

Clinical Presentation and Treatment of Black Widow Spider Envenomation: A Review of 163 Cases

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Study objective: To review cases of black widow spider envenomation to describe the clinical presentation and evaluate the efficacy of treatment.

Design: Retrospective chart review.

Setting: An urban toxicology referral center.

Type of participants: All patients attended by the toxicology service and discharged from our hospital between January 1982 and December 1990 with a diagnosis of black widow spider envenomation.

Interventions: Inclusion criteria were either a positive black widow spider identification or a visible envenomation site ("target lesion"). Depending on the clinical presentation, patients were categorized as grade 1, 2, or 3 in severity. The efficacy and side effects of treatment alternatives were evaluated.

Measurements and main results: One hundred sixty-three patients met the inclusion criteria. The most common sites of envenomation were the upper and lower extremities. The most common presenting complaint was generalized abdominal, back, and leg pain. One hundred eighteen patients initially presented to our institution, and 45 were transfers. Pain relief of grade 2 and 3 envenomations was achieved most effectively with either black widow spider-specific antivenin alone or a combination of IV opioids and muscle relaxants. Fifty-eight patients received antivenin with complete resolution of symptoms in a mean time of 31 ± 26.7 minutes. Of the 118 patients initially seen at our institution, the mean total duration of symptoms was 9 ± 22.7 hours in patients receiving antivenin and 22 ± 24.9 hours in patients not receiving antivenin. Fifty-two percent of patients not receiving antivenin required hospitalization, whereas only 12% of those receiving antivenin were admitted. One patient died of severe bronchospasm after receiving antivenin. Calcium gluconate was not effective in providing symptomatic relief in this series, with 96% of the grade 2 and 3 envenomations treated initially with calcium gluconate requiring the addition of IV opioids or other analgesics for symptomatic relief. Fifty-five percent of patients initially receiving IV morphine and 70% of those initially receiving both IV morphine and benzodiazepines obtained symptomatic relief without additional medication.

Conclusion: One hundred sixty-three envenomations by black widow spiders were reviewed and graded according to severity with treatment modalities evaluated. Although calcium gluconate usually has been considered the first-line treatment of severe envenomations by black widow spiders, we found it ineffective for pain relief compared with a combination of IV opioids and benzodiazepines. The use of antivenin significantly shortened the duration of symptoms in severe envenomations.

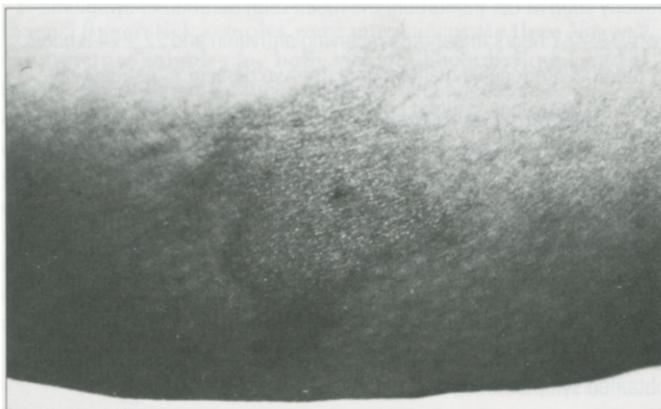
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INTRODUCTION

Superstitions surrounding spiders were reported in Greek mythology, when the jealous goddess Aphrodite transformed Arachne into a spider. In the 17th century, southern Europe experienced a panic over the bite of a spider that is thought to have been a type of wolf spider, *Lycosa tarantula*, and a dance called a "tarantella" was devised to protect bite victims. Much of the folklore concerning bites by large hairy spiders (most of which are harmless) originated from this era. Medical reports of spider bites during this period proclaimed to be from tarantulas more likely were from *Latrodectus tredecimguttatus*, a European species related to the North American black widow.¹

Black widow spiders (*Latrodectus* sp) produce one of the most potent known venoms by volume.² The venom is chiefly a neurotoxin in human beings, with symptoms most often manifested as severe skeletal muscle pain and cramping³ and autonomic disturbances such as diaphoresis and hypertension.³ A variety of treatments have been tried for severe *Latrodectus* envenomations. Muscle relaxants, IV calcium gluconate, opioids, and *Latrodectus*-specific antivenin have been used with reported success.²⁻⁷ Small studies have been undertaken to assess the efficacy of therapy,^{4,8} but the

Figure 1. Typical target lesion, demonstrating the central punctate site of envenomation, a surrounding area of blanching, and the outer erythematous ring



authors could draw no conclusions. We retrospectively reviewed 163 cases of envenomations by black widow spiders to describe the clinical presentation and evaluate the efficacy of treatment.

MATERIALS AND METHODS

The charts of 172 consecutive patients with a diagnosis of black widow spider envenomation directly managed by the toxicology service of an urban hospital and regional toxicology referral center from January 1982 through December 1990 were reviewed retrospectively. The species of black widow found in Arizona is *Latrodectus hesperus* (LH), bites of which are clinically similar to those reported with the more ubiquitous *Latrodectus mactans* and *Latrodectus variolus*.⁹ Venom from *Latrodectus mactans* and *Latrodectus hesperus* are so structurally similar that envenomations by each would be expected to respond similarly to various treatment regimens.^{10,11}

Inclusion criteria for entry into the study were either a positive LH identification by the patient (or hospital staff when the spider was brought to the emergency department) or the presence of an erythematous envenomation site or "target lesion" (Figure 1) on physical examination associated with characteristic symptoms of envenomation. We have found the target lesion a reliable sign of LH envenomation.^{11,12}

Each chart was reviewed for data pertaining to patient age, anatomic location of the bite, time and circumstances of the bite, vital signs, presenting complaint, physical examination findings, total duration of symptoms, laboratory results, transfer data from referral facilities, and treatment including outcome and adverse reactions. "Relief of symptoms" was defined as subjective pain relief as recorded in each patient's medical record for 30 minutes or longer after treatment administration. We divided study patients into grade

Table 1. Grading scale of signs and symptoms following *Latrodectus* envenomations

Grade	Description	Total in Series (%)
1	Asymptomatic Local pain at envenomation site Normal vital signs	15 (9)
2	Muscular pain in envenomated extremity Extension of muscular pain to abdomen if envenomated on lower extremity or chest if envenomated on upper extremity Local diaphoresis of envenomation site or involved extremity Normal vital signs	60 (37)
3	Generalized muscular pain in back, abdomen, and chest Diaphoresis remote from envenomation site Abnormal vital signs: Hypertension (systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mm Hg) Tachycardia (pulse >100) Nausea and vomiting Headache	88 (54)

1, 2, and 3 envenomations depending on severity of symptoms, physical findings, and vital signs (Table 1). Pediatric patients in this study were defined as victims less than 13 years of age, and they were excluded from analysis of vital signs. Grading of envenomations in this group of patients was based on the remaining criteria.

Retrospective follow-up information concerning delayed hypersensitivity reactions was sought on all patients receiving antivenin. All patients receiving antivenin at our institution are educated extensively concerning signs and symptoms associated with delayed hypersensitivity reactions such as rashes, myalgias, pruritus, and fever. Each patient (or accompanying parent for children) was requested to notify the poison center if signs or symptoms of delayed hypersensitivity reactions were observed so that the patient could be re-evaluated or prescriptions ordered if needed. Follow-up data concerning these reactions were recorded by the poison center, and these data were reviewed on patients treated since 1986 for any observed and reported delayed hypersensitivity reactions. In addition, telephone follow-up was attempted to all patients who received antivenin.

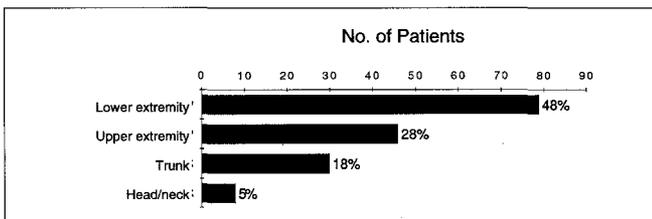
Statistical analysis was performed using Student's *t*-tests and χ^2 analysis. *P* < .05 was taken as statistical significance.

RESULTS

One hundred seventy-two charts with the diagnosis of "black widow spider envenomation" were reviewed, and 163 met inclusion criteria. Ninety-nine patients (61%) were male. Ninety-four patients (58%) were bitten at their residence, and 24 (15%) were bitten by a spider that was in their clothing or shoes as they dressed. Sixteen patients (6%) were bitten in bed. The average age of all patients was 31.6 years, with an age range of 8 months to 88 years. The study group included 18 pediatric patients.

A positive identification of the spider was recorded in 117 charts (72%), whereas a target lesion was mentioned among the recorded physical examination in 79 patients (48%). Patients most often were bitten on the lower extremity (Figure 2). The average time from envenomation until onset of symptoms was 1.15 ± 1.64 hours (ranging from immediately to 12 hours). The average time from onset of symptoms until presentation to a health care facility for all patients was 6.15 ± 7.83 hours (range, 30 minutes to 48 hours).

Figure 2. Locations of *Latrodectus hesperus* envenomation



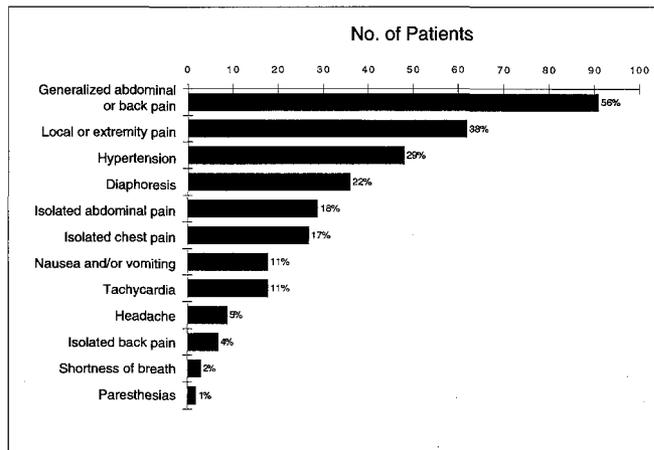
The most common presenting complaint was generalized muscular abdominal, back, and leg pain, although a variety of complaints were recorded (Figure 3). Thirty-six patients (22%) were diaphoretic on presentation. Most adult victims presented with normal vital signs, but 45 (31%) were hypertensive (systolic blood pressure, 140 mm Hg, or diastolic blood pressure, 90 mm Hg). Only six of these patients had a documented history of hypertension. Fourteen adult patients (10%) presented with tachycardia (pulse >100).

The majority of all envenomations were grade 2 (37%) and 3 (54%) in severity (Table 1). Eighty-nine male victims (90%) and 59 female victims (92%) were grade 2 or 3 envenomations. Eighty grade 2 or 3 patients (54%) were 31 years old or younger.

Twenty-two patients (14%) in this series initially were sent home after evaluation in an ED or physician's office but returned to an ED with recurring pain. One hundred eighteen patients (72%) in the study initially were seen at our institution. Forty-five patients (28%) were transferred to our institution from another facility due to treatment failures of grade 2 or 3 envenomations. Of the 45 transferred patients, 15 (33% of those transferred) had received either calcium gluconate alone or in combination with a muscle relaxant such as methocarbamol. Only six (13%) had received a trial of IV or IM opioids. The remainder of patients had received some combination of oral analgesics, IV muscle relaxants, or other therapies. None had received antivenin.

Laboratory testing was performed on some severe envenomations (Table 2). Twenty-one of 54 patients with laboratory work performed had abnormal laboratory findings, the most common being leukocytosis. Although 38 patients with severe muscle pain and cramping were evaluated with total creatine phosphokinase levels, only seven were found to have elevated values (highest, 1,350; mean, 718 IU/L). Myoglobinuria was not evaluated.

Figure 3. Common signs and symptoms associated with *Latrodectus hesperus* envenomations



Patients in this series received an assortment of medications (Figure 4). Twenty-four patients with grade 2 or 3 envenomations initially received calcium gluconate (mean total dose, 1,400 mg; range, 100 to 4,000 mg). Twenty-three of those patients (96%) reported no relief after calcium administration and continued to experience severe pain, requiring the addition of antivenin (five) or some combination of parenteral opioids and benzodiazepines (18) for relief of symptoms. Seventy-five grade 2 or 3 patients initially were treated with parenteral opioids (49 patients; IV or IM morphine [mean total, 15 mg; range, 2 to 80 mg] or meperidine [mean total, 88 mg; range, 25 to 475 mg]) or a combination of parenteral opioids (mean total morphine, 20 mg; mean total meperidine, 50 mg) and benzodiazepines (26 patients; diazepam [mean total, 15 mg; range, 2 to 60 mg] or lorazepam [mean total, 4 mg; range 2 to 10 mg]). In this group, 27 (55%) initially treated with parenteral opioids and 18 (70%) initially treated with a combination of parenteral opioids and benzodiazepines obtained symptomatic relief without additional medication.

A total of 58 patients received antivenin; 46 (79%) were grade 3. All patients receiving antivenin had complete resolution of symptoms in a mean time of 31 ± 26.7 minutes (ranging from immediately to 120 minutes) from the end of the infusion. No relapses in symptoms were recorded. Fifty patients were recorded as describing relief of pain after one vial and required no further pain medication, whereas seven patients required an additional vial. No patient required more than two vials.

Patients initially seen at our institution were grouped into those who received antivenin (42, antivenin group, excluding one fatality) and those who did not (76, no-antivenin group) to compare efficacy of treatment. All antivenin patients and 69 no-antivenin patients (88%) were either grade 2 or 3 envenomations. Excluding grade 1 envenomations, the average time from onset of symptoms to presentation in the ED was not significantly different between antivenin and no-antivenin groups (Table 3). However, the average duration of symptoms after envenomation in the antivenin group was

9 ± 22.7 hours compared with 22 ± 24.9 hours ($P < .05$, Student's *t*-test) in the no-antivenin group.

Thirty-nine no-antivenin patients (52%) required admission to the hospital for an average of 1.46 days, whereas only five antivenin patients (12%) were admitted (mean, 1.14 days). Four of the five patients admitted after receiving antivenin were admitted for overnight observation after urticarial reactions to antivenin infusion. The remaining patient, who had a history of coronary artery disease, had a brief episode of chest pain and some nonspecific ST-T wave changes on ECG before receiving antivenin. She was admitted for observation, and myocardial infarction was ruled out. All no-antivenin patients hospitalized required admission for repeated administration of parenteral analgesics.

One patient receiving antivenin suffered a fatal respiratory arrest with severe anaphylactic bronchospasm following its administration. This individual reportedly had a history of asthma. Bronchospasm occurred rapidly after antivenin was infused and was refractory to epinephrine and other resuscitative measures. There was no mortality recorded in the patients not receiving antivenin.

Retrospective telephone follow-up to evaluate delayed hypersensitivity reactions was attempted in the 50 antivenin patients with available telephone numbers. Nine were contacted, and none reported any symptoms resembling delayed hypersensitivity reactions. Poison center follow-up data were available and reviewed on nine additional antivenin patients since 1986, but none reported any symptoms consistent with delayed hypersensitivity reactions.

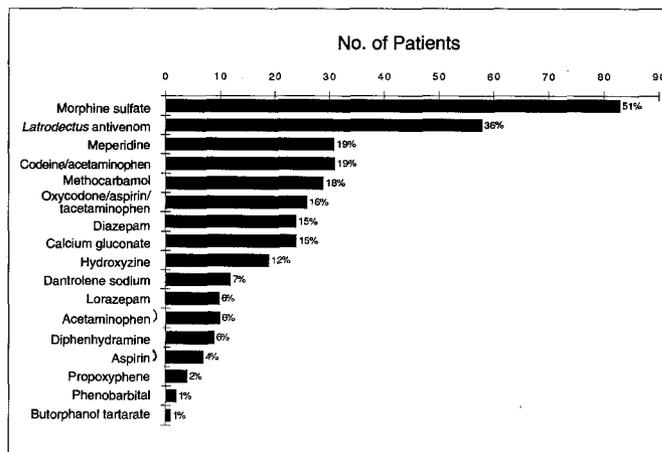
DISCUSSION

Of the 20,000 spiders species found in the United States, all except two are considered venomous. Only 50 of these species have fangs that can penetrate human skin.² Small quantities of venom and weak delivery systems limit severe toxicity in this group.²

Table 2.
Laboratory results from 54 patients envenomated by *Latrodectus hesperus* in this series

Test	Total Performed	No. Abnormal
CBC	44	14
Total creatine phosphokinase	38	7
Electrolytes, blood urea nitrogen, creatinine, glucose	30	0
SMA 20	10	5
Urinalysis	10	2
ECG	4	1
Chest radiograph	2	0
Most Common Abnormalities	No.	
Elevated WBC	14	
Elevated creatine phosphokinase	7	
Elevated lactic dehydrogenase	4	

Figure 4.
Medications used in treatment of *Latrodectus hesperus* envenomations



Latrodectus genus spiders have been the leading cause of death from arachnid envenomation in this country.³ Five species are found in the United States, with at least one in every state except Alaska.³ The most common are *Latrodectus mactans* and *Latrodectus variolus*, which are located abundantly in southern and eastern states. The venoms of *Latrodectus* sp are virtually identical and thought to act at the neuromuscular junction by binding to glycoproteins or gangliosides on the presynaptic membrane and opening cation channels.¹³ Large quantities of acetylcholine then are released from the presynaptic neuron while the reuptake of choline is inhibited simultaneously. The result is pain and cramping of large muscle groups. Severe envenomations also have been reported to cause weakness,⁵ hypertension,⁵ priapism,¹⁴ and, rarely, death.⁵

As with any retrospective study, our analysis was limited by the accuracy of the medical records. We have attempted to limit these biases by establishing operational definitions for data entry with strict inclusion and exclusion criteria. In addition, envenomated patients at our medical center are cared for by a small group of toxicologists, providing more uniform medical record documentation.

Our data agree with those of previous reports in that most bites occur on the extremities and that generalized pain in the back or abdomen is the most frequent presenting complaint of patients seeking medical help after *Latrodectus* envenomation. We have noticed several trends in the presentations we have encountered. Diaphoresis was common in our review and often presents in unusual distributions. Perspiration may be confined to the bitten extremity or even to the skin immediately overlying the site of envenomation. The face and especially the forehead and nose also are frequently diaphoretic when other body parts are dry.

Hypertension was noted in 31% of adult patients in this study and has been reported as a frequent finding by others.^{3,8} Elevations in blood pressure have been proposed to result from action of the venom on vasomotor centers in the brain stem and spinal medulla.¹⁵ It also is possible that acetylcholine liberated at cholinergic sympathetic ganglia may result in postganglionic release of norepinephrine-stimulating peripheral α -receptors, leading to vasoconstriction.⁹

Envenomation-induced hypertension usually responds to treatment with antivenin and may respond to analgesics, but patients with underlying medical conditions and severe hypertension may require additional antihypertensive therapy. Hypertensive patients who are not candidates for antivenin and do not respond to supportive pain management are likely to require admission.

Symptoms in victims of severe *Latrodectus* envenomation have been noted to “wax and wane.”⁹ From our experience, many patients will demonstrate this clinical pattern and will appear to improve regardless of treatment if they are observed for a period after the envenomation. If they are not treated with antivenin, pain often returns, requiring additional medical management. This is probably the rationale behind reports of successful treatment of severe envenomations with medications such as calcium gluconate.^{2,4,6,7,11}

There is limited scientific evidence supporting the use of calcium for *Latrodectus* envenomations. Animal data suggest that *Latrodectus* venom increases the permeability of the nerve terminal membrane to calcium³ and that high extracellular concentrations of calcium antagonize the releasing effects of black widow spider venom on neurotransmitters at nerve endings.¹⁶ Most human experience with calcium gluconate is anecdotal, with symptoms often recurring within 20 minutes of infusion.⁹ We found that very few patients received any pain relief from calcium gluconate infusion, and all except one subsequently required IV or IM opioids for pain relief. We therefore recommend that patients with severe envenomations who are not candidates for antivenin be treated with parenteral opioids or a combination of parenteral opioids and sedative-hypnotics such as diazepam or lorazepam. Many of these patients will need admission for observation and pain control, but symptoms usually resolve within 24 to 48 hours.

This is the largest reported series of *Latrodectus* envenomations and the largest series to receive *Latrodectus*-specific antivenin. A significant difference was found in duration of symptoms in the antivenin group versus the no-antivenin group. Patients receiving antivenin rarely required admission, and those who did predominantly were for observation following mild urticarial reactions noted during antivenin infusion. No patient required additional pain medication once pain relief was obtained after receiving antivenin.

The fatality reported by our data demonstrates the need for prudence in the administration of this equine serum product. Patients with allergies to horse serum products and those who previously had received antivenin or horse serum products are at risk for immunoglobulin E-mediated immediate hypersensitivity reactions. As with all equine serum preparations, rapid administration of antivenin can induce histamine release and anaphylactoid signs and symptoms in most patients.

We have found that slow administration of antivenin, especially at the beginning of the infusion, usually is well tolerated. We place one vial of antivenin in 50 to 100 mL of 5% dextrose

Table 3.
Comparison of *Latrodectus*-specific antivenin versus no antivenin in treatment of severe *Latrodectus hesperus* envenomations presenting initially to our institution

	Antivenin	No Antivenin
No. of total grade 2 or 3 patients	42	65
Time from onset of systems until presentation (hr)	3.1 ± 2.9* (<i>P</i> > .05, Student's <i>t</i> -test)	5.2 ± 4.6
Duration of symptoms (hr)	8.7 ± 22.7* (<i>P</i> < .05, Student's <i>t</i> -test)	22.1 ± 24.9
No. of patients admitted	5 (<i>P</i> < .05, χ^2)	39
Average length of hospitalization for admitted patients (days)	1.14 (<i>P</i> > .05, Student's <i>t</i> -test)	1.46

*Excluding one fatality.

or normal saline solution and infuse the combination over 20 to 30 minutes. Skin testing before administration may detect a highly allergic individual, but a negative skin test cannot rule out completely the occurrence of hypersensitivity reactions. Pretreatment with histamine₁ or histamine₂ blockers may be beneficial in preventing histamine release, but their efficacy in this situation is unproven. We advise that the administration of antivenin be reserved for severe grade 2 or 3 envenomations in patients without risk factors for immediate hypersensitivity reactions.

CONCLUSION

We studied 163 cases of *Latrodectus* envenomation for clinical presentation and graded each according to severity. The presenting complaints in this study parallel those of previous reports. Although calcium gluconate has been considered the first-line treatment of severe *Latrodectus* envenomations, we found it ineffective for pain relief compared with antivenin or a combination of parenteral opioids and benzodiazepines. *Latrodectus*-specific antivenin was found to be effective in rapidly and irreversibly relieving symptoms in severe envenomations. The use of *Latrodectus*-specific antivenin should be restricted to patients who have severe envenomation and no allergic contraindications and in whom IV or IM analgesics were unsuccessful for pain relief.

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