

Arthropod Envenomation in North America



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KEYWORDS

- Arthropods • Spiders • Scorpions • Hymenoptera • Bees • Ants • Ticks
- Centipedes

KEY POINTS

- Black widow spider bites cause painful muscle spasms, secondary to neurotoxicity, and are responsive to antivenom therapy.
- Brown recluse spider bites result in hematoxicity and most commonly manifest locally as skin necrosis.
- Scorpion stings in North America produce severe localized pain with occasional neurotoxic systemic effects.
- Hymenoptera stings from bees and wasps can result in local skin reaction to severe anaphylactic reactions and are responsible for more fatalities than any other venomous arthropod.
- Fire ant stings can cause multiple painful localized skin reaction and pustules.

SPIDERS

There are nearly 40,000 species of spiders worldwide (class Arachnida). Most species cannot inflict serious bites to humans because they do not have fangs long enough to penetrate the human skin.^{1,2,3} As a result, most exposures are often unnoticed and do not need treatment. In North America, approximately 50 species of arachnids potentially cause human morbidity. Spiders use their venom to paralyze and liquefy their prey. There are only a few medically relevant spiders that produce toxic venoms that can lead to local reactions, systemic illnesses, hematoxicity, and neurotoxicity.

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Black Widow Spiders

Introduction

The *Latrodectus* genus of spiders includes 5 primary species found in North America: *Latrodectus mactans*, *Latrodectus bishop*, *Latrodectus geometricus*, *Latrodectus hesperus*, and *Latrodectus variolus*.³ They live in dimly lit, secluded areas such as woodpiles, stonewalls, cabins, barns, stables, and outhouses. They are present in southern Canada and every US state except Alaska.⁴ Black widows are jet black with an iconic red hourglass marking on the ventral aspect of the abdomen (Fig. 1). The red hourglass is specific to *L. mactans*; other species have distinctive ventral markings, such as triangles and spots. There is a seasonal variation in the number of black widow bites, starting to increase in spring, peaking in September, and reaching a nadir in January to February.⁴

Black widows are docile and nocturnal and bite when their web is disturbed. The female black widow is generally considered poisonous to humans and is more aggressive if guarding her egg sac. The male black widow spider has smaller jaws with minimal venom production and is not significantly poisonous to humans. These spiders use striated muscles to control the amount of venom they inject, and about 15% of bites do not deliver venom.⁵ The venom's toxicity is due to the presence of α -latrotoxin. This toxin facilitates exocytosis of synaptic vesicles and the release of the neurotransmitters norepinephrine, γ -aminobutyric acid, and acetylcholine.⁶ The toxin also causes degeneration of motor end plates, resulting in denervation. The venom destabilizes nerve cell membranes by opening ion channels, causing a large influx of calcium into the cell and depletion of acetylcholine from presynaptic nerve terminals.

Patient evaluation overview

Latrodectism is the clinical syndrome that follows a black widow bite. The bite produces a pinprick sensation that often goes unnoticed. With careful examination, 2 small fang marks may be noticed. Within the first few hours, local irritation develops, including erythema, urticaria, or a characteristic halo-shaped target lesion. These local symptoms may be followed by generalized symptoms of pain and muscle spasms in the chest, abdomen, and lower back. Typically, the pain is concentrated to the chest with upper extremity bites and abdomen with lower extremity envenomation. Abdominal rigidity can be severe and may be mistaken as an acute abdomen.^{7,8} Signs and symptoms in small children are wound erythema, irritability, constant crying, sialorrhea, agitation, and seizures. Victims experience pain on the wound site, muscle



Fig. 1. Black widow spider, *Latrodectus mactans*. (Courtesy of CDC/Paula Smith; and James Gathany.)

spasms, abdominal and thoracic pain, and fine tremors.⁹ About one-third of patients will go on to have systemic symptoms.² These systemic symptoms include hypertension, sweating, salivation, dyspnea with increased broncho-secretions, and seizures. Less common effects include myocarditis,¹⁰ compartment syndrome of the upper extremity,¹¹ and priapism.^{12,13} Death is rare from black widow envenomation alone, with no recent cases reported in the US literature, and only a few documented worldwide.^{14–16}

Pharmacologic treatment options

Tetanus immunization should be updated, but antibiotics are unnecessary unless there is evidence of a wound infection. Oral and parenteral analgesics are administered if pain is severe. Muscle spasms may require large doses of benzodiazepines. With administration of these drugs, attention should be given to the patient's airway status because of the concomitant neurotoxicity of the venom.

Historically, administration of calcium gluconate was considered because of concern for the development of hypocalcemia following black widow envenomation. This practice is currently not advocated, because studies have proven no benefit to the administration of calcium.^{7,17} Likewise, dantrolene administration has not been shown to be clinically efficacious for muscle spasms.

Nonpharmacologic treatment options

Pain at the bite site may be relieved with application of an ice pack. The wound can be cleansed with soap and irrigated with water.

Combination therapies

In extreme cases with severe symptoms, *Latrodectus* antivenom is recommended.¹⁸ Currently, in North America, the most widely available product is black widow antivenin (Lyovac, Merck). Black widow antivenin is a horse serum-derived product containing immunoglobulin G antibodies to *L. mactans* venom. The dose of antivenom is one vial diluted in 50 mL of normal saline administered intravenously over 15 minutes. A more highly purified equine F(ab)₂ antibody black widow spider antivenom is also under investigation.¹⁹ The use of *Latrodectus*-specific antivenom is restricted to patients with severe envenomation (eg, seizures, hypertensive crisis, respiratory compromise, or intractable pain), with no allergic contraindications, in whom opioids and benzodiazepines are ineffective. If available, young children and elderly patients with severe toxicity should receive antivenom early in the clinical course.²⁰

Treatment resistance/complications

There has traditionally been reluctance to use antivenom because of concern for anaphylaxis. Two reviews of antivenom use in the United States have demonstrated low rates of adverse reactions.^{4,14} There have only been 2 deaths reported after black widow antivenom administration.^{7,21} Patients receiving antivenom may experience flu-like symptoms or serum sickness 1 to 3 weeks following treatment. This entity is generally self-limited and responsive to antihistamines and steroids.

Evaluation of outcome and long-term recommendations

In adults, the pain will gradually subside after several hours but may remain for 2 to 3 days. A small child bitten by a black widow spider has a greater chance of morbidity and mortality. As with snake envenomation, the volume of distribution and milligrams per kilograms dose of the venom is relatively larger in children than adults. A dose that may cause painful muscle spasms in an adult may lead to respiratory arrest in a child.¹ Any symptomatic patient who has suffered a bite from a black widow spider should be admitted for observation and pain control. Pregnant patients should undergo fetal

monitoring. If there is cardiopulmonary compromise or seizures, the patient should be admitted to the intensive care unit for stabilization and antivenom administration. Symptoms of latrodectism typically last days, but some patients can have intermittent muscle weakness and spasms for weeks.

Brown Recluse Spiders

Introduction

The 6 species of recluse spiders in North America are *Loxosceles arizonica*, *Loxosceles deserta*, *Loxosceles devia*, *Loxosceles laeta*, *Loxosceles rufescens*, and *Loxosceles reclusa*. Of these, *L. reclusa* is the most common. These spiders are reclusive nocturnal hunters and are active from spring to fall.^{22,23} Victims typically are bitten on the extremities while rummaging in confined spaces such as a closet or an attic, while putting on a boot, or when using a blanket or sleeping bag that a spider is trapped in.

The brown recluse gets its name because of its reclusive nature and brown- or fawn-colored body. It is approximately 1 to 5 cm in length, with a characteristic violin- or fiddle-shaped marking on the dorsal cephalothorax (**Fig. 2**). They have long, slender legs and 6 eyes rather than eight, which is the norm for other spiders.²⁴

The venom of the recluse spider, per volume, is more potent than that of the rattlesnake and can cause extensive skin necrosis. The venom acts directly on cell walls, causing immediate injury and cell death. It contains the calcium-dependent enzyme sphingomyelinase D, which in combination with C-reactive protein has a direct lytic effect on RBCs. The local tissue destructive effects are due to hemolytic enzymes and a levarterenol-like substance that induces vasoconstriction. Following cell wall damage, intravascular coagulation causes a cascade of clotting abnormalities and local polymorphonuclear leukocyte infiltration, culminating in a necrotic ulcer.



Fig. 2. Brown recluse spider, *L. reclusa*. (Public domain image by Alex Wild; "Insects Unlocked" project, University of Texas at Austin.)

Patient evaluation overview

Most brown recluse bites occur in predawn hours and are often painless. The seasonality of brown recluse bites and the geographic area should be considered when making this diagnosis. One study demonstrated that 95% of brown recluse bites occurred between the months of April and October.²² *L. reclusa* is primarily found in the south central United States.²⁵ The clinical response to loxoscelism ranges from cutaneous irritation (necrotic arachnidism) to a life-threatening systemic reaction. Most signs and symptoms of envenomation are localized to the bite area.²⁶ Most (90%) result in nothing more than a local reaction and resolve spontaneously.²⁷ Within a few hours, the patient experiences itching, swelling, erythema, and tenderness over the bite site. Classically, erythema surrounds a dull, blue-gray macule circumscribed by a ring or halo of pallor. Gradually, over 3 to 4 days, the wound forms a necrotic base with a central black eschar. In 7 to 14 days, the wound develops a full necrotic ulceration.²⁸ Bites that are in fatty areas, such as the thigh or buttocks, tend to cause more extensive necrosis.²⁹ Several sources call for stricter diagnostic criteria and claim that the diagnosis of necrotic arachnidism secondary to brown recluse spiders is overreported and often mistaken for skin abscesses (eg, MRSA [methicillin-resistant *Staphylococcus aureus*]) and other dermatologic causes.^{30–32}

The systemic reaction, which is less common than the cutaneous reaction, is associated with a higher morbidity. The reaction rarely correlates with the severity of the cutaneous lesion. Within 24 to 72 hours following the envenomation, the patient experiences fever, chills, myalgias, and arthralgias. In severe systemic reactions, the patient may suffer coagulopathies, hypotension, jaundice, disseminated intravascular coagulation (DIC), seizures, renal failure, and hemolytic anemia.^{33,34} In rare cases, a patient may succumb to the systemic reaction.²⁷

Hobo Spider

The Hobo spider (*Eratigena agrestis*, formerly *Tegenaria*), also known as the aggressive house spider, is found in the Pacific Northwest region of the United States and Canada.³⁵ This spider was traditionally included with *Loxosceles* species when discussing cases of necrotic arachnidism; however, recent studies are calling this into question.³⁵ Similar symptoms lead many to incorrectly attribute hobo spider bites to that of the brown recluse, which is less indigenous to the northwest United States. This species is more aggressive and bites with minor provocation.³⁶ Hobo spiders are brown with gray markings and have a herringbone pattern on the abdomen (Fig. 3).



Fig. 3. Hobo spider (*E. agrestis*). (From Whitney Cranshaw, Colorado State University, Bugwood.org.)

Pharmacologic treatment options

The management of envenomation by the brown recluse or hobo spider depends on whether the reaction is local or systemic. It is difficult to predict which type of wound will eventually progress to a disfiguring necrotic ulcer. Tetanus immunization should be updated, but antibiotics are only indicated if there is a secondary wound infection. Antihistamines and analgesics can be beneficial. Many treatment modalities, including dapsone, triamcinolone, diphenhydramine, colchicine, and trypsin, have been studied, but none have prevented the formation of an ulcerative lesion.³⁷

Nonpharmacologic treatment options

Proper care includes wound cleansing, immobilization, and elevation of the affected extremity to reduce pain and swelling. Early application of ice to the bite area will lessen the local wound reaction, whereas heat will exacerbate the symptoms. A suggested method of treating expanding wound necrosis due to brown recluse spider bites is hyperbaric oxygen treatment. However, results with such treatment have been mixed, and little evidence exists to support its use.^{27,38}

Combination therapies

Although not proven in clinical trials, glucocorticoids may provide a protective effect on the red blood cell (RBC) membrane, thus slowing hemolysis. The patient should be monitored in a hospital setting for the development of DIC. Transfusion of RBCs and platelets may be necessary. Plasma exchange for refractory hemolysis has been recently described following brown recluse spider envenomation.³³ Urine alkalization with bicarbonate may lessen renal damage if the patient is experiencing acute hemolysis.

There continues to be ongoing research with brown recluse antivenom.³⁹ However, there is little evidence to support its efficacy, particularly against local dermatologic effects.⁴⁰ Institutions in Mexico and Brazil currently produce antivenom for *Loxosceles* bites, but the product is not commercially available in the United States.

Surgical treatment options

Early excision of ulcers is not recommended because wound healing is slowed and scarring is more severe if excised early in the clinical course. Complications of early surgical intervention include recurrent wound breakdown as well as long-term distal extremity dysfunction. Delayed excision of ulcers after the necrotic process has subsided (usually within 6–8 weeks), followed by secondary closure with skin grafting, is the preferred method of managing necrotic ulcers. In a normal host with appropriate wound care, most bite wounds heal well with only 10% occurrence of major scarring. Immunocompromised patients and those with diabetes mellitus often have a more prolonged and complicated healing process.

Treatment resistance/complications

Historically, the use of the polymorphonuclear leukocyte inhibitor, dapsone, was advocated to diminish scarring and subsequent surgical complications. Its use, however, has not proven effective in any large study with human or animal models.³⁸ Because of the potential for dapsone to induce methemoglobinemia and hemolytic anemia, particularly in children and those patients with glucose-6-phosphate dehydrogenase deficiency, administration is not advised.

Evaluation of outcome and long-term recommendations

Patients who are asymptotic following a period of observation in the emergency department (ED) and have normal baseline laboratory values may be discharged home with close outpatient follow-up for wound care within 24 to 48 hours. Systemic

effects of brown recluse spider bites are rare but can be life threatening, and the patient should be evacuated if in a remote setting.

Tarantulas

Introduction

Tarantulas are feared because they are the largest of all spiders (**Fig. 4**). They inhabit the deserts of the western United States and Mexico, but have been discovered as far east as the Mississippi River Valley. These large, hairy spiders are relatively harmless. They are extremely shy and bite only when vigorously provoked or roughly handled.

Patient evaluation overview

Tarantula bites usually cause minimal pain and surrounding edema with minimal necrosis and no serious systemic effects. Although tarantula bites are usually of little consequence to humans, they can be more severe in domestic animals, especially canines. The growing trade of these arachnids as exotic pets should prompt the clinician to inquire about this as a possible cause an unusual skin lesion.⁴¹

Pharmacologic treatment options

Tetanus prophylaxis should be updated, and nonsteroidal anti-inflammatory agents can be given to alleviate pain. If needed, the patient is treated with antihistamines and topical glucocorticoids.

Nonpharmacologic treatment options

Treatment of bites consists of local wound care, and involved limbs should be raised and immobilized.

Treatment resistance/complications

Exposure to the hairs on the abdomen of the tarantula is more concerning than the actual bite. These hairs can be flicked off in large numbers as a defense mechanism and are capable of producing urticaria and pruritus that may persist for several weeks. The hairs may also get into the eyes and cause keratoconjunctivitis or ophthalmia nodosa, a nodular, granulomatous lesion in the cornea.^{42,43} Patients with these complaints after exposure to a tarantula should be referred to an ophthalmologist. Without appropriate care, these eye lesions may progress to keratitis, uveitis, retinitis, and orbital cellulitis.



Fig. 4. Mexican red-kneed tarantula, Mexican red-kneed birdeater, female (*Brachypelma smithi*). (Photo by: George Chernilevsky, Vinnytsya, Ukraine.)

SCORPIONS

Introduction

Scorpion stings can cause significant morbidity and mortality.⁴⁰ Scorpions are arachnids that resemble crustaceans and are among the oldest terrestrial animals. Worldwide, about 2 billion people are at risk for scorpion envenomation, with over one million stings and thousands of deaths annually.⁴⁴ In North America, scorpion deaths only accounted for 0.3% of the venomous and nonvenomous animal deaths reported to the Centers for Disease Control and Prevention in the last decade.⁴⁵ Nevertheless, they remain a public health concern throughout the South and southwest United States and among outdoor enthusiasts camping and hiking in desert regions.

The scorpion has a pair of anterior legs with pinchers, a long mobile tail equipped with venom glands and a stinger, known as the telson (**Fig. 5**). Although members of the genera *Hadrurus*, *Vejovis*, and *Uroctonus* are capable of inflicting painful wounds, only the southwestern desert scorpion (*Centruroides exilicauda*, formerly *Centruroides sculpturatus*) poses a serious health threat in the United States. They are called bark scorpions because they cling to the bottom of fallen brush and trees. They are tan-brown in color, vary in length from 1 to 6 cm, and are most active at night. The chitin shell of this scorpion will fluoresce under an ultraviolet or Wood's lamp, aiding in rapid identification (**Fig. 6**). *Centruroides* venoms are neurotoxic, causing repetitive firing of axons by activation of sodium channels. This activation causes spontaneous depolarization of both the sympathetic and the parasympathetic nervous systems.

Patient Evaluation Overview

Unless the scorpion is identified, the diagnosis is based on clinical symptoms. Most victims will have localized tenderness, with an increased sensitivity to touch over the area of the sting, exacerbated by tapping on the area. Patients suffering more serious envenomation manifest the venom effects from overstimulation of the sympathetic, parasympathetic, and central nervous systems. Elevation of blood pressure and heart rate typically occurs within an hour of envenomation, and tachydysrhythmias may develop during this time. Pediatric victims are at a greater risk for severe reactions. Disconjugate, "roving" eye movements are common in children, along with other neurologic findings, including muscle fasciculations, weakness, agitation, and



Fig. 5. Bark scorpion, *C exilicauda*. (Photo by: Gail Hampshire, Cradley, Malvern, U.K.)



Fig. 6. Arizona bark scorpion glowing under ultraviolet light. (Photo by: Bryce Alexander.)

opisthotonos. Less common sequelae are severe ataxia, respiratory distress, seizures, and posterior reversible encephalopathy syndrome.⁴⁶

Pharmacologic Treatment Options

Analgesics and tetanus prophylaxis should be administered. Benzodiazepines and opioids are indicated for agitation and muscle spasms. Tachydysrhythmias and hypertension may be treated with β -blockers, such as esmolol or labetalol. Advanced life support and airway control may be required for more severe envenomations.

In the United States, *Centruroides*-specific antivenom, an immune F(ab')₂ equine injection (Anascorp), was recently approved for severe envenomation by the US Food and Drug Administration.⁴⁷ Scorpion antivenom for other species has been produced for clinical use in several other countries. As with all animal-derived antivenoms, both immediate and delayed allergic reactions including serum sickness are possible. In a linked set of prospective trials of an equine F(ab')₂ antivenom, more than 1500 patients were treated with antivenom. There were only 1/500 acute adverse reactions and 1/200 delayed reactions, most of which were mild and did not require hospitalization or ED evaluation.⁴⁸ Although this study demonstrated antivenom can be administered safely, there remains concern that it may not be cost-effective. For this reason, *Centruroides*-specific antivenom (Anascorp *Centruroides* scorpion immune F[ab]₂ equine injection) should be reserved for cases of severe systemic toxicity.⁴⁹

Nonpharmacologic Treatment Options

The treatment of *Centruroides* envenomations is supportive. Cool compresses or ice packs and local wound care are used for the local symptoms and pain.

Evaluation of Outcome and Long-Term Recommendations

Clinical score predicting the need for hospitalization in scorpion stings has been described.⁵⁰ It is recommended that victims with systemic symptoms be observed for 24 hours, and children be admitted to the hospital for monitoring. Most patients with localized pain at the site of the sting can be safely discharged home with adequate pain medications.

HYMENOPTERA

Introduction

The order Hymenoptera includes bees, vespids (hornets and wasps), and fire ants. Bees and vespids cause more than one-fourth of all reported envenomations in the

United States and an estimated 50 annual deaths.⁴⁵ In the United States, 10% of all cases of anaphylaxis are attributed to stinging insects or hymenoptera.⁵¹ Although hymenoptera venoms possess intrinsic toxicity, it is their ability to sensitize the victim and cause subsequent anaphylactic reactions that makes them so potentially lethal.

Bees and Vespids

Honeybees (*Apis mellifera*) are insects with alternating black and yellow body stripes. The female honeybee's stinger is a modified ovipositor that is connected to a venom sac. Because honeybees lose their barbed stinger after stinging and die, they generally only sting in defense when provoked or stepped on. Their venom causes a much greater release of histamine per gram than does other hymenoptera venom and thus is potentially more dangerous.

Africanized honeybees, or "killer bees" (*Apis mellifera scutellata*) (Fig. 7), are now found in Texas, Arizona, California, and most of the temperate southern states.⁵² In the 1950s, African bees were imported into Brazil for breeding experiments designed to improve honey production and disease resistance. Many escaped and subsequently mated with other imported European honeybees.⁵³ These hybrids have since migrated northward along the coasts and temperate regions of the continent. Although the toxicity of their venom is equal to that of their native counterpart, they are far more aggressive. A hive can respond to a perceived threat with more than 10 times the number of bees within seconds. When the ovipositor is pulled from the bee's abdomen after stinging a victim, it releases a pheromone, isoamyl acetate. This pheromone attracts other bees to the victim and incites multiple stings. Massive numbers of stings from an attack of Africanized bees can result in multisystem damage and death from severe venom toxicity. Acute tubular necrosis and renal involvement with myoglobinuria are well-known complications of massive envenomation.⁵⁴ In swarms, these bees can overwhelm and kill even healthy nonallergic victims.⁵⁵ Envenomation from these aggressive arthropods has become a public health issue and is most dangerous to very young or elderly patients and those with concomitant medical conditions.⁵⁶

The most common hornets in the United States are the yellow jackets (*Vespa pennsylvanica*). They are usually seen around garbage cans, beverage containers, and various foods. They are aggressive and sting with little provocation. Wasps (*Polistes annularis*, the paper wasp) have thin, smooth bodies and a formidable sting. They build



Fig. 7. Adult African killer bee, *A mellifera scutellata*. (From Jeffrey W. Lotz, Florida Department of Agriculture and Consumer Services, Bugwood.org.)

their nests in the eaves of buildings. Unlike honeybees, these vespids are carnivorous and able to use their smooth unbarbed stingers multiple times.^{57,58}

Hymenoptera venoms contain enzymes (phospholipase A and hyaluronidase) that directly affect vascular tone and permeability. Most of the toxicity of the venom results from bradykinin, acetylcholine, dopamine, histamine, and serotonin. Although their enzymes are similar, there is little immunologic cross-reactivity between bee and vespid venoms. Although a bee sting may not sensitize a person to yellow jacket venom, a yellow jacket sting is more likely to sensitize one to wasp venom.⁵⁹

Patient evaluation overview

Four possible reactions are seen after hymenoptera stings: a local reaction, toxic reaction, systemic anaphylaxis, and a less common delayed-type hypersensitivity reaction.^{36,60}

Local reactions

Local reactions are the most common reactions resulting from the vasoactive effects of the venom and are generally mild. The most common response includes pain, erythema, edema, and pruritus at the sting site. Local reactions occurring in the mouth or throat can produce swelling that may compromise and lead to upper airway obstruction.

Toxic reactions

Toxic reactions may occur when a patient suffers from multiple stings. Africanized bees are notorious for such attacks, but an aggressive native hive may elicit a similar response. The essential lethal dose is approximately 20 stings per kilogram in most mammals.⁵⁷ Symptoms of a toxic reaction may resemble anaphylaxis, but gastrointestinal manifestations (vomiting and diarrhea) and sensations of light-headedness and syncope may also occur. Headache, fever, drowsiness, involuntary muscle spasms, edema (without urticarial), and seizures may ensue. Although urticaria and bronchospasm are not always present, severe envenomations may lead to respiratory arrest. Hepatic failure, rhabdomyolysis, coagulopathies, and DIC have been reported in victims. In addition, myocardial infarctions, cerebrovascular accidents, and intracranial bleeds have been described.⁶¹ Toxic reactions are thought to occur from a direct multisystem effect of the venom.

Anaphylactic reactions

Anaphylactic reactions are generalized systemic allergic reactions that may occur after envenomation. They are thought to occur from an immunoglobulin E-mediated mechanism, leading to the release of pharmacologically active mediators within mast cells and basophils. Symptoms are initially mild, but severe reactions can lead to death within minutes. Unlike the toxic reaction, there is no correlation between systemic allergic reactions and the number of stings. Most allergic reactions occur within the first 10 to 15 minutes and nearly all occur within 6 hours. Fatalities that occur within the first hour of the sting usually result from airway obstruction or anaphylactic shock. Initial symptoms typically consist of ocular pruritus, facial flushing, and generalized urticaria. Symptoms may intensify rapidly with chest or throat constriction, wheezing, dyspnea, abdominal cramping, diarrhea, vomiting, vertigo, fever, laryngeal stridor, and syncope.

Delayed reactions

Delayed reactions, appearing 1 to 2 weeks after a sting consist of serum sickness-like signs and symptoms of fever, malaise, headache, urticaria, lymphadenopathy, and polyarthritis. This reaction is thought to be immune complex mediated.⁶⁰

Pharmacologic treatment options

With more severe local reactions, there is a more sustained inflammatory response, and the swelling may spread to the entire extremity and persist for several days. A short course of antihistamines and prednisone (1 mg/kg/d for 5 days) may decrease the duration of symptoms. Systemic reactions occur in approximately 1% of hymenoptera stings. No specific antivenom currently exists for Hymenoptera stings. In all but the mildest of systemic reactions, the mainstay of treatment is epinephrine (Table 1). Epinephrine counteracts the bronchospastic and vasodilatory effects of histamine. Epinephrine can be given as an intramuscular injection (0.01 mL/kg of 1:1000 solution; not to exceed 0.3 mL). In more severe life-threatening reactions, the intravenous or endotracheal route is preferred (0.1 mL/kg of 1:10,000 solution). The dose may be repeated at 15-minute intervals as needed. Early intubation is indicated if there is evidence of severe laryngeal edema or stridor because airway obstruction is the leading cause of death in anaphylaxis. Antihistamines are given early, but not as a substitute for epinephrine. An H₂-receptor blocker (eg, famotidine or ranitidine), in addition to an H₁-receptor blocker (diphenhydramine), may aid in inhibiting the vasodilatory effects of histamine. Adjunctive therapy for bronchospasm includes inhaled β₂-agonists (eg, albuterol). When hypotension ensues, isotonic fluid resuscitation and pressor agents are instituted.

A biphasic allergic reaction can occur in up to 20% of patients. A general rule is that urticaria plus involvement of any other organ system constitutes anaphylaxis.⁶² A delayed serum sickness-like reaction may appear 10 to 14 days following the initial sting. This immune complex disorder may be treated with a short course of prednisone.

Nonpharmacologic treatment options

If present, the embedded stinger should be removed manually. Previous sources recommended cautiously scraping the stinger off with lateral pressure, rather than grasping it, to avoid compression of the venom sac resulting in further venom release. Recent studies have demonstrated that this is erroneous because the venom has likely been completely released within seconds of envenomation.⁶³ Treatment is symptomatic, with ice or cold compresses.

Combinations therapies

An emergency insect sting kit generally contains a tourniquet, epinephrine in a 1:1000 dilution, and an antihistamine. These kits are widely available, and susceptible patients should carry them whenever they venture into the wilderness or remote settings.

Treatment resistance/complications

Most serious reactions to bee stings occur in the first 30 to 60 minutes. The local effects of a sting may persist for 2 or 3 days, or even weeks if there is a retained stinger. Delayed hypersensitivity may occur 7 to 10 days after the sting.⁶²

Table 1 Hymenoptera sting treatment	
Medication	Dose
Glucocorticoids	Methylprednisolone 125 mg intravenously (IV)
Antihistamine	Diphenhydramine: 25–50 mg IV or orally (PO)
Epinephrine	0.01 mL/kg of 1:1000 solution, do not exceed 0.3 mL intramuscularly
H2 blocker	Famotidine: 20 mg IV/PO Ranitidine: 50 mg IV/PO
Albuterol	2.5–5 mg every 20 min for 3 doses as needed

Evaluation of outcome and long-term recommendations

Essential to the treatment of any systemic reaction is the prevention of future reactions. Patients who have had a systemic reaction should be instructed to wear protective clothing and avoid hymenoptera-infested habitats. Portable epinephrine kits (Epi-Pen and Epi-Pen Jr) are available. They should be prescribed before the patient leaves the ED. The patient should be urged to carry the kit at all times when in the wilderness setting and to use epinephrine for any systemic symptoms. Even if symptoms are mild, the patient should seek emergency care. The patient should also be instructed to wear a medical alert tag.

Referral to an allergist is indicated for any patient who has experienced life-threatening respiratory symptoms or hypotension. Venom immunotherapy desensitization is very effective in preventing further systemic reactions, with 95% to 100% protection after 3 months of treatment. Victims who have only urticaria or angioedema do not require venom immunotherapy. Only 10% of these patients will have systemic reactions with subsequent stings.⁶³

FIRE ANTS

Introduction

Five known species of fire ants belonging to the family Formicidae and genus *Solenopsis* are found in North America. Two of the species were imported into the United States, the red fire ant (*Solenopsis invicta*) and the black fire ant (*Solenopsis richteri*), of which *S invicta* is the predominant species and responsible for 95% of clinical cases (Fig. 8). They were imported aboard ships from Brazil in the 1940s and introduced in



Fig. 8. Fire ants (*S invicta*). (From United States Department of Agriculture Agricultural Research Service, Image Number K5388-1. Photo by Scott Bauer.)

Alabama. They subsequently spread throughout the Southeast and are presently found in 13 southern states, from Florida to Texas. Their geographic range is limited by soil, temperature, and moisture.⁶⁴

S invicta are 2 to 5 mm in size and red in color. They live in colonies and build large mounds up to 3 ft in diameter, which are interconnected by underground tunnels up to 100 ft long. These mounds are found most commonly in yards, parks, and open fields.⁶⁵ Fire ants are aggressive insects with no natural enemies and tend to attack in swarms, with multiple stings. In endemic areas, nearly 50% of the exposed population is stung each year. Stings occur most frequently on the ankles and feet during the summer months. Fire ants sting in a 2-phase process. The ant first bites the victim with powerful mandibles, then, if undisturbed, will arch the body and swivel around the attached mandibles to sting the victim repeatedly with the stinger or ovipositor. The sting sites produce a characteristic circular pattern of papules around 2 central punctures. Fierce fire ant attacks ensue in response to an alarming pheromone released by an individual or group of ants.

Bee and wasp venoms are made of proteins. Conversely, fire ant venoms are 95% alkaloid,⁵⁷ and the remaining 5% is very immunogenic, which can sensitize a victim to the venom. This sensitization creates a risk for future anaphylaxis, and 10% of victims have some degree of hypersensitivity.⁶⁶ The venoms have cytotoxic, bactericidal, insecticidal, and hemolytic properties. They also activate the complement pathway and promote histamine release.

Patient Evaluation Overview

Clinical manifestations reflect the venom's effects and are predominantly dermatologic reactions. The initial bites and stings cause a sharp burning pain associated with circular wheals or papules around the central hemorrhagic punctures. The wheal-and-flare reactions resolve within 1 hour, but then develop into sterile pustules within 24 hours. The pustules slough off over 48 to 72 hours, leaving shallow ulcerated lesions. The pustules are pruritic and often become contaminated after the victim scratches the lesions. Secondary infections may ensue but are usually minor. Approximately 25% of victims develop more severe local reactions, characterized by an exaggerated wheal-and-flare response, followed by the development of erythema, edema, and induration greater than 5 cm in diameter. These lesions are intensely pruritic, may resemble cellulitis, and persist for 24 to 72 hours.⁶⁵

Pharmacologic Treatment Options

Topical glucocorticoid ointments, local anesthetic creams, and oral antihistamines are useful for the itching associated with these reactions. No intervention has been shown to prevent or resolve the pustules. Prophylactic antibiotics are generally not indicated.

Nonpharmacologic Treatment Options

Treatment consists of local conservative measures including application of ice or cool compresses for symptomatic relief and gentle, frequent cleansing of the affected areas to prevent secondary infections.

Combination therapies

Immunotherapy may be appropriate for persons with severe hypersensitivity to fire ant venom or those who have had a previous anaphylactic reaction to a fire ant sting. The efficacy of immunotherapy has been variable, but it has been reported to provide protection as high as 98%.^{64,67}

Treatment resistance/complications

Anaphylactic reactions have been estimated to occur after as many as 1% of fire ant stings. Anaphylaxis may occur several hours after a sting and is known to occur more frequently in children than in adults. Those victims demonstrating severe allergic reactions should be referred for more comprehensive allergy skin testing.

Ticks

Ticks, which also belong to the class Arachnida, are vectors of human disease. With the recent changes in climate and global warming, they are increasing their North American distribution. Although less feared than spiders, they cause a higher morbidity because of transmission of infectious disease such as Rocky Mountain spotted fever. The bite of a tick is usually painless, but the victim may later have neurologic manifestations, including difficulties walking, weakness, flaccid paralysis, slurred speech, and visual disturbances. The victim usually has a history of recent outdoor activity. Two species responsible in North America are *Dermacentor andersoni* (wood tick) and *Dermacentor variabilis* (dog tick). The blacklegged tick (*Ixodes scapularis*) (Fig. 9) transmits *Borrelia burgdorferi* known to cause Lyme disease. Patients with a dermatologic “target lesion” or erythema migrans following a tick bite should be evaluated for Lyme disease (Fig. 10). These patients are treated with doxycycline or (other appropriate antibiotics if allergic) to prevent delayed neurologic and cardiotoxic manifestations. Investigations are ongoing with vaccine in development for Lyme disease.⁶⁸

Centipedes, millipedes, and caterpillars

Several species of caterpillars (order Lepidoptera) as well as centipedes and millipedes (class Myriapoda) secrete substances that cause severe burning pain, numbness, pustular dermatitis, edema, vomiting, and headache.⁶⁹ Oropharyngeal exposure can cause mucosal edema and irritations. Centipedes are generally considered more venomous than millipedes. A recent case report describes a case of erucism and renal failure following *Lonomia* caterpillar envenomation.⁷⁰



Fig. 9. The blacklegged tick (*I. scapularis*), the primary vector for Lyme disease in the central and eastern United States. (From Gross L. A new view on Lyme disease: rodents hold the key to annual risk. PLoS Biol 2006;4(6):e182.)



Fig. 10. *Erythema migrans* in Lyme disease depicting the pathognomonic erythematous rash in pattern of a “bull’s eye” lesion. (Courtesy of CDC/James Gathany; and James Gathany.)

Pharmacologic Treatment Options

Centipedes can inflict bites that cause erythema and edema. Treatment is usually local soaks and analgesics. Analgesics should be used as needed, and more supportive therapy may be needed for severe envenomation.

Nonpharmacologic Treatment Options

Treatment consists of washing the area thoroughly with soap and water and removing any spines or hairs present. Spines of caterpillars can be removed with adhesive tape or by applying white water-soluble glue. Locally applied ice packs, a paste of baking soda paste, or topical lidocaine⁷¹ may be beneficial.

OTHER ARTHROPODS

Many other arthropods such as beetles (order Coleoptera) can cause local skin reactions and allergic reactions, depending on the individual’s sensitivity. Patients are treated symptomatically with local steroid creams and antihistamines. Conenose bugs or “kissing bugs” may cause severe local and systemic allergic reactions and have recently reached epidemic numbers in North America⁷² (**Fig. 11**). Treatment with antihistamines and local wound care, depending on the degree of reaction, are generally all that is needed.



Fig. 11. Three species of kissing bugs: *Triatoma protracta*, the most common species in the western United States; *Triatoma gerackeri*, the most common in Texas; *Triatoma sanguisuga*, most common in the eastern United States. (From Curtis-Robles R, Wozniak EJ, Auckland LD, et al. Combining public health education and disease ecology research: using citizen science to assess Chagas disease entomological risk in Texas. PLoS Negl Trop Dis 2015;9:e0004235.)

Mosquitoes (class Insecta, family Culicidae), although technically not considered venomous arthropods, are abundant and annoying throughout North America. They can be dangerous vectors for diseases such as malaria, dengue fever, Chikungunya, and Zika virus in tropical regions of Africa, Asia, and South and Central America. Recently, Zika virus has been reported in North America in persons traveling from Brazil and the Caribbean.^{73,74} Mosquitoes responsible for the transmission of Zika virus include *Aedes albopictus* and *Aedes aegypti* (Fig. 12).

Protection and Prevention

Protection from arthropod bites is best achieved by avoiding infested areas, wearing protective clothing, and using insect repellents. Insect repellents containing *N,N*-diethyl-meta-toluamide (DEET) are the most effective products on the market, providing broad-spectrum repellency lasting several hours. DEET's peak duration of action plateaus at a concentration of 50%, with no added benefit from products containing higher concentrations.⁷⁵ Topical insect repellents (often combined with sunscreen products) generally do not provide complete protection. However, products containing ethyl butylacetylaminopropionate can provide protection for up to 3 hours and can be safely added to sunscreen lotions without potential side effects.⁷⁶ Mosquitoes bite untreated skin and may even bite through clothing. Deerflies, midges, black flies, and ticks prefer to bite around the head and will crawl into the hair to bite unprotected areas. Wearing protective clothing with long sleeves and pants, including a hat, reduces the chance of being bitten. Treating clothes and hats with permethrin in addition to spraying with DEET on the skin offers the greatest protection. Mesh insect tents or bedding provides additional lines of defense. Finally, avoiding hikes or outdoor activities at dawn or dusk can diminish arthropod encounters.



Fig. 12. *A. aegypti* mosquito, biting a human. (From US Department of Agriculture Agricultural Research Service, Image Number K4705-9.)

Outdoor enthusiasts traveling throughout the wilderness or to a part of the world where insect-borne disease is a potential threat should educate themselves concerning indigenous arthropods as well as the toxicities and diseases they may transmit.

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