CHAPTER 153

Envenomation

CRAIG S. KITCHENS – Snakes Native to the United States, STEVEN A. SEIFERT – Snakes Non-Native to the United States, CLAUDIA L. BARTHOLD – Spiders and Scorpions, and JENNIFER A. OAKES – Marine Envenomation

INTRODUCTION

This review will discuss envenomation by snakes (both native and nonnative to the United States), spiders, scorpions, and marine animals. Clinical and laboratory manifestations of envenomations are due to a spectacular array of substances that gain entry into the victim and cause symptoms. A great deal of attention has been paid to the biochemistry and mechanisms regarding venoms. As complex and varied as venoms are, one should expect that the symptoms and severity can range from mild to serious, or even be fatal, and the treatment can range from supportive to the administration of various therapeutic substances (antivenoms) to neutralize the venoms. Over several decades, the scientific approach to understanding venoms and their manifestations has converted the approach to envenomation syndromes from folklore and anecdotal first-aid nostrums to an evergrowing and sophisticated scientific discipline.

SNAKES NATIVE TO THE UNITED STATES

Man has had a long and storied relationship with snakes, with references several millennia ago found in the third chapter of Genesis. Despite most references’ depiction of dread, the medical profession’s positive regard for snakes is attested by the universally accepted sign of the medical profession: a snake intertwined on the staff of Aesculapius.

This portion of the chapter will deal with our management style regarding snake envenomation by snakes native to the United States; other physicians’ styles may be less conservative; few will be more so. First, these facts not only underscore differences in therapeutic philosophy, but also acknowledge that there exists a considerable range in morbidity and mortality in envenomation based partly on the bitten host, but especially on the species of the offending reptile—we treat what we see. Second, one can deduce that there is no clear “standard of care.”

The second part of the chapter will address envenomation by snakes not native to the United States. Unfortunately, this separation sometimes is blurred by the increasing number of exotic snakes kept either professionally by herpetologists who work in zoos, research, or the pharmaceutical industry, or by private collectors who keep a variety of exotic venomous snakes.

A mere century ago, the treatment of North American snakebites was shrouded in mystery, folklore, and old wives’ tales, and indeed, was not even considered a medical problem. As clinical observation followed by clinical investigation became more commonplace in the study of snake envenomation syndromes, snakebite management has become an important area of clinical medicine (1,2). In the United States, there are two broad categories of venomous snakes. The first, and the less common, is the coral snake, members of the family Elapidae, with two genera and several species. This snake represents the only venomous snake in North America that is not a pit viper, does not have cat eye–shaped pupils, and has a rather small head. Only 1% to 2% of all US snakebite envenomations involve coral snakes. As the epidemiology, symptomatology, and treatment of coral snake envenomation is entirely different and apart from pit viper envenomation, it will be discussed separately.

The pit vipers account for about 95% of US snakebites. These are members of the family Viperidae, subfamily Crotalinae and comprise rattlesnakes, water moccasins, and copperheads. Pit vipers are composed of three genera and numerous species, which will be briefly discussed separately. As pit vipers, they have two heat-sensing pits approximately halfway between their nostrils and eyes. Because of their considerable venom apparatus, they appear to have heads significantly larger than one might expect, given the size of their bodies. Rattlesnakes have a series of distal specialized skin attachments that cause the rattlesnake to generate the distinctive rattle when it shakes its tail. The remaining 2% to 3% of all US snakebites are inflicted by exotic venomous snakes, which are covered in the second part of this chapter, Snakes Not Native to the United States.

Identification of offending animals should be done if possible, but without undue risk of further bites to the victim or others. Because the US pit viper and coral snake antivenoms are polyvalent, it is only necessary to identify a snake to the family level. Identification charts are available and experts such as local herpetologists may be consulted in certain cases.

Coral Snake Envenomation

Coral snakes are rather small and brilliantly colored secretive reptiles. As opposed to most snakes, which prefer isolation, they are often found around newer housing projects and may be encountered in one’s garden or yard. They are not aggressive, supporting stories that children may play with them for hours to days without being bitten. Additionally, their anatomy is such that they cannot open their mouths as widely as the pit vipers, so they typically bite only at the tips of fingers or the webbed space between the thumb and first finger. Lacking long fangs, envenomation requires hanging on to a small anatomic part for 10 to 30 seconds in order to work venom into the skin. Activity most victims will not tolerate, again accounting for the rather small number of victims. This colorful snake has several nonpoisonous look-alikes with which it is sometimes confused. In the United States, the coral snake has a black nose, with alternating rings of red, yellow (sometimes white), and black encircling the entire body of the snake. Hospitals should have a snake identification chart, but accurate or consistent identification of snakes from pictures by patients, let alone by younger patients or patients in an inebriated state, is notoriously poor.
Coral snake envenomation is complicated by the fact that, in direct contrast to pit viper envenomation, there is little or no local tissue damage; therefore, the characteristic triad of immediate local pain, swelling, and discoloration, while characteristic of pit viper envenomation, does not develop. It is, accordingly, possible to misconstrue a serious bite from a coral snake as one from either a “dry bite” by a venomous snake or a bite by a nonvenomous snake. This can lead to an unfortunate outcome.

Symptoms and Manifestations

Symptoms may be delayed up to 12 hours, yet are dangerous and can progress rapidly once they appear; therefore, patients are often observed for 24 hours to determine whether an envenomation has occurred, particularly if they are also inebriated. As the venom is chiefly neurotoxic, neurologic signs and symptoms are declared in approximately the following ascending order and frequency: a mild numbness in the bitten extremity; and euphoria, often precipitously followed by cranial nerve symptoms, with diplopia being the one that the patient most often first notices, whereas a distinct flat dysarthria (similar to patients with myasthenia gravis) is the one that health care professionals usually first notice. Stridor, inability to swallow and, finally, respiratory arrest may rapidly ensue. During progression from dysarthria to respiratory arrest, aspiration pneumonia is extremely common and comprises one of the major morbidities of coral snake envenomation. Should cranial nerve involvement be noted to develop, it is important to prophylactically and preemptively endotracheally intubate the patient in order to protect the airway.

Lacking the large fangs characteristic of pit vipers, visible puncture wounds are absent. Rather, if one squeezes the bite site, one may see minute pinpoints of blood welling up from the tissue, indicating that the teeth of the coral snake have successfully worked their way into the subcutaneous tissue, thereby allowing the deposition of venom. We had reported (3) a triad of risk factors which, in our experience, if any two are present, warrant consideration for antivenom: (a) the snake is positively identified as a coral snake; (b) there is a history of the snake “hanging on” the bitten site for at least 15 to 30 seconds, thus allowing sufficient time to work the venom under the skin; and/or (c) one can observe pinpoints of blood following applied pressure to the bitten area. We typically do not administer antivenom for the presence of only one feature of this triad but frequently observe the patient for about a day.

The primary manifestation of envenomation is paralysis of the entire nervous system, with the primary threat to life being respiratory arrest, with or without aspiration pneumonia. Our local experience suggests that the natural history (i.e., without antivenom treatment or severe reaction to antivenom such that therapy is aborted) of those patients who develop respiratory arrest do so for approximately 7 to 10 days before the effects of the venom naturally abate; mentation is not affected. One must be able to support a totally flaccid patient for this period of time, with particular attention to maintenance of respiratory care and respiratory hygiene. Long-term sequelae following either successful treatment or the natural history of the envenomation syndrome may include several months of dysesthesias and paresthesias in the bitten extremity, but these generally fade after several months to a year.

Antivenom Administration

The antivenom for coral snake envenomation supplied by Wyeth (Antivenin [Micrurus fulvius] [equine origin]) is, unfortunately, no longer being manufactured. Should antivenom be procured, and if symptoms are deemed either imminent or present, three to five vials of the antivenom are usually given intravenously about every 8 to 12 hours until symptoms stop progressing; typically, a single treatment might be sufficient. If symptoms develop an hour or more before antivenin administration, it is notoriously difficult to reverse the neurologic blockade, and repeated administration of antivenom is not only futile, but in this time of extremely limited supplies, is probably unwise for society in general.

The shortage of coral snake antivenom and uncertainty of both its indication and efficacy has resulted in an increasingly conservative approach to its administration in an effort to minimize infusion if antivenom is unnecessary. It has recently been suggested to wait until symptoms begin to develop in monitored patients prior to both the preparation and administration of this valuable antivenom, as many to most patients never progress to this stage (3a).

It appears that antivenom prepared in South America for South American members of the Micrurus family is variably effective against the Micrurus species in the northern hemisphere (4,5). A coral snake antivenom, prepared in Mexico (Coralym, Bioclon), is available in emergencies. Presently, it is recommended to call one’s regional poison center (1–800–222–1222) to assist in acquisition, as most of the Mexican product in the United States is held by zoos. See below, Snakes Not Native to the United States, for further information.

PIT VIPER ENVENOMATION

Genera

Crotalus

This family, Crotalidae, consists of three genera found within the United States. The largest genus, composed of some 15 to 20 species and subspecies, is Crotalus, the rattlesnakes, distinctly New World animals. The rattle is composed of specialized scales that produce a rattling sound when the reptile shakes its tail. The most serious bites are those of the two largest snakes, namely the easterndiamondback rattlesnake (Crotalus adamanteus) and the western diamondback rattlesnake (Crotalus atrox). Some special comments will also be made about specific effects of the venoms of the canebrake rattlesnake (Crotalus horridus atricaudatus) and the Mojave rattlesnake (Crotalus scutulatus). The remaining rattlesnakes tend to be smaller and located mostly in the desert southwest and California.

Sistrurus

Two other species of rattlesnakes are in the second genus, Sistrurus. Sistrurus catenatus (also known as the massasauga) is mostly encountered in the upper Midwest from western Pennsylvania and New York across to Michigan and Iowa. Sistrurus miliarius (also known as the pygmy rattlesnake) is seen chiefly in Florida and up into the Atlantic Coast states. Both species of Sistrurus are smaller rattlesnakes with poorly developed rattles. Their bites are characterized by a very low morbidity and virtually zero mortality (6,7). We use antivenom...
only occasionally (approximately 10% of the time) in pygmy rattlesnake bites and primarily in patients at the extremes of age or with bites about the head or face.

**Agkistrodon**

The third genus of the family Crotalidae is *Agkistrodon*, which is composed of two species. The copperhead (*Agkistrodon contortrix*) is the most common pit viper from Georgia up through the Atlantic Coast states. In two reviews (8,9), antivenom was only rarely administered. No patients died, none had meaningful coagulation test abnormalities, none bled, and none required surgical procedures. *Agkistrodon piscivorus* (commonly known as the water moccasin) is also in the Atlantic Coast states, in Florida, and westward through Alabama and Mississippi and into eastern Texas. Neither species of *Agkistrodon* is extremely venomous. Bites characteristically cause significant edema but virtually no mortality (10). Significant in vitro coagulation abnormalities are rare (10). We employ antivenom in only about 25% of victims of water moccasin envenomations and those chiefly for patients either at the extremes of age, multiple bites, or with significant comorbidities.

**Range of Venom Effects**

Bites from these species of pit vipers vary enormously, from the least lethal with no documented deaths (*S. miliarius*—pygmy rattlesnake) to the most lethal (*C. adamanteus*—eastern diamondback rattlesnake). The variability of the virulence is due to the variability of the venom. All pit viper venoms are very complex, containing upward to 20 to 40 proteinaceous substances, about half of which are enzymes designed to help spread the venom throughout the prey's tissues and to predigest the intended prey, and another equal number of nonenzymatic proteins that have many other effects, including those affecting the autonomic nervous system. Indeed, pit viper venom is one of the more complex mixtures of poisons known to exist. Snake venom is best regarded as an offensive weapon against an accidental prey.

The complexity of the venom is demonstrated by its multiple effects. At one time, it was fashionable to describe venom as “neurotoxic” or “hematoxic,” but those notions tend to break down. It is fair to regard the venom of the coral snake as “neurotoxic” or “hematoxic,” but those notions tend to be chiefly, if not exclusively, neurotoxic. Several excellent reviews exist regarding the complex nature of pit viper venoms (11–17).

The mixture of venom components vary enormously not only within the family, but also within the genus and species. In fact, even within the same subspecies, there is considerable variation in the relative concentrations of various components in the venom. Even individual members of a species, studied over time, display variability in their venom pattern (18). This is important when one considers the antivenom that is currently available. CroFab ([Crotalidae polyvalent immune Fab [ovine] [FabAV], Therapeutic Antibodies, Inc., Nashville TN) is a mixture of Fab fragments prepared from purified immunoglobulins, produced in healthy sheep that have been repeatedly injected with venom from one of the following four snakes: *C. atrox*, *C. adamanteus*, *C. scutulatus*, or *A. piscivorus*. The Fab fragments from all four preparations are then mixed together to produce a polyvalent mixture. As there are variable degrees of immunogenicity and responses from the sheep to the injection of multiple and variable components (antigens) within the venom of these four pit vipers, it should be realized that not all venom components will be neutralized to exactly the same degree. Because many of the venom principles within other species of this genus may be shared with other genera, there is a variable degree of crossover of the Fab antivenom against the venom of species to which the sheep was never exposed, such as *Crotalus horridus atricaudatus*, *S. miliarius*, and others. This no doubt explains, in part, the variability of the response of some envenomation syndromes from other snakebites to the same Fab antivenom. As an example, the author has had experience (unpublished data) with a patient envenomated by a pet mottled rock rattlesnake (*Crotalus lepidus*), a small and rather rarely offending reptile. The victim of this bite had essentially no salubrious response to repeated administrations of FabAV. One may deduce that there exist few Fab fragments directed against that snake's individual venom pattern. On the other hand, the venom of the Southern Pacific rattlesnake (*Crotalus helleri*) is not injected into those snake, yet the envenomation syndrome resulting from this reptile seems to respond well to FabAV (19).

Recently, a new pit viper antivenom has been approved by the FDA for release in 2018. It is an F(ab')2 preparation named Anavip ([Instituto Biecolon, S.A., de C.V.]). It is prepared from injecting horses with venom from two South American pit vipers (*Bothrops asper* and *Crotalus durissus*). It had been theorized that, being a larger molecule than Fab, its half-life might be longer and thus may prove to minimize “recurrence syndrome” (see Clinical and Laboratory Findings, below). Early studies support this notion (19a). As it is yet to be released, further comments about its dosage, safety, and efficacy cannot be elaborated upon.

**Symptoms and Manifestations**

The near-immediate onset of the triad of symptoms occurring in human victims of pit viper envenomation—namely, pain, swelling, and discoloration—supports the concept of disruption and digestion of tissue due to the venom. Digestive enzymes such as phosphatases, hyaluronidases, proteinases, phospholipases, and other substances dissolve connective tissue and proteins, and attack nerve endings (16,17). Edema is largely brought about by disruption of the endothelium of capillaries and lymphatics due to a variety of proteins that directly attack endothelial integrity. Discoloration results from extravasation of red cells through the disrupted microcirculation (17). A far smaller role in local hemorrhage is played by perturbations of the coagulation system, which is discussed in more detail below. Evidence for this concept is that, while hemorrhage within soft tissues may be spreading and progressive, it is typically confined to the bitten extremity as hemorrhage only rarely occurs systemically in victims of bites from snakes native to the United States; this is not always the case with bites from many snakes not native to this country.

Pain, swelling, and discoloration (beginning immediately to approximately 2 hours at the latest from the bite) serve as excellent evidence for envenomation. On the other hand, lack of pain, swelling, and discoloration usually indicate that the victim has been fortunate to be one of the 15% to 30% of pit viper victims in which the reptile did not inject venom and thus require no antivenom. One caveat is that some patients may be envenomated by a pit viper but fail to display any local
signs of pain, swelling, or discoloration, yet are clearly ill as attested by their profuse weakness, fasciculations, diaphoresis, hypotension, nausea, vomiting, diarrhea, mental status alterations (which include confusion and stupor), and the off-mentioned “metallic taste” experienced by several victims. This situation occurs in approximately 5% to 10% of envenomations, and is best attributed to injection of the venom more or less directly into a vessel or a muscular bed rich in capillaries such that local pain, swelling, and discoloration are bypassed as the venom goes more directly into the circulatory system. Sites in which such situations occur are the muscular areas within the hands (thenar or hypothenar eminences) as well as the calf, or even more proximally in the great muscles of the legs or arms.

Many of the venom components that cause pain, swelling, and discoloration are neutralized by the currently available FabAV. A great many of these principles are shared within the Crotalid family; however, not all are. The venom of some native snakes contains a principle that is quite myotoxic and this appears to be less promptly neutralized by FabAV. Reptiles that characteristically cause massive rhabdomyolysis with extreme elevations of the serum creatine phosphokinase (CPK)—including the CPK-MB band, but with negative troponin assays—include the canebrake rattlesnake (Crotalus horridus atricaudatus) (20) of the southeastern United States and the Mojave rattlesnake (C. scutulatus) (21) of the desert southwest. Additionally, neurologic symptoms are more pronounced in the Mojave rattlesnake victim than in victims of most other Crotalid species (22). Efficacy of FabAV has been demonstrated in reviews of both pediatric populations (23) and among patients adjudged to have been severely envenomed (24).

Clinical and Laboratory Findings

Coagulation abnormalities, both clinical and laboratory, have always been of great interest to those who treat pit viper envenomations. They are by far most pronounced within the Crotalus genus and rarely encountered in the Agkistrodon (9,10) and rarely, if ever, in the Sistrurus genera (10). Laboratory coagulation abnormalities that have been described in bite victims of Crotalus subspecies have been most thoroughly studied in the bites from the eastern diamondback (C. adamanteus) (10) and the western diamondback (C. atrox). The venom of these snakes contains a thrombin-like enzyme (crotalase) that rapidly and efficiently, yet only partially, cleaves fibrinogen by cleaving the A-peptide off the α-subunit as does thrombin but, unlike thrombin, crotalase does not complete fibrinogen cleavage as it neither cleaves the B-peptide from the β-subunit nor activates factors V, VIII, or XIII; this partially clotted non-cross-linked fibrinogen forms only a loose web-like gel that is exquisitely sensitive to any fibrinolytic activity. A mild, transient thrombocytopenia may be seen for a few hours suggesting a passive temporary entrapment of platelets in this web-like gel. Also different from thrombin’s actions, crotalase neither activates platelets nor consumes antithrombin III.

These are distinct and durable differentiating points from disseminated intravascular coagulation (DIC); in DIC, consumption of fibrinogen is typical and is accompanied by thrombosis of blood vessels in several organs as well as severe depletion of platelets, factor V, and factor VIII, which occurs from the bite of some exotic snakes (15).

Crotalase does not activate plasminogen directly (i.e., in vitro or in vivo) but does so indirectly, most likely by release of endothelial-secreted tissue plasminogen activator (tPA). Plasma levels of tPA spike in a reflex response to the deposition of the partially formed fibrin on the endothelial surface, and a brisk fibrinolysis occurs, producing massive quantities of circulating fibrin degradation products (FDPs), as essentially the total body fibrinogen component (15–20 g) is nearly totally converted into FDPs within an hour of the envenomation (10). Crotalase is necessary in only extremely small amounts to totally defibrinogenate an adult human. This hypothesis is supported by three lines of evidence. The first is that even the most trivial bite from the smallest of eastern diamondbacks may be associated with total defibrinogenation as the sole clinical or laboratory manifestation of envenomation. Therefore, the coagulation end point (visible fibrin clot) of routine coagulation tests, such as prothrombin time (PT) and partial thromboplastin time (PTT), is so impaired that the blood seems “incoagulable.” Thrombin generation via the intact coagulation cascade is totally retained to promote intact hemostasis, despite incoagulability in vitro PTs and PTTs. Thrombin generation is sufficient to support platelet adhesion at sites of wounds and, with even limited amounts of remaining fibrinogen, to secure a reasonable clot.

A second line of evidence that crotalase need be present in only very small amounts is evidenced by an event termed “recurrence syndrome” (25). In this clinical situation, despite total arrest of the envenomation syndrome—as defined by a lack of progression of present swelling at the bite site, a lack of new swelling, cessation of nausea and vomiting, normalization of vital signs, and, at least temporarily, total correction of the PT and PTT (26)—after several days, the PT and PTT may revert to incoagulability as defibrinogenation recurs, most likely as a result of a return of crotalase from the wound circulating in the absence of antivenom. The third line of evidence is the astounding efficacy and rapidity of readministration of FabAV to correct the recurrence of coagulopathy. There is great and healthy debate as to whether or not the recurrence syndrome should be treated (25). Patients who have been clinically stable for several days following prompt administration of FabAV may, and usually do, remain totally free of any symptoms, including any clinical signs of abnormal hemostasis, only to be found to have incoagulable PTs and PTTs as they are being prepared for hospital discharge.

A stumbling block for the majority of clinicians is drawing interpretations and conclusions based on their prior experiences from clinical situations which result in equally impaired PTs and PTTs, and then comparing those situations to this fairly benign defibrinogenation syndrome (27). The defibrinogenation syndrome is very easily and promptly reversed by the readministration of FabAV. However, recurrence may happen yet again if unneutralized venom principles continue to enter the general circulation from the wound site after the clearance of the circulating antivenom. The clinical significance of recurrence, particularly as manifest by return of coagulation abnormalities from victims of North American pit vipers, is yet to be clarified. Recently, there have been reports of low-dose continuous infusion therapy with FabAV being efficacious in recurrence syndrome (28).

These recurrences have been discovered and defined as the result of study and follow-up of patients bitten by rattlesnakes and administered FabAV. The discovery of recurrence
syndrome was enabled by research, development, and observation from clinical protocol-driven prospective studies of patients treated with FabAV, which garnered the largest and most extensively followed group of patients (29). In fact, in a retrospective study, Bogdan et al. (30) found data showing that, among 354 consecutive patients treated for North American Crotalid bites, 112 exhibited coagulopathy. Of these, 31 had undergone coagulation testing sufficient to detect whether a recurrence occurred; of these 31, 14 (45%) had a recurrence of the coagulopathy to include severe hypofibrinogenemia or thrombocytopenia. Apparently, none of these patients experienced spontaneous hemorrhage despite these overt laboratory abnormalities.

Boyer et al. (29), in studying FabAV-treated Crotalid envenomations in 38 patients, found that 20 (53%) had recurrent, persistent, or late coagulopathy, some occurring 13 days following envenomation and treatment; no patient experienced significant spontaneous bleeding. Of their 20 patients, 16 were observed with no further FabAV treatment, and all fared well. Two patients who received supplemental doses of FabAV had prompt normalization of laboratory findings. Of interest, all their patients with defibrinogenation on presentation showed significant increases in their plasma fibrinogen levels following FabAV treatment, which is a major laboratory criterion for a therapeutic response to FabAV.

Ruha et al. (31) studied 28 cases of rattlesnake envenomation in Arizona, noting that in some cases, despite initial control of coagulopathy, there was return of either coagulation defects and/or thrombocytopenia. It was their opinion that one need not wait for total normalization of all the coagulation and platelet studies as a therapeutic end point for FabAV therapy. Odeleye et al. (32) noted, in two cases of rattlesnake envenomation, that thrombocytopenia was difficult to reverse either with FabAV and/or platelet transfusions, and suggested that unless bleeding occurs, transfusion of platelets and blood products might best be withheld.

Camilleri et al. (33) concluded that despite “critical value” coagulopathies, close observation without further therapeutic intervention is appropriate. Similar conservative conclusions were made from South American pit viper experiences by de Oliveira et al. (34) regarding their experience with Bothrops, and by Sano-Martins et al. (35) regarding the South American cascabel (Crotalus durissus).

Postmortem Findings

Death from American pit viper envenomation is rare, and full autopsies are even rarer. Dart et al. (36) reviewed the few reports regarding 16 deaths up to 1989. Central nervous system edema and hemorrhage were reported in a few cases, but cerebral hemorrhage was deemed the cause of death in only one. They also opined that the exact cause of death may be difficult to determine, deducing that the most common cause was progressive shock leading to multiorgan failure and death hours to a few days later. Generalized edema from extravasation of fluid into the heart, lung, and brain was implicated; it appeared that edema was a result not of frank hemorrhage, but of direct effect of the toxin on the circulatory endothelial integrity and the microcirculation in particular. It was frequently noted in their review that delayed therapy and/or inadequate therapy, or even no antivenom therapy, seemed to be disproportionately encountered among fatal cases.

Prehospital Treatment

The key to good, effective therapy that minimizes the chance of loss of life, limb, or function is prompt transportation to a medical care facility. In areas where snakes are endemic, almost all hospitals have at least a modicum of antivenom available.

Initial scene management is to prevent further bites and to calm the patient. If successful transport is anticipated within an hour, it is probably best to forgo any local therapy other than to gently splint the bitten extremity, keeping it at or slightly below heart level, and transport the patient to an appropriate health care facility. The use of topical cold packs may provide some relief of severe pain, if properly applied. Incising or excising the wound, the application of electrical currents, or other traumatic manipulations are contraindicated. Suction devices remove at best 2% of the venom load, are likely to be clinically insignificant, and, if used, should not delay transport. The use of a tourniquet with pressure sufficient to impede either arterial or venous flow is contraindicated. A lymphatic constriction band (LCB) ideally a blood pressure cuff inflated to 15 to 25 mmHg or a band that allows a finger to pass easily beneath) or a properly applied pressure immobilization bandage (PIB) may be considered if there are immediate life-threatening effects or a prolonged (>1 hour) transport time.

Hospital Treatment

While there is often an undue amount of unfounded anxiety (2), the treatment of victims who have been envenomed by North American snakes will not be encountered by most physicians. Although approximately 5,000 to 10,000 bites occur in the United States yearly, death from envenomation by North American pit vipers occurs only about 5 to 10 times (0.1%) per year, representing an approximate 99.9% survival rate. Reasons for this fairly enviable situation, especially when compared to higher mortalities in other countries, include three facts. First, medical care is far more accessible than it is in many countries in which envenomations occur; second, venoms of North American pit vipers do not cause true DIC with organ thrombosis and/or DIC-type bleeding; third, employment of prompt and sound medical care, including fluid resuscitation and monitoring of vital signs, to minimize morbidity. Table 153.1 outlines the essentials of appropriate management of such patients.

Immediate Management

Confirm the Bite

First, confirm that the patient was bitten by a snake and, particularly, a venomous snake. With the exception of coral snake
envenomation, this usually includes the presence of puncture wounds. Most patients experience the prompt triad of pain, swelling, and discoloration confined to the bite site, usually within minutes of the event, but up to 2 hours later in atypical cases. If a patient does have puncture wounds consistent with pit viper envenomation, and does not have pain, swelling, and discoloration, or any systemic symptoms such as hypotension, nausea, vomiting, diarrhea, constipation, mental status changes, fasciculations, or diaphoresis, one may strongly consider that the patient has been bitten yet not envenomated. A caveat for this pronouncement is that many children, when anxious, frequently vomit, which may be a misleading sign. An alarming number of victims of snakebites are not at their normal mental status, given the frequency of concomitant inebriation from alcohol or other substances. This impedes obtaining a detailed history and the patient’s full cooperation. In most situations, only a minority of bites are accidents in the true sense of the word.

**Determine the Genus and Species**

Determine the family and/or genus and species of snake if at all possible. The majority of victims know not only that they were in proximity to a venomous snake, but also the snake’s common name, yet still are compelled to taunt, toy with, kiss, or otherwise handle the venomous animal for reasons that are not clear; in such patients, snake identification is not difficult. Another 25% to 30% will bring the snake to the health care facility in conditions ranging from badly mutilated to quite alive. Identification by charts or consulting herpetologists or other experts is quite useful in determining the species of the snake, whereas it is not of much benefit for the victim if he or she cannot identify the type of snake that inflicted the bite. Whether by confusion or the desire to please, children will agree that the picture of nearly any snake presented to them is indeed the offending reptile. Several online sites, such as http://www.pitt.edu/~mcs2/herp/SoNA.html, are available to assist identification.

One can occasionally augment identification of an offending snake by the symptom complex its bite produces, as is demonstrated in Table 153.2. The prognosis is generally species dependent, but also related to the time to presentation, time to antivenom administration, the health of the host, and other factors. Management will be based on a mixture of observed and anticipated symptoms and physical findings, as well as one’s prior experience in handling this emergency.

**Determine Systemic Signs and Manifestations**

Assuming the patient does have signs of local envenomation, next in order is to determine whether there are any systemic signs of envenomation, remembering the fact that no one dies of local envenomation, but only from systemic manifestations. As a general rule, in mild and moderate envenomations, the symptoms are due primarily to the local pain, swelling, and discoloration, which, while quite alarming, are not usually of a life-threatening nature. Systemic symptoms such as nausea, vomiting, diarrhea, and diaphoresis, as well as fasciculations—particularly in *Crotalus* envenomations—do portend the possibility of a more serious outcome. Many coagulation abnormalities seen in *Crotalus* envenomations are often spectacular in their laboratory manifestations but systemic hemorrhage is uncommon. Altered mental status to include a noticeable stupor, and a foul metallic taste is often reported by patients with serious envenomations.

**Assign Degree of Severity**

In attempting to assign a degree of severity from mild to moderate to severe, one must recognize several principles. The first is that the envenomation syndrome is progressive and, secondly, evaluation is ongoing and time dependent. Two patients may be bitten to a similar degree. If the first patient is seen in 15 or 20 minutes after the bite, very few local signs of pain, swelling, or discoloration will be seen, whereas a similar patient requiring 2 hours to arrive for emergent care will report more advanced and obvious pain, swelling, and discoloration, although with exactly the same prognosis. It is the rate of change in signs, symptoms, and other manifestations that is important in grading the severity of the bite, as well as in grading the effect—or lack of effect—of the administration of antivenom.

**Antivenom Administration**

Because of the present lack of prospective, outcome-based studies, practices regarding perceived indications for the use of antivenom vary. Most practitioners will not administer antivenom to a patient without envenomation (“dry bites”) or to

---

**TABLE 153.2 Clinical Characteristics of Envenomation That Potentially Aid in Identification of Offending Pit Viper Species**

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Scientific Name</th>
<th>Distribution</th>
<th>Neurologic Symptoms</th>
<th>Coagulopathic Findings</th>
<th>Rhabdomyolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern diamondback rattlesnake</td>
<td><em>Crotalus adamanterus</em></td>
<td>Southeastern United States</td>
<td>+</td>
<td>Prolonged Pt/Ptt; minimal thrombocytopenia</td>
<td>+</td>
</tr>
<tr>
<td>Canebrake rattlesnake</td>
<td><em>Crotalus horridus atricaudatus</em></td>
<td>Eastern United States</td>
<td>Nil</td>
<td>Nil</td>
<td>+++</td>
</tr>
<tr>
<td>Mojave rattlesnake</td>
<td><em>Crotalus scutulatus</em></td>
<td>Desert Southwest United States</td>
<td>+++</td>
<td>Nil</td>
<td>+++</td>
</tr>
<tr>
<td>Timber rattlesnake</td>
<td><em>Crotalus horridus</em></td>
<td>Eastern United States</td>
<td>Nil</td>
<td>Prolonged Pt/Ptt; moderate to severe thrombocytopenia</td>
<td>Nil</td>
</tr>
<tr>
<td>Massasauga</td>
<td><em>Sistrurus catenatus</em></td>
<td>Upper midwestern States</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Pygmy rattlesnake</td>
<td><em>Sistrurus miliarius</em></td>
<td>Southern Atlantic Coast states</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Copperhead</td>
<td><em>Agkistrodon contortrix</em></td>
<td>Atlantic Coast states</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Water moccasin</td>
<td><em>Agkistrodon piscivorus</em></td>
<td>Atlantic and Gulf Coast states</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Pt, prothrombin time; Ptt, partial thromboplastin time.

+,, usually minimally present; ++, usually moderately present; ++++, usually extensively present; ++++, always present.
those who have only minimal envenomation, particularly if it is by the Sistrurus or Agkistrodon species. Bites by the copperhead (A. contortrix) are usually not treated (7–9) with antivenom unless the patient is at the extremes of age or with many comorbid conditions. Envenomation by the water moccasin (A. piscivorus) is notorious for a large amount of local edema but not much in the way of systemic symptoms and laboratory manifestations (10), and even less in the way of mortality. Their swelling can be so massive that, if untreated for any reason, bites of the hand may progress up the arm, chest wall, neck, face, and even abdomen; all of which is reversible.

Severe envenomations are often apparent by the time they arrive at the emergency department (ED), primarily because of the rapidity with which the venom initially gains entry into the circulatory system. While it is common to see someone progress from minimum envenomation to moderate envenomation, it is quite rare to see one, in our experience, progress from moderate envenomation to severe envenomation. Rather, when they arrive—even within minutes of the event—severely envenomated patients may be considerably hypotensive with lethargy, nausea, and vomiting, and require immediate and aggressive therapy (Table 153.3); suggested therapy is outlined in Table 153.4. It is useful to outline the leading edge of proximal progression of the swelling with an ink pen or felt marker. In this manner, one can observe whether the swelling is progressive or arrested. Whereas some relatively slow progression is tolerated—particularly if one elects not to treat the patient or if antivenom is not immediately available—rapid swelling, particularly with concomitant systemic symptoms, usually justifies prompt and aggressive therapy.

We do not administer antivenom in patients who have no envenomation; about 10% to 15% of people with minimal envenomation, half of those patients with moderate envenomation, and all patients with severe envenomation are administered antivenom. The offending reptiles in one’s locale and the experience of those evaluating the patient may override our simplification. Reasons for not administering antivenom to all, or nearly all, victims are several: (a) the extremely low mortality rate of envenomation by snakes native to the United States, (b) the admittedly very low rate (<0.01%) of serious and mild (14%) allergic reactions, (c) the modest rate (15%) of serum sickness–like late reactions (occurring typically 8–12 days after administration) to FabAV (1), and (d) the cost of antivenom treatment, which can easily exceed $50,000. As antivenom is more efficacious the earlier it is administered, once the decision has been made to employ the drug, it should be done promptly. Control of the envenomation syndrome is adjudged by the slowing, or preferably the cessation, of progressive local swelling (27). One should not expect extant swelling to regress or any areas of local damage to the bite site such as a swollen or discolored area to regress, as such damage has already resulted prior to the patient’s arrival and treatment. Hemorrhagic bleb formation at the site of the bite is not an important sign in and of itself, although it generates much attention; these are best left alone.

Compartment syndromes are seen rarely, and indications for surgical intervention as justified by pressure measurements in only about 1% to 2% of all envenomated patients in the United States. The degree of swelling in and of itself is not a reliable sign of compartment syndrome given the elasticity of skin. More reliable signs are total lack of function and exquisite pain of the muscles contained within a compromised compartment and, often, an intense hardness of the site owing to the nonelasticity of fascial tissue which, while limiting swelling, allows pressure to increase in tissues locked beneath the fascial plane. The palmar aspect of the hand and lateral compartment of the tibia may be so involved. Direct measurement of pressure within an anatomic compartment may be of use, yet adequate antivenom therapy and elevation will usually result in normalization of pressures. Orthopedic consultation may be indicated, but in experimental animal models, fasciotomy has not been shown to result in improved outcomes.

The mainstay for treatment for North American pit viper envenomation is ovine FabAV for bites in both adults and children (23,27). The Fab portions of sheep immunoglobulins are made by enzyme cleavage and elimination of the Fc fragment, which is regarded as the more immunogenic part of the intact immunoglobulin molecule, and by further enzymatic cleavage of the resulting Fab fragment. Pretreatment skin or conjunctival testing is neither required nor recommended prior to the administration of FabAV. The small FabAV molecule has the theoretical advantage of a larger volume of distribution and

<table>
<thead>
<tr>
<th>TABLE 153.3 Severity of Envenomation by Pit Vipers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>No envenomation</td>
</tr>
<tr>
<td>Minimal envenomation</td>
</tr>
<tr>
<td>Moderate envenomation</td>
</tr>
<tr>
<td>Severe envenomation</td>
</tr>
</tbody>
</table>

TABLE 153.4 Summary of Therapeutic Measures for Pit Viper Envenomation

- Obtain IV access and administer crystalloid as indicated.
- Obtain complete blood count, prothrombin time, partial thromboplastin time, and platelet count every 6–12 hrs.
- Estimate severity of envenomation
  - Species of snake
  - Age, health status of victim
  - Rate of progression of signs/symptoms
- Administer FabAV per Table 153.3.
- Follow rate of progression of signs/symptoms after FabAV administration.
- Determine tetanus vaccination status.
- Seek consultation from experts or a poison center (1–800–222–1222), especially if one is less experienced in treating snake envenomation.
the potential to neutralize more venom at the bite site. On the
other hand, as it has a more rapid distribution and shorter
half-life than intact IgG, periodic readministration during the
initial treatment period is important.

Another general rule of thumb for pit viper envenomation is
that approximately half of the total swelling expected to occur
does so within the first 2 hours of envenomation, and nearly
all of it occurs by 12 hours after envenomation. This seems
congruent with one study that involved timed rate of change in
swelling. Accordingly, if a patient presents over 12 hours after
the bite, it would be unusual to experience significantly more
swelling, and most systemic symptoms should have occurred
and abated. We rarely initiate administration of antivenom
treatment more than 12 hours after a bite, and essentially
never after 24 hours of the bite. One may reintiate or continue
antivenom administration after 24 hours in selected situations,
such as in the management of continued coagulopathic effects
or in the management of recurrence syndrome.

We hold that the defibrinogenation syndrome itself is not
such a clear and present risk for spontaneous hemorrhage or
that its presence alone requires administration of antivenom,
or that its recurrence represents an established reason to read-
administer antivenom (10,26). As the literature and experience
garnered thus far supports that defibrinogenation alone seems
benign, the administration of blood products such as fresh fro-
zen plasma (FFP) or cryoprecipitate is usually not warranted,
even prior to a surgical procedure, as the risks of these blood
products probably outweigh their (unproven) benefit. If one
does encounter a patient with systemic hemorrhage, or should
unacceptable bleeding follow a surgical procedure, adminis-
tration of additional antivenom plus cryoprecipitate (8–10
bags in an adult) is the fibrinogen source of choice (10). We
advise against preemptive or prophylactic transfusion of blood
products for potential or concern for bleeding reserving blood
products only for actual hemorrhage and after antivenom has
been administered (37).

Some species of snakes, particularly the timber rattlesnake
(*Crotalus horridus*), have a principle in their venom that
causes significant thrombocytopenia, which appears rather
resistant to reversal by antivenom therapy (38). If platelet
counts are significantly falling and/or are less than 10,000 to
20,000 cells/μL, administration of additional antivenom and
infusion of platelets may be indicated, particularly if there is
evidence for systemic bleeding. In general, with most Crotalid
envenomation, there is a mild thrombocytopenia in the range
of 50,000 to 150,000 cells/μL that is thought to be due to pas-
sive entrapment of platelets within the previously described
soft fibrin network; this does not support a diagnosis of DIC.

**Support**

A surgical procedure for the wound is rarely indicated, and there
are several case series and experimental studies suggesting that sur-
gical procedures correlate with a delayed outcome, some with a
paradoxic increase in permanent loss of tissue, loss of anatomic
function, and nonspecific stiffness (37,39,40). Antibiotics are
generally not employed as they are of questionable assistance,
and their routine use is not recommended (37,41,42). If there
has been significant surgical manipulation of the wound in
the field, such as with repeated knife wounds, that stance may
need to be reconsidered. Tetanus vaccination status should be
ascertained as being up to date. It is best to have the extremity
clearly visible so as not to compromise the evaluation; we do
not advocate any covering dressings or wraps. Once the patient
is at the hospital and receiving antivenom, the extremity should
be elevated above the level of the heart. Monitoring is usually
best performed in the ED, with subsequent admission to the
intensive care unit (ICU), although ICU therapy should not be
considered, in our opinion, as a necessary standard of care—
the careful and frequent nursing care available in the ICU is,
however. The usual length of hospitalization is 4 to 6 days. We
often observe patients for up to 24 hours—either in the ED
or in the hospital—who are deemed to have no envenomation
or mild envenomations, and who do not receive antivenom
because of the high incidence of concurrent inebriation.

**Prognosis**

Nearly all North American pit viper bites result in some near-
instantaneous local tissue destruction, which should not be
expected to be totally absent or to resolve, even with the very
best and most rapid care. Most edema and swelling that does
occur after antivenom treatment lasts only for a month or two,
with longer recovery times seen in older or debilitated patients.

In general, there is a total return of function to the bitten
extremity, although some patients can experience mild stiff-
ness, atrophy, and weakness for up to a year or more (43,44).
The loss of tissue, including fingers or limbs, is very rare, and
often occurs with the injudicious prehospital use of ice or tour-
quoise or, perhaps, very delayed care. Unfortunately, patients
who are bitten by snakes tend to continue their risky behavior,
resulting in the finding that reenvenomation is not rare.

**SNAKES Not NATIVE TO THE UNITED STATES**

This section summarizes the epidemiology, pathophysiology,
diagnosis, and treatment of nonnative snake envenomations
in the United States. Envenomations by reptile, amphibian,
arthropod, or marine species not native to the United States
pose special challenges to the clinician as they are likely to be
unfamiliar with the clinical spectrum of exotic envenomation
and its current management. Antivenoms, if they exist, may
not be available or may take many hours to locate and deliver
to the location of the envenomated patient. Zoos, aquaria,
and academic institutions may obtain and stock antivenoms to
non-native animals in their possession for potential treatment
of their workers. The problem is compounded by private col-
lections, whose existence is not usually known to their regional
health care system until an exposure occurs and whose keepers
are unlikely to possess the appropriate antivenoms. Policies
and procedures governing acquisition, storage, handling, anti-
venom, and preparations for managing envenomations range
from comprehensive to nonexistent.

The severity and spectrum of effects in envenomation varies
widely. A significant number of bites and stings do not result in envenomation. However, life-threatening effects may
be seen and fatalities in venomous snakebite occur at a much
higher rate than for native envenomations, because of the
inherent toxicity of non-native species, difficulties and delays
in obtaining appropriate antivenom and clinical unfamiliar-
ity with management of these envenomations. Identification to
the species level of the envenomating organism is important in
Epidemiology

There are about 3,000 snake species in the world, of which fewer than 300 are dangerous to humans (45). Venomous reptiles include the families Atractaspidae, Colubridae, Crotalidae, Elapidae, Hydrophiidae, and Helodermatidae (45). Between 40 and 50 nonnative snake envenomations occur per year in the United States. Although nonnative envenomations in the United States involved dozens of species over the past 20 years (46,47), certain families, genera, and species are more commonly encountered. Cobras (family Elapidae) account for one-third of all nonnative venomous snake exposures, and 86% of Elapid envenomations. Viperids account for 46% of all nonnative venomous snake exposures, with Bothrops, Bitis, and Lachesis genera accounting for the 53% of all Viperid envenomations (46,47).

Compared with other etiologies of critical illness, venomous snakebites account for fewer ICU admissions per year. Nevertheless, almost one-third of non-native envenomations develop major to moderate symptoms and signs of disease, and are admitted to an ICU. The case fatality rate of approximately 1% is significantly greater than in native snakebites. Males are involved in 84% of bites, a similar percentage to that in native bites. Almost 15% are aged 17 years or less, and approximately 7% are aged 5 years or younger, most likely as a result of private collections in home settings (47). Identification of the snake in nonnative bites is usually not difficult, as zoos, aquaria, and academic institutions will know their collections to the species or subspecies level and have procedures in place to identify the biting snake. The private collector is also usually well informed. However, the bitten individual with a private collection may not be capable of communication, and potential penalties for possession of venomous animals in some jurisdictions may result in the withholding of critical information (48). A qualified herpetologist should be consulted for the identification of nonnative snakes that are otherwise unidentified. The presence of a puncture and typical appearance of the site, progression of findings, and consistent laboratory abnormalities of a snakebite indicate the possibility even when the history is not available.

Pathophysiology

The venom glands of poisonous snakes are modifications of salivary glands (49). The venom of a single snake is a complex mixture of enzymes, nonenzymatic proteins and peptides, and other substances (50,51). These substances exert simultaneous toxic or lethal effects on the integumentary, hematologic, nervous, respiratory, muscular, and cardiovascular systems. The clinical picture also can be complicated by the effects of endogenous mediator release, such as histamine, cytokines, and nitric oxide (52). Some of these components may be found in all venomous snakes, with mixed clinical effects. The most important deleterious components of snake venom are shown in Table 153.5. Hyaluronidase is found in all venoms and produces hydrolysis of connective tissue stroma, allowing the dispersion of other toxic components (53). Zinc-dependent metalloprotease enzymes damage vascular membranes and produce local and systemic hemorrhage (54,55). Phospholipases are found in most snake venoms, with a variety of effects (50), including destabilizing biologic membranes and abolishing the selective membrane ion channel permeability to ions such as calcium (56,57). Crotalid venom is rich in proteinases, amino acidases, and phospholipases, and typically produces findings of cellular destruction, increased membrane permeability, and coagulation impairment. Coagulation abnormalities may result from multiple mechanisms, including consumption, aggregation or inhibition of platelets, or effects on the coagulation cascade, such as activation or inhibition of coagulation factors, procoagulant activity, defibrinogenation, prothrombin action, collagenase-like activity, and other effects (16,58,59). Elapid venoms vary widely among species but contain more neurotoxins and cardiotoxins (51), resulting in various expressions of neurologic and cardiac toxicity; sea snakes have venom similar to elapids.

Diagnosis and Monitoring

The spectrum of symptoms and signs produced in a victim by a given venomous snakebite varies with the species of snake, the natural variability in venom composition between snakes, and, in any given snake over time, the quantity of venom injected, bite location, and the age and health of the victim.

Size and Species

In general, larger snakes contain and deliver more venom, but fatal envenomations may result from small species and juvenile snakes. Toxicities of the venom will depend on the species and other factors that affect venom production.

Quantity Injected

As many as 30% of Crotalid bites and 50% of Elapid bites may result in no envenomation (60). When venom is injected, the amount may be reduced by poor penetration of the fang or high tissue pressures, as in fingertips. The volume of available venom may also be reduced by recent previous feedings.
Bite Location

Tissues and anatomic areas with a low capacity for swelling, or which are functionally important, such as the fingers or hand, are particularly at risk of both short- and long-term impairment. The destructive effects of proteolytic enzymes may directly damage tissues. Also, even where no true compartments exist, tissue pressures may be significantly elevated and vascular compromise may occur. True muscle compartments may be subject to elevated pressures, either because of direct injection of venom with intracompartmental edema, from passage of venom into a compartment via direct spread or lymphatics, or as a result of extrinsic pressure on a compartment secondary to subcutaneous edema. Lower extremity bites may accumulate enough edema fluid to affect hemodynamic stability, particularly in children. They may also damage venous valves and produce long-term dependent edema. Decreased mobility and mobilization after a bite may predispose to deep venous thrombosis or other morbidity. Upper extremity, torso or head and neck bites may result in airway compromise secondary to edema.

Age and Health of the Victim

Those at greatest risk of morbidity and mortality include patients with long delays to treatment, those with significant comorbid conditions, and those at the extremes of age. Because of smaller body mass, children receive a relatively greater dose of venom. As with native envenomations, some private collectors may be under the influence of alcohol at the time of envenomation, which may affect their ability to avoid envenomation, predispose to multiple bites, and delay seeking care.

Symptoms and Manifestations

Since various factors may affect the quantity and specific components available and delivered, it is difficult to make an a priori determination of the clinical potential of the envenomation. The manifestations of snake envenomations can be divided into local and systemic effects.

Local Effects

Snake venom that produces local effects causes pain and edema at the bite site, erythema, ecchymosis, and occasional bleb formation. Later, the increased membrane permeability and cellular destruction produced by proteases result in spreading edema both distally and proximally, and may cause tissue necrosis. If the bite is on an extremity, elevated tissue pressures may compromise vascular supply or result in elevated compartmental pressures. Periodically marking—with an ink pen or felt marker—the extent over time of proximal spread of edema directly on the skin is useful in documenting the progression of local venom effects and response to treatment. The leading edge is usually palpable as a sharply demarcated ridge and differs from later redistribution of tissue edema, which more gradually transitions to normal tissue. Edema may spread from an extremity onto the trunk or involve the head and neck, compromising the airway (61,62). Pain, possibly requiring opioid-level management, is common and cannot be used to diagnose compartment syndrome. Because of the similarity of findings with compartment syndrome, if there is concern for elevated tissue or compartmental pressures, they should be measured directly (Stryker Intra-Compartmental Pressure Monitor System, Stryker United Kingdom; COACH Transducer, MIPM GmbH, Mammendorf, Germany). Local venom effects will respond to adequate amounts of antivenom with cessation of progression of proximal edema and reduced tissue pressures. Recurrence of progression of local effects may occur, particularly with Fab antivenoms, which have a larger volume of distribution and, thus, its circulating concentrations fall more quickly than F(ab’2) or IgG antivenoms. Locally acting venom components are usually exhausted by 24 to 36 hours, although the resulting tissue injury may continue to develop over days to weeks. Starting on the second day post envenomation, the clinical appearance of the bitten extremity, with increased heat and inflammation of the lymphatics, may be difficult to distinguish from an infective process. Overall, the incidence of infection is low, but will vary depending on the snake, the host, and factors such as the development of necrosis and wound manipulation. Potentially life-threatening infections such as nectrotizing fasciitis and disseminated osteomyelitis have been reported following snakebites (63–65).

Hematologic Effects

Coagulation alterations result from proteases acting on various parts of the coagulation cascade and may occur singly or in any combination. Fibrinogenolysis may occur, resulting in decreased levels of fibrinogen and increased levels of FDPs (16,65–68). Platelet inhibition, aggregation, or consumption may occur with abnormal function and/or decreased platelet counts (16,69). Intravascular hemolysis has also been reported with some snake venoms (70). The coagulopathic effects may result in local or systemic bleeding, including life-threatening hemorrhage as well as thrombotic events (70–75). Laboratory tests, including a complete blood count (CBC) with platelet count, PT/international normalized ratio (INR), PTT and fibrinogen, should be obtained on arrival and periodically reassessed. A single d-dimer (or fibrinogen degradation product) test should be obtained at least two hours post bite to assess whether fibrinogen destruction is occurring. Regardless of whether frank hypofibrinogenemia develops during hospitalization, patients with an elevated d-dimer are at risk of recurrent or delayed coagulopathy. Most patients who will develop hematologic abnormalities will demonstrate them within 1 to 2 hours, although early use of antivenom may mask this finding; normal hematologic values at 6 hours suggest an absence of such effects. If abnormalities are present, the use of antivenom may halt (e.g., fibrinogenolysis) or reverse (e.g., platelet aggregation) venom effects. The timing of repeat labs is based on the use of antivenom, clinical findings, and laboratory trends. Unneutralized venom components responsible for hematologic effects may remain active in the body for up to 3 weeks, resulting in delayed, persistent, or recurrent hematologic abnormalities (29,76,77).

Neurologic Effects

These may result from Atractaspis, Elapid, Helodermaid, Hydrophiid, or Viperid envenomations. Clinical effects can include sweating, numbness, paresthesias, convulsions, coma, muscle fasciculation, muscle weakness, and respiratory arrest. Respiratory muscle paralysis is the primary cause of death with most Elapid and Hydrophiid venoms. Viperid snakes rarely cause clinically significant respiratory compromise. Coma may be secondary to hypovolemia or to a direct effect of the toxin (67). Neurologic effects may develop rapidly, with respiratory arrest occurring within 15 to 30 minutes, but also may be delayed by many hours (78,79). Measures such as the
application of a PIB may also delay the onset of neurotoxicity (80). Even with delayed onset, once neurologic effects occur, they may progress very rapidly. Patients should be observed for a sufficient period of time, and preparations to manage the airway should be readily available. It should be kept in mind that some Elapids produce little to no local effects, and therefore, their absence cannot be relied upon to confirm nonvenomation. Once muscle weakness or paralysis has occurred, it may be difficult to reverse, although both antivenom and cholinergic agonists will generally stop the progression of effects and have been reported to result in either dramatic or more rapid improvement than would otherwise be expected (81–83). Extubation criteria are based on standard tests of respiratory sufficiency.

**Nonhematologic Systemic Effects**

These include effects on the cardiovascular, respiratory, and neurologic systems. In general, snakes from any family may produce any of these effects, although certain effects predominate within families. Type I hypersensitivity reactions to venom (IgE or non-IgE mediated) with or without hypotension may occur; the incidence is believed to be approximately 1% (84). Type I hypersensitivity reactions are characterized by wheezing, urticaria, laryngeal edema, and/or hypotension. Airway compromise from laryngeal edema may also occur, and direct myocardial depression, injury, or dysrhythmic effects of venom have been reported (84–89). The clinical picture may be complicated by possible adverse reactions to antivenom. The incidence of type I hypersensitivity to antivenoms varies from less than 5% to 25%. Other systemic findings common in snakebites are nausea, vomiting, diaphoresis, and pulmonary edema, especially in more severe cases. These usually resolve in response to antivenom and rarely persist beyond the immediate postbite period. Adverse reactions to antivenoms can complicate care. Type III hypersensitivity reactions—“serum sickness”—may occur in any patient who has received antivenom and are the result of circulating immune complexes. The frequency of occurrence is dependent on the amount of antivenom received as well as the type (e.g., source animal, immunoglobulin fragment). Type III reactions usually occur between 5 and 21 days after receiving antivenom and vary widely in incidence by antivenom utilized, from less than 5% to 100% (90–94). Symptoms and signs usually consist of muscle and joint aches, low-grade fever, and/or an urticarial rash; severe cases may have severe symptoms, including renal insufficiency.

**Diagnosis**

The diagnosis of snakebite may be a clinical one and should be suspected in any unknown presentation with any of the above clinical manifestations. Although immunoassays and bioassays have been used to identify various snake venoms in tissue within endemic areas, such tests are not available in the United States (95,96). In the United States, envenomations are likely to occur in zoo, academic, and private collector settings (47). Snake identification may be inaccurate in noninstitutional settings, yet obtaining an accurate identification of the snake is of utmost importance in order to select the appropriate antivenom. When dealing with private collectors, consideration should be given to independently verifying the snake species. A local zoo or aquarium may be of assistance in identifying the snake.

**Management**

The management of clinically significant snake envenomation can be divided into first aid, specific antivenin therapy, and supportive therapy (Table 153.6).

**Online Antivenom Index**

Initiation of efforts to obtain the appropriate antivenom should not wait until symptoms or signs develop; rather, this should be done immediately following the bite. The Online Antivenom Index is a resource for determining the appropriate antivenin(s) for any given snake and maintains a continuously updated listing of zoo antivenom stocks and contact information. It is accessible by regional poison centers (1–800–222–1222), which can assist in the identification and acquisition of an appropriate antivenom and in the clinical management of a snake envenomation.

**First Aid**

In general, the patient should get away from the snake and the snake should be secured by a qualified individual. Pre-existing medical information, information regarding the biting species, and any available antivenom should be transported with the patient. The bitten body part should be splinted to slow the central compartment spread of venom and reduce the risk of out-of-hospital respiratory arrest, and thus should be routinely employed (98,99). With Viperid envenomations, the risk of rapidly developing life-threatening systemic effects is generally less. Although the use of a PIB prolonged survival in an animal model, it also resulted in increased tissue pressures; thus, the potential benefits must be weighed against the risk of increased...
local injury in Viperid envenomations (100). Hypotension, airway compromise, or other signs of a severe type I hypersensitivity reaction would be examples of appropriate indications for the use of a PIB or LCB in a Viperid bite. In general, prior to arrival at a hospital and administration of antivenom, the bitten area should be kept at or slightly below the level of the heart. A dependent position may be used if rapid, severe systemic effects are occurring. These measures can be instituted on arrival at the hospital if they have not been done previously. Transport to a health care facility should be by paramedic ambulance. The initiation of two, large-bore intravenous lines is a sensible precaution. The PIB or LCB should not be removed until antivenom has been obtained and is infusing, if nonenvenomed, or a decision has been made not to administer it, keep a bitten extremity elevated with periodic assessment of edema (and tissue pressures if indicated), and monitor for development or progression of systemic symptoms. Management of progressive tissue edema and elevated tissue or compartmental pressures is by adequate amounts of antivenom and elevation, if tolerated. Frankly necrotic tissue should be debrided. There is little to no role for dermotomy or fasciotomy.

### Hospital Care

At the hospital, basic wound care should be provided, including updating the tetanus status, if needed. If, after a sufficient period of observation, which varies from 8 to 24 hours depending on the species of the snake, the victim demonstrates no signs or symptoms of envenomation, the person can be released from the hospital (Tables 153.7 to 153.9).

### Pain Control

Opioid analgesics are best deferred until after hospital evaluation because of the risk of potentiating respiratory depression. An ice pack applied to the bite site, with customary precautions, may provide some pain relief without risking additional tissue injury (97,101). Opioid-level analgesia, however, may be required and its judicious use can be considered.

### Antibiotics

Most authors recommend against routine prophylactic antibiotics. Antibiotics are suggested only for those with necrosis or clinical or laboratory evidence of infection (102).

### Antivenom

Antivenom is composed of antibodies raised in an animal such as a sheep or horse to the venom of one or more species of snakes. A single snake's venom may be used to produce a monovalent antivenom, effective only against that snake or other snakes with the same or a subset of venom components. Since, in their endemic areas, it may not always be possible to identify the biting species, many antivenoms are polyvalent; that is, they are designed to provide neutralizing efficacy for a number of different snake species. Venoms range from those that are relatively unpurified—whole IgG immunoglobulins, containing other proteins and immunoglobulin fractions—to highly purified specific IgG, F(ab)′2, or Fab immunoglobulin fragments. In general, horse serum–based products are more immunogenic than sheep-based antivenoms. IgG has a smaller volume of distribution, longer half-life, and higher rates of type I and type III hypersensitivity reactions, while Fab antivenoms have the largest volume of distribution, shortest half-lives, and lowest rates of allergic reactions. There is both considerable overlap and considerable variation of venom components within genera and species. When possible, species-specific antivenom that claims efficacy for the particular snake should be used. Antivenoms effective against other

---

**TABLE 153.7 Hospital Snakebite Site and Wound Management**

- If previously applied, a pressure immobilization bandage (PIB) or lymphatic constriction band (LCB) should not be removed until antivenom is being administered or a decision has been made to observe without antivenom.
- Wash the bite site, apply antibiotic ointment, leave it otherwise uncovered, and provide tetanus immunization updating as needed.
- Once antivenom has been initiated, or a decision has been made not to administer it, keep a bitten extremity elevated with periodic assessment of edema (and tissue pressures if indicated), and monitor for development or progression of systemic symptoms.
- Management of progressive tissue edema and elevated tissue or compartmental pressures is by adequate amounts of antivenom and elevation, if tolerated.
- Frankly necrotic tissue should be debrided.
- There is little to no role for dermotomy or fasciotomy.

**TABLE 153.8 Hospital Snakebite Antivenom Management**

- Antivenom is the definitive management of snake envenomation, when it is available.
- Antivenom for an exotic species can be located via the Online Antivenom Index. Poison centers (1-800-222-1222) can assist.
- When available, species-specific antivenom should be used.
- Skin testing is indicated if recommended by the manufacturer.
- Skin tests are neither sensitive nor specific to predict hypersensitivity reactions and are not recommended.
- A positive reaction does not preclude antivenom administration.
- Skin testing should not delay administration of antivenom in a life- or limb-threatening envenomation.
- Exotic antivenoms are imported under Investigational New Drugs licenses and if used, appropriate reports need to be made to the hospital’s institutional review board (IRB) and the Food and Drug Administration (FDA).

**TABLE 153.9 Hospital Snake Bite Symptom Management**

- Hypotension
  - May be due to a type I hypersensitivity reaction to venom or to antivenom, cardiotoxins, or fluid loss.
  - Management is with Trendelenburg positioning, crystalloid fluid expansion, pressors, anaphylaxis treatments (epinephrine, H1- and H2-blockers), and antivenom (if believed to be secondary to venom).
- Neurologic effects
  - Should be managed with antivenom and mechanical airway support as needed.
  - Cholinergic agonists, such as neostigmine, may be used as adjunctive or substitute management of muscle weakness in some Viperid envenomations.
- Hematologic effects
  - Severe or multicomponent abnormalities are managed primarily with antivenom.
  - Blood products are reserved for clinically significant hemorrhage, and given with additional antivenom if needed.
  - Some effects (e.g., platelet aggregation) may be readily reversed, while other processes (e.g., fibrinogenolysis) may be stopped, with components returning to normal levels by their natural replenishment.
- Other systemic effects are managed with symptomatic and supportive care.
  - Parenteral opioids may be required for pain.
  - Recurrence of local and/or hematologic venom effects may occur.
  - Patients at high risk should be closely monitored, especially post discharge.
  - Additional antivenom should be considered for recurrent local effects in the first 24 h or recurrent severe or multicomponent hematologic abnormalities.
snakes in the same genus may be tried if species-specific antivenom is not available. Antivenoms for nonnative snakes are imported into the United States under Investigational New Drug (IND) application. As such, their use carries additional Food and Drug Administration (FDA) and institutional review board (IRB) reporting requirements. As no US hospital routinely stocks antivenoms for nonnative species, such antivenoms are generally acquired by zoos and other institutions against the species they have in their collection for use in the event of one of their workers being envenomed. Zoos have traditionally made their antivenoms available to physicians on a compassionate basis. Since an IND antivenom will usually be brought into a hospital from an outside, nonhospital source, questions may be raised by the pharmacy regarding storage conditions, expiration dates, and other issues relating to its administration. If the potential for a nonnative envenomation can be anticipated, such as a known zoo or university collection, it is prudent to have an existing protocol as well as having obtained prior IRB approval (103).

Antivenom is considered the definitive treatment for all clinical effects of snake venom, although for a variety of reasons, such as incorrect snake identification, geographic variation of venom components, irreversible or time-dependent toxicity, and so forth, it may have limited to no observable efficacy against any particular venom effect (104–107). In addition, there are rarely prospective, controlled clinical trials to document appropriate indications, efficacy, and safety or to establish optimal dose and dosing regimens. Since antivenoms carry a risk of allergic reactions, potential benefits must be weighed against the risks of administration. Skin tests are neither sensitive nor specific enough to predict type I hypersensitivity reactions and their use is discouraged. If performed, however, the result should not serve as a contraindication to administration when indicated, and preparations to manage an allergic reaction should always be immediately available. Some antivenoms with known high rates of adverse reactions may routinely be recommended to co-administer with epinephrine or other medications. Expert guidance is suggested. Regardless, skin testing should not delay administration of antivenom in a life-threatening envenomation.

Treatment with antivenom alters venom component distribution pharmacokinetically. Venom components bound to antibody become inaccessible to target tissues and are thus neutralized. Therefore, the dose of antivenom should be great enough to theoretically bind/neutralize the entire venom dose injected by the snake. These doses have been determined by knowledge of typical snake venom loads, neutralization properties of antivenoms in animal studies, and clinical studies. In most cases, it would be best to give doses of antivenom to ensure adequate venom neutralization on the assumption of a severe envenomation, since the degree of envenomation is difficult to appreciate early in the course. Such neutralization, however, occurs predominantly in the vascular compartment, and there may be unneutralized venom components remaining in the tissues. Venom may thus redistribute from target tissues and continue to produce toxicity if the antivenom dose is inadequate or if unbound antivenom has been eliminated. These pharmacokinetic relationships illustrate why antivenom administration as soon as possible following envenomation is beneficial and why the use of shorter-acting antivenoms may result in recurrent hematologic effects. Also, because of difficulty reaching damaged tissue and despite the use of antivenom early in the course of a snake envenomation, there may still be limitations as to the effectiveness of antivenom in preventing worsening of local tissue damage, and it will not benefit already devitalized tissue.

Indications, timing, and doses of antivenom will vary and expert guidance should be sought. Since the required dose of antivenom is that needed to neutralize a given amount of venom in the body, it is not dosed by patient weight, and children may require larger doses than adults. Over a 10-year period in the United States, antivenom was only used in 26% of nonnative snake envenomations, possibly because of difficulties in determining, locating, and obtaining appropriate antivenom in a timely manner (47,103). Antivenom is most effective in preventing or ameliorating local venom effects when given early in the course. Since most local reactions have stopped progressing within 24 to 36 hours, giving an initial dose of antivenom after this time frame is not likely to be of any benefit. Antivenin is also most effective at preventing or reversing hematologic effects when given early, but may still be beneficial for weeks after an envenomation if there are still circulating venom components (66,76,108). Clinically significant hemorrhage is managed with additional antivenom as well as blood component therapy. Large doses may be required to stop or reverse some effects.

Finally, zoos may only have or choose to send expired antivenom. Expired antivenoms may have decreased efficacy and thus may require higher doses, but barring discoloration or frank contamination, there is otherwise no contraindication to their use. The regional poison center should be contacted for further assistance (1–800–222–1222).

Surgical Management

Frankly devitalized tissue, usually becoming evident several days following an envenomation, should be debrided. Because high concentrations of venom have been found in blisters overlying the bite area, unroofing these should be considered. Fasciotomy or dermotomy have been advocated for compartment syndrome or tense tissue edema potentially affecting blood flow. Unfortunately, a true compartment syndrome is difficult to diagnose by clinical means, since the typical signs and symptoms of snake envenomation mimic classic compartment syndrome findings, and early surgical intervention often leads to prolonged convalescence, increased tissue damage, decreased function, and greater scarring. Finally, there is no evidence of improved outcome, and there is animal-model evidence of increased myotoxicity with fasciotomy (109). Reported fasciomy reaction rates vary by geographic region and historical practice, ranging from 0% to greater than 10%. Fasciotomy should only be considered in patients with objective evidence of a compartment syndrome (i.e., a documented significant increase in intracompartmental pressures), vascular impairment, unusual entrapment syndromes, or other tissue threats that are unresponsive to an adequate trial of antivenom and elevation (110–114). Mannitol and hyperbaric oxygen have also been used in conjunction with antivenom (115); noninvasive vascular studies may identify patients at risk for ischemia (116) and ultrasound may help to establish the location of edema (116a).

Other Supportive Therapies

These include basic wound care and updating tetanus status. Blood products should be reserved for significant hemorrhage or hemolysis and administered with additional antivenom. Ventilatory support and hemodialysis may be necessary for pulmonary and renal complications of severe envenomation. Corticosteroids may be used for hypersensitivity reactions...
to venom or antivenom. Antibiotics are indicated for documented infection or in the presence of frank necrosis.

**Hypersensitivity Reactions**

If a type I hypersensitivity reaction develops, the antivenom infusion should be stopped. Anaphylactoid reactions are primarily related to rate of infusion, and stopping the infusion often results in rapid improvement. Anaphylactic reactions (i.e., those IgE mediated) are often dramatic and continue to progress after the infusion has been stopped. There is, as one might expect, considerable clinical overlap between the reactions (117). Standard managements should be used. If symptoms persist, the patient should be treated with H₁-blockers (e.g., diphenhydramine, 50 mg IV) and H₂-blockers (e.g., ranitidine, 50 mg IV). Wheezing may respond to β-adrenergics by nebulizer (e.g., albuterol). If there is hypotension or laryngeal edema, epinephrine, either subcutaneously or intravenously, should be considered (118). Antivenom should be withheld until the reaction has subsided and then a determination made whether to restart it. If restarted, the patient should receive pretreatment with H₁- and H₂-blockers and the infusion begun more slowly.

Type III reactions are usually managed with nonsteroidal anti-inflammatory drugs (NSAIDs) and H₁- and H₂-blockers. More severe cases may require opioid-level pain relief, as well as corticosteroids. All patients receiving antivenom should be cautioned regarding the possibility of a type III reaction occurring after discharge.

**Postdischarge Considerations**

It is desirable to see patients at least once after discharge to monitor for persistent or recurrent hematologic effects, if indicated, or tissue injury and its sequelae, and to refer for physical or occupational therapy in order to maximize functional recovery. Patients treated with a Fab antivenom may need monitoring for more than a week to detect and manage possible late coagulopathy. Patients should also be cautioned about the possible risk of sensitization to snake venoms or antivenoms regarding possible future envenomations (Table 153.10).

**Nonrecommended Treatment**

Some treatments are ineffective or dangerous and are therefore not recommended.

---

**TABLE 153.10 Postdischarge Management Following Snakebite**

- Physical therapy may be helpful in minimizing the extent and duration of functional impairment.
- Type III hypersensitivity reactions (“serum sickness”):
  - They usually develop 5–14 days following antivenom administration.
  - The incidence varies from <5% to >80% of cases depending on the antivenom, host, and other factors.
  - Nonsteroidal anti-inflammatory drugs and antihistamines are usually sufficient for symptomatic care.
  - Severe reactions may have renal involvement and require steroids and, in rare cases, rehospitalization.
- Patients with significant hematologic abnormalities, especially those treated with Fab antivenoms, may be at risk of recurrent effects post discharge.
  - Close follow-up is necessary for at least 2–4 days to detect recurrence.
  - Consider readministration of antivenom for clinical bleeding or multicomponent or severe hematologic abnormalities, especially with comorbid conditions.
  - There is no evidence for efficacy, and there is potential for additional injury, with arterial or venous tourniquets, incision or excision of the wound, or the application of heat, cold, or electricity.
  - Suction apparatuses remove only a small amount of venom, have not been shown to improve outcome, and may serve only to delay transport and definitive care (119,120).
  - Although some snake venoms also contain procoagulant factors, and the overall clinical picture is DIC-like, the conditions are not identical, so heparinization and other treatments for DIC are not applicable in snakebites.
  - In the absence of necrosis, prophylactic antibiotics also are of no proven value.
  - Corticosteroids are of no proven value for acute venom effects.

---

**SPIDERS AND SCorpIONS**

**Native Spiders**

Spiders of medical significance can be found worldwide (121), while in the United States, only two groups of spiders are typically considered medically significant. These are the widow or *Latrodectus* spiders and the brown spiders belonging to the *Loxosceles* genus.

**Widow Spiders (Latrodectus Genus)**

Widow spiders, including the well-known black widow, belong to the *Latrodectus* genus. These spiders are among the most medically important spiders, and representatives are found almost worldwide. In the United States, the widow spiders are found throughout most of the country but are most common in the southeast, with the black widow (*Latrodectus mactans*) believed to cause most envenomations. The female black widow has a shiny black abdomen and a characteristic bright red hourglass marking on her underside and is considered more harmful to humans secondary to longer fangs than her male counterparts (122). Widow spiders are considered shy spiders and can be found in dark, secluded areas such as under leaf litter (123). All widow spiders worldwide are believed to have similar venom characteristics and similar clinical symptoms.

**Pathophysiology**

The primary component of widow spider venom that causes human clinical effects is α-latrotoxin. It binds to neuronal tissue and causes neurotransmitter release in at least two ways: (a) it binds to and helps form ion channels, which allow calcium and other ions to leak, causing a calcium-dependent release of neurotransmitter; and (b) it binds to the latrophilin receptor on neuronal tissue, and causes a calcium-independent release of synaptic vesicles (124). This neurotransmitter release, either through calcium-dependent or calcium-independent means, is believed to cause the clinical symptoms seen after widow spider envenomation.

**Diagnosis**

Diagnosis is primarily clinical and historical, as there are no laboratory tests to confirm envenomation. Typically, bite victims will recall a painful pin prick–like bite, but the bite can be painless. Bites may occur in dark, outdoor places such as woodpiles when dressing or putting on shoes, especially if they are left outside, or even while in bed (125).
Clinical Effects

Bites from the widow spiders can produce mild local irritation. The bite is classically described as two small punctures with a small area of erythema surrounding a minimally blanched area centrally, producing a “halo” or “target” effect (125). Local injection of venom is not believed to cause necrotic wounds and superinfection is considered uncommon.

The more medically significant effects following widow envenomation are the constellation of systemic symptoms known as latroductism. Typically, symptoms begin within an hour after the bite. What may begin as local muscle cramps can progress to involve larger muscle groups, spreading continuously from the site of the bite. Priapism (126), ileus (127), elevations in creatine kinase (125), and myocarditis (127,128) have been reported as associated with a Latrodectus bite. Though no reported cases of spontaneous abortion have been reported in pregnant patients (129), concern exists for premature delivery given the intense muscle cramping and hypertension that can occur following a widow spider envenomation. Hypertension has been reported (125) and could be life threatening in susceptible populations.

Management

While the Latrodectus venom is very potent, the volume of venom is minuscule. There is no role for tourniquets, incision, or excision at the venom injection site. Initial control of pain and muscle contraction should be accomplished through administration of opiates and benzodiazepines. Benzodiazepines are preferred as muscle relaxants, given their wide therapeutic window and minimal hemodynamic and cardiac side effects when compared to agents such as cyclobenzaprine or methocarbamol. Intravenous calcium has not been shown to provide significant benefit (122,125) and is no longer considered a first-line agent.

An antivenom specific to L. mactans is available ([L. mactans] Black Widow Spider Antivenin, Equine Origin, Merck & Co., Inc.). As with administration of other IgG antivenoms, there is a risk of hypersensitivity reactions, including anaphylaxis (125) and serum sickness (130). While skin testing is recommended by the manufacturer, it is insufficiently sensitive or specific to either predict or exclude the likelihood of a type I hypersensitivity reaction (122). Type III hypersensitivity reactions (“serum sickness”) have been reported (130), though they are believed to be rare given the small volume of antivenom necessary to neutralize the injected venom.

The use of antivenom is controversial. Most would agree that when dealing with patients in the extremes of age, pregnant patients, or those with intractable muscle cramping and pain, the use of antivenom should be strongly considered. For those with mild to moderate envenomations, clinicians can attempt a trial of benzodiazepine and opioid therapy. Moss and Binder (130) found that most bite effects were self-limited and needed only minimal pharmacologic intervention, while others found that antivenom was associated with minimal adverse events and rapid resolution of symptoms, and should therefore be considered early in the course after moderate to severe envenomations (122,125,131,132). If administered, the antivenom should be administered in a controlled, monitored environment, with treatments available immediately for acute allergic reactions. There is no evidence that pretreatment with any of these agents is efficacious in preventing a reaction, and caution should be used before administering antivenom in anyone with risk factors for immediate hypersensitivity reactions (125). The dose for adults or children is the contents of one restored vial (2.5 mL) of antivenom; typically it is administered as a slow intravenous infusion (133). It can be redosed if needed, but one vial of antivenom is usually sufficient (132). The clinician at the bedside must weigh the small risk of adverse reactions to the possible benefit from reversal of the venom’s effects. A purified F(ab)2 fragment antivenom currently undergoing phase 3 trials may prove to be a preferred alternative to the current antivenom (134).

Follow-Up

Unless antivenom is administered, in which case monitoring for serum sickness should be arranged, there are no long-term sequelae expected from a widow spider envenomation (130). Local wound care should be satisfactory for the bite site, and prophylactic antibiotics are not warranted.

Brown Spiders (Loxosceles Genus)

Loxosceles spiders are found primarily in the southern half of the United States. While at least 30 species of Loxosceles can be found on several continents, the Loxosceles reclusa species (“brown recluse”) is the most common and medically important in the United States (122,135). As their name implies, these are considered shy spiders, hiding in woodpiles and dark corners, only biting when threatened. Bites are more common in warmer months and are often presumed to occur when a spider is caught next to skin by clothing or linens (135). True epidemiology is difficult, as necrotic wounds, which can occur because of Loxosceles envenomations, are often inaccurately attributed to spider bites when other insect bites, skin infections, or other dermatologic conditions are truly responsible.

Pathophysiology

Venom from Loxosceles spiders is a complex mixture of cytotoxic components that indirectly cause impressive, delayed local symptoms and have the potential for causing human systemic toxicity. Hyaluronidase in the venom causes significant tissue destruction, allowing spread of other venom components in the soft tissues following an envenomation (136). Sphingomyelinase D in Loxosceles venom is believed responsible for the dermal inflammation seen after bites (137). Venom injected in the skin starts a cascade of cellular reactions including neutrophil migration and degranulation, which leads to potentially severe local tissue injury (138).

Diagnosis

Because the bite is usually painless and thus unnoticed at the time, unless a Loxosceles bite is witnessed and positive identification of the spider occurs, the diagnosis is typically a historical and clinical one. The necrotic wounds found with Loxosceles spider bites can mimic numerous other common cutaneous conditions, such as bites by other spiders or other insects, soft tissue bacterial infections, or a vasculitis. A broad differential, including these, as well as conditions such as erythema nodosum, pyoderma gangrenosum, pyogenic granuloma, and herpes infections, should be reviewed before a necrotic wound is attributed to a Loxosceles spider in the absence of a known bite (139). Cases of necrotic wounds have been linked to other US spiders such as the hobo spider (140), though clear and well-accepted causation between these spiders and dermonecrotic wounds is still not established (134,141). Positive laboratory identification by enzyme-linked immunosorbet assay
(ELISA) or hemagglutination is possible to confirm Loxosceles envenomation in research settings (142), but is not at this time clinically useful.

**Clinical Effects**

Unlike the widow spiders, the majority of clinical effects seen from Loxosceles spiders are a result of local tissue injury. The characteristic necrotic wounds are described as having a “red, white, and blue” appearance, though clearly demarcated color rings are rare and not needed to make a diagnosis. Local tissue inflammation occurs over the first day after envenomation, causing skin erythema. In the center of this reddened skin, a small necrotic or “blue” area develops that is surrounded by a halo of blanched tissue appearing gray or “white.” Often the wound is not noted until it begins to cause significant pain or the necrotic area becomes prominent.

Rarely, a Loxosceles spider bite can lead to a clinical syndrome known as systemic loxoscelism. Cases, many of them in children, begin as low-grade febrile illness with arthralgias and other nonspecific symptoms (143). Within 24 to 48 hours after the bite, these symptoms can progress to a potentially life-threatening illness characterized by hemolysis and shock (135,143,144). Systemic loxoscelism should be in the differential of unexplained hemolysis associated with shock (144).

**Management**

Many pharmacologic and surgical treatments have been proposed in the management of the necrotic dermal wounds associated with Loxosceles spiders, but none has been proven to have significant effects in preventing or reversing damage. These include hyperbaric oxygen (145,146), steroids (147), dapsone (145–149), nitroglycerin (150), and early surgical debridement, and are not recommended. The venom spreads rapidly after a bite, and early attempts to “core” out affected areas to prevent venom spread result in poor wound healing and worsened scarring (148). If significant cosmetic defects occur as a result of the necrotic wound, surgical intervention, including skin grafting, should be delayed at least 4 to 12 weeks (151).

Systemic loxoscelism should be treated with symptomatic and supportive care. Successful treatment of proven loxoscelism cases has included aggressive fluid resuscitation, blood product transfusion, and vasopressor use. A case report detailed the use of therapeutic plasma exchange in the care of a teen-age patient with refractory hemolysis (144). Within 24 to 48 hours after the bite, these symptoms can progress to a potentially life-threatening illness characterized by hemolysis and shock (135,143,144).

**Nonnative Spiders**

The funnel web spiders (Hadronyche and Atrax spp.), native to Australia, and the banana spider (Phoneutria spp.), native to South America, are considered far more dangerous than the native Latrodectus and Loxosceles spiders. In the United States, these can be found through collectors or as accidental stowaways in goods transported internationally. The funnel web spider venom contains a potent neurotoxin that can cause fasciculations, weakness, and autonomic instability, with coma and pulmonary edema complicating the clinical course. An antivenom available in Australia has been successfully used in severe envenomations (153).

The South American spiders belonging to the genus Phoneutria have a neurotoxic venom that can cause pain and neurologic and gastrointestinal symptoms, as well as shock and pulmonary edema in severe cases (154). An equine antivenom is available in South America. These antivenoms may be located in the United States through the Online Antivenom Index, with the assistance of a regional poison center (1–800–222–1222).

**Scorpions**

In the United States, there is only one medically significant species of scorpion, Centruroides exilicauda. Found in the southwestern United States, primarily in southern Arizona, it is commonly known as the bark scorpion. Stings occur by the tail, with the venom containing neurotoxins and other components. Children are at greatest risk of having clinically significant symptoms associated with such a scorpion sting. Symptoms can be minor, with only some local paresthesias but, for some, symptoms can be severe, including cardiac manifestations such as tachycardia and hypertension, neurologic manifestations such as roving eye movements and agitation, and respiratory manifestations, including tachypnea and stridor (155,156).

An antivenom, Centruroides (Scorpion) Immune F(ab′)2 (Equine) injection was approved for use in 2011. This intravenously administered antivenom is indicated for those patients who manifest clinically important signs of envenomation such as loss of muscle control, respiratory distress, or excessive oral secretions (157). A continuous midazolam infusion, ventilatory support, and otherwise supportive and symptomatic care were mainstays of treatment prior to the development of this antivenom (158,159) and remain important.

**MARINE ANIMALS**

This section will review exposures to venomous marine creatures, but organisms that are poisonous when ingested will not be covered. Marine envenomations can occur from interaction with both vertebrate and invertebrate organisms. In the vertebrate category are stingrays, sea snakes, catfish, scorpionfish, and leatherjacks, among others. Invertebrates encompass a much larger grouping, including coelenterates (Cnidaria), echi- noderms, annelid worms, and mollusks.

**Stingray**

Eleven different species of stingray are found in US waters, seven of which are found in the Atlantic Ocean (160,161). These animals have long, sharp, serrated barbs along the dorsal surface of their tails, which can cause significant tissue damage and death due to abdominal and chest trauma and exsanguination has been reported, even without envenomation (162,163). Secondary bacterial infection is also common due to severity of the wounds (160,162,164,165). Rays will often burrow into the sandy bottom of temperate shallow waters where they may be inadvertently stepped on or otherwise startled to lash out with their tail. The tail barbs are also covered in an integumentary sheath that encases two ventrolateral venom glands. The venom is a complex mixture that includes phosphodiesterase, nucleosidases, and serotonin (160,161).

**Clinical Effects**

Burning pain at the wound site typically intensifies with time, and local symptoms may last up to 48 hours (162); and pain may be out of proportion to extent of visible injury. Venom...
can cause initial vasodilation and edema at the bite site, then vasoconstriction with hemorrhagic necrosis of tissue and inflammatory infiltrate (160,161,164). Cardiac conduction abnormalities ranging from bradycardia to atrioventricular nodal blocks with dysrhythmias and cardiac arrest from asystole have been reported. Systemic venom effects also include nausea/vomiting/diarrhea and abdominal pain, as well as ataxia, tremor, paralysis, seizure, coma, hypotension, and respiratory distress/depression (160–162).

Treatment

Treatment is symptomatic and supportive. Radiographic imaging as well as local wound exploration is necessary to evaluate for retained foreign body in the wound. Tetanus prophylaxis should be administered if needed. Prophylactic antibiotics to cover marine microorganisms should be considered, as secondary bacterial infections are common, particularly with Vibrio species (160,164,165). Pain control with opiate analgesia is often required, and immersion of the limb in hot water (110°F [43°C]) may aid in pain relief (162,163). Care should be taken to not produce thermal injury. Consider an observation period of at least 4 to 6 hours to ensure that symptoms do not progress to systemic effects.

Scorpaenoida

This group is composed of a number of venomous fish, and is the most common marine vertebrates that sting humans, both in the wild and in home aquaria. They are found in the warm waters of the Gulf of Mexico and Florida Keys, as well as the Pacific, including around Hawaii, and the Indian Ocean. Fish in this group include lionfish (Pterois), zebrafish (Danio), scorpionfish (Scorpaena), and stonefish (Synanceia) among many others. Venom apparatus is a collection of spines along the body of the fish, each composed of paired venom glands covered by an integumentary sheath, located near the tips of the spines. The dorsal spines are typically the most numerous and can inject the most venom (161,166). The venom of the fish in this phylum is a complex mixture, and most contain significant amounts of inflammatory mediators such as thromboxane and prostaglandins (160,166,167). The chemical makeup and potency of venom varies by species within this group, and clinical effects range from very severe (stonefish) to mild (lionfish). The stonefish is by far the deadliest of this group; pain and clinical effects range from very severe (stonefish) to mild

Sea Snakes

There are approximately 50 species of sea snakes in several subfamilies. They are found primarily in the warm tropical waters of the Indo-West Pacific. None are found in the Atlantic Ocean or Caribbean Sea. Envenomations are likely the result of such snakes being kept in zoos or academic institutions or kept by private collectors, and 150 to 170 deaths are recorded per year, with an overall mortality rate of approximately 3% (167,175). All are venomous, with seven species known to be fatal to humans Astrotia stokesii, Enhydrina schistosa, Hydrophis ornatus, H. cyanocinctus, Lapemis hardwickii, Pelamis platurus, and Thalassophina viperina.

The venom of sea snakes is most similar to that of the Elapids, with neurotoxicity, and potentially respiratory arrest, as the primary clinical effect. An IgG equine–derived, polyvalent sea snake antivenom from Enhydrina schistosa and Notechis scutatus (Tiger snake) is available, and has some cross-reactivity against many other sea snake venoms (167,175,176). See the section on non-native snake envenomations (above) for further management considerations.

Invertebrates

Five phyla constitute the venomous invertebrates: Cnidaria, Porifera (sponges), Echinodermata (sea urchins, starfish), Molusca (octopi and cone snails), and Annelida (bristle worms). There are over 10,000 species in the phylum Cnidaria (formerly Coelenterata), and several hundred are dangerous to humans. This grouping includes jellyfish (class Scyphozoa), the
the most concerning effect of which is significant systemic hypertension (184). The effects can be severe enough to lead to cardiovascular symptoms, and even end-organ damage including myocardial infarction, cardiomyopathy, and intracerebral hemorrhage; and death has been reported (184,189,190). Other effects include anxiety, restlessness, headache, nausea/vomiting, tachycardia, and localized and systemic pain (184,189,191). Pain and hypertension may be mitigated by administration of calcium channel blockers, specifically nifedipine, and magnesium sulfate intravenously (184,189,192,193). Otherwise care is symptomatic and supportive. Fire coral (Millepora) is not a true coral, rather a relative of fresh water hydra, but has nematocysts to envenomate its prey. They are found in shallow tropical waters, and the nematocysts may penetrate deeply. The stings cause local burning pain, urticaria, and intense pruritus (186). These wheals may take weeks to heal completely and may leave hyperpigmented scars; corticosteroids may be of use to treat persistent rash. The Scyphozoa contain the “true” jellyfish, including the deadly box jellyfish (Chironex fleckeri or sea wasp), which is not found in US waters, and is present here in zoos, institutional, and possibly private collections only. It is usually found in tropical climates of the Indian and Pacific Oceans, including the coastal waters of Australia. The box jellyfish is so named because of its four translucent panels that roughly form a box. The sting of the box jellyfish is painful and can cause death within minutes from hypotension, profound muscle spasm, respiratory paralysis, and even rapid cardiovascular collapse (194–196). Each box jellyfish contains enough venom to prove fatal to several adult humans. An antivenom is available and should be stocked by the institutions that house these creatures; antivenom can be located by contacting the regional poison center (1–800–222–1222) (185,197).

The Scyphozoa also include sea nettles (Dactylometra quinquecirrhia), which pose a greater chance of exposure to swimmers of this country, but the sting in most cases is a minor annoyance, although systemic symptoms similar to those seen with Physalia envenomations have been reported (178,186).

**Clinical Effects**

Most organisms in this grouping, with the exception of the Portuguese man-of-war, cause only mild local effects in humans. These local effects consist of burning pain at the site of the sting, which may be severe, with swelling, erythema, and possible vesicle formation and ulceration of the area (186,187). Regional lymphadenopathy may be seen, and secondary infection and scarring are common.

Anaphylactoid reactions can occur as well. Systemic effects, if any, are mild, but immune reactions such as erythema nodosum and reactive arthritis have been reported (180,181,183,186,187). Ulceration, secondary infection, and scarring can result.

Irukandji syndrome is a constellation of both local and systemic symptoms that occur in a delayed fashion, but typically within 30 minutes, after envenomation by an Australian jellyfish (Carukia barnesi); but also after exposure to Malo maxime and other species. There have been reports of a similar syndrome occurring in swimmers and divers off the coast of southern Florida, and Thailand, although the all responsible organisms has not yet been identified (184,188). Systemic release of catecholamines, leading to a hyperadrenergic state thought to be mediated via Na⁺ and Ca²⁺ channel agonism, the most concerning effect of which is significant systemic

---

**Chapter 153**

**Envenomation**

---

**Treatment**

Swimmers and divers in waters endemic for venomous animals and health care providers caring for victims of envenomations should wear gloves and clothing for personal protection. Irrigation with copious seawater initially is the safest intervention. If stung, any nematocysts still on the skin should be inactivated with 5% acetic acid (vinegar) and then removed by “shaving” the area with a dull-edged knife or the edge of a credit card (178,192,197,198); the shaving cream may aid in the shaving process. Adhesive tape may also be effective at removing unseen nematocysts. Papain meat tenderizer has been reported to improve symptoms but should be used with caution (176). Alcohol or fresh water may cause the remaining nematocysts to fire and should be avoided. A few species’ nematocysts will fire in the setting of acetic acid, including the American sea nettle, the little mauve stinger jellyfish, and the hairy or lion’s mane jellyfish. For these few, a slurry of baking soda should be applied for at least 10 minutes over the affected area. If tentacles remain attached to the skin, a vinegar or baking soda slurry should be applied, then shaving cream and dull-edged scraping to remove the tentacles. Many components of the venoms of these organisms are heat labile, and immersion of the
affected area in non-scaling hot water (110°F [43°C]) may aid in pain relief (160,161,176,178,198). Tetanus prophylaxis should be given as needed and a third-generation cephalosporin used for secondary infection. Pain should be treated with both NSAIDs and opioids as needed. Persistent pruritus and swelling should be treated with antihistamines. Systemic steroids have not been shown to be of any benefit.

**Sea Lice (Seabather’s Eruption)**

The prolific time period for the appearance of sea lice is March through June on the southeast coast of Florida. A contact dermatitis can develop with exposure to the larvae of sea lice (*Linuche unguiculata*). The larvae attach to the fibers in bathing suits and cause a rash in the distribution of the swimwear, thus “seabather’s eruption.” The rash is pruritic, erythematous, and maculopapular, and typically resolves spontaneously in hours to days without sequelae (181,199–201). Topical treatment with antihistamines and calamine lotion may give relief.

**Palythoa Coral**

Palytoxin can be found in myriad species and the most common source of exposure is via ingestion of fish and crustaceans that produce the toxins, as well as *Ostreopsis dinoflagellates* and *Trichodesmium cyanobacterium* entering the food chain; however an increasingly important source of exposure is via palythoa soft corals that are very popular in home aquaria (202). The first description in the literature is from the legend of *Limu make o hana*, a zoanthid seaweed-like coral originally from Hawaii. This toxin has been found to be responsible for several human fatalities and nonfatal but clinically significant toxic exposures. Inhalational exposures have been described from aerosolized toxin from algae blooms as well as toxin in home aquaria corals, and dermal exposures from both wild and home coral contact (202–206). It is a highly toxic agent, with an LD₅₀ in mice of 0.15 μg/kg, compared to tetrodotoxin of 8.7 μg/kg (202,204). Avoidance of exposure is key and persons who have these corals in home aquaria should handle them only with thick rubber or nitrile gloves and wear respiratory masks. Attempts to kill the corals with boiling water or during attempts to clean the tanks may be impacted as well, either directly or indirectly (202,207). Palytoxin effects at other tissue types are suspected as the causative species involved in serious or fatal human envenomations are mild and limited to local effects, but at least 36 deaths have been reported and serious symptoms have been described in over 50 more (184,210). Palytoxin effects at other tissue types are suspected as the causative species involved in serious or fatal human envenomations are mild and limited to local effects, but at least 36 deaths have been reported and serious symptoms have been described in over 50 more (184,210). *C. geographus* are most commonly identified as the causative species involved in serious or fatal human envenomations with cone snail encounters, although other species have also been implicated; and children are usually more severely affected than adults. Death is typically due to cardiovascular collapse and respiratory muscle paralysis (184,210,212).

**Treatment**

Removal of spicules with adhesive tape or the edge of a dull knife may aid in symptom control (160,161,181,209). Antihistamines and NSAIDs may be used for symptom control.

**MOLLUSCA**

**Conus Snails**

Cone shell snails have an ejectable tooth at the end of a long flexible proboscis, and envenomate their prey by sinking this tooth deep into the flesh (210). The venom contains primarily neurotoxins that act by ion channel effects (210–212).

**Clinical Effects**

Clinical effects include local burning pain, numbness, and paresthesias, as well as systemic effects of nausea/vomiting, laceration, salivation, perioral paresthesias, cranial nerve palsies including dysphonia, dysphagia and blurred vision, ataxia, coma, respiratory muscle paralysis, and cardiovascular collapse (184,210). Of known and reported cases, the majority of human envenomations are mild and limited to local effects, but at least 36 deaths have been reported and serious symptoms have been described in over 50 more (184,210). Of known and reported cases, the majority of human envenomations are mild and limited to local effects, but at least 36 deaths have been reported and serious symptoms have been described in over 50 more (184,210).

**Treatment**

Treatment is primarily symptomatic and supportive. Conus species have been estimated to produce up to 700K different conopeptides across the nearly 700 species within the genus; with each snail producing 200 to 1,000 individual peptides (213,214). In depth discussion is well beyond the scope of this chapter, but the toxins are roughly grouped into 3 main collections based on effects: “lightning-strike cabal” which stun fish via effects at Na⁺ channels; the “motor cabal” which cause paralysis via effects at both Na⁺ and calcium channels effecting neuromuscular transmission, and finally the “nirvana cabal” which through as of yet unknown mechanisms narcotize and sedate prey (210,212,213). The primary functions of the main toxins found across many of the species: α, and θ conotoxins are to cause cellular depolarization and neuronal hyperexcitability by preventing closure of voltage-gated ATPase channel, turning the channel into a non-selective monovalent cation pore, which leads to cell membrane electrical destabilization and often even cell lysis (202,205,207,208). Binding also leads to uncoupling of ion transport and protracted channel opening at this and possibly other pumps; calcium, potassium, and other ion channels may be impacted as well, either directly or indirectly (202,207). Palytoxin effects at other tissue types are suspected and are under investigation but are beyond the scope of this chapter. The clinical picture includes dermal irritation, rash, fever, hemolysis, leukocytosis, myalgias, and muscle spasm with elevated creatinine protein kinase, although rhabdomyolysis has rarely been reported. Additionally, paresthesias, nausea/vomiting, abdominal cramping, dyspnea with bronchospasm, cardiac conduction abnormalities and fatal dysrhythmias, eventually leading to hypotension and death, have also been reported after inhalational and aerosol exposures (202,204–207). Dermal exposures can have many of the same above signs and symptoms, however no fatalities have been reported (203,205,206). Corneal damage has been described (205). Treatment is symptomatic and supportive; there is no antidote or specific target treatment available.

**Sponges**

Some sponges contain spicules composed of calcium carbonate and silica, which can cause local irritation and itching of skin upon contact. This is also known as “skin diver’s” or “sponge fisherman’s” disease. The fire, red, and bun sponges also have toxins in their coatings that can cause local irritation, which may be painful and pruritic and produce erythema (161,175,219). Pain and paresthesias after contact may persist for weeks (161,175,209).

**Treatment**

Remove spicules with adhesive tape or the edge of a dull knife or credit card. Washing the area with 5% acetic acid may aid in symptom control (160,161,181,209). Antihistamines and NSAIDs may be used for symptom control.
Na” channels, holding them in their open state, blocking K” efflux from cells, paralysis via inhibition of voltagegated Ca” channels on pre-synaptic membranes, inhibition of acetylcholine release from post-synaptic nicotinic receptors, and effects at Na” channels at the neuromuscular end-plate, inhibiting the production of action potentials and muscular contraction leading to paralysis are primarily mediated by μ conotoxins. (kohn, cruz, conoserver). There are also neurotransmitter and receptor effects that have not yet been fully elucidated, that cause disorientation and sedation to prey fish after envenomation. ω-conotoxin MVIIA is a cyclotide neurotoxin that has a synthetic analog (ziconotide acetate derivative) that is currently marketed as a chronic pain management agent, due to actions at both sodium and calcium channels. These conotoxins have been found to inhibit both pre- and postganglionic N-type calcium channels on nerve terminals, resulting in complete inhibition of cardiac autonomic neurotransmission. Peripheral antagonism of these channels has been demonstrated in animal studies as well as in vitro tissue models and likely contributes to peripheral sympathetic effects leading to hypotension. Conantokin G is an NMDA receptor antagonist that has shown promise in in vitro and animal models to have efficacy in managing neuropathic pain (215–219).

Clinical Effects
Local effects predominate, such as burning pain and local hemorrhagic injury. Secondary infection and retained foreign body from broken spines are not uncommon. Systemic symptoms are rarely reported but may include nausea and vomiting; muscle weakness and paralysis have also been noted in severe envenomations. Immersion of the limb in non-scalding hot water (110°F [43°C]) may aid in pain relief, as the venom components are heat labile (161,163,167,220). Opiate analgesics may be required.

Sea Urchins

Many sea urchins have long, sharp, brittle spines composed of calcium carbonate that cause local injury, but most are not venomous. Deep tissue injury and extension of spines into organs and joint spaces may cause tissue destruction and morbidity from secondary infection. If it is a venom-containing species, the gland is located at the end of the spines and in their pedicellariae (the mouth-like apparatus at the end of a flexible stalk used to gather food). Venom is composed of a mixture of steroid glycosides, serotonin, proteases, cholinergic-like substances, and others (161,179).

Clinical Effects
Local pain, erythema, and edema are typically self-limited. Partial paralysis of the envenomated limb has been reported with exposure to some species (161,220). Rare systemic symptoms are noted in the literature.

Treatment
The affected area should be immersed in non-scalding hot water (110°F [43°C]), with oral analgesics and local wound care, and removal of any embedded spines as needed, which may require operative removal as deeply embedded spines can cause long-term tissue injury and infection if left in situ. Care is otherwise symptomatic and supportive.

Annelid Worms

The common bristle worm, found in Floridian and Caribbean waters, causes intense local inflammation with edema, erythema, and urticaria (161). No systemic reactions have been reported, and the toxin is unknown. Removal of any bristles adherent to the skin and otherwise simple symptomatic and supportive care are the mainstays of treatment.

Key Points

Snakes Native to United States

- Presentation
  - Determine historical facts (prior snakebite? accidental? pet?).
  - Ascertain species (native or exotic? coral snake or viper?).
  - Learn activities following accident (delay, running, nausea, vomiting?).
- Diagnosis
  - “Dry bite” or envenomation? (pain, swelling, discoloration)
• Only local or systemic signs? (nausea, vomiting, shock, hemorrhage)
• Signs and symptoms? (stable, progressive, or rapidly progressive)
• Treatment
• Make early as possible decision to treat with antivenom or not.
• Efficacy of antivenom best with earlier than later use.
• Treat pit viper envenomations as per Table 153.3 until signs and symptoms of envenomation resolve or cease to progress, typically following initial six vials antivenom.
• Be aware of “recurrence syndrome” (primarily hematologic laboratory abnormalities) 24 to 72 hours after last infusion of antivenom.

Snakes Not Native to the United States
• Up to 30% of Viperid and 50% of Elapid bites do not result in envenomation.
• Signs and symptoms of envenomation may be delayed by many hours.
• Identification of the snake to the species level is required for antivenom selection.
• Viperid venoms usually produce local tissue injury and hematologic abnormalities, and may also include cardiovascular effects and neurologic effects.
• Elapid venoms usually produce neurologic toxicity, progressing to respiratory muscle paralysis, and may also include local tissue injury and hematologic abnormalities.
• Type I hypersensitivity reactions (anaphylaxis) may occur to venom or antivenom.
• Anaphylaxis, cardiotoxins, or fluid loss may produce hypotension.
• Local tissue injury may result in severe swelling, pain, and elevated tissue and/or compartmental pressures. Functional impairment, necrosis, and tissue loss may occur.
• Hematologic effects include impairment or consumption of platelets, fibrinogenolysis, hypofibrinogenemia, prolongation of PT/PTT, procoagulant effects, and other abnormalities, either singly or in combination; also, significant bleeding may occur.
• Neurologic effects include diplopia, paresthesias, fasciculations, respiratory muscle paralysis, and arrest. Viperid may cause weakness, but usually not respiratory compromise.
• Other venom effects include tachycardia, nausea, vomiting, diaphoresis, and anxiety.
• Wound infection is uncommon, documented in less than 5% of cases.
• Local effects may continue or recur for the first 24 to 36 hours, and hematologic effects may continue or recur for up to 3 weeks.

Snakes and Scorpions
• Widow spider bites are classically painful and manifest pain and muscle spasm extending from the site of the bite.
• Antivenom is available for widow spiders and the bark scorpion and is appropriate for use in severely symptomatic patients.

• Envenomation from Loxosceles species spiders (e.g., brown recluse) can cause a necrotic wound for which basic wound care and supportive care are the best treatment.
• Systemic illness from Loxosceles spider envenomation can present with fever and myalgias, which may progress to hemolysis and shock in rare circumstances.
• Envenomation by nonnative spiders should prompt a call to a regional poison center for advice regarding antivenom usage.

References


