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THE GLOBAL EPIDEMIOLOGY, SYNDROMIC CLASSIFICATION, MANAGEMENT, AND PREVENTION OF SPIDER BITES

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Abstract. Spiders are carnivorous arthropods that coexist with humans and ambush or ensnare prey. Unlike other arthropods, spiders rarely transmit communicable diseases, and play a critical role in the ecosystem by consuming other arthropods that frequently transmit human diseases, such as mosquitoes and flies. There are more than 30,000 species of spiders, most of which are venomous, but they cannot inflict serious bites due to delicate mouthparts and short fangs. The differential diagnosis of spider bites is extensive and includes other arthropod bites, skin infections, and exposure to chemical or physical agents. However, approximately 200 species from 20 genera of spiders worldwide can cause severe human envenomings, with dermonecrosis, systemic toxicity, and death. Spider bites can usually be prevented by simple personal and domestic measures. Early species identification and specific management may help prevent serious sequelae of spider bites.

INTRODUCTION

The largest phylum in the animal kingdom is the phylum *Arthropoda*, including more than a million insects classified, and half a million or more insects yet to be classified.[1] Most arthropods are benign and beneficial plant pollinators, but others, such as mosquitoes, flies, and ticks, can transmit serious human diseases. Although spider bites may be secondarily infected by soil- or water-dwelling (*Clostridium* spp., *Mycobacterium* spp.) or human skin-dwelling (*Staphylococcus aureus*) microorganisms, spiders do not often transmit communicable diseases.

Many spiders produce toxic venoms that can cause skin lesions, systemic illnesses, neurotoxicity, and death. Although the collective term "arachnidism" is often used to refer to envenoming spider bites, arachnidism also includes bites by other arachnids, such as scorpions. The preferred collective term for envenoming spider bites is "araneism," with spider bites further stratified by systemic manifestations, such as necrotic araneism (for *Loxosceles* and *Cheiracanthium* bites) or latrodectism (for *Latrodectus* species or widow bites).[2] Necrotic araneism is characterized by dermonecrotic ulceration at spider bite sites due to combinations of cytotoxicity from venom components and autoimmune responses from lymphocytes and cytokines.

MATERIALS AND METHODS

A 30-year MEDLINE search of the world's salient scientific literature of case reports, case series, and reviews was conducted to determine the frequency of venomous spider bites, the confirmation of definite spider bites, and the expert identification of spiders inflicting venomous bites. In addition, a global distribution and syndromic classification of venomous spiders was developed, and the pathophysiology, clinical management, and prevention of spider bites were described. The pathophysiologic manifestations of envenoming spider bites were classified into six distinct clinical syndromes: 1) latrodectism and family-related steatodism, 2) loxoscelism, 3) non-*Loxosceles* necrotic araneism, 4) funnel-web neurotoxicity, 5) phoneutrism, and 6) allergic and foreign body araneism.

Although spider bite–induced systemic illnesses have not been previously classified by syndrome, these six clinical syndromes are all individually supported by case reports and series. Specific supporting references are cited in the descriptions of each syndrome. Although steatodism is the most recent spider bite syndrome described, *Steatoda* spiders, like *Latrodectus* spiders, are members of the family Theridiidae, and inflict painful bites with systemic effects similar to, yet milder than, *Latrodectus* bites. Steatodism was therefore considered a variant of latrodectism. Although necrotic araneism has been most commonly associated with *Loxosceles* bites, it may also follow bites by several other species, including *Cheiracanthium*, *Argiope*, *Badumna*, *Lampona*, *Lycosa*, *Sicarius*, and possibly *Tegenaria agrestis*. Necrotic araneism was therefore logically separated into *Loxosceles* and non-*Loxosceles* induced syndromes of necrotic araneism. Funnel-web neurotoxicity has been well established by Australian investigators, and phoneutrism has long been recognized as a distinct entity by Brazilian investigators. Finally, the last distinct clinical syndrome, allergic and foreign body araneism, included not only the well recognized dermatitis and *ophthalmia nodosa* caused by dermal or ocular-embedded therapsid hairs, but also the allergic manifestations induced by inhalation of urticating hairs and by conjunctival contact with squashed spider contents from several venomous species.

RESULTS

Spider anatomy, feeding behavior, venom delivery, and taxonomy. Unlike insects, spiders have four pairs of legs; paired pedipalps, often mistaken for legs, and used to differentiate sex (males have larger pedipalps specialized for sperm packet transfer); a cephalothorax with multiple, often paired dorsal eyes; delicate connecting pedicles; and unsegmented abdomens with ventral silk glands and paired spinnerets. Spiders are predaceous feeders, subsisting on the predigested body juices of their prey, previously subdued by their venoms. The spider venom-delivery apparatus includes paired chelicerae or jaws suspended from the anterior end of the cephalothorax, paired hollow fangs hinged onto the distal tips of stubby chelicerae, and paired venom glands serving each fang and housed within the chelicerae and cephalothorax. When spiders feed, their fangs are folded into grooves on the distal chelicerae. The sharp edges of the paired chelicerae and maxillae then cut, crush, and chew the prey; digestive enzymes

secreted by maxillary glands bathe the prey; and the feeding appendages present predigested prey to the mouth for aspiration into the stomach. Since spiders predigest their prey over hours and cannot consume intact insect exoskeletons, undigested remains often adorn spider webs or burrows or get woven into egg sacs.

Spiders are simply classified into two major suborders based on whether their fangs, operate in parallel requiring a snakelike strike (Mygalomorphae), or open side-to-side in an opposing manner (Aranaeomorphae), like most insects. The mygalomorph spiders or mygales include the highly venomous Australian funnel-web spiders and the docile, long-lived tarantulas, frequently sold as pets worldwide. The aranaeomorph spiders are considered true spiders, are more widely distributed than mygalomorphs, and also include venomous families, such as widow spiders, brown recluse spiders, and running or sac spiders.

Spider ecology. There are more than 30,000 species of spiders, all of which are venomous, with the exception of the family Uloboridae.[2] Like the majority of arthropods, many spiders cannot inflict serious human bites because of their small size, delicate chelicerae, short fangs, and venoms designed to stun web-ensnared insects. In addition, many spiders produce venomous toxins that are specific for receptors in preferred, usually invertebrate, prey. Nevertheless, most spider species have not had their venoms tested for animal or human toxicity.

Spider venoms are composed of complex proteins and proteolytic enzymes that are either designed to initiate digestion of prey entrapped by web-spinners or to incapacitate prey ambushed by hunting spiders. In general, hunting spiders, such as brown recluse spiders (*Loxosceles* spp.), funnel-web spiders (*Atrax* and *Hadronyche* spp.), and South American armed spiders (*Phoneutria* spp.) have more potent venoms than web-spinners, with the notable exception of widow spiders (*Latrodectus* spp.). Some species of spiders, notably tarantulas, can use their hind legs to launch urticating hairs from their dorsal abdomens to irritate the skin, eyes, and mucous membranes of pursuing attackers. Finally, some species of spiders are ubiquitously distributed globally, such as *Latrodectus* or widow spiders, whereas other spiders have regional distributions, such as Sydney funnel-web spiders (*Atrax robustus*), which live within the Sydney metropolitan area and along the southeastern Australian seaboard.

The epidemiology of spider bites. The epidemiologic analysis of spider bites is confounded by several factors including the extensive differential diagnosis of dermal bite-like lesions, suspected versus definite spider bites, and precise identification of biting spiders by arachnologists.[3] To date, most studies of spider bites have been retrospective, bites have not been confirmed by eyewitnesses, and spiders have not been kept alive for identification, or identified incorrectly.[3] Only prospective studies of definitely confirmed spider bites with expert identification of the envenoming species will contribute to the development of evidence-based methods to precisely describe venomous spiders and the outcomes of their bites.[3]

There are no national or international registries for spider bites, but the American Association of Poison Control Centers (AAPCC), the Australian Poison Information Center (PIC), and several academic health centers in Australia and South America (Brazil and Chile) do report annual or periodic descriptive data on spider bites. In 1994, the AAPCC recorded 9,418 possible spider bite telephone calls, but a disproportionate number of suspected bites (1,027, [10.9%]) were reported from the Pacific northwest region of the United States, which comprises only 4% of the U.S. population.[4] In addition, more spider bites from the Pacific northwest (781, [76.1%]) were inflicted by unidentified species, as compared with the rest of the United States, where only 57.1% of the spider bites were inflicted by unidentified species, and 42% of the bites were caused by *Latrodectus* or *Loxosceles* spiders.[4] This discrepancy in AAPCC-reported spider bites ultimately prompted the U.S. Centers for Disease Control and Prevention (CDC) to initiate a search for an unidentified species of venomous spider in the Pacific northwest.[4,5]

In a retrospective analysis of spider bites in the Pacific northwest (1988–1995), the CDC subsequently reported that a non-native species, *Tegenaria agrestis*, the hobo spider, which was introduced into the area from western Europe in the 1930s, was possibly responsible for an increasing number of unidentified spider bites with extensive dermal necrosis and permanent scarring.[5] Nevertheless, *T. agrestis* has never been conclusively identified as the cause of necrotic araneism in the Pacific northwest of the United States because the CDC report was based on retrospective telephone reports of suspected bites without expert identification of biting spiders.

In a prospective analysis of 1,474 suspected spider bites in Australia over a 27-month period, Isbister and Gray reported that 539 were witnessed as definite bites, but the investigators never received the spiders for identification, and that 750 bites were confirmed by eyewitnesses, with biting spiders later identified by experts.[6] Most (84%) of the severe envenomings were caused by *Latrodectus hasselti* (redback) spiders, and in contrast to the reports from the United states, there was no evidence of necrotic araneism in the Australian experience.[6]

In a retrospective analysis of 1,348 suspected spider bites in Chile over a 40-year period, Schenone reported that 16.6% of the dermonecrotic lesions were caused by *Loxosceles* spiders, 28.1% were due to other arthropod bites or stings, 44.2% were due to infectious etiologies, and 11.1% of the lesions were caused by various chemical or physical exposures.[7] In another South American retrospective study of 515 wolf spider (family Lycosidae) bites in Sao Paolo, Brazil over a five-year period, Ribeiro and others reported that wolf spider bites occurred in all age groups, were more frequent in males (56%), occurred mostly on the hands and feet (79%), and caused mild pain without local necrosis.[8] These investigators concluded that most wolf spider bites were mild, very few ($n = 3$) required antivenom therapy, and that previous wolf spider bites with local necrosis were probably misdiagnosed *Loxosceles* bites.[8] In a retrospective analysis of 91 definite mygalomorph spider bites in Sao Paulo from 1966 to 1991, Lucas and others reported that envenoming by South American mygalomorph spiders, in contrast to Australian mygalomorph bites, were usually mild and represented less than 1% of all spider bites reported during the study period.[9]

The anatomic location of spider bites appears to be far more dependent on the activity of human victims at the time of bites, rather than on the biting spiders' preferred habitats or feeding habits.[10] In a prospective analysis of Australian

sparassid (huntsmen spiders) and *Lampona* (white-tail spiders) bites, Isbister and others reported that huntsmen spiders usually inflicted distal extremity bites when disturbed (86%) or handled, and that white-tail spiders inflicted distal bites (25%) when victims were sleeping, dressing, or drying off after bathing.[10,11] These investigators concluded that huntsmen and white-tail spider bites caused minor effects with initially painful bite wounds with no local necrosis or major systemic toxicity.[10,11]

The differential diagnosis of spider bites. In the study of Schenone in Chile, only 16.6% of local dermonecrotic lesions were caused by *Loxosceles* bites.[7] The differential diagnosis of necrotic araneism, often ascribed to *Loxosceles* spider bites, is extensive. Vetter and Bush have emphasized repeatedly that the diagnosis of brown recluse (*Loxosceles reclusa*) bites is frequently overused for dermonecrotic lesions of uncertain etiology, especially in locations in the United States where the spider is not even endemic.[12,13] In a retrospective analysis of suspected brown recluse bites in four western American states over a 41-month period, Vetter and others collected 216 diagnoses of brown recluse spider bites, but could only confirm 35 brown recluse or Mediterranean recluse sightings in those same four states over the study period.[14]

Antivenom therapy in araneism. The most important groups of envenoming spiders causing the greatest adult morbidity and pediatric mortality include the widely distributed widow (*Latrodectus* spp.) and recluse (*Loxosceles* spp.) spiders and two spiders confined to single countries: the Australian funnel-web spiders (*Atrax* spp. and *Hadronyche* spp.) and the Brazilian armed spider (*Phoneutria* spp.). Although antivenom use has reduced pediatric mortality from spider bites, antivenoms are often withheld, underused, administered too late, or reserved for the most severe envenomings. With the exception of *Loxosceles* antivenom, effective antivenoms are now available for the remaining highly venomous spiders including four widow antivenoms, Sydney funnel-web antivenom, and armed spider antivenom. In addition, all of these antivenoms demonstrate excellent antigenic cross-reactivity among different spider species of the same genera or related families and have a low incidence of side effects, excluding serum sickness. Although *Phoneutria* antivenom is rarely indicated for armed, mygalomorph spider bites in Brazil, Sydney funnel-web antivenom has been effectively administered for *Atrax* spp. and *Hadronyche* spp. bites in Australia, and redback spider antivenom has been used effectively for black widow bites in the United States.[15]

DISCUSSION

Species identification, global distribution, syndromic diagnosis, clinical manifestations, and management of definite spider bites. *Latrodectism: Widow spiders (Latrodectus spp.).* *Latrodectus* species spiders live outdoors in dark spaces in temperate and tropical latitudes worldwide, spinning trip web-wires that often trail below their dark crevice retreats. Preferred habitats include brick and rock piles, woodpiles, embankment and wall crevices, crawl spaces, exterior gas and water meters, barns, stables, trash piles, and outhouses. Females are always darker, more venomous, and significantly larger (30–40-mm leg span) than males (16–20-mm leg span), which are quite capable of biting, but rarely inflict severely envenoming bites.[16,17] Most *Latrodectus* females are dark gray to black and exhibit red to orange hourglass or geometric patterns, spots, or stripes on their ventral abdomens. *Latrodectus* spiders are most abundant and active during the warm months of the year. These spiders are naturally nonaggressive, prefer to retreat when threatened, and bite only if handled or trapped.

Latrodectism from *Latrodectus* species bites is caused by a neurotoxic component of *Latrodectus* venom, alpha-latrotoxin, which causes massive presynaptic release of most neurotransmitters including acetylcholine, norepinephrine, dopamine, and glutamate. Following a mildly to severely painful, stinging bite without surrounding inflammation, latrodectism occurs within 30 minutes to a few hours of the spider bite and is characterized by generalized pain, muscle cramps and, rarely, fasciculations. Muscular spasms often begin at the bite site, and spread initially to local lymph nodes, and then to the face and abdomen.[16] Apparently, muscle fasciculations are inconsistent manifestations of latrodectism, and are more common following American black widow bites than after Australian redback spider (*L. hasselti*) bites and South African brown widow bites (*L. geometricus*).[17,18] Lower leg pain with burning feet and lower extremity sweating may occur, even after upper extremity bites.[17] The face may be contorted into grimacing expressions, *facies latrodectismica*, resembling tetanic *risus sardonicus*.[16] The abdomen may become rigid, mimicking the acute abdomen of appendicitis.[16–18] Rarely, thoracic myospasm followed by weakness may result in restrictive hypoventilation and respiratory arrest.[16] Rhabdomyolysis and seizures are uncommon. Associated signs may include arthralgias, bronchorrhea, regional and generalized diaphoresis, fever, hypertension, hyperreflexia, regional lymphadenopathy, nausea, vomiting, paresthesias, priapism, ptosis, restlessness, salivation, and tremor. Latrodectism usually resolves over a 3–7-day period, with few deaths.[16–21]

The notorious *Latrodectus* biters include *L. mactans*, *L. hasselti*, *L. curacaviensis*, *L. geometricus*, *L. hesperus*, *L. indisdinctus*, *L. lugubris*, *L. menavodi*, *L. tredecimguttatus*, and *L. variolus*.[16] Although the clinical picture of latrodectism caused by different *Latrodectus* species is similar, there are unique features that characterize the initial clinical presentation of widow bites in different countries.[16–21]

In a prospective analysis of 68 redback spider (*L. hasselti*) bites in Australia, Isbister and Gray reported pain after all bites, severe pain in 42 cases (62%), prolonged (more than 24 hours) pain in 45 cases (66%), pain-associated insomnia in 22 cases (32%), and systemic effects in 24 cases (35%), notably local or regional diaphoresis in 23 cases (34%).[17] In addition, intramuscular redback spider antivenom therapy appeared relatively ineffective since only one of six patients treated with redback antivenom was pain-free within 24 hours.[17]

In a retrospective study of 45 black (*L. indistinctus*) and brown (*L. geometricus*) bites in South Africa, Muller reported that black widow bites (n = 30) were twice as common and more severe than brown widow bites (n = 15), and were characterized by generalized muscle pain and cramps, abdominal muscle rigidity, profuse sweating, hypertension, and tachycardia.[18] Conversely, brown widow bites were associated with markedly less pain and muscle cramping, always localized to the bite extremity.[18]

In a 10-year (1980–1990) retrospective analysis of latrodectism in Brazil, Lira da Silva and others reported that most (57%) widow bites occurred in cities, affected predominantly men (70%), and were most commonly inflicted by *L. curacaviensis*.[19] The clinical presentation was characterized by limb pain (29%), tremor and rigidity (29%), generalized sweating (28%), distal paresthesias (21%), and abdominal cramping (17%).[19] Although treatment was mainly supportive (67%), 21% of widow bite victims required antivenom therapy, with most patients (64%) being discharged within 24 hours.[19]

In a 10-year (1984–1994) latrodectism study in Spain, Diez Garcia and others reported only 12 confirmed Mediterranean black widow (*L. tredecimguttatus*) bites, most characterized by generalized pain and abdominal rigidity and cramping (n = 10), and local pain (n = 8) and erythema (n = 10) at the bite sites.[20] Laboratory abnormalities were unusual and included leukocytosis (n = 4), elevated levels of creatine kinase (n = 4), and proteinuria (n = 3).[20] *Latrodectus* antivenom therapy was not indicated in any case.[20]

In an American retrospective chart review of 163 black widow bites in Arizona, Clark and others reported that the most common initial manifestations included generalized abdominal, back, and leg pain.[21] The extremities were the most common bite sites.[21] Intravenous calcium gluconate was ineffective for pain relief compared with a combination of intravenous opioids and benzodiazepines, and antivenom as indicated by severity of envenomings.[21,22] Fifty-eight patients received antivenom therapy, with one death from severe bronchospasm.[21] Fifty-two percent of those patients not receiving antivenom therapy required hospitalization, compared with only 12% of those 58 bite victims who received antivenom, all of whom experienced complete resolution of symptoms within one hour.[21] The investigators concluded that although calcium gluconate had been recommended for analgesia in the past, it was ineffective compared with intravenous opioids and benzodiazepines, and that antivenom therapy significantly shortened the duration of symptoms in severe black widow envenomings.[21,22]

The local wound care of *Latrodectus* bites should include thorough wound cleansing, ice pack application, oral or parenteral analgesics, and tetanus prophylaxis. Symptomatic children, pregnant women, and elderly patients with hypertension or coronary artery disease should be hospitalized for observation. Initial laboratory evaluation should include complete blood count, serum glucose and creatine kinase, and urinalysis.

Latrodectus antivenom therapy is indicated for patients manifesting severe regional or systemic latrodectism, or for uncontrolled hypertension, seizures, or respiratory arrest.[21–27] Antivenom, 1–3 vials, diluted in 100–250 mL of 0.45% sodium chloride should be infused intravenously over a 1–2-hour period.[21–23,26,27] Unrefined *Latrodectus* antivenom is often produced in horses exposed to *Latrodectus* bites, and has been associated with serum sickness, anaphylaxis (0.5% in an Australian series[10]), and death.[21,23,26,27] Purified, Fab-fragment *Latrodectus* antivenoms are now readily available in Australia and South America, and rarely cause severe immunologic complications, although serum sickness remains possible.[21–23,25–27] In a retrospective analysis of all antivenom use in Australia over a one-year period, Sutherland reported that redback spider (*L. hasselti*) antivenom was the most common antivenom administered (n = 258), followed by Sydney funnel-web antivenom (n = 3), and that serum sickness occurred in only three patients receiving redback spider antivenom.[23] In severe envenomings, especially in children, antivenom may be effective in reversing latrodectism up to 90 hours after an envenoming bite.[24]

In 2001, Graudins and others demonstrated significant cross-species efficacy of Australian redback spider antivenom to antagonize the toxicity of both North American and European widow venoms in both laboratory and animal models.[26] Daly and others confirmed the effectiveness of redback spider (*L. hasselti*) antivenom in neutralizing the effects of two North American widow venoms, *L. hesperus* and *L. mactans*, in a mouse model.[27] In conclusion, *Latrodectus* antivenom therapy should be the mainstay of pharmacotherapy for all severe widow envenomings with high therapeutic efficacy, excellent antigenic cross-reactivity among *Latrodectus* and family-related (*Steatoda*) species, and little risk of serum sickness or death from anaphylaxis.[21,22,26–30]

Steatodism: Spider bites by Steatoda spp of the Family Theridiidae. The family Theridiidae contains the well-known *Latrodectus* or widow spiders and the less well-known comb-footed spiders of the genera *Steatoda* and *Achaearanea*.[28] In a prospective cohort study of 28 definite spider bites caused by non-*Latrodectus* theridiid spiders in Australia, Isbister and Gray reported 23 bites by *Steatoda* spp. and 5 bites by *Achaearanea* spp.[28] In addition to being more common, *Steatoda* bites were always more severe and more likely to cause systemic effects than *Achaearanea* bites.[28] Steatoda bites occurred year round, during waking hours, with 78% occurring indoors, and 48% while dressing indoors.[28] The clinical presentation of *Steatoda* bites was characterized by moderate to severe regional pain (26%), with a mean duration of six hours, and systemic effects in 30%, notably nausea, headache, malaise, and lethargy.[28] These investigators used the term "steatodism" to describe the clinical syndrome of *Steatoda* bites, with pain and systemic effects similar to, but milder than, *Latrodectus* bites, with the exception of the diaphoresis, which is pathognomonic of *Latrodectus* bites.[28] Although most patients received supportive care only, one patient with severe *Steatoda* envenoming was inadvertently treated with redback spider (*Latrodectus hasselti*) antivenom, with all pain and systemic effects resolving within one hour.[28] The investigators concluded that redback spider antivenom cross-reacted with and neutralized *Steatoda* venom and could be an effective therapy for severe *Steatoda* envenomings.[28]

In a separate case report of a *Steatoda* bite in Australia, Graudins and others successfully treated a 22-year-old woman with severe *Steatoda grossa* (cupboard spider) envenoming and a presentation suggesting latrodectism with redback spider antivenom.[29] In addition, these investigators demonstrated the reversal of *S. grossa* toxicity with redback spider antivenom in an isolated, *in vitro* chick biventer cervicis nerve-muscle preparation.[29]

Steatoda spiders are not confined to Australia, and are ubiquitously distributed worldwide.[28–30] *Steatoda* spiders are common in Europe and along the Mediterranean coast (*S. nobilis* and *S. paykulliana*), and *S. nobilis* was recently introduced into England from the Canary Islands.[30–33] Experts anticipate that *Steatoda* bites will be more commonly reported outside of Australia, and some may even require Australian redback spider antivenom therapy.[30] Recent labora-

tory investigations in Italy and in Russia have now confirmed the similar cationic channel-forming properties of *Latrodectus* and *Steatoda* theridiid spider venoms on bilayer lipid membranes, supporting the use of Australian redback antivenom therapy in severe *Steatoda* envenomings.[31–33]

Loxoscelism: Brown recluse spiders (Loxosceles spp.). *Loxosceles* spiders are medium-sized spiders that build messy webs, often wedged in crevices or behind furniture or pictures, and live both indoors and outdoors in dark spaces in temperate and tropical latitudes worldwide. Preferred habitats includes rock piles, wood piles, rat holes, attic and basement crawl spaces, indoor trash and clothing piles, cardboard boxes, and storage sheds. *Loxosceles* species spiders are most abundant and active at night during the warm months of the year.

All *Loxosceles* spiders are rather drab brown in color, often have no unique identifying markings except for the female brown recluse (*Loxosceles reclusa*), and are often simply described as brown spiders.[34–36] Brown recluse, violin, or fiddleback spiders are more accurate and descriptive common names for *Loxosceles* species spiders.[34,36] Females are more venomous and larger (20–30-mm leg span) than males (10–35-mm leg span), which rarely inflict severe envenoming bites.[34,36] The *Loxosceles* female is dull fawn to dark brown with an even darker brown, distinctive pattern on the dorsal cephalothorax. In the female brown recluse spider, this identifying pattern looks like a violin, fiddle, or cello with the base at the head end, bordered by three pairs of eyes, and the neck of the design pointing toward the abdomen.[34,36,37] Like *Latrodectus* spiders, *Loxosceles* spiders are naturally nonaggressive, reclusive, prefer to retreat when threatened, and bite only if handled or trapped in garments or bed linens.[34,36,37] Most human bites will occur in the early mornings and will cluster wherever bed linens, bedclothes, or other garments squeeze the female between fabrics and the victim's skin.[34,36,37] Thus, most *Loxosceles* bites will occur under the arms, at the waist, or on the lower extremities under socks, stockings, or pants.[34–39]

Necrotic araneism, the dermonecrotic ulceration at spider bite sites, is caused by cytotoxic and proteolytic components of the species-specific venoms.[37] The primary cytotoxic component of *Loxosceles* venom has now been identified as sphingomyelinase D.[37,38] In *Loxosceles*-induced necrotic araneism, or loxoscelism, an initially painless to transiently stinging bite is followed by painful blistering with surrounding erythema within 2–8 hours, progressing to a central darkness of pending necrosis surrounded by concentric erythema ("red, white, and blue target sign") by 24–48 hours, and then ulcerating in an eccentric pattern by 48–72 hours ("flowing downhill ulcer sign"), with eschar formation and slow healing with scarring over weeks to months.[34,36,37,39]

The exact mechanisms of both cytotoxic and systemic loxoscelism have not been conclusively elucidated. Since red blood cell hemolysis and local and disseminated intravascular coagulation characterize loxoscelism, sphingomyelinase D must play a major role in initiating loxoscelism after *Loxosceles* bites.[37–39] Within 2–7 days of a *Loxosceles* bite, systemic loxoscelism may occur more commonly in children than adults and is characterized by arthralgias, chills, fever, leukocytosis, maculopapular rash, nausea and vomiting, followed by thrombocytopenia, hemolytic anemia, disseminated intravascular coagulation, hemoglobinuria, myoglobinuria, febrile seizures, coma, and acute renal failure.[34–39]

With proper wound management, necrotic wounds will heal over a 1–2-month period with a 10–15% incidence of major scarring.[34–37] Ulcerating or necrotic wounds from a myriad of other insect-induced, infectious, or physical sources are often misdiagnosed as *Loxosceles reclusa* bites with necrotic araneism in the United States. Systemic loxoscelism is also rare in the United States, with a 3% incidence rate and no deaths in a population of 111 patients with expert-confirmed brown recluse (*Loxosceles reclusa*) bites in a 1997 survey in the United States.[34] Systemic loxoscelism is much more common following South American *Loxosceles* species bites (*L. gaucho*, *L. laeta*, *L. intermedia*) with a prevalence rate of 13.1% and a case fatality rate of 1.5% in 267 cases of expert-confirmed *L. laeta* or *L. intermedia* bites.[35]

The local wound care of *Loxosceles* bites should include thorough wound cleansing, cold compresses, elevation of the bite extremity, immobilization, oral or parenteral analgesics and antihistamines, and tetanus prophylaxis.[34–37] Any patient manifesting significant necrotic araneism or evidence of systemic loxoscelism should be hospitalized for observation and specific therapy.[34–37,39] Initial laboratory evaluation in cases of expanding dermonecrosis and loxoscelism should screen for evidence of diabetes, hemolysis, and intravascular coagulation.[34–37,39] Unsuspected patients with diabetes may develop neuropathic foot ulcers or soft tissue infections following minor trauma that may be misdiagnosed as *Loxosceles* bites. Recommended laboratory tests include complete blood count, serum glucose, platelet count, prothrombin time, partial thromboplastin time (international normalized ratio), fibrinogen, fibrin split products, renal function tests, and urinalysis.[34–37,39]

Early excision of bite lesions and intralesional injection of corticosteroids are contraindicated and could extend the dermonecrosis.[34–37] Wound care should include debridement of necrotic tissues, culture-directed antibiotic therapy for secondary wound infections, and delayed excision of eschars, with split-thickness skin grafting as indicated.[34–37]

The orally administered leukocyte microtubular inhibitors, such as dapsone (100 mg orally twice a day for two weeks) or colchicine (12 mg orally tapered over a four-day period), were initially recommended to halt the expanding dermonecrosis of *Loxosceles*-induced necrotic araneism. The microtubular inhibitors were presumed to halt expanding dermonecrosis by limiting both leukocyte migration to and subsequent leukocyte degranulation and cytokine discharge at *Loxosceles* bite sites.[34,36–39] However, the efficacy of oral leukocyte inhibitors in necrotic araneism has not been supported by randomized controlled drug trials, and their use may pose significant toxicity risks. Since dapsone can induce hemolysis and methemoglobinemia in hereditary glucose-6-phosphate dehydrogenase (G6PD) deficiency and in NADH methemoglobin reductase (NADH-MR) deficiency, baseline G6PD and NADH-MR levels and liver function tests should be ordered prior to initiating dapsone therapy in any patient. Hyperbaric oxygenation has also been recommended to halt and reverse the expanding dermonecrosis of loxoscelism, but has shown mixed treatment outcomes, and remains unsupported by controlled trials.[38] Renal protection from extracellular hemoglobin or myoglobin may require fluid loading, osmotic diuresis, or even temporary hemodialysis for acute renal insufficiency.

Although *Loxosceles*-specific antivenoms remain under investigation in both the United States and South America, no antivenoms are universally available, except in South America, and reports of the efficacy of systemically administered *Loxosceles* antivenoms have been mixed to date.[34–38]

Gomez and others have now characterized the antigenic cross-reactivity of the two medically important North American *Loxosceles* species venoms from *L. reclusa* and *L. deserta* by inducing common protein bands on Western blot comparative analyses of the two venoms.[40] In another laboratory investigation, Gomez and others were able to significantly attenuate by both observation and measured myeloperoxidase activity (a measure of neutrophil accumulation and activity) the cytotoxic and dermonecrotic activity of *L. deserta* venom in rabbits by the prior intradermal administration of anti-*Loxosceles* Fab fragments.[41]

Non-Loxosceles necrotic araneism: running and sac spiders (Cheiracanthium spp.). Although the exact toxicokinetic mechanisms remain unclear, non-*Loxosceles*-associated necrotic araneism has been reported following suspected and definite spider bites by several species including *Cheiracanthium*, *Argiope*, *Badumna*, *Lampona*, *Lycosa*, *Sicarius*, and possibly *T. agrestis* (only in the United States).[42–49] The running and sac spiders (*Cheiracanthium* spp.) of the family Clubionidae have now been definitely implicated in increasing cases of necrotic araneism throughout the world, particularly in South Africa.[42–46] The venoms of *Cheiracanthium* spiders have not been well studied, but are now known to contain several proteolytic enzymes including alkaline phosphatase, deoxyribonuclease, esterase, hyaluronidase, lipase, and ribonuclease.[43–47] Young and Pincus clearly demonstrated the presence of hyaluronidase and proteases in the digestive extracts of both *Badumna insignis* and *Lampona cylindrata*, and concluded that these enzymes contributed to the dermonecrotic effects of bites by these spiders.[49]

Digestive collagenases and proteases may also play a primary role in non-*Loxosceles*-associated necrotic araneism.[47,49] Atkinson and Wright demonstrated that collagenases, capable of inducing cytotoxic disruption of mouse skin in tissue culture, were present in the midgut extracts of 13 Australian spider species.[46] Foradori and others also demonstrated the presence of collagenases in the midgut extract of *Argiope aurantia* (garden spider).[47] When injected intradermally into rabbits, however, the *Argiope* collagenases did not cause dermonecrotic lesions.[47] Like sphingomyelinase D, proteases and collagenases can also cause necrotic araneism with significant local tissue destruction, lysis of red blood cell membranes, local intravascular coagulation, tissue ischemia, and fat necrosis.[40–42,44–47] Non-*Loxosceles* necrotic araneism is often associated with mild systemic toxicity without hematological abnormalities.[42–47]

Like *Latrodectus* spiders, *Cheiracanthium* spiders may be found worldwide, but lack any distinctive features, and exhibit a kaleidoscope of colors from yellow to green to brown. *Cheiracanthium* spiders are small (10–18-mm leg span), often have one longitudinal stripe on the dorsal abdomen, and have long, delicate legs. *Cheiracanthium* or sac spiders prefer to live indoors, snugly encased in woven silk sacs, and favoring the folds of drapes and curtains or warm windowsills. They forage and feed at night, can run fast, and become aggressive and bite when provoked, especially at night.

A *Cheiracanthium* spider bite is often very painful and followed by a mildly pruritic, erythematous wheal surrounded by paresthesias within 30 minutes.[43–45] Most *Cheiracanthium* bites do not ulcerate and become asymptomatic within two days.[43–45] Some *Cheiracanthium* species spider bites (*C. lawrencei* and *C. japonicum*) may rarely be associated with early ulceration and limited necrosis, and usually heal spontaneously within 7–10 days.[43–47] *Cheiracanthium* bites may also be associated with a mild systemic syndrome characterized by low-grade fever, severe headache, nausea, abdominal cramps, and vomiting.[43–45]

Provided secondary infections are prevented, most *Cheiracanthium* bites will heal without significant scarring within 7–10 days.[43–45] Treatment should include thorough wound cleansing, tetanus prophylaxis, cool compresses, elevation of the bite extremity, immobilization, analgesics, antihistamines, antiemetics as indicated, antibiotic therapy only for secondary infections, and conservative debridement of necrotic tissue, if indicated.[43–45]

Possible non-Loxosceles necrotic araneism: hobo spiders (T. agrestis). *Tegenaria agrestis*, also known as the hobo spider or "aggressive" house spider, is a relatively recent Western European émigré to the United States, settling comfortably in the Pacific northwest of the United States and the Canadian Pacific around 1936.[42,48] Since other spiders capable of inducing necrotic araneism, such as *Loxosceles* and *Cheiracanthium* spiders, are rare to non-existent in the colder climates of the North American Pacific coast, the hobo spider may be the principal cause of necrotic araneism in the colder latitudes of the North American Pacific coast.[12–14] Since the hobo spider is considered innocuous in Europe, however, it remains unclear and unproven whether the hobo spider in the United States is really the major cause of necrotic araneism in the North American Pacific northwest.[12–14,42,48]

Hobo spiders are large and moderately hairy brown spiders with black splotches or chevron-like stripes on their dorsal abdomens. Male hobo spiders are almost as large as females (30–50-mm leg span), more aggressive and more venomous than females, and more likely to bite humans, unlike diminutive *Latrodectus* and *Loxosceles* males. As running spiders, hobo spiders move fast, running up to one meter/second, and as hunters, they are aggressive and will attack if disturbed, particularly males. Hobo spiders have poor eyesight, are poor climbers, remain near ground level, and hunt and attack by sensing vibrations. They build ground-level webs in moist, peri-domestic areas, such as woodpiles, compost and debris piles, rock garden walls, basement crawl spaces, baseboards, sub-floors, and home perimeters.

Although the initial features of envenoming *Tegenaria* bites with necrotic araneism resemble *Loxosceles* bites, the following characteristics may differentiate dermonecrosis caused by *Tegenaria* bites from dermonecrosis caused by *Loxosceles* bites: 1) a completely painless or mildly stinging initial bite; 2) local painful induration within 30 minutes surrounded by an expanding ring of concentric erythema that can reach a diameter of 5–15 cm; 3) multiple small blisters developing within the indurated area within 15–35 hours; and 4) rupture and coalescence of blisters with serous exudates encrusting a cratered wound by 48–72 hours.[5,42] An eschar with underlying necrosis that sloughs over a 30–40-day period leaving a permanent scar may occur, especially in fatty areas, such as the underarms. *Tegenaria* bite lesions will generally heal spontaneously over prolonged periods.[5,42]

The most common systemic syndrome associated with *Tegenaria* bites is a constellation of severe headache, nausea, vomiting, weakness, fatigue, temporary memory loss, and vision impairment within 10 hours of the bite.[5] Protracted systemic effects are very rare and may include intractable vomiting, chronic watery diarrhea, and aplastic anemia, which can be fatal.[5,42] The optimal management strategies for *Tegenaria* bites are not well established, but should include thorough wound cleansing, tetanus prophylaxis, cool compresses, elevation of the bite extremity, immobilization, analgesics, antibiotic therapy for secondary infections, and eschar excision with split-thickness skin grafting, as indicated.

In an elegant laboratory investigation designed to compare the venom toxicities of hobo spiders from the United States and Europe, Binford analyzed the venoms of *T. agrestis* spiders from Washington, United Kingdom, and Switzerland by both liquid chromatography and insect bioassays.[48] Chromatographic profiles were different between the sexes, but similar within sexes between hobo spiders from the United States and the United Kingdom. Insect toxicity studies showed no differences between venom potencies in spiders from the United States and the United Kingdom, but female venoms were more potent than male venoms.[48] Binford concluded that these results did not support the common claims that hobo spiders, particularly the larger males, commonly cause necrotic araneism in the northwestern United States.[48] In several recent studies of necrotic araneism and spider ranges, Vetter and others concluded that the majority of dermonecrotic lesions in the United States are misdiagnosed as necrotic araneism from spider bites, particularly *Loxosceles reclusa* and *T. agrestis* bites, especially in regions where such species are either not endemic or rarely reported.[12–14]

Funnel-web neurotoxicity: funnel-web spiders. The Australian funnel-web mygalomorph spiders are very large (15–45-mm body length and a 45–60-mm leg span) dark black spiders belonging to two major genera (*Atrax* and *Hadronyche*) within the family Hexathelidae, subfamily Atracinae. Although all funnel-web spiders are venomous, only three *Atrax* species and at least six *Hadronyche* species have so far proved capable of causing severe, potentially lethal human bites. These include 1) the Sydney funnel-web spider (*Atrax robustus*) of the Sydney metropolitan area and the southeastern Australian seaboard, and 2) a related species from the eastern Australian seaboard, the arboreal funnel-web (*Hadronyche formidabilis*) of the highlands of New South Wales.[50–53] All funnel-webs produce neurotoxic venoms, with the smaller males being more aggressive and venomous than females and inflicting more bites, especially during the summer months.[51] The Sydney funnel-web spider is among the world's most dangerous spiders, capable of causing death from a neurotoxic bite within 15 minutes, especially in children.[52,54–57]

Australian funnel-webs are large and formidable, with a shiny, ebony black cephalothorax, prominent fangs, and a velvety black to plum abdomen with prominent spinnerets. Both *Atrax* and *Hadronyche* funnel-webs build distinctive silk-lined, funnel-shaped webs, either in trees (*Hadronyche formidabilis*) or on the ground in burrows, rotting logs, and between tree roots (*Atrax robustus*), with warning trip webwires extending out from their webs. Smaller female funnel-web spiders prefer to remain at home with their large families of 100–150 spiders, but the larger, mature males soon become roving vagrants in metropolitan areas, such as Sydney, posing greater human threats than females.

There are clearly two phases of envenoming following funnel-web bites. Initially, there is mass autonomic nervous system excitation with simultaneous nicotinic, cholinergic, and adrenergic components.[50,51,53] In Stage I funnel-web envenoming, local piloerection and muscle fasciculation begin within minutes of an intensely painful bite, with little local inflammation and no blistering or subsequent dermonecrosis.[50,51,53] Piloerection and fasciculation extend proximally, become generalized within 10–20 minutes, and are quickly accompanied by an autonomic crisis with both adrenergic components (diaphoresis, tachydysrhythmias, hypertension, noncardiogenic pulmonary edema), and cholinergic components (apnea, bronchorrhea, coma, diarrhea, salivation, lacrimation).[50,51,53] Without emergency management at the scene, fatal respiratory arrest may result from apnea, laryngospasm, and pulmonary edema.[50–56] The Stage I autonomic storm will subside within 1–2 hours; consciousness often resumes in Stage II, but progressive hypotension, respiratory depression, and pulmonary edema may persist.[50–56]

Funnel-web venom is composed of at least three major classes of peptides: delta-atracotoxins, omega-atracotoxins, and Janus-faced atracotoxins.[54] The delta-atracotoxins are responsible for the biphasic, primate specific autonomic syndrome following funnel-web envenomings.[54] Delta-atracotoxins induce spontaneous repetitive firing and prolongation of action potentials in all excitable cells, especially in the autonomic nervous system.[54] This autonomic storm results from a hyperpolarizing shift of the voltage-dependence of neural activation and a slowing of voltage-gated sodium channel inactivation.[54] This action is due to the voltage-dependent binding of delta-atracotoxins to neurotoxin receptor site-3 on insect and primate voltage-gated sodium channels in a manner similar to scorpion and sea anemone toxins.[54] The omega- and Janus-faced atracotoxins have not been as well studied as the delta-atracotoxins, and appear to be insect receptor-specific neurotoxins.[54]

Since 1927, 13 fatalities from *Atrax robustus* envenoming have occurred in Australia, with children being particularly susceptible.[57] An effective *Atrax robustus* antivenom was released in 1981, and administered to more than 40 patients by 1991, with no deaths or adverse effects, other than serum sickness, reported.[50,52,54–60]

The Australian mouse spiders (*Missulena* spp.) of the family Actinopodidae appear to have neurotoxic venom components similar to the funnel-webs. Although *Missulena* venom has not been fully characterized, Sydney funnel-web antivenom has been shown to be highly effective in reversing *Missulena* envenoming, indicating significant cross-reactivity.[54] Sydney funnel-web antivenom is also effective in reversing the toxic effects of other *Atrax* and of several *Hadronyche* species of funnel-webs.[50,58,59] In 1989, Dieckmann and others successfully used Sydney funnel-web antivenom to reverse all symptoms in three patients who were bitten by *Hadronyche* spiders and did not receive immediate first aid.[60]

Antivenom therapy with Sydney funnel-web antivenom (Commonwealth Serum Laboratories, Parkville, Victoria, Australia) is the cornerstone of management of Australian funnel-web spider bites and severe envenomings by Australian *Missulena* mouse spiders.[50–52,55–60] The reader is referred to several recent reviews.[50–52,56,57,60] Treatment of funnel-

web envenoming is very specific, must begin immediately, and basically includes 1) splinting and then gently wrapping the length of the bitten extremity with a crepe or elastic bandage to retard the lymphatic movement of the venom towards the central circulation (the Australian pressure-immobilization technique); 2) immobilizing the bite victim to retard potential circulation of neurotoxic venom; 3) evacuating the victim to the nearest hospital with Sydney funnel-web (*Atrax robustus*) antivenom on hand with the pressure immobilization splint-bandage in place; 4) intravenously administering Sydney funnel-web antivenom for confirmed bites by *Atrax* or *Hadronyche* species of funnel-webs or for severe envenomings by *Missulena* mouse spiders); 5) continuing to administer 1–2 ampules of antivenom every 15 minutes until neurotoxic symptoms resolve if any symptoms or signs of autonomic neurotoxicity continue to occur on slow release of lymphatic compression (many funnel-web bites are non-envenoming to mildly envenoming); and 6) removing the pressure bandage during full hemodynamic monitoring in an intensive care setting.[50–52,55–60] The prophylactic administration of antihistamines prior to antivenom administration is no longer recommended.[61]

Phoneutrism: armed spiders (Phoneutria spp.). The *Phoneutria* spiders of South America are large, nocturnal, and aggressive spiders with neurotoxic venoms.[62–64] *Phoneutria nigriventer* is the most common species, often as large as a tarantula (80–95-mm leg span), with males being slightly smaller than females. *Phoneutria nigriventer* is dull gray-brown with a white longitudinal band on the dorsal abdomen.[62–64] *Phoneutria* species spiders are also known as armed or armed-banana spiders, but should not be confused with harmless *Cupiennius* spiders, also commonly called banana spiders in South America.[62–64] Since both *Phoneutria* and *Cupiennius* spiders frequent banana clusters, are similar in size, and have a distinctive brush of red hairs surrounding their chelicerae, they are often confused and require expert identification by arachnologists.[62–64] *Phoneutria* spiders do not build webs, forage only at night, and often enter houses at daybreak, hiding in clothing closets and laundry rooms. *Phoneutria* spiders inflict 600–800 spider bites each year in the Sao Paulo, Brazil metropolitan area.[63,64]

Phoneutria venom is composed of a very complex mixture of aspartic acid, glutamic acid, histamine, hyaluronidase, lysine, serotonin, and other unidentified kallikrein-kinin activating factors that collectively target both peripheral and central nervous systems to induce and potentiate repetitive nerve action potentials.[63,64] Within 10–20 minutes of a severely painful bite, often characterized by very localized sweating and piloerection at the bite site, pain radiates proximally up the bitten extremity to the trunk.[62–64] The *Phoneutria* bite victim will experience tachycardia, hypertension, profuse diaphoresis, hypothermia, salivation, nausea, vomiting, vertigo, visual disturbances, priapism (especially in boys less than 10 years old), and rarely death within 2–12 hours.[62–64] Most bite victims recover within 24–48 hours, and few victims will require antivenom therapy. In a descriptive analysis of 422 patients with confirmed *Phoneutria* spider bites in Brazil in 1984–1996, Bucaretchi and others[64] reported mild envenoming requiring supportive treatment only in most patients (89.8%); severe envenoming in a few patients (0.5%); antivenom administration in 10 patients (2.3%), 2 with severe envenomings and 8 children with moderate envenomings; and 1 death from delayed (9 hours post-bite) pulmonary edema in a nine-year-old boy who received antivenom.[64]

The treatment of *Phoneutria* bites should include thorough wound cleansing, tetanus prophylaxis, warm compresses to achieve local peripheral vasodilation, elevation of the bite extremity, immobilization, non-sedating analgesics, local anesthetic infiltration of the bite site, antivenom skin testing, and antivenom (Sero Antiaracidico Polivalente; Instituto Butantan, Sao Paulo, Brazil) administration (1–5 ampules intravenously or intramuscularly).[63,64] The prophylactic administration of antihistamines prior to antivenom therapy is no longer recommended.[61] Antivenom response may be monitored by relief of pain at the bite site and resolution of priapism, if present.[61,63,64]

Allergic and foreign body Araneism: tarantulas. The tarantulas of the Family Theraphosidae are the world's longest-lived and largest spiders (18–24-cm leg span), and are among the most docile and brightly colored and patterned of all spiders. Tarantulas continue to be popular household pets, with environmentally threatened and endangered Amazonian species often imported worldwide. Tarantulas live in most tropical regions of the world, and are very common in the New World with more than 1,500 species, and 40 species in the southwestern United States alone. They are very territorial and stick close to their birthplaces, do not build webs, and live in underground burrows beneath rocks and embankments. Females prefer to remain in their burrows with their large families and can live for 25–30 years. Males rarely live for more than a year after reaching maturity by the age of 10–12 years. Tarantulas rest in their burrows or shady spots during the day and hunt at night. They have poor eyesight and detect and ambush prey by sensing vibrations. Although tarantula bites in dogs are often fatal, tarantulas rarely inflict envenoming bites on humans.[65] Their major form of defense is to launch their urticating hairs posteriorly and rapidly retreat from threats.

The venom of the U.S. tarantula, *Aphonopelma hentzi,* contains a mixture of nucleotides, spermine, and, principally hyaluronidase, and resembles scorpion venom in composition and biologic effects. Escoubas and others have now demonstrated that tarantula venom components also contain a variety of specific peptide ligands that target specific neuroreceptors in excitable cell cationic channels, particularly sodium, potassium, and calcium cationic channels.[66] Recently, Bode and others used a tarantula peptide ligand (GsMtx-4) from the venom of *Grammostola spatulata* to suppress the incidence and duration of induced atrial fibrillation in rabbit hearts.[67] The investigators concluded that the antiarrhythmic effects of GsMtx-4 were due to specific inhibition of the potassium-selective, atrial-stretch-activated ion channels.[67] In addition, they suggested that GsMtx-4 could be the first of an entirely new class of antiarrhythmics directed against the causes rather than the symptoms of atrial fibrillation.[67]

Tarantula envenoming in humans usually causes mild stinging, resembling a bee or wasp sting, with minimal surrounding inflammatory reaction, no dermonecrosis, and no serious systemic sequelae.[65] Although tarantula bites are usually innocuous in humans, tarantula bites are often lethal in domestic animals, particularly dogs.[65] In a combined nested-prospective study of spider bites and a retrospective case series of definite tarantula bites in humans and dogs in Australia, Isbister and others described nine tarantula bites in hu-

mans and seven in dogs.[65] The 16 bites included 2 bites each by *Selenocosmia* spp. tarantulas and *Phlogiellus* spp. tarantulas.[65] The nine human bites caused only mild effects including local pain, severe in four cases, puncture marks, and transient bleeding from puncture sites.[65] Mild systemic toxicity occurred in one of the nine human cases.[65] All seven canine victims died within 0.5–2 hours of the confirmed tarantula bites.[65]

Four genera of New World tarantulas (*Acanthoscurria*, *Brachypelma*, *Grammostola*, and *Lasiodora*) and many other tarantula species possess several types of urticating hairs on their dorsal abdomens, which can be flicked off by the thousands to irritate and incapacitate pursuing aggressors. In human victims, these urticating hairs can penetrate the skin causing severe pruritic reactions or lodge in the cornea causing ophthalmia nodosa.[68–73] In a classic investigation, Cooke and others described and classified four types of tarantula urticating hairs, ranging in length from 0.6 to 1.5 mm and distinguished by distal barbs on electron microscopy.[73] The U.S. tarantula, *Aphonopelma hentzi,* possess only Type I hairs that cannot deeply penetrate the skin, but can cause ophthalmia nodosa.[73] Type II hairs are not launched in the face of attackers, but are defensively incorporated into tarantulas' tunnel retreats.[73] Type III hairs can penetrate up to 2 mm in human skin, and are most likely to cause intense skin inflammation and ophthalmia nodosa.[73] Type IV hairs are found only in the South American *Grammostola* tarantulas, and are designed to induce irritation in the upper respiratory tract of pursuers.[73]

Although ophthalmia nodosa was initially reported after caterpillar hairs lodged in human corneas, ophthalmia nodosa with transient, steroid-responsive keratoconjunctivitis has also been reported in association with the handling of pet tarantulas, often by children.[68–75] In 1997, Blaikie and others reported three British cases of keratoconjunctivitis after handling domestic pet tarantulas.[71] One patient with a pet Thailand black tarantula (*Haplopelma minax*) presented with a steroid-responsive ophthalmia nodosa characterized by transient anterior chamber inflammation and no long-term sequelae.[71] The other two patients, both of whom handled pet Chilean rose-haired tarantulas (*Grammostola cala*), developed more serious pan-uveitis lasting for years, and leading to glaucoma and reduced visual acuity in one patient.[71] In 1998, Belyea and others reported another case of ophthalmia nodosa in a 17-year-old American girl with a pet Chilean rose-haired tarantula.[72] Following tapering topical steroids, all ocular inflammation and associated periorbital inflammation resolved by 10 months with two urticating hairs still lodged in the corneal stroma on slit-lamp examination.[72]

The management of tarantula bites should be conservative and symptomatic with thorough wound cleansing, tetanus prophylaxis, elevation of the bite extremity, immobilization, and oral analgesics as needed. All superficially embedded urticating hairs that can be identified by microscopy or slit-lamp examination should be removed if possible, and topical or systemic antihistamines and corticosteroids prescribed for pruritus from allergic response to fragmented and remaining urticating hairs.[68–72,75] Prolonged topical ophthalmic corticosteroid therapy, rather than corneal excision, is often indicated for ophthalmia nodosa due to embedded corneal tarantula hairs.[68–72,75] Patients recovering from urticating hair-induced ophthalmia nodosa should be followed by an ophthalmologist with periodic slit-lamp examinations and visual acuity and intraocular pressure measurements.[68–72,75] If enthusiasts must handle their pet tarantulas or even clean their terrariums, they should wear gloves and eye protection, avoid rubbing their eyes, and thoroughly wash their hands after any contact with tarantulas or their terrariums.[71,75]

Other spider-induced injuries. In addition to the eye injuries caused by tarantula hairs, both Fuller and Isbister have described acute conjunctivitis following eye contact with squashed spider contents.[76,77] Fuller reported a patient who developed acute conjunctivitis, periorbital edema, and mild systemic toxicity following eye contact with squashed black widow (*Latrodectus hesperus*) contents.[76] Recently, Isbister reported a 46-year-old male who smashed an unidentified spider with a newspaper and suffered immediate eye pain, severe photophobia, acute conjunctivitis, periorbital edema, and loss of visual acuity.[77] Following topical anesthesia and vigorous eye irrigation, the symptoms and signs resolved over 2 hr.[77] Other unusual spider injuries include urticaria caused by skin-embedded tarantula hairs, and occupational asthma caused by the inhalation of tarantula hairs.[78,79]

Miscellaneous mildly envenoming spiders. As discussed, *Steatoda* spiders, sparassid spiders (huntsmen spiders), Australian mouse spiders, *Lycosa* (wolf) spiders, and most mygalomorphs can inflict severe bites, some even requiring treatment with cross-reacting antivenoms. In addition, many other species of spiders may cause medically notable human bites with mild envenoming, local pain and erythema, and without necrosis or significant systemic manifestations other than regional lymph node tenderness, contiguous arthralgias, malaise, nausea, and low-grade fever. On rare occasions, spiders previously considered completely harmless, such as the grass spider (*Agelenopsis aperta*), may inflict severely envenoming bites, especially in children.[80] Miscellaneous spider bites are a frequent source of telephone calls to poison information centers, especially in Australia, South America, and the United States (Table 1).

General management of the unknown spider bite. Any unknown spider bite or other spider-associated injury should be confirmed by a history of spider bite or spider body or content contact and observed biting or other contact by eyewitnesses. The general management of any unknown spider

TABLE 1
Some miscellaneous mildly envenoming spiders

North America	Australia	South America	Africa
Agelenopsis	*Achaearanea*	*Cupiennius*	*Harpactirella lightfooti*
*Araneus**	*Badumna**	*Lycosa**	*Palystes natalius*
*Argiope**	*Delena*		*Sicarius*
Bothriocytrum	*Heteropoda*		
Drassodes	*Holconia*		
Heteropoda	*Isopeda*		
Herpyllus	*Isopedella*		
*Liocranoides**	*Lampona*		
*Lycosa**	*Neosparassus*		
Misumenoides	*Supunna*		
*Neoscona**			
Peucetia			
*Phidippus**			
Trachelas			
Ummidia			

* Necrotic araneism is possible following envenoming bites by these spider species.

or other insect bite should be conservative and symptomatically directed and include thorough wound cleansing, elevation of the bite extremity, immobilization, cool compresses (except for *Phoneutria* bites), tetanus prophylaxis, analgesics, and antipruritics. Broad spectrum antibiotic therapy is indicated only for evidence of infection and should be directed by culture and sensitivity testing. Secondary wound infections are uncommon after most spider bites.[6] In their prospective analysis of 750 definite spider bites in Australia, Isbister and Gray reported a 0.9% incidence of secondary wound infections in spider bite sites.[6]

Prevention and control of spider bites. Outdoor spider bites may be prevented by wearing gloves, long sleeves, and long pants tucked into socks, especially when trekking outdoors, selecting firewood, and clearing brush. Campers and hunters should clean out privies, outdoor toilets, tents, cabins, and all potential campsites areas filled with spider webs with a broom or branch before settling in. Additional protection while outdoors can come from spraying clothing with synthetic pyrethroids and, possibly, by applying N, N-diethyl-*m*-toluamide (DEET)–containing insect repellants to any nonmucosal, skin-exposed areas, especially on the extremities. Most spider bites will occur during daytime activities outdoors or indoors, and during the spring and summer, when the potential for human-spider encounters are the greatest.

Simply maintaining a clean domestic environment, moving beds away from corners and walls, and careful storage of clothing and linens, particularly soiled clothing and linens, will reduce the chance of indoor spider bites, especially when dressing, grooming, or sleeping. In addition, checking shoes, socks, gloves, hats, sheets, and towels and all clothing and linens before donning or using will also expose hiding spiders that might bite on reflex when squeezed in clothing, towels, or bed linens. Indoor spider bites may also be prevented by properly insulating homes, especially all windows and exterior doors, attics and basement crawl spaces, and by removing all spider webs with brooms or vacuums, and by applying safe indoor insecticides, such as synthetic pyrethroids, or even natural pyrethrins, derived from chrysanthemums. Nevertheless, spiders and their preferred insect prey often retreat into difficult-to-reach spaces during the day, such as under baseboards and floorboards, within curtains and draperies (*Cheiracanthium* spp.), and behind pictures and mirrors (*Loxosceles* spp.). Some house-dwelling spiders, such as *T. agrestis*, may be relatively resistant to most pesticides due to frequent exposures and are better controlled with domestic measures and spider traps indoors.

The major problems with indoor insecticide use include eliminating natural predatory spiders and other, harmless arthropods, and forcing venomous spiders to flee to safer, unseen and unreachable spaces. In such cases, the simplest preventive measures are best, especially maintaining a hygienic domestic environment, eliminating litter, sealing all cracks and leaks with insulation materials, clearing all yard debris away from home foundations and outdoor recreational spaces.

Tarantulas should always be handled away from the face with glove and eye protection. Tarantula pet owners and zookeepers should also wear gloves and eye protection when cleaning tarantula terrariums.[69–72,75,78,79] If necessary, nuisance or threatening spiders should be smashed or sprayed at a distance to avoid any skin, ocular, or respiratory tract contact with aerosolized spider parts or contents.[76,77] Finally, the safest way to prevent a spider bite should an unwelcome venomous spider land on you is simply to flick the spider off with a finger, rather than squishing the spider against the skin which serves only to open the chelicerae by reflex, causing the fangs to spring into biting position.

CONCLUSIONS

Unlike other arthropods, spiders do not usually transmit communicable diseases to humans, and play a critical role in the ecosystem by consuming other arthropods that often transmit human diseases. Most spiders are venomous, but cannot inflict serious bites on humans due to delicate mouthparts and fangs. The differential diagnosis of spider bites is extensive and includes other arthropod bites, skin infections, and exposure to chemical and physical agents. However, approximately 200 species from 20 genera of spiders worldwide can cause severe human envenomings. Spider bites can be prevented by relatively simple domestic and personal protective measures. Early species identification and specific management may help prevent serious sequelae of spider bites.

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