Venomous snakes are found in 47 of the 50 US states. The majority of venomous snakebites occur in the southwestern United States. Approximately 4700 human exposures to venomous snakes are reported to poison control centers annually. It is estimated that 150,000 animals, primarily dogs and cats, are bitten in the United States every year. Although human mortality following snakebite in the United States is low (0.06%), reported mortality in dogs ranges from 1% to 30%. Snakebite poses a significant risk of morbidity in humans as well as domestic animal species. Veterinarians must be aware of the venomous snakes in their practice area, be able to recognize the clinical picture typical of an envenomation by these snakes, and be equipped to treat these patients.

VENOMOUS SNAKES OF NORTH AMERICA

Venomous snakes in North America that have been reported to cause illness in domestic animals are members of the family Elapidae or Crotalidae. The coral snake species are the only Elapids native to North America. Table 1 gives a listing of coral snakes located in North America with their approximate geographical distribution. Several nonvenomous snakes are easily mistaken as coral snakes. Coral snakes are marked with broad bands of bright colors and, in contrast to the pit vipers, have round pupils and no pit on their face. The red and yellow bands on a coral snake are in direct contact and completely encircle the body. Coral snakes make up approximately 2% of the envenomations that occur in humans every year. Elapids have small fixed front fangs and they must chew on their prey in order to envenomate, making envenomation by these snakes much less common. Coral snake venom is the most toxic per milligram of dried weight of any snake venom in the United States.
States; fortunately, approximately 60% of all coral snakebites do not result in envenomation.5,6

Snakes in the family Crotalidae make up the largest percentage of snakebite exposures each year.3 Snakes in this family are the pit vipers including rattlesnakes, cottonmouths, and copperheads. Pit vipers are distinguished by their diamond-shaped heads, elliptical pupils, heat-sensing pit on their face between their eye and their nose, and retractable front fangs.1 Pit vipers have the ability to control the amount of venom they inject and can bite without injecting venom, resulting in a “dry bite.” Approximately 25% of all pit viper bites are dry bites.2 A defensive strike may be a “dry bite” or inject very little venom in contrast to an offensive bite, in which they will inject a controlled amount of venom, or an agonal bite, where they will discharge their venom gland entirely.1

There are several different species of rattlesnakes in North America (Figs. 1–3). Table 2 provides a listing of rattlesnakes in North America and their approximate geographical locations. Approximately 65% of venomous snakebites are caused by rattlesnakes.2 Rattlesnake envenomation results in more deaths and a higher morbidity than any of the other pit vipers found in North America.3 The species of rattlesnakes most commonly reported with bites are the Eastern diamondback rattlesnake, the Western diamondback rattlesnake, the prairie rattlesnake, the Pacific

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Common Name</th>
<th>Geographical Distribution</th>
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<tbody>
<tr>
<td>Micruroides euryanthus</td>
<td>Sonoran Coral Snake</td>
<td>Central and SE Arizona, SW New Mexico</td>
</tr>
<tr>
<td>Micrurus fulvius fulvius</td>
<td>Eastern Coral Snake</td>
<td>N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana</td>
</tr>
<tr>
<td>Micrurus fulvius tenere</td>
<td>Texas Coral Snake</td>
<td>Texas, Louisiana, Arkansas</td>
</tr>
<tr>
<td>Micrurus fulvius barbouri</td>
<td>South Florida Coral Snake</td>
<td>South Florida</td>
</tr>
</tbody>
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Fig. 1. Crotalus horridus horridus (timber rattlesnake). Note the thick, solid dark tail characteristic of the timber rattlesnake. (Courtesy of John N. Gilliam, DVM, MS, DACVIM, DABVP, Stillwater, OK.)
rattlesnake, the timber rattlesnake, and the pygmy rattlesnake. Of these species, the Eastern and Western diamondback rattlesnakes are most often associated with mortality.\(^2\) Rattlesnake venom varies from species to species and within a species; therefore, the clinical picture resulting from rattlesnake envenomation is largely variable.

Copperhead (Fig. 4) bites are the second most common snake envenomation in the United States (25%), followed by cottonmouths (about 10%).\(^3\) Table 2 shows the approximate geographical distribution of these snakes. Cottonmouth moccasins are semiaquatic snakes that are capable of biting while under water.\(^2\) Copperhead and cottonmouth envenomations generally result in significantly less mortality and morbidity than does rattlesnake envenomation.

**TOXIC EFFECTS AND CLINICAL SIGNS**

Snakes swallow their prey whole; it can take up to 14 days for complete digestion to occur.\(^2\) Putrefaction of the prey may cause the snake to regurgitate before digestion.
<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Common Name</th>
<th>Geographical Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crotalus adamanteus</strong></td>
<td>Eastern Diamondback rattlesnake</td>
<td>N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana, Florida</td>
</tr>
<tr>
<td><strong>Crotalus atrox</strong></td>
<td>Western Diamondback rattlesnake</td>
<td>California, Nevada, Arizona, New Mexico, Texas, Oklahoma, Arkansas</td>
</tr>
<tr>
<td><strong>Crotalus cerastes</strong></td>
<td>Mojave Desert Sidewinder</td>
<td>California, Nevada, Arizona, Utah</td>
</tr>
<tr>
<td><strong>Crotalus concolor</strong></td>
<td>Midget Faded rattlesnake</td>
<td>Wyoming, Utah, Colorado</td>
</tr>
<tr>
<td><strong>Crotalus horridus</strong></td>
<td>Timber rattlesnake</td>
<td>Texas, Minnesota, Wisconsin, Iowa, Nebraska, Kansas, Oklahoma, Arkansas, Missouri, Tennessee, Kentucky, Illinois, Indiana, Ohio, N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana, Florida, Pennsylvania, New Jersey, Maryland, Delaware, Virginia, W. Virginia, New York, New England</td>
</tr>
<tr>
<td><strong>Crotalus lepidus</strong></td>
<td>Rock rattlesnake</td>
<td>Arizona, New Mexico, Texas</td>
</tr>
<tr>
<td><strong>Crotalus mitchelli</strong></td>
<td>Speckled rattlesnake</td>
<td>California, Nevada, Arizona</td>
</tr>
<tr>
<td><strong>Crotalus molossus</strong></td>
<td>Black-tailed rattlesnake</td>
<td>Arizona, New Mexico, Texas</td>
</tr>
<tr>
<td><strong>Crotalus pricei</strong></td>
<td>Twin-spotted rattlesnake</td>
<td>Arizona</td>
</tr>
<tr>
<td><strong>Crotalus scutulatus</strong></td>
<td>Mojave rattlesnake</td>
<td>Nevada, SW Texas, S. California, Tuscon to Phoenix, Arizona, New Mexico</td>
</tr>
<tr>
<td><strong>Crotalus ruber</strong></td>
<td>Red Diamond rattlesnake</td>
<td>Washington, Oregon, Idaho</td>
</tr>
<tr>
<td><strong>Crotalus tigris</strong></td>
<td>Tiger rattlesnake</td>
<td>Arizona</td>
</tr>
<tr>
<td><strong>Crotalus viridis</strong></td>
<td>Western rattlesnake</td>
<td>Oregon, Idaho, Arizona, New Mexico, Texas, Montana, S. Dakota, N. Dakota, Nebraska, Iowa, Utah, Colorado, Kansas, Oklahoma</td>
</tr>
<tr>
<td><strong>Crotalus viridis viridis</strong></td>
<td>Prairie rattlesnake</td>
<td>Oregon, Idaho, Arizona, New Mexico, Texas, Montana, S. Dakota, N. Dakota, Nebraska, Iowa, Utah, Colorado, Kansas, Oklahoma, Wyoming, Alberta Canada</td>
</tr>
<tr>
<td><strong>Crotalus viridis abyssus</strong></td>
<td>Grand Canyon rattlesnake</td>
<td>Arizona</td>
</tr>
<tr>
<td><strong>Crotalus viridis helleri</strong></td>
<td>Southern Pacific rattlesnake</td>
<td>California</td>
</tr>
<tr>
<td><strong>Crotalus viridis lutosus</strong></td>
<td>Great Basin rattlesnake</td>
<td>Oregon, Idaho, California, Nevada, Arizona, Utah</td>
</tr>
<tr>
<td><strong>Crotalus viridis oreganus</strong></td>
<td>Northern Pacific rattlesnake</td>
<td>Washington, Oregon, Idaho, California, Nevada</td>
</tr>
<tr>
<td><strong>Crotalus willardi</strong></td>
<td>Ridge-nosed rattlesnake</td>
<td>Arizona</td>
</tr>
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(continued on next page)
The role of venom, therefore, is to predigest the prey, allowing it to be fully digested more rapidly, within 2 to 5 days. The proteins and enzymes that allow for immobilization and predigestion of the prey are responsible for the clinical signs we see in our patients. To better understand the clinical picture of these envenomated patients, it is helpful to have a working knowledge of the individual venom component’s effect on the body. It is perhaps easiest to discuss these venom components in conjunction with the clinical signs that they cause.

**CLINICAL SIGNS OF ELAPID ENVENOMATION**

Close examination of a suspect elapid bite victim, focusing on the lips, muzzle, and distal limbs, should be performed to look for the presence of fang puncture wounds. Coral snake fang punctures are small, looking more like scratches, and are easily missed. Clinical signs of coral snake envenomation are largely attributed to the venom’s neurotoxic effects and typically have a delayed onset, making it difficult, initially, to determine if envenomation has occurred. Clinical signs may occur within 1 hour of envenomation but can be delayed up to 18 hours. Interestingly, coral snakebites often do not result in severe pain. Swelling in the area of the bite is not an indicator of severity of envenomation as fatal envenomation can occur with minimal

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**Table 2 (continued)**

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Common Name</th>
<th>Geographical Distribution</th>
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<tbody>
<tr>
<td><em>Sistrurus catenatus</em></td>
<td>Massasauga rattlesnake</td>
<td>Arizona, New Mexico, Texas, Michigan, Wisconsin, Minnesota, Nebraska, Iowa, Colorado, Kansas, Oklahoma, Arkansas, Missouri, Illinois, Indiana, Ohio, New York, Pennsylvania</td>
</tr>
<tr>
<td><em>Sistrurus miliarius</em></td>
<td>Pigmy rattlesnake</td>
<td>Texas, Oklahoma, Arkansas, Missouri, Tennessee, Florida, N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana</td>
</tr>
<tr>
<td><em>Agkistrodon contortix</em></td>
<td>Southern Copperhead</td>
<td>Kansas, Oklahoma, Arkansas, Missouri, Tennessee, Kentucky, Illinois, Indiana, Ohio, N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana, Pennsylvania, New Jersey, Maryland, Delaware, Virginia, W. Virginia, New York, New England</td>
</tr>
<tr>
<td><em>Agkistrodon piscivorus</em></td>
<td>Eastern/Western Cottonmouth</td>
<td>Texas, Nebraska, Iowa, Kansas, Oklahoma, Arkansas, Missouri, Tennessee, Kentucky, Illinois, N. Carolina, S. Carolina, Georgia, Alabama, Mississippi, Louisiana, Virginia</td>
</tr>
</tbody>
</table>

local tissue damage. Dogs envenomated by coral snakes typically become lethargic and exhibit vomiting and ptalism acutely due to the venom’s excitatory effects on the autonomic nervous system. The postsynaptic action of the neurotoxin at the acetylcholine receptor site eventually results in generalized muscle weakness, quadriplegia, and paralysis. The neurotoxicity may manifest itself as ptosis and weakness of the extrinsic musculature of the eyeball. The most common clinical signs seen in 9 dogs envenomated by coral snakes were lethargy and lower motor neuron weakness, marked ptalism, vomiting, and reddened urine. Cardiac arrhythmias have been reported secondary to coral snake envenomation but are not common. Death typically occurs secondary to respiratory paralysis. Coral snake envenomation in the cat is not widely reported; however, in one case series of 3 cats suspected of having coral snake envenomation, common clinical signs were sedation, peracute onset of ascending flaccid paralysis, hypothermia, decreased nociception, loss of spinal reflexes, and loss of cutaneous trunci reflex.

**CLINICAL SIGNS OF PIT VIPER ENVENOMATION**

Clinical signs of pit viper envenomation tend to be more severe in dogs than cats as cats seem to be more resistant to pit viper venom on a milligram of venom–per–kilogram of body mass basis. Species, age, size, location of the bite, postbite excitability, and health status at the time of the bite are all factors that will affect the severity of envenomation in a given individual. Concurrent medications at the time of the bite may also affect the severity of the clinical signs (eg, nonsteroidal anti-inflammatory drugs further inhibit platelet function; beta-blockers may mask early onset of anaphylaxis). The primary factors related to the snake that affect severity of envenomation are the quantity and toxicity of the venom. The quantity of venom available for injection can be affected by season, time since last discharge of venom, age and size of the snake, and motivation of the snake (offensive vs defensive vs agonal).

Puncture wounds that are oozing blood or serum are a characteristic clinical sign of pit viper envenomation (Figs. 5–9). It is important to note that the presence of fang marks does not confirm envenomation due to the high percentage of “dry bites.” If there is absent to minimal swelling observed 1 hour post bite and the animal is not
showing any systemic signs of envenomation, it is very unlikely that envenomation occurred. With moderate to severe envenomation, local tissue damage is evident within 10 minutes of the bite (exception may be the Mojave rattlesnake), the area is painful, and there is often local hemorrhage.

Acute pain, marked swelling and edema, and ecchymosis at the bite site are also characteristic of pit viper envenomation (Figs. 6 and 8). Tissue damage and necrosis in the area of the bite is the most commonly recognized clinical sign following North American pit viper envenomation. Tissue damage is most likely a combination of the direct effect of the venom on the tissues and damage caused by inflammation and swelling secondary to edema formation and hemorrhage.
Multiple venom components are involved in causing tissue damage and necrosis. Venom metalloproteinases (VMPs) cause local myonecrosis and skin damage as well as hemorrhage and systemic inflammation. They cleave pro–tumor necrosis factor alpha (pro-TNFα) and release activated TNFα, a normal mediator of the inflammatory response. Activated TNFα results in production of similar human metalloproteinases (HMPs) which break down extracellular matrix proteins, resulting in further tissue damage. HMPs also cleave pro-TNFα and result in a vicious cycle of inflammation. Venom hyaluronidase and collagenase lead to deeper venom penetration through connective tissue. Hyaluronidase decreases connective tissue viscosity by catalyzing the cleavage of internal glycoside bonds and mucopolysaccharides while collagenases digest collagen.

Local tissue reactions are less dramatic with cottonmouth and copperhead snakes than rattlesnakes. There are rare occasions where fatal pit viper envenomation can occur without local tissue effects (Fig. 9). This is most likely to occur with one of the snakes that have primarily neurotoxic venoms such as the Mojave rattlesnake. The Mojave rattlesnake, timber rattlesnake, and canebrake rattlesnake all possess a neurotoxin. The Mojave toxin can cause a flaccid paralysis; however, weakness and paralysis are not commonly seen following Mojave rattlesnake envenomation. This toxin is thought to work presynaptically by blocking the calcium channels in the presynaptic motor neuron at neuromuscular junctions. This blockade prevents the release of acetylcholine, preventing the activation of the acetylcholine receptor on skeletal muscle and thus preventing muscle contraction. Calcium channel blockade by the Mojave toxin will not improve with calcium therapy. Effects of Mojave toxin...
experimentally are greatest on the motor axon terminals of the diaphragm, which could lead to respiratory paralysis. The venom of the Mojave found near Phoenix is thought to be less neurotoxic than that of the Mojave found in southwestern Arizona and southeastern California.

The primary neurotoxic sign seen with timber rattlesnake envenomation is myokymia, a type of muscle fasciculation that resembles a wave or wormlike movement below the skin. The proposed mechanism also involves calcium channels at the presynaptic neuromuscular junction. Intravenous calcium does result in clinical improvement.

Further clinical signs seen with pit viper envenomation include but are not limited to petechiae, increased salivation, vomiting, diarrhea, urinary and fecal incontinence, excessive thirst, severe hypotension, regional lymphadenopathy, altered respiratory rate, pulmonary edema, cyanosis, cardiac arrhythmias, bleeding, obtundation, shock, coma, and convulsions.

Indications of coagulopathy such as petechiae or spontaneous bleeding occur with severe envenomations. One retrospective study found that the presence of petechiation was negatively correlated with survival in a group of dogs envenomated by pit vipers.

Lethargy, increased salivation, vomiting, diarrhea, and urinary and fecal incontinence are most likely due to the venom’s excitatory effect directly on visceral smooth muscle or indirectly on the autonomic nervous system.

Severe hypotension is multifactorial. A myocardial depressor protein has been demonstrated in Western diamondback venom that could directly result in hypotension.
Rattlesnake venom contains kininogenases that act on plasma globulins to form bradykinins, potent vasodilators that can result in profound hypotension. Bradykinins can stimulate the body’s natural phospholipase A2, resulting in the production of prostaglandins and thromboxane A2. Prostaglandins E2 and I2 cause vasodilation, which results in decreased systemic arterial pressure and contributes to hypotension. Prostaglandins can also cause severe congestion in the lungs, increased vascular permeability and hemorrhage. Indomethacin, a cyclooxygenase inhibitor, has been shown to improve Mojave rattlesnake venom–induced hypotension in a mouse model, suggesting the role of prostaglandins in venom-induced hypotension.

Large amounts of fluid may be lost in acute envenomation, resulting in hypotension. Fluid losses are attributed to third space losses secondary to severe endothelial damage, vomiting, and hemorrhage. A lethal factor in Crotalus venom has been shown to cause lysis of plasma membranes resulting in microangiopathic vascular permeability, which allows plasma proteins and red blood cells to leak into the surrounding tissues. This extravascular fluid loss can lead to volume depletion and hypoperfusion followed by hemoconcentration, lactic acidosis, and hypovolemic shock.

Another contributor to venom-induced hypotension is blood pooling. Crotalidae venom has been shown to cause pooling of blood in the hepatosplanchnic vasculature of dogs and in the lungs of cats. Victims may have an altered respiratory rate, pulmonary edema, and cyanosis. Cardiac perfusion will suffer with prolonged or untreated hypotension, resulting in a further decrease in cardiac output. Cardiac arrhythmias may be seen. No direct effect of pit viper venom on the heart has been specifically identified. At present it is uncertain whether cardiac arrhythmias are due to direct or secondary effects of North American pit viper and elapidæ venom.

Bites to the head or neck can result in severe edema and swelling of the pharyngeal area resulting in respiratory distress or asphyxia. Dogs are most commonly bitten on the head; second most commonly the legs, and rarely the body. Cats are most commonly bitten on the front legs, followed by the head and then the body. In cases
of head bites, there may be epistaxis, which can appear frothy, and swelling of the face may prevent opening of the eyelids, resulting in temporary blindness.\textsuperscript{16}

Venom travels via the lymphatics; therefore, regional lymphadenopathy may be recognized. This lymphadenopathy is often mistaken for secondary infection; however, it rarely is associated with infection in human patients.\textsuperscript{22} Bites to extremities may continue to have edema for weeks to months due to reduced lymphatic function.\textsuperscript{12}

**DIFFERENTIAL DIAGNOSES**

Differential diagnoses for coral snake envenomation include tick paralysis, polyradiculoneuritis, botulism, and myasthenia gravis.\textsuperscript{5} Differential diagnoses for pit viper envenomation include trauma, angioedema (ie, insect bite or sting), a nonsnake animal bite, abscess, non–snakebite wound–induced cellulitis, or puncture wound.\textsuperscript{1,16}

**EMERGENCY FIELD TREATMENT/FIRST AID**

Over the years many recommendations have been put forth for the field treatment of snakebites. Scientific studies of these methods have proved that many are ineffective and some are even harmful. Keeping the animal as restricted and calm as possible and transporting them the nearest veterinary facility is the best response to a snakebite.\textsuperscript{8} In the case of coral snake envenomation, it is ideal to get the animal to a facility that can offer mechanical ventilation in case it is needed.\textsuperscript{6} Antivenin availability is also very important. Most medical facilities in areas where poisonous snakes are endemic will have access to antivenin. Therapies that are contraindicated include cryotherapy, hot packs, electroshock therapy, incision and suction of the bite site, and tourniquet application.\textsuperscript{1} Compression bandages have been shown to be beneficial in Australian Elapid envenomation; thus, they may have a place in field treatment of coral snake envenomation.\textsuperscript{6} They have not, however, been demonstrated to be beneficial in pit viper envenomation. Keeping the venom concentrated in one area may only result in increased tissue necrosis.\textsuperscript{1,2,12} Due to the difficulty with appropriate application in the case of coral snake envenomation and the potential contraindication in pit viper envenomation, the authors cannot recommend the use of compression bandages. The Extractor is a negative suction device that has been evaluated for its use as a first aid device with snake envenomation.\textsuperscript{23–25} If applied within 3 minutes of envenomation, 23% of venom could be extracted after 3 minutes of suction and 34% after 30 minutes of suction.\textsuperscript{24} However, the distance between fang tip punctures in defensive bites of western diamondback rattlesnakes were measured and it was concluded that The Extractor could not simultaneously cover both puncture wounds, indicating that 2 of these devices may be necessary to aspirate venom from a bite site.\textsuperscript{25} The Extractor did not reduce local venom induced tissue injury in an artificial model of rattlesnake envenomation in pigs.\textsuperscript{26} In addition, this model indicated local skin damage may occur secondary to prolonged application of the device.\textsuperscript{26} Application of this device has not been reported in veterinary medicine. Hair-covered skin may present a challenge to establishing negative pressure with the device and more information on the product’s application to the veterinary species is needed.

It is not uncommon for cats to be bitten by a snake on the body. A localizing circumferential compression device has been evaluated in pigs experimentally envenomated with Eastern diamondback rattlesnake venom on the torso and was found to be beneficial in delaying the onset of signs of envenomation.\textsuperscript{27} This device may or may not be practical in our veterinary patients. Application to feline patients may be very difficult and stressful, making it impractical.
Snakebite victims that are treated appropriately within 2 hours of being bitten have an excellent prognosis. Many attempts at field first aid ultimately delay appropriate care in the hospital. Such a delay was a common denominator in human victims who died secondary to rattlesnake bite.

Although it is helpful to have identification of the snake, owners should not risk capturing the snake for identification purposes. These efforts can result in the owner getting bitten and will delay appropriate treatment for the animal. Owners should be cautioned that dead and decapitated snakes can still envenomate.

**DIAGNOSTIC TESTING**

A minimum database should be collected on a patient presented for snakebite even if signs of envenomation are not present initially. Laboratory abnormalities may be present that will confirm envenomation prior to clinical signs becoming apparent. A baseline complete blood count (CBC) and blood chemistry panel should be performed. Common CBC findings are nonspecific and include mild to severe anemia, leukocytosis (may or may not have a left shift), and thrombocytopenia. Anemia in dogs bitten by coral snakes may be due to severe hemolysis. The proposed mechanism is the action of venom phospholipase A2 (PLA2) on red blood cell membranes. This has not been documented in cats bitten by coral snakes. In North American pit viper envenomation, the anemia is more commonly due to hemorrhage as hemolysis is uncommon in the absence of disseminated intravascular coagulation. The chemistry panel should include but not be limited to creatine phosphokinase (CPK), creatinine, blood urea nitrogen, sodium, potassium, chloride, calcium, and glucose.1

Rhabdomyolysis may occur secondary to envenomation and may, at least in part, be due to the venom protein myotoxin a. Myotoxin a affects calcium regulation within the cell, causing increases in intracellular calcium and eventual skeletal muscle cell necrosis. The exact mechanism of myotoxin a is not known. Myotoxin a is absent in Western diamondback rattlesnake venom. Venom PLA2 may also play a role in rhabdomyolysis by damaging muscle cell membranes, disrupting organelles, and allowing increased influx of calcium. Increased intracellular calcium may result in necrosis. Muscle fiber proteins can be damaged by venom proteolytic enzymes RNase, DNase, and 5’ nucleotidase if the venom is injected directly into a muscle. Profound swelling of an area may result in an ischemic myonecrosis secondary to the envenomation. In veterinary patients, pain indicative of a typical rhabdomyolysis may not be exhibited; therefore, the syndrome may not be recognized without evaluating CPK. A marked early increase in CPK is an indicator of severe envenomation.

Hypokalemia has been documented secondary to pit viper envenomation and may contribute to signs of weakness and cardiac dysfunction.

A blood smear should be examined to look for the presence or absence of echinocytosis. Echinocytosis has been reported in the literature secondary to coral snake and rattlesnake envenomation. Although there are no reports of echinocytosis secondary to copperhead envenomation in the literature, it has been seen in at least 2 dogs with documented copperhead envenomation (Robin Allison, DVM, DACVP, Stillwater, OK, personal communication, March 2011) (Fig. 10). Exposure of human, canine, equine, and feline red blood cells to Western diamondback rattlesnake venom resulted in echinocytosis in an in vitro study. Low venom concentrations resulted in Type I and Type II echinocytes. Type III echinocytes, spheroechinocytes, and spheroocytes occurred with increased venom concentrations. The absence of echinocytosis does not indicate that envenomation did not occur. Rattlesnake venoms are reported to cause more severe coagulopathies than those of other pit vipers; therefore, a coagulation panel including activated clotting time...
(ACT), prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen, fibrin degradation products (FDPs), and an accurate platelet count should be evaluated.\(^1\) Decreased platelet counts and/or increased ACT, PT, and PTT indicate envenomation has occurred and the degree of change is an indicator of severity of envenomation.\(^{13}\) Common findings on a coagulation panel from animals with moderate to severe North American pit viper envenomation are hypofibrinogenemia, increased FDPs, and prolonged PT and PTT.\(^{10}\) In contrast, animals with coral snake envenomation are more likely to have a hyperfibrinogenemia.\(^6\)

Venom disrupts the coagulation process by one or more mechanisms that differ from species to species and even within the same species of snake.\(^{12}\) Venom fibrinolysins destroy both fibrinogen and fibrin, while venom thrombin-like enzymes result in the construction of a weak fibrin chain by inadequate fibrinopeptide cleavage.\(^{12}\) In addition, thrombin-like enzymes do not activate factor XIII. The net result of these venom activities is defibrination characterized by inadequate fibrin clot formation, hypofibrinogenemia, increased FDPs, abnormal coagulation profiles, and diminished to absent intravascular clotting.\(^{12}\) Snake-bitten patients suffering from defibrination alone are often misdiagnosed with disseminated intravascular coagulation (DIC) because of their abnormal coagulation profiles; however, platelet function and numbers are normal, factor VII is unaffected, and clinical bleeding is unusual in these animals.\(^{12}\)

Phospholipids must be available for use in the clotting cascade—in particular, for the activation of factor X. Venom PLA2 forms complexes with phospholipids, preventing them from being used for clotting protein activation.\(^{19}\) The result is a dysfunctional clotting cascade and a diminished clotting ability manifested with an increased PT and PTT.

Platelet function and number can be affected in crotalid snake envenomation patients. The mechanisms by which venom-induced thrombocytopenia (VIT) occurs are not understood. Effects of rattlesnake venom on the bone marrow resulting in decreased production have not been demonstrated.\(^{33}\) Two other basic mechanisms have been proposed: aggregation and consumption/destruction. Several rattlesnake venoms have been noted to cause platelet aggregation resulting in thrombocytopenia.\(^{34}\) Crotalocytin, a specific serine protease isolated from timber rattlesnake venom, has been shown to cause platelet aggregation in vitro.\(^{33}\) Venom PLA2 can result in

![Fig. 10. Blood smears demonstrating type III echinocytes caused by pit viper envenomation. A, Dog bitten by a rattlesnake. B, Dog bitten by a copperhead. The arrows point to polychromatophils, which are always unaffected. (Courtesy of Robin W. Allison, DVM, PhD, DACVP, Stillwater, OK.)](image-url)
production of prostaglandin E2 and thromboxane A2, which also cause platelet aggregation.\textsuperscript{19} Phospholipases have been implicated in damaging platelet membranes and resulting in their ultimate destruction. In addition, envenomation can result in a tremendous amount of endothelial damage, which results in platelet adherence and sequestration at the bite site.\textsuperscript{33}

Coagulopathies may exist in the face of normal platelet number due to abnormal platelet function. A protein found in Western diamondback rattlesnake venom, catrocollastatin, inhibits platelet adhesion to collagen, resulting in abnormal platelet function in the face of normal platelet numbers.\textsuperscript{35} Crovidisin, a toxin found in prairie rattlesnake venom, binds to collagen fibers and prevents platelets from interacting with collagen. This prevents platelet adhesion, release reaction, thromboxane formation, and aggregation.\textsuperscript{36}

Hemorrhagic toxins damage capillary endothelial cells and vessel wall basement membranes resulting in extravasation of erythrocytes.\textsuperscript{22} The smaller blood vessels tend to be more susceptible to these toxins.\textsuperscript{22} Upon necropsy of animals that have died from snake envenomation, there is often a large amount of hemorrhage in the tissues surrounding the bite site.

When evaluating the pit viper envenomated patient for coagulopathies, it is important to realize that DIC rarely occurs in snakebite victims and abnormal coagulation profiles as well as observed increased bleeding are more likely due to one or more of the many direct effects of the venom.\textsuperscript{12}

A baseline urinalysis should be performed to look for hematuria, hemoglobinuria, myoglobinuria, proteinuria, or glucosuria.\textsuperscript{1} The presence of pigmenturia is an indicator of severe envenomation.\textsuperscript{13} Renal compromise can occur in snakebite patients and is most likely a secondary rather than primary effect of envenomation.\textsuperscript{30} Hypotension, hypoperfusion, microthrombosis, myoglobinuria, and hemoglobinuria may all contribute to renal compromise and/or damage in these patients.

Electrocardiograms are indicated in any patient with severe envenomation or with suspect cardiac toxicity. Measuring cardiac troponin I may be beneficial in detecting myocardial damage.

Animals bitten on an extremity should have circumferential measurements taken of the limb just above and just below the bite site at presentation.\textsuperscript{1} These measurements should be repeated every 15 minutes until they are static over 4 measurements.

Snakebite severity scores have been developed to aid in determining if antivenin is indicated.\textsuperscript{37} These scores may aid the clinician in evaluating not only the severity of the envenomation but also the progression. They can assist in determining the necessity of antivenin therapy. Table 3 shows a human snakebite severity score that has been adapted for use in veterinary patients.

\textbf{IN HOSPITAL TREATMENT}

Treatment of a snakebite victim should first involve determining whether envenomation has occurred followed by a combination of supportive care and therapy aimed at reversing the adverse effects of the venom. Snakebite victims should be hospitalized for a minimum of 8 hours to determine the severity of a potential envenomation.\textsuperscript{1} The snakebite severity score sheet should be filled out on presentation and repeated 6 hours after presentation. It is imperative to have a baseline and at least one comparison to be certain subtle changes are not occurring that would indicate the patient’s impending decline.\textsuperscript{1} Circumferential measurements should also be made at this time (see section on diagnostic testing).

Some clinicians may choose to treat patients with diphenhydramine at presentation for its sedative effects. Keeping the animals as calm as possible is necessary.
Table 3
Snakebite severity score
Scoring should occur at presentation and at 6-hour intervals thereafter. Maximum possible score is 20. Risk of mortality increases with increasing scores

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: slight dyspnea</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: respiratory compromise, tachypnea, use of accessory muscles</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: cyanosis, air hunger, extreme tachypnea, respiratory insufficiency or respiratory arrest from any cause</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: tachycardia, general weakness, benign dysrhythmia, hypertension</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: tachycardia, hypotension (tarsal pulse still palpable)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: extreme tachycardia, hypotension (nonpalpable tarsal pulse or systolic blood pressure &lt;80 mmHg), malignant dysrhythmia or cardiac arrest</td>
</tr>
<tr>
<td>Local Wound</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: pain, swelling, ecchymosis, erythema limited to bite site</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: pain, swelling, ecchymosis, erythema involves less than half of extremity and may be spreading slowly</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: pain, swelling, ecchymosis, erythema involves most or all of one extremity and is spreading rapidly</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Very severe: pain, swelling, ecchymosis, erythema extends beyond affected extremity, or significant tissue necrosis</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: abdominal pain, tenesmus</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: vomiting, diarrhea</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: repetitive vomiting, diarrhea, or hematemesis</td>
</tr>
<tr>
<td>Hematological</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: coagulation parameters slightly abnormal, PT &lt; 20 sec, PTT &lt; 50 sec, platelets 100,000 to 150,000/mm3</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: coagulation parameters abnormal, PT 20–50 sec, PTT 50–75 sec, platelets 50,000 to 100,000/mm3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: coagulation parameters abnormal, PT 50–100 sec, PTT 75–100 sec, platelets 20,000 to 50,000/mm3</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Very severe: coagulation parameters markedly abnormal with bleeding present or the threat of spontaneous bleeding, including PT unmeasurable, PTT unmeasurable, platelets &lt;20,000/mm3</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal: apprehension</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate: chills, weakness, faintness, ataxia</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe: lethargy, seizures, coma</td>
</tr>
</tbody>
</table>

Antihistamines have no direct effect on the venom or its effects; however, its administration has been positively associated with survival in dogs envenomated by pit vipers. Therapies for coral snake envenomation in the United States are currently supportive as coral snake antivenin is not available. Supportive care of these patients involves maintaining hydration, appropriate care for the paralyzed patient, and prevention of aspiration pneumonia. Intravenous crystalloid fluids are indicated to maintain hydration and should be initiated early since clinical signs are often delayed. If significant hemolysis or rhabdomyolysis occurs, animals should be maintained on intravenous fluids until evidence of hemolysis and muscle damage have diminished in order to prevent renal damage.

Antivenom is a key component of most severe pit viper envenomation treatments. Not all envenomated patients will require antivenom. One hundred cases of prairie rattlesnake envenomation in dogs found most dogs did not require antivenin for resolution of clinical signs. Very few copperhead bites require treatment with antivenom. It has been widely accepted that the smaller the victim, the more severe the envenomation and thus the higher the dose of antivenom. A study of 31 dogs bitten by the Eastern diamondback rattlesnake showed that the smaller dogs had a worse prognosis. However, a study of 114 cases of snake envenomation in children refuted this fact as all children did well with conservative treatment and did not require antivenom therapy. These conflicting facts confirm that the outcome of each individual envenomation is dependent on several things, size being only one of them. The choice to administer antivenom should be made based on the clinical picture of the patient. The Snakebite Severity Score may aid in this decision. Four common indications for antivenom administration are:

1. Rapid progression of swelling
2. Significant coagulopathy, defibrination, or thrombocytopenia
3. Neuromuscular toxicity
4. Shock

It is important for clinicians and owners to remember that antivenom will not prevent all the effects of the venom. Currently available veterinary antivenom does not have antibodies against myotoxin and, if not administered within 20 minutes of envenomation, will not reverse or block the effects of venom metalloproteinases. Thrombocytopenia induced by timber rattlesnake venom is not responsive to antivenom. These facts do not, however, preclude the use of antivenom as it is very beneficial in reversing most systemic effects of the venom such as coagulation deficits, fluid loss, neurologic signs, and cardiac dysrhythmias. Specific doses for antivenom have not been established. In the veterinary patient, cost is often the greatest factor in determining a dose of antivenom. Any amount of venom that is bound is less venom in circulation causing detrimental effects. The inability to give a large dose of antivenom should not discourage the clinician from giving what is feasible. The average dose for dogs and cats is 1 to 2 vials; however, resolution of clinical signs could require as many as 12 vials. Antivenom is most effective when administered early on, but there is evidence that as long as there is circulating venom, antivenom will be beneficial. Larger doses of antivenom have been associated with a lower chance of survival, although this may be due to the fact that the most severe envenomations are most likely to receive the higher doses of antivenom. 

*Crotalidae Polyvalent Antivenin, Boehringer Ingelheim Vetmedica, Inc.*
The human literature describes skin testing prior to antivenom administration; however, this is not practiced in veterinary medicine. The slow administration of antivenom coupled with the diligent observation of the patient should allow early identification of an allergic reaction. Hyperemia of the inner pinna is a good indicator of early systemic reactions.\textsuperscript{13} It is very important to have all items necessary to treat anaphylaxis immediately available while administering antivenom.\textsuperscript{12} When reconstituting antivenom it should not be shaken but can be swirled and warmed to body temperature in order to facilitate more rapid dissolution.\textsuperscript{1} Recommended dilution is 1 vial of antivenom to 100 to 250 ml of crystalloid fluid.\textsuperscript{1} This dilution may have to be adjusted for very small patients to avoid volume overload when administering the entire antivenom dose.\textsuperscript{1} Antivenom should be administered intravenously and should not be administered directly at the bite site.

If an anaphylactoid reaction is noted during antivenom administration, the drug should be stopped and the animal should be treated, most commonly with diphenydramine. The infusion can typically then be resumed after a short period of time.\textsuperscript{1} If anaphylaxis is noted the antivenom administration is stopped and the animal is treated typically with epinephrine plus or minus corticosteroids and intravenous crystalloid fluids.\textsuperscript{1} In a group of 218 pit viper envenomated dogs, 7% experienced acute reactions to antivenom,\textsuperscript{4} which is much lower than the 23% to 56% rate reported in humans.\textsuperscript{40}

A patient that receives antivenom should remain in the hospital for at least 24 hours.\textsuperscript{22} If laboratory abnormalities were noted initially, these tests should be repeated after antivenom therapy before discharging the patient.

A newer antivenom is available that is a purified and lyophilized ovine Fab immunoglobulin fragment product.\textsuperscript{1} This product does not contain the Fc immunoglobulin fragment, making it much less likely to cause an allergic reaction. Currently this product is cost prohibitive for the veterinary patient. A recurrence phenomenon has been well documented with this ovine antivenom.\textsuperscript{41} Patients receive antivenom and clinical signs improve and 2 to 14 days later clinical signs of envenomation recur.\textsuperscript{42} It is thought that venom is sequestered in the tissues and is released slowly over time as reperfusion and healing to the envenomated area occur. Venom has been detected in a human patient up to 6 days after envenomation, indicating a prolonged elimination time.\textsuperscript{43} The smaller Fab fragments are thought to be cleared from circulation rapidly and are then not available to continue to bind venom that is released over time.\textsuperscript{41} The whole IgG equine antivenom (veterinary product) stays in circulation longer and has been found in urine 4 months post administration.\textsuperscript{41}

Colloids are controversial in the treatment of snakebite patients. As described earlier, the venom has profound effects on the vasculature resulting in large amounts of fluids leaking into the extravascular fluid spaces. If colloids are leaked outside the vascular space, they will act as an osmotic draw for more fluid to exit the vasculature. One location this is likely to occur, particularly in cats, is the pulmonary vasculature, resulting in pulmonary edema.\textsuperscript{1} Whole blood transfusions, however, may be necessary if hemorrhage or hemolysis is severe.\textsuperscript{44}

Snakebite patients are often very painful. Care must be taken when manipulating these patients. Initial analgesia should consist primarily of narcotics. NSAIDs are contraindicated as long as a coagulopathy is present. Morphine-induced histamine release can be confused with antivenom anaphylaxis so other opiates such as fentanyl are preferred.\textsuperscript{1}

Corticosteroids have been very controversial in snakebite victims over the years. Work in humans has failed to show any beneficial effect of steroids with envenomation.\textsuperscript{45} Use of steroids in some species has been reported to be detrimental even increasing mortality.\textsuperscript{1}
Heparin has been used to inhibit the venom thrombin-like enzymes; however, they are not inhibited by heparin and therefore its use is not indicated.1

Broad-spectrum antibiotics are often administered to animals suffering from snake envenomation. This is a controversial practice in human medicine. Regional lymph-adenopathy as a result of venom traveling up the lymphatics is often misdiagnosed as a sign of infection in the area of the bite. Infections secondary to snake envenomation in human patients are not common22; however, the nature of our patients and the environment in which they live are quite different, perhaps leading to a bigger concern about wound infection. Venom is thought to be sterile but the snake’s mouth contains a variety of aerobes and anaerobes that are undoubtedly inoculated at the time of a bite.46 When dogs envenomated by pit vipers were treated with fluoroquinolone antimicrobials the odds of survival were greater.4 Interestingly, dogs treated with other antimicrobials had no increased odds of survival over those untreated.4 It is the general consensus among the veterinary literature that broad-spectrum antibiotics are still indicated in snake envenomation patients.

Fasciotomy is rarely indicated in snake envenomation patients. In order to determine if fasciotomy will be beneficial, one must first diagnose compartment syndrome. This is challenging and not frequently done in the veterinary patient. Compartment syndrome does not commonly occur in snakebite victims.

Tetanus antitoxin has been advocated in the treatment of canine snake envenomation. Tetanus is rare in dogs and C tetani has not been isolated from the snake’s mouth, so its necessity is questioned.10,17

A rattlesnake vaccine (Red Rock Biologics, Woodland, CA, USA) is marketed for the dog and the horse. Empirical data have been conflicting, with some veterinarians reporting much lesser degrees of illness secondary to envenomation in vaccinated dogs (Stacey McLoud, DVM, Spearman, TX, personal communication, March 2011) and others reporting no difference.1 Efficacy studies with this product are in vitro and an in vivo challenge study has not been published. Safety data on the vaccine indicate the product is safe. One author’s personal experience is that animals that are bitten more than once typically have a milder reaction with each subsequent bite (L.G.). This could support the theory of naturally protective titers. More peer-reviewed research needs to be presented on this product in order to determine its in vivo efficacy.

COMPLICATIONS

It is not uncommon for aspiration pneumonia to occur secondary to coral snake envenomation. This is most likely due to dysphagia from neurologic dysfunction to the larynx and pharynx.5 The hypersalivation that occurs secondary to envenomation further complicates the picture.

Serum sickness secondary to antivenom administration has been reported in a dog.47 In people it can occur in up to 50% of patients who receive more than 8 vials of antivenom and is characterized by fever, malaise, nausea, diarrhea, arthralgia, myalgia, lymphadenopathy, peripheral edema, and dermatopathy.47 In the dog, serum sickness was manifest as fever, chemosis, urticaria, focal purpura, and limb edema, which was responsive to steroids. These signs occurred at the third day after antivenom administration, which is earlier than what is typically seen in people (1 to 2 weeks post administration).12,47

SUMMARY

North American snake envenomation can result in significant morbidity in the veterinary patient. An understanding of the mechanisms of the snake’s venom
endemic to your practice area will facilitate appropriate treatment of these patients. Client education on field treatment of snakebites may result in the patient being transported for medical attention in a timely manner. Envenomation does not occur with every snakebite. Victims should be monitored closely for 8 hours for signs of envenomation. If signs do not occur in this time period, it is very unlikely that envenomation occurred. Attempts should be made to evaluate severity of envenomation by physical examination, calculation of serial Snakebite Severity Scores, and evaluation of hematology and blood chemistry values with particular attention paid to the presence/absence and severity of echinocytosis. The foundation of snake envenomation treatment is supportive care and antivenom. Antivenom is typically only necessary with cases of severe envenomation. Patients receiving prompt and appropriate care have an excellent prognosis for recovery.

REFERENCES


