified ovipositors that protrude from the abdomen and act as hypodermic needles to administer the venom. The barbed stinging apparatus of the bee is quite prominent. The stinging action pulls the stinger from the bee, thereby eviscerating the insect and killing it.

The wasp, which has an unbarbed stinger, may inflict many stings without damaging itself or its stinging apparatus. The venom is produced in one or two tubular glands that empty into a venom reservoir. The venom reservoir has a duct that connects to the stinger. The venom is composed of several classes of substances varying in composition among different species. Proteins, as in snake venom, make up most of the venom by dry weight. Peptides, amino acids, carbohydrates, lipids, and other low-molecular-weight substances are also found. The most common enzymes are phospholipase A and hyaluronidase. Peptides are common in some species and constitute up to 50% of the dry weight. Most of the toxicity of the venom results from substances of low molecular weight (e.g., bradykinin, acetylcholine, dopamine, histamine, and serotonin). Many other antigenic substances are also described in these species.
substances have been identified in bee and wasp venom, and they account for the induction of hypersensitivity and anaphylaxis in humans.37,38

Clinical Features

The signs and symptoms of bee and wasp stings vary, depending on the degree, type, and location of envenomation, as well as the characteristics of the victim. Bee and wasp venom can cause serious injury other than allergic types of reactions, depending on the number of stings, the species of insect, the size and previous health of the victim, and the anatomic area stung. For example, a stinger in the tongue or throat may quickly compromise the airway. Honeybee venom causes a much greater release of histamine per gram than does other hymenoptera venom and thus is more dangerous. Certain species of honeybee release a pheromone, isoamyl acetate, when the ovipositor is pulled from the abdomen after stinging a victim. This pheromone attracts other bees to the victim and thus incites multiple stings.

There is little antigenic overlap among species, which may explain the variability in reaction to stings reported by victims. Victims who are allergic to honeybees and who mistakenly identify a yellow jacket as a honeybee may not have a systemic reaction and thus may think that they are no longer allergic to honeybees.39

The most consistent finding is immediate pain at the site of the sting, followed by local swelling, redness, and itching. A sensitive victim may experience swelling, urticaria, coughing, wheezing, coma, and respiratory arrest. Some large and especially venomous hornets have been known to cause muscle necrosis and renal damage. Most serious reactions to bee stings occur in the first 30 minutes; however, the local effects of a sting may persist for 2 or 3 days. Delayed hypersensitivity may occur 7 to 10 days after the sting.40-42

“Killer Bees.” Health officials have been concerned about a particularly aggressive species of bee imported from Africa to Brazil in 1956 that has been known to attack humans and cattle with fatal results. This bee has managed to compete with native species in the southeastern United States, including California, Arizona, and Texas, where the mean high temperature is at least 60°F. This type of bee is not more toxic, only more aggressive.

Fire Ants. Another unwelcome import to the United States is the fire ant. This insect is a member of the family Formicidae and is another of the Hymenoptera that is harmful to humans. Several species of fire ant are known, some native to North America and some imported. The species responsible for 95% of clinical cases, Solenopsis invicta, was imported from Brazil to Alabama in the 1930s. This ant is now found in nine southern states and is replacing many native species and inhabiting new niches. The only limiting factor keeping the fire ant from progressive migration seems to be cold winters. This ant is small and light reddish brown to dark brown. Its venom is unique to the animal kingdom in that it is 99% alkaloid. The remaining 1% is quite immunogenic and can sensitize an individual to the venom. Properties of this venom include hemolysis, depolarization of membranes, activation of the alternative complement pathway, and general tissue destruction. The sting is produced when the ant bites the victim with its jaws and, while holding tight, pivots around and stings the victim with its ovipositor. The sting usually produces a sterile pustule within 24 hours. Other symptoms include local burning, redness, and itching. With multiple stings and in sensitive individuals, urticaria, angioedema, dyspnea, nausea, vomiting, wheezing, dizziness, and respiratory arrest may occur. Approximately 10% of victims have some degree of hypersensitivity reaction.44

Management

Home Care. First aid for Hymenoptera envenomation depends on the degree of reaction to the sting. For simple stings an ice bag wrapped in a towel and applied to the sting area usually relieves the pain and swelling. In the event of an anaphylactic reaction, basic life support is administered until further medical help arrives. Many people allergic to Hymenoptera envenomation carry an emergency insect sting kit containing a tourniquet, epinephrine in a 1:1000 dilution, and an antihistamine. These kits are readily available, and both the patient and the patient’s family should be instructed in the treatment of a severe allergic reaction.

Emergency Department Care. No specific antivenin exists for Hymenoptera stings. Treatment consists of local wound care and general supportive measures. A history of any previous allergic reactions to bee stings, hay fever, asthma, or drug reactions is obtained. The circumstances surrounding the sting and the number and location of stings are noted. In patients with a single sting and only a local reaction, the sting area is inspected for evidence of a venom apparatus, which, if present, can be removed by scraping the edge of a scalpel blade parallel to the skin and lifting the apparatus away from the skin without squeezing the venom sac. An ice bag wrapped in a towel may then be applied and the patient given an oral antihistamine (e.g., 50 mg of diphenhydramine). The patient is monitored, and if no further reaction is observed, he or she may be discharged with instructions to return to the emergency department if wheezing, dyspnea, hives, dizziness, or dysphagia occurs.

Adults in whom a severe urticarial reaction, dyspnea, or hypotension develops are treated with 0.3 mL of epinephrine in a 1:1000 dilution intramuscularly, 50 mg of diphenhydramine intravenously, and 50 mg of ranitidine intravenously. Although no evidence exists, it is recommended that patients with severe hypertension or cerebrovascular disease or those taking monoamine oxidase inhibitors be given epinephrine cautiously because of the potential for adverse reactions. Patients who are taking beta-blockers may not respond to epinephrine and should be given glucagon 1 to 2 mg intravenously. Based on their body weight, children are treated with 0.01 mL of a 1:1000 dilution of epinephrine per kilogram intramuscularly and 1 mg of diphenhydramine per kilogram intravenously.40 These patients must be watched closely for signs of respiratory problems and treated accordingly. After 1 hour, these individuals should be totally free of symptoms (except for some itching around the sting site). A biphasic allergic reaction can occur in up to 20% of patients. Any patient requiring epinephrine should be watched for at least 6 hours and may require 23-hour observation. There is a possibility of recurrence of the reaction up to 72 hours, and patients should be warned of this in their discharge instructions. Patients with allergic reactions to a single sting should be given an emergency insect sting kit and instructed in its use and referred to an allergist for desensitization.

A general rule is urticaria plus involvement of any other organ system constitutes anaphylaxis.45 Epinephrine is the treatment of anaphylaxis or anaphylactoid reaction and is given if these types of reactions are suspected. Patients who are wheezing after an insect sting are demonstrating a systemic reaction; they require intravenous access, inhaled beta-agonist therapy, intravenous steroids, and H1 and H2 blockers. Patients who have life-threatening reactions (hypotension, respiratory arrest, and cardiac arrest) may be given 0.1 mg of epinephrine in at least a 1:10,000 dilution, very slowly intravenously. The intramuscular route is preferred for all but the most extreme reactions.
Treatment of allergic reactions to fire ant stings is the same. The skin lesions should be kept clean with soap and water. Ice bags may be applied initially to relieve burning and pain. Prophylactic antibiotics are not needed.

Of patients who have a systemic reaction to an insect sting, 60% can have a future allergic reaction if they have a positive skin test result. These patients should be desensitized to any specific venom to which they are allergic. Purified insect venom is currently available for most Hymenoptera, including fire ants.45 Patients seen in the emergency department with systemic reactions to stings should be referred for skin testing and desensitization. These patients should be given emergency insect sting kits with instructions for use and should avoid activities that place them in proximity to Hymenoptera species.

### Spiders and Scorpions

The class Arachnida contains the largest number of venomous species known, with approximately 34,000 species of venomous spiders and 1400 species of venomous scorpions. Virtually all known species are venomous, but most are not harmful to humans. Only approximately 50 species of arachnids in the United States cause human illness because most species do not have fangs or stingers sufficiently long to penetrate human skin. Humans fear spiders and scorpions, for good reason in certain cases. Ticks, which also belong to this class, are less feared but probably cause more morbidity because of transmission of infectious diseases, such as Rocky Mountain spotted fever and Lyme disease. Some spider bites are never diagnosed because of lack of significant symptoms and the fact that they occur while the victim is sleeping. Many nonspider bites are incorrectly diagnosed as spider bites, and unfortunately there is no gold standard for making the diagnosis.

#### Black Widow Spider

The black widow spider, *Latrodectus mactans*, may be the most recognized venomous spider in the world. Several other closely related species of *Latrodectus*, or widow spiders, are found throughout the United States, including *Latrodectus hesperus*, which is common in Arizona and other western states. The diagnosis and treatment of the bites of all species are the same.

The black widow is found throughout the United States (except Alaska) and in southern Canada. The female is approximately twice as large as the male, and although both are venomous, only the female is able to envenomate humans. The black widow is glossy black, occasionally with red stripes, and has a bright red marking on the abdomen. This marking may have a hourglass shape or may appear only as two spots. Abdominal markings may vary, and related *Latrodectus* species may be similar in appearance and toxicity. The combined length of the black widow’s head and abdomen is approximately \( \frac{1}{2} \) inch, and the spider is approximately 1½ inches long, including the legs. It is found in protected places, such as under rocks, in woodpiles, and in outhouses and stables. The female is not aggressive except when guarding her eggs.

The venom apparatus of the black widow is a modified first appendage of the head known as the chelicera. The spider is able to control the amount of venom injected into its prey. The venom of the black widow is complex and contains both protein and nonprotein compounds.

Spiders normally use the venom to paralyze their prey and also to liquefy the tissues of the prey for digestion. The venom probably evolved from digestive glands analogous to the salivary glands in snakes. The ingredient most toxic to humans is thought to be a neurotoxin. This toxin destabilizes neuronal membranes by opening ionic channels, causing depletion of acetylcholine from presynaptic nerve terminals and increasing the frequency of spontaneous miniature endplate potentials at neuromuscular junctions.

**Clinical Features.** The classic symptomatology of the black widow bite is initially a pinprick sensation that may be followed by minimal local swelling and redness. If the area is examined closely, two small fang marks may be noticed. Sometimes the bite is not felt, especially if the victim is working when the bite occurs. From 15 minutes to 1 hour later, dull crampy pain develops in the area of the bite and gradually spreads to include the entire body. Usually, the pain is concentrated in the chest after upper extremity bites or in the abdomen after lower extremity bites. The abdomen may become boardlike, and the patient may complain of severe crampy pain. The abdominal manifestation may mimic pancreatitis, a peptic ulcer, or acute appendicitis, except that abdominal tenderness is usually minimal. Pregnant women may go into premature labor and precipitous delivery. Associated symptoms include dizziness, restlessness, ptosis, nausea, vomiting, headache, pruritus, dyspnea, conjunctivitis, facial swelling, sweating, weakness, difficulty speaking, anxiety, and cramping pain in all muscle groups. The patient is usually hypertensive, and cerebrospinal fluid pressure is sometimes elevated. There may be electrocardiographic changes similar to those produced by digitalis.

In adults, the signs and symptoms begin to abate after several hours and usually disappear in 2 or 3 days. A small child bitten by a black widow spider, however, may not survive.47 As with snake envenomation, the volume of distribution of black widow venom is much smaller in children than in adults. A dose that may cause only a few hours of pain in an adult may lead to complete cardiac decompensation and respiratory arrest in a child. Adult patients with preexisting hypertension, cerebrovascular disease, or cardiovascular disease are also at greater risk for complications. Symptoms usually persist for 8 to 12 hours and then subside, although in severe cases muscle cramps may continue for several days.

**Management.** First aid for a black widow spider bite consists of applying an ice pack to the bite area for relief of pain and transporting the victim to a hospital where supportive, symptomatic, and definitive treatment can be administered. The rescuer should obtain the specimen if possible because many dangerous spiders resemble harmless species and vice versa. The patient is monitored en route to the hospital, and basic life support is initiated if necessary. Bites in the neck or mouth area may cause airway compromise through muscle spasm. Emergency department care consists of obtaining a history of the circumstances surrounding the bite, a description of the appearance of the spider, any significant past medical history, current medications, and allergies to insect bites, horses, or horse serum.

The wound site is inspected for fang marks and cleansed with soap and water. As with any puncture wound, the patient’s tetanus immunization status is assessed. The patient is observed for approximately 6 hours. If symptoms do not develop and the spider was not positively identified as a black widow, the patient may be discharged with instructions to return to the emergency department if any symptoms develop.

All patients with symptoms of moderate envenomation, pregnant women, children, and those with preexisting cardiovascular disease or hypertension require intravenous access, a complete blood count, electrolytes, blood urea nitrogen, creatinine, coagulation studies, urinalysis, and an electrocardiogram.

Symptomatic treatment involves controlling the muscle cramps responsible for most of the discomfort associated with the bite. Diazepam or other benzodiazepines given intravenously are useful for relieving muscle spasms. There is one preliminary report in the literature supporting the benefit of dantrolene sodium both orally and intravenously to provide muscle relaxation for *Latrodectus* envenomation.48 Parenteral analgesics may be necessary to control pain; these drugs may affect an already compromised respiratory condition, and therefore their use must
be closely monitored. Patients with moderate symptoms are admitted to the hospital and monitored until symptoms subside; usually 1 day is sufficient. Fetal monitoring is initiated for pregnant women, and patients with severe symptoms are admitted to the intensive care unit for cardiovascular monitoring.

**Latrodectus Antivenin.** In general, pediatric patients, pregnant women, and the elderly may need to be given *Latrodectus* antivenin (LyoVac), which is derived from horse serum. Clinical judgment is used to adjust for the age and category of patients needing antivenin. Candidates for antivenin include patients with severe envenomation manifesting as seizures, respiratory failure, or uncontrolled hypertension; pregnant women; and patients not responding to other therapy. The dose of the antivenin is one vial diluted in 50 mL of normal saline and administered intravenously over a period of 15 minutes. Precautions for allergic reactions should be taken before antivenin is administered. A dose of subcutaneous 1:1000 epinephrine may prevent allergic reactions when given before horse serum antivenin. This antivenin is also useful with other species of the *Latrodectus* genus.46

**Brown Recluse Spider**

Several deaths were attributed to the brown recluse spider, *Loxosceles reclusa*, in the 1950s, primarily in the south-central United States, thus drawing the attention of the medical community. Many species of *Loxosceles* are venomous to humans, and at least five are found in the United States. These spiders are approximately 1 inch long, including leg span, and range in color from tan to dark brown. The most distinguishing mark is a violin-shaped darker area found on the cephalothorax. Close examination may reveal that the brown recluse has three pairs of eyes rather than the usual four.

These spiders, as their name implies, are not aggressive and are usually found under rocks, in woodpiles, and occasionally in attics and closets. Their range is concentrated in the south-central United States, especially Missouri, Kansas, Arkansas, Louisiana, eastern Texas, and Oklahoma. However, they have been reported in several large cities outside this range.

The venom apparatus is similar to that of most spiders, including the black widow. The composition of brown recluse venom has not been completely determined, but sphingomyelinase D is a primary component. The local tissue destructive effects are thought to be primarily caused by hemolytic enzymes and a levanterenol-like substance that induces severe vasocostriction. The systemic symptoms seem to be an allergic phenomenon and vary according to the individual’s immune response to the venom.49

**Clinical Features.** The symptoms of a brown recluse spider bite are both local and systemic. Initially they are similar to those caused by bites of many other spiders and other conditions, including pyoderma gangrenosum, furuncles, viral and fungal infections, and foreign body reactions. The victim may notice some burning pain in the area of the bite. Some victims do not notice the initial bite at all. Pain usually develops within 3 or 4 hours, and a white area of vasocostriction begins to surround the bite. A bleb then forms in the center of this area, and an erythematous ring arises on the periphery. The lesion at this stage resembles a bull’s-eye. The bleb darkens, necroses over the next several hours to days, and continues to spread slowly and gravitationally, with involvement of skin and subcutaneous fat. The most common mimic of *Loxosceles* or other necrotic spider bite is a methicillin-resistant *Staphylococcus aureus* (MRSA) skin infection.50,51

Systemic symptoms include fever, chills, rash, petechiae, nausea, vomiting, malaise, and weakness. Hemolysis, thrombocytopenia, shock, jaundice, renal failure, hemorrhage, and pulmonary edema are the usual signs of severe envenomation. Fatalities are more common in children, most often the result of severe intravascular hemolysis.51

**Management.** First aid for a brown recluse spider bite is simple. The specimen is secured if possible and the victim transported to a medical facility. Because the lesion develops over a period of days, there may not be any local treatment of the lesion that is effective. The emergency department evaluation involves a history of the circumstances surrounding the bite; the time elapsed since the bite; past history of allergic reactions, medications, or medical problems; and an assessment for systemic toxicity. If a specimen is available, identification may be facilitated by recruiting the help of a local entomologist. If signs of systemic toxicity develop, an intravenous line is placed in an unaffected extremity and a complete blood count, metabolic and coagulation profile, and urinalysis are performed. Vital signs and urine output are closely monitored. Patients with delayed presentation with a necrotic lesion require standard wound management and cultures for MRSA. Excision of the lesion has not been shown to aid healing and may be detrimental. Lesions have been known to cause extensive scarring, infection, and necrosis. Bites that are in fatty areas, such as the thigh or buttocks, may cause more extensive necrosis.

Dapsone, 50 to 200 mg/day, has been shown to be helpful in preventing local effects of the venom.51 If used within 48 hours, it may limit the size of the lesion that develops. However, dapsone may cause methemoglobinemia and hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency. Hyperbaric oxygen has been shown to decrease lesion size in animal models.52,53 Analgesics and antibiotics should be used as indicated during the course of the disease, although infection is not common. All patients with signs of systemic envenomation require hospital admission for monitoring; dialysis may be necessary if acute renal failure develops, and surgical consultation should be obtained for evaluation of the wound.

The Instituto Butantan in Sao Paulo, Brazil, and Instituto Bioclon, Mexico, both produce an antivenin for *Loxosceles* bites, but they are not available in the United States.

**Other Spiders**

Several other spiders can cause envenomation but are uncommon in the United States. Some of these spiders are large and can be quite aggressive. Most are imported either intentionally or as stowaways on cargo ships. Tarantulas, wandering spiders, funnel-web spiders, pallid spiders, and crab spiders are a few of the imported venomous spiders. Many of these species can cause envenomation similar to that of the brown recluse spider, and some produce neurotoxins.

Antivenin is produced for some of these groups (e.g., Brazilian *Phoneutria* and Australian *Atrax* species) but is usually available only in the country in which the species is generally found.54 Emergency care therefore involves symptomatic and supportive treatment. An outbreak of bites by a species of *Tegenaria*, known as the *hobo* or aggressive house spider, has been reported. This species was imported from Europe to the Pacific Northwest. This spider is a small brown spider with a herringbone pattern on its abdomen. The lesions are similar to those caused by the brown recluse spider, but systemic symptoms include headache and weakness. Treatment is largely supportive.

Tarantulas are popular pets in the United States, and most native species are relatively nontoxic. Tarantulas are unusual in that the abdominal hairs can be thrown by the spider and embedded in human skin and the eye. These hairs can cause allergic reactions and severe conjunctivitis and must generally be removed under a slit lamp or by an ophthalmologist. A recent import from Thailand, the cobalt blue tarantula, *Haplopelma lividum*, is a very aggressive spider with toxic venom.55
Scorpions

Scorpions are arachnids that resemble crustaceans and are among the oldest terrestrial animals. Scorpions are found throughout the world, and several species are located in the southwestern United States. Only one species, Centruroides sculpturatus (formerly Centruroides exilicauda), which is found in Arizona, is particularly dangerous. Scorpions are nocturnal predatory animals that usually spend the day under rocks, logs, or floors and in crevices. C. sculpturatus, or the bark scorpion, is found on or near trees (Fig. 62-5).

The scorpion has a tail-like structure that is actually the last six segments of its abdomen. The last segment, or the telson, contains the two venom glands and stinger. The toxicity of scorpion venom varies greatly from species to species. In general, the less dangerous species produce more local reactions, and the more dangerous species cause more systemic reactions. Several proteins have been identified in their venom; some cause hemolysis, local tissue destruction, and hemorrhage. The venom of C. sculpturatus is predominantly a neurotoxin that causes or enhances repetitive firing of axons by activation of sodium channels.

Clinical Features. Envenomation causes severe and immediate pain at the sting site. Local edema and erythema may or may not be present, depending on the species. After envenomation by C. sculpturatus, the victim may have heightened sensitivity to touch in the area of the sting along with local numbness and weakness. The diagnosis is often made by tapping on the site of the sting and causing an increase in pain at the site. Systemic symptoms may then develop, including anxiety, restlessness, muscle spasms, nausea, vomiting, excessive salivation, itching of the nose and throat, hyperthermia, blurred vision, myoclonus, and respiratory arrest. Various systemic complications may occur, depending on the species of scorpion. Tityus trinitatis scorpion stings cause pancreatitis to develop in 80% of victims. A wave of symptoms sometimes occurs over a 24-hour period, or respiratory failure may develop in the first 30 minutes. As with most envenomations, children are at a greater risk for severe reactions. A grading system has been developed to guide management of bark scorpion stings.56,57

Management. First aid for a scorpion sting consists of applying an ice bag to the area of the sting and transporting the victim to the hospital. A history of the circumstances surrounding the sting, any previous medical problems, and a description of the scorpion if no specimen is present should be obtained. It is relatively difficult for a layperson to differentiate the various scorpions. A serum Western blot test has been developed that can differentiate various scorpion venoms and thus help with diagnosis of Centruroides species, but it is not commercially available.57 Anascorp (Centruroides [scorpion] immune F[ab]2 equine injection) is horse serum derived and has been shown to be effective and safe in both blinded and open studies of 1534 patients. It was effective in children if given within 4 hours of the sting.60 Epinephrine 1:1000 can be given before Anascorp to prevent allergic reactions, although the incidence should be less than with whole immunoglobulin. Narcotic analgesics and barbiturates have been reported to increase the toxic effects of the venom and should be avoided.36,57

Approved antivenin is recommended in all cases of severe envenomation. Victims should be observed for 24 hours, and children should be admitted to the hospital for monitoring. Intravenous diazepam or another benzodiazepine may be used for myoclonus and muscle spasms. Phenobarbital, previously used in large doses in children, may be more dangerous than efficacious and may have contributed to deaths in the past. Atropine may be administered to control hypersalivation and bradycardia. Nitroprusside and prazosin have been used to control hypertension. Ventilatory assistance may be necessary, especially in children.

Other Arthropods

Ticks are vectors of human disease, and certain pregnant female ticks also secrete a toxin that causes a progressive ascending paralysis in humans and animals. The precise mechanism and structure of the toxin are unknown. The two species responsible in the United States are Dermacentor andersoni (wood tick) and Dermacentor variabilis (dog tick). The bite of the tick is usually painless, but the victim later has difficulty walking, weakness, flaccid paralysis, slurred speech, and visual disturbances.39 The victim is usually a child, often with a history of recent outdoor activity. Treatment is removal of the offending tick before the paralysis has progressed too far. Any patient with ascending paralysis should be closely examined for the presence of a tick, especially on the head and back.

Several species of beetle, millipede, and caterpillar secrete irritating substances that cause severe burning pain, numbness, pustular contact dermatitis, edema, nausea, vomiting, and headache. Oropharyngeal exposure can cause mucosal edema and irritation.60 No deaths have been reported. Treatment consists of washing the area thoroughly with soap and water and removing any spines or hairs present. Spines can be removed with adhesive tape or by applying white glue or facial peel. Locally applied ice bags and a paste of baking soda and water may be of benefit. Analgesics should be used as needed, and supportive therapy may be necessary for severe envenomation.61

Centipedes can inflict bites that cause erythema and edema. Treatment is usually local soaks and the use of analgesics. Cone-nose bugs, or “kissing bugs,” may cause severe local and systemic allergic reactions. Treatment with antihistamines and supportive care, depending on the degree of reaction, are all that is necessary. Many other arthropods can cause local skin reactions and severe allergic reactions, depending on the individual’s sensitivity. Patients are treated symptomatically with local steroid creams, antihistamines, and other symptomatic supportive measures.

VENOMOUS MARINE ANIMALS

Epidemiology

Almost 2000 species of animals found in the ocean are either venomous or poisonous to humans, and many can produce severe illness or fatalities. An estimated 40,000 to 50,000 marine envenomations occur annually. In recent years the number of injuries caused by these animals has increased dramatically because of the greater number of scuba divers, snorkelers, surfers, and others
engaging in water sports. These animals are not usually aggressive, and many are completely immobile. Most of the venomous marine animals injure humans with defensive or food-procuring devices. Most venomous marine animals in the United States are found along the California, Gulf of Mexico, and southern Atlantic coasts. These animals range in complexity from sponges to bony fishes and contain some of the most complex and toxic venoms known.

**Venom Delivery**

In general, venomous marine animals are divided into three main classes according to the mechanism of venom delivery: bites, nematocysts, and stings.

**Bites**

Biting animals include several species of cephalopods, most often octopi. Although popular media portray a giant deadly creature that squeezes its victims to death, the most dangerous octopi are seldom larger than 20 cm. Several fatalities have been reported after a bite by the blue-ringed octopus, *Hapalochlaena maculosa*. Most victims are bitten on the upper extremity as they disturb this normally nonaggressive creature. The octopus has a pair of modified salivary glands that secrete venom into the wound produced by the animal’s beak. The venom contains a potent vasodilator and an inhibitor of neuromuscular transmission similar to tetrodotoxin.62 No known antivenin exists, and treatment is largely supportive, with respiratory support being the most important lifesaving intervention.

**Nematocysts**

The second type of venom mechanism is the nematocyst found in coelenterates (*Cnidaria*). This group of animals includes the Portuguese man-of-war, true jellyfish, fire corals, stinging hydroids, sea wasps, sea nettle, and anemones. Most of these organisms are sessile, but some are free floating. Because of their large numbers, this group accounts for the greatest number of envenomations by marine animals.

Many different types of nematocysts are known, but the basic mechanism is a “spring-loaded” venom gland that can, on mechanical or chemical stimulation, suddenly exert and discharge a structure that penetrates the prey and delivers the venom through a connecting tube. These nematocysts, found on the animal’s tentacles, can number in the hundreds of thousands. Tentacles can be up to 100 feet long in some giant species. Nematocysts can still function even if the animal is dead or if the tentacles are separated from the animal’s body. These stinging cells can remain active for weeks after an animal becomes beached. Often, not all nematocysts fire on initial contact but may discharge later during attempted rescue and treatment. Certain marine species have evolved methods of using ingested nematocysts for their own defense.

Toxicity. Nematocyst venom contains various peptides, phospholipase A, proteolytic enzymes, hemolytic enzymes, quaternary ammonium compounds, serotonin, and other toxic compounds. The venom of the coelenterates is antigenic, and allergic reactions are often seen. The severity of the envenomation is related to several factors. First, the severity of the injury is directly proportional to the number of nematocysts discharged. Second, the toxicity varies from species to species. It is unlikely that the victim or the treating physician will be able to identify the species from the appearance of the wound. Symptoms may range from simple isolated stinging to respiratory paralysis, cardiovascular collapse, and death. Therefore the diagnosis must be made according to the clinical findings. Third, the victim’s autopharmacologic response to the venom may turn a relatively minor envenomation into a fatal anaphylactic reaction. Any clinician who regularly treats this type of injury should become acquainted with the common species in the particular area.

Although lethal and potentially lethal jellyfish exist worldwide, the extremely toxic specimens are found off the coast of Australia and in other Indo-Pacific waters. Probably the most notable and most toxic coelenterate is the box jellyfish (*Chironex fleckeri*), also known as the “sea wasp.” More dangerous than the famed great white shark, this small animal causes several deaths along the Australian coast annually.64 Cardiac arrest may occur within minutes, and early aggressive resuscitation offers the best chance of recovery. Intravenous verapamil and box jellyfish antivenin are advocated for use in treatment.65,66

Another north Australian jellyfish, *Carukia barnesi*, also produces a devastating envenomation known as *Irukandji syndrome*. This causes major catecholamine release, hypertensive crisis, and passive death.67

The Portuguese man-of-war (*Physalia physalis*) is found along the southern U.S. coastline. This organism is not a true jellyfish but a hydroid colony. Envenomation is usually limited to local pain and paresthesias, but it may progress systemically to nausea, headache, chills, and even cardiopulmonary collapse. This organism has also been responsible for several deaths.68

Most other envenomations are minimal, and the danger is either drowning after being stung or an allergic reaction to the venom. The symptoms resulting from coelenterate envenomation usually consist of a severe burning sensation accompanied by raised erythematous lesions where nematocysts have discharged into the skin. The symptoms may progress, depending on the species and the number of nematocysts, to include nausea, vomiting, chest pain, muscle cramps, dyspnea, diarrhea, cough, convulsions, angioedema, and respiratory arrest. The initial pain and redness may last from a few hours to 2 or 3 days, depending on the therapy.

A related type of envenomation is caused by various species of coral, particularly fire coral (*Millepora*). These injuries combine nematocyst envenomation with wound contamination. Animal protein and calcareous material left behind in these wounds cause infection and chronic inflammation.

**Stings**

Some marine animals cause a “sting” that is produced by a specialized apparatus that punctures the victim’s skin and then introduces venom. Common examples of this type of animal are sea urchins, cone shells, bristle worms, sea snakes, crown-of-thorns starfish, stingrays, scorpion fish, weever fish, catfish, stonefish, rabbit fish, and zebra fish. Sea urchins, cone shells (*Conus californicus*), catfish, scorpion fish, and stingrays account for most of the venemous marine animal injuries in the United States.

**Sea Urchins.** Sea urchins belong to the Echinoidea phylum along with starfish and sea cucumbers. These animals produce injury and envenomation mostly through toxin-coated spines. These spines often break off and introduce calcareous material and debris into the wound, thereby potentiating severe infection. Symptoms most often include severe local burning, pain, and discoloration, but they may progress systemically in some patients. The degree of envenomation is usually related to the number of spines involved and the species of animal encountered.

**Cone Shells.** Cone shells are much more toxic than sea urchins, and some species have been responsible for fatalities in the Indo-Pacific region. The venom apparatus is a tubular gland that connects to several teeth at the end of a retractable proboscis. All envenomations reported have occurred in persons handling the shells. The venom contains several proteins, protein-carbohydrate complexes, and 3-indolyl derivatives that act mainly on skeletal muscle and cause variably spastic and flaccid
Management

Much of the venom from marine animals can be neutralized at the scene, and most fatalities can be prevented. The most important step is to remove the victim from the water. Drownings after minimal envenomation may account for more fatalities than the end effects of severe envenomation. The patient should be questioned about the circumstances of the bite, allergies, and systemic symptoms. If a severe allergic reaction has occurred, the victim is treated for this emergency before the wound is addressed. The type of wound care largely varies according to the type of venom apparatus involved. All marine stings from either bony fish or stingrays are treated with immersion in hot (110°F) water for 30 to 90 minutes. This therapy usually improves pain within minutes, but supplemental analgesics may be needed. As with all wounds encountered in the emergency department, appropriate cleansing, debridement, and tetanus prophylaxis are paramount. Prophylactic antibiotics, such as ciprofloxacin, are recommended when residual foreign body is suspected. Specific antivenins are available for some species, such as the box jellyfish and stonefish.

Bite injuries are treated with basic life-support measures and general wound care consisting of cleansing, debridement, and irrigation. Systemic signs and symptoms are treated as appropriate, with aggressive attention paid to the cardiac and respiratory systems.

Nematocysts

Nematocyst injuries are treated by first removing the nematocysts without allowing them to discharge. Tentacles are removed with a gloved hand or forceps. The remaining nematocysts are fixed by pouring vinegar (dilute acetic acid) over the wound area. For Physalia (man-of-war) stings, hot water may be useful or hot vinegar may be even better.76 Baking soda and alcohol have also been shown to be effective, and deactivation of nematocysts may be species specific. Fresh water is not used, because it may stimulate continued nematocyst discharge.74 Other methods include scraping off residual material with the use of a shaving cream or baking soda slurry. The affected area is then debrided and cleansed. Hot water immersion may relieve pain. Most lifeguard stations in areas where coelenterate stings are common have the necessary materials for this regimen. Supportive pharmacologic therapy (e.g., analgesics, antihistamines, and steroid creams) is indicated for all but the most trivial envenomation. Delayed cutaneous reactions may persist despite optimal therapy.7

Fish

Puncture injuries are treated by removing the spine or sting if possible. An x-ray film of the involved area is obtained because many spines and sheaths are radiopaque. Sea urchin spines usually break off in the wound; they are so fragile that removing them is difficult without the proper instruments. The stinger of the stingray should be removed with forceps, although these stingers with their sheaths have been known to penetrate body cavities and require surgery for removal. Although not usually present in the wound, the fish spines of bony fish should be removed with forceps. In all cases the wound should be copiously irrigated. Most venom injected through puncture wounds are heat labile. Significant analgesia can be achieved by submersion of the wound in hot (110°F) water for 30 to 90 minutes or until symptoms improve. Patients envenomated by unknown or unfamiliar organisms should be observed for systemic signs and symptoms. Careful discharge instructions are provided to the patient, warning him or her to return for increasing pain, numbness, difficulty breathing, and signs of infection.

KEY CONCEPTS

- Snake venom causes neurotoxicity and hematotoxicity, but one usually predominates, depending on the species of snake.
- The amount of crotalid antivenin given depends on the grade of envenomation, from 0 (minimal or no sign of envenomation) to IV (severe envenomation).
- Pit vipers have a characteristic pit found midway between the eye and the nostril on both sides of the head.
- Arthropods account for more deaths from envenomation than snakes, usually as a result of allergic reactions.
- Nematocyst (jellyfish) stings should be immediately neutralized with vinegar or hot water, and fish stings with hot water.
- Spider bites may be difficult to diagnose without identification of the offending spider.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.