Brown Recluse Spiders (*Loxosceles reclusa*): Process of Envenomation and Medical Diagnosis

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Abstract

The brown recluse spider, *Loxosceles reclusa*, is the most medically important recluse spider species in North America because it occurs in high concentrations in close proximity to humans. The range of *Loxosceles reclusa*, in the United States, extends from ‘southeastern Nebraska to southernmost Ohio and south into Georgia and most of Texas’ (da Silva et al., 2004). The brown recluse is not an aggressive spider and prefers to live in dark, secluded areas. The venom it produces is used to subdue prey or as a self defense mechanism. Loxoscelism, the bite of a brown spider, is associated with many well-known symptoms. The initial bite may be painless and a victim may not be aware of the incident. Mild to severe pain begins anywhere from two to eight hours after a bite, followed by itching, swelling, and tenderness (da Silva et al., 2004). In the next 24 hours an initial blister will appear and within a week the wound may progress into the characteristic necrotic lesion. The cutaneous reaction just described is common and severity varies based on the response of each individual subject with the majority of reactions being far from severe. Less commonly, the legion may progress to a systemic infection that is usually mild and self-limiting, but in rare cases may lead to renal failure and death. Initial treatment involves the use of elevation, ice, and antibiotics. Outside of the United States, *Loxosceles* antiserum may be administered, but is not proven to be highly effective in humans. The diagnosis of brown recluse spider bites is usually based solely on clinical symptoms due to the fact that few patients bring the spider specimen.
Diagnosis is always difficult and physicians should take into account the distribution and epidemiology of the spider. Many medical reports of brown recluse spider envenomation originate from areas of North America where the spiders are not endemic, are extremely rare, or have never been found, making them highly unlikely to be the source of the wounds (Vetter and Bush 2002). A multitude of other medical problems are associated with necrotic lesions and many go untreated when spider bites are misdiagnosed.

**Introduction**

The brown recluse spider, *Loxosceles reclusa*, is the most widely dispersed member of its genus in the United States and is most often implicated in necrotic arachnidism (Zeglin 2005). Brown recluse spiders range in size from eight to fifteen millimeters with most being roughly the size of a quarter. Their legs appear to be disproportionately long when compared to the length of their bodies and they range from pale brown to dark brown in color. Brown recluse spiders, as well as the other members of their genus *Loxosceles*, are most readily identified by their eye pattern. These spiders have six eyes ‘arranged in pairs with one anterior dyad and another lateral dyad on each side’ (da Silva et al., 2004). An additional method of identification for the brown recluse is its body structure. There is a violin-shaped pattern on its cephalothorax that is a slightly different brown from the rest of its body, but this characteristic is unreliable and sometimes overlooked (Swanson and Vetter 2005). The pattern is fairly consistent in adult brown recluse specimens, but becomes faded when they are preserved. It may be absent entirely in immature brown recluse spiders and other *Loxosceles* species.

The venom of the brown recluse is used to paralyze insect prey and as a defense mechanism. They prefer to avoid humans and only attack when they feel threatened.
Loxoscelism is the term used to describe bites from brown spiders of the genus *Loxosceles* and has been reported in ‘South America, North America, Europe, Africa, the Middle East and some parts of Asia, Israel, and Australia’ (da Silva et al., 2004). The brown recluse spider is not endemic to all parts of the United States. The native range of *Loxosceles reclusa* is located in the central and southern states that include ‘Nebraska, Kansas, Oklahoma, Texas, Louisiana, Arkansas, Missouri, Kentucky, Tennessee, Mississippi, Alabama, northern Georgia, and southern portions of Ohio, Indiana, Illinois, and Iowa’ (Swanson and Vetter 2005).

Brown recluse spiders are not aggressive, nocturnal, and prefer to live in dark areas. These spiders occur in areas with temperatures ranging from eight to forty-three degrees Celsius and can survive anywhere from days to months without available food and water (da Silva et al., 2004). It is commonly believed that humans transport the brown recluse out of its native range. The spider is known to seek shelter in stored boxes located in dark basements and attics. Those boxes, and the spiders residing in them, can be brought to nonendemic areas when possessions are transported. While this scenario is possible, there is no proof it is true for a large enough number of brown recluse spiders to cause the number of necrotic lesions reported. This unsubstantiated belief has led to incorrect diagnosis of many more brown recluse spider bites in non-endemic areas than these spiders could possibly cause (Bennett and Vetter 2004).

Medical misdiagnosis of necrotic lesions that are not caused by *Loxosceles reclusa* is dangerous for patients and physicians. Many illnesses have similar symptoms and receiving a misdiagnosis leading to incorrect treatment puts patients health at risk and exposes physicians to possible litigation. Since brown recluse spiders are so rare in
areas of nonendemicity, the diagnosis of a presumptive bite is most likely an error that reinforces the assumption that brown recluse spiders are common local causes of necrosis (Vetter and Bush 2002).

**Envenomation**

Out of the nearly 40,000 species of spiders that have been identified worldwide, *Loxosceles* spiders are one of the few groups where there is enough human and research evidence to link spider bites to necrotic arachnidism (Isbister and White 2004). Many spiders do have defensive venom, but the majority of identified venoms have been tested and proven to have little or no effect on mammalian tissue. The venom of the brown recluse spider is one of the exceptions to this statistic. A bite from a brown recluse spider can result in a simple, well-healed wound, with minimal localized pain; a more intense wound with severe pain, known as necrotic arachnidism; or the development of a systemic illness that cause fever, nausea, and can ultimately be fatal (Zeglin 2005). The severity of the reaction in each individual depends upon a variety of factors. These include the amount of venom injected, the age of the victim (children being more likely to have a severe reaction), the health of the victim, location of the bite, the speed at which treatment is received, and other minor factors. Most bites produce only mild reactions and heal within three weeks leaving no scarring, while only approximately twenty percent involve necrotic ulcers that take months to heal and may result in permanent scarring (Mold and Thompson 2004).

The initial bite of *Loxosceles reclusa* may be painless. Itching, pain, and erythema (redness of the skin) appear within the first day. This can be followed by the center of the bite site turning bluish-purple, which signals the beginning of tissue necrosis.
Blisters can erupt and the area can become surrounded by a ring of white, dying flesh. All of these symptoms together are known as the ‘red, white, and blue sign’ and are the defining characteristic of necrotic lesions (Zeglin 2005). Most necrotic lesions will show up within two days after a bite or not at all.

The venom contains about eight known enzymes and proteins. Among these are sphingomyelinase D (SMD), hyaluronidase, and lipase. The primary component of the toxin is SMD. SMD is toxic to endothelial and red blood cells and becomes incorporated into cell membranes in the skin, triggering an inflammatory response while intensifying the response to pain (Mold and Thompson 2004). Hyaluronidase increases the permeability of skin cells allowing the venom to spread, while lipase is responsible for the depressed scarring (Zeglin 2005). Other components are still being studied and may lead to better therapy in the future.

**Diagnosis**

According to the Centers for Disease Control and Prevention, brown recluse spider bites are not a reportable illness and “there are no reliable estimates of the incidence of such bites or how often medical attention is sought for them” (Zeglin 2005). The main characteristic of brown recluse spider bites that makes them hard to diagnose, is the lack of initial pain when the bite occurs. Many bite victims are not even aware they were bitten until pain starts hours later, at a time when the spider can no longer be found. Therefore, patients who believe they were bitten rarely bring the spider with them and fail to provide a specimen. This causes diagnosis to be based on epidemiological and historical findings, clinical signs and symptoms, and the oral report of the patient (da Silva et al., 2004).
When physicians rely on symptoms and epidemiology, diagnosis can be fairly reliable. The oral report of a patient tends to be far less reliable. This was shown in a case study (Swanson and Vetter 2005) in which six hundred patients, who believed they had received spider bites, were observed at the University of Arizona Hospital and the Los Angeles County Hospital. Of the six hundred people examined, eighty percent had bites that were clearly caused by other arthropods (e.g., ticks, triatomid bus, hymenoptera, bedbugs, fleas, flies, mites, blister beetles, blistering lepidoptera, solpugids, crickets, or even grasshoppers) (Swanson and Vetter 2005). This study shows the challenge facing physicians diagnosing spider bites.

The diagnosis of brown recluse spider bites becomes increasingly difficult because oral reports made by patients are mostly unreliable. The magnitude of this problem is portrayed by the fact that more than ninety percent of the time, the arachnid is not available to be identified by an expert. Physicians should suspect a spider bite when the medical history of a patient implies an encounter with spiders, the bite occurred in a geographical area where the suspected spider is endemic, and the proper clinical signs are present (Zeglin 2005). These tactics are currently the most promising way to achieve a correct diagnosis. Perhaps a commercially available diagnostic test will be produced in the future.

Treatment

Medical reports tend to highlight extreme cases of *Loxosceles reclusa* bites. This may make most physicians unaware that the majority of bites are ‘self-limited and self-healing without any long-term consequences’ (Swanson and Vetter 2005). Mild wounds are cleaned, iced, and elevated, and patients are told to avoid strenuous activity. When a
patient does display necrotic lesions, there is an established therapy of dapsone, acetylsalicylic acid, and antibiotics. Surgery may be required in extreme cases (da Silva et al., 2004). Treatment of mild cases is fairly standard, but treatment of severe lesions is controversial. Dapsone, considered the primary therapy to minimize necrosis, has very little data to support its efficacy in humans and can produce adverse side effects. In a letter to the American Journal of Emergency Medicine, a leading expert in the field wrote, “Would treating physicians even consider dapsone (which is well-known to have serious side effects and questionable efficacy) if they hadn’t first made the diagnostic leap-of-faith that an idiopathic lesion was a brown recluse spider envenomation?” (Vetter ad Bush 2004). Treating severe necrosis by surgically removing the tissue and grafting of new skin is also questioned because it may increase tissue damage and slow the healing process.

There are some alternative treatments for severe brown spider bites being considered including, hyperbaric oxygenation, nitroglycerin patches, electric shock, and heparin therapy (Zeglin 2005). Hyperbaric oxygenation and nitroglycerin are thought to increase blood flow to the infected area resulting in decreased venom effectiveness. Heparin may decrease blood clotting, which slows necrosis, and electric shock therapy may inactivate enzymes in the venom, helping to neutralize the toxin (Zeglin 2005). All of these treatments are still experimental and have no conclusive data to support their efficacy in humans.

One last treatment being studied is *Loxosceles reclusa*-specific anti-venom, which has been shown to stop necrosis after envenomation. This has only been tested in lab animals where it was shown to be effective systemically, but was not shown to be
especially effective against local effects at the site of the bite (da Silva et al., 2004). There have been no clinical studies on humans and the anti-venom is not used in the United States. While all of these treatments show some promise, there is no perfect method for treating severe reactions to a *Loxosceles reclusa* envenomation.

There have been very few studies conducted on human patients who have been bitten by a brown recluse spider. One of the human case studies that did occur (Mold and Thompson 2004) used a group of family physicians that documented patients with suspected brown recluse spider bites over a five-year period. Physicians provided the care they would normally give, while also providing topical nitroglycerin patches and vitamin C tablets at no cost for those patients who wished to use. Patient data was collected and weekly follow-ups were conducted until healing occurred. The researchers were provided with healing time, amount of scarring, and treatment methods used. No treatment approach was identified that was sufficiently promising to warrant a clinical trial in humans. The case study just described contained all of the weakness that most known studies of treatment methods for brown recluse spider bites possess. There was no way of knowing if lesions on the patients were actually *Loxosceles reclusa* bites, a substantial number of patients (twenty-eight percent) were unavailable for follow-up consultations, and the number of patients treated for bites, but not enrolled in the study was unknown (Mold and Thompson 2004). Until more consistent methods of studying therapies for brown recluse spider bites are constructed, there will never be an accurate way to determine which treatments are the most beneficial and effective.
Misdiagnosis

Over the last fifty years, the growing belief that spiders cause most cases of skin necrosis has resulted in the presumption that brown recluse spiders are to blame, even in areas where they are extremely rare, or nonexistent (Swanson and Vetter 2005). Far too many cases are occurring in locations where *Loxosceles reclusa* is not endemic and where patients may submit a spider less than ten percent of the time. A large number of infections and diseases may show similar symptoms to those produced by the brown recluse and are misdiagnosed to the detriment of the patient. These include, ‘staphylococcal or streptococcal infection, herpes simplex, herpes zoster, diabetic ulcer, fungal infection, pyoderma gangrenosum, lymphomatoid papulosis, chemical burn, toxicodendron dermatitis, squamous-cell carcinoma, neoplasia, localized vasculitis, syphilis, the Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema nodosum, erythema multiforme, gonococcemia, purpura fulminans, factitious injury, sporotrichosis, and Lyme disease’ (Swanson and Vetter 2005). The vast numbers of illnesses that can be misdiagnosed, make proper knowledge of brown recluse spider epidemiology and spider identification (when possible) critical requirements for diagnosing physicians.

The fact that brown recluse spiders rarely attack humans, even in their endemic range, should exemplify the questionable nature of a diagnosis in a nonendemic area. One article (Isbister and White 2004) describes a Kansas homeowner who collected 2055 brown recluse spiders (over 400 large enough to bite) in his home. Even with this surprising number of spiders residing in the house, no one was bitten over a six-month collection period, or during the six years the family lived in the house. Therefore, any
diagnosis of loxoscelism should be considered highly suspect, even in infested households, if the spider is not caught in the act.

One team of scientists (Vetter, Edwards, and James 2004) compared reports of brown recluse spider bites over six years in Florida to a hundred years of Florida arachnological data. In one hundred years, there were only eleven finds of an actual brown spider specimen, all located within ten Florida counties. Ironically, in just six years of reports made by medical professionals, there were one hundred twenty-four diagnosed brown spider bites, located within thirty-one Florida counties. Another group (Vetter, Cushing, Crawford, and Royce 2003) collected data in California, Oregon, Washington, and Colorado over a forty-one month period. During that time, they were informed of two hundred sixteen loxoscelism diagnosis even thought they could only find historical evidence of thirty-five brown recluse spiders ever collected form those four states. The increasing problem of medical misdiagnosis of brown recluse spider bites is substantiated by the findings obtained in both of these studies.

Conclusion

It was less than a century ago when the first scientist, L. S. Schmaus, established the connection between spider bites and human skin injury in a report documenting the bite of *Loxosceles reclusa* (Swanson and Vetter 2005). Since that time, the belief that spiders cause the majority of skin necrosis cases in the United States has become widely popular. It has been shown by many case studies that the perceived threat of spider bites far exceeds the actual risk. Nevertheless, physicians continue to over-diagnose spider bites even when epidemiological data and historical facts contradict their findings, and patients continue to neglect questioning the diagnoses they receive from medical
professionals. All cases of brown recluse spider bites are not misdiagnoses. Patients do receive bites from \textit{Loxosceles reclusa} and physicians continue to do the best they can with the knowledge and technology available. In a letter to the Lancelet, one scientist writes, “Although it is correct that large numbers of verified spider bites are difficult to accumulate, the medical community should be more persistent in ferreting out these difficult-to-obtain data rather than rely on speculative, presumptive, and quite often erroneous scraps of information which have been the basis for spider envenomation theory and therapy for several species” (Vetter 2004). Scientists and physicians in the field of arachnidology should strive towards establishing a consistent methodology to use as a basis for diagnosing and treating \textit{Loxosceles reclusa} bites. These methods should not be based upon historical, unreliable case studies in which some patients may not even have been bitten by a brown recluse spider, but upon new case studies where efforts were made to be consistent in the diagnosis and the use of various existing therapies. When this is accomplished, perhaps medical professionals will be better informed and the number of incorrect diagnoses in the United States, as well as other countries where errors in diagnosis occur, can be drastically reduced.
References


