

# The Clinical Characteristics of Brown Recluse Spider Bites Treated by Family Physicians

## An OKPRN Study

Jim Cacy, PhD, and James W. Mold, MD  
Oklahoma City, Oklahoma

**BACKGROUND.** The brown recluse spider (*Loxosceles reclusa*) has been recognized as a cause of necrotizing bites since at least 1957, but most of the literature consists of laboratory studies using animals, human sera, or case reports of more dramatic examples of bite reactions. Our goal was to develop a more comprehensive clinical description of the brown recluse spider bites treated by family physicians.

**METHODS.** Two preprinted, postage-paid cards were given to physician members of the Oklahoma Physicians Research Network. One card was used for recording examination and treatment data, and the other was for tracking the progress of the bite until it was completely healed. For comparison, similar information was collected from the local poison control center.

**RESULTS.** From April 1996 to August 1998, the physicians recorded 149 bites. Most of the victims were women aged 18 to 65 years, and most sought treatment within 3 days. Pain was common but not universal. Most bites were located on the extremities. Erythema was always present, but necrosis was present in only 40% of the bites. Some systemic signs or symptoms were common. The most frequent forms of treatment were systemic antibiotics (66% of cases) and conservative wound management (56%). Only 1 hospitalization occurred; 43% of the bites healed within 2 weeks; and only 13% resulted in scarring.

**CONCLUSIONS.** The brown recluse spider bite is a relatively common problem treated by family physicians in Oklahoma. Most bites are not serious. More research at the practice level is needed to develop diagnostic criteria and to explore the effectiveness of various treatment options.

**KEY WORDS.** Research; spider; arachnidism; epidemiology. (*J Fam Pract* 1999; 48:536-542)

**L***oxosceles reclusa* is known by many names, including brown recluse spider, violin spider, Arizona brown spider, fiddle or fiddleback spider, and necrotizing spider. Its color is tan to brown with a violin-shaped marking on the dorsum of the cephalothorax (Figure 1). The adult is approximately 9 mm in length, with a leg span of approximately 25 mm. Brown recluse spiders are found predominantly in the South Central and Southeastern United States, from Oklahoma to Georgia and Iowa to Louisiana. Outdoors, they are typically found in warm, dry places, such as under the bark of dead trees, under stones, and in piles of lumber or firewood. They may also be found in outbuildings or inside the home in places that are dark, dry, and rarely disturbed by humans.<sup>1,3</sup> Victims are typically bitten while dressing in clothing that has been stored undisturbed for some time, when rolling over onto a spider that has crawled into the bed in search of food, when moving boxes stored in an attic or basement, or when dis-

turbing a pile of wood or rocks. Controlling infestations is difficult, because this spider can survive for 6 months without food or water, and chemicals potent enough to kill it are also hazardous to humans.<sup>4</sup>

This spider was identified as a cause of necrotizing bites by 1957,<sup>5</sup> and perhaps as early as 1893.<sup>6</sup> The victim may not feel the bite initially, but within 2 to 3 hours a stinging sensation is usually followed by intense pain and erythema. A small dark blister may appear, and a large area around the bite may become congested, swollen, and hard to the touch. The tissue gradually sloughs away, and healing usually takes 6 to 8 weeks, leaving a sunken scar. Figure 2 depicts a brown recluse bite in the early stages; Figure 3 is the same bite in later stages but before it is completely healed.

Patients in poor physical condition, the very young, and the elderly may experience serious systemic reactions. There have been reports of death, thought to be primarily due to renal failure following a bite.<sup>7,9</sup> Systemic reactions are relatively rare, however, and brown recluse bites do not always produce the necrotic lesion.<sup>10,11</sup>

This bite is often confused with other bites and disease states.<sup>12-17</sup> Russell and Gertsch<sup>16</sup> listed 13 disease states that have been observed to cause necrotic lesions that may appear similar to the brown recluse bite (erythema chronicum migrans, Stevens-Johnson syndrome, Lyells

Submitted, revised, April 21, 1999.

From the Department of Family and Preventive Medicine, the University of Oklahoma, Oklahoma City. Reprint requests should be addressed to Jim Cacy, PhD, the University of Oklahoma, Department of Family and Preventive Medicine, 900 NE 10<sup>th</sup> St, Oklahoma City, OK 73104. E-mail: jim-cacy@ouhsc.edu.



FIGURE 1

Brown recluse spider.



Image courtesy of Thomas R. Fasulo, extension entomologist, University of Florida.

syndrome or toxic epidermal necrosis, erythema nodosum, erythema multiforme, infected herpes simplex, purpura fulminana, diabetic ulcer, bed sore, poison oak, poison ivy, chronic herpes simplex, and gonococcal arthritic dermatitis). They also reported that necrotic lesions have been noted in bites determined conclusively to have been caused by solpugids, ticks, assassin bugs, and even Jerusalem crickets and grasshoppers.

There have been a number of laboratory studies of brown recluse venom<sup>18-37</sup> using animals and human sera. Sphingomyelinase-D is thought to be the component of brown recluse venom that is the primary cause of local and systemic reactions. The local reaction is also associat-

ed with polymorphonuclear (PMN) leukocyte infiltration. Severe systemic reactions are associated with hemolysis, hemolytic anemia, or hemoglobinuria.

Diagnostic laboratory tests have been developed and proposed, but no commercial test is available.<sup>38-42</sup> Proposed treatments have included dapsone,<sup>18,43-48</sup> colchicine,<sup>49</sup> corticosteroids,<sup>50-54</sup> antihistamines,<sup>55-59</sup> hyperbaric oxygen,<sup>43,48,60-63</sup> high-voltage direct current (HVDC),<sup>65-69</sup> early surgical excision, late surgical excision,<sup>44,45,51,68-70</sup> nitroglycerin patches,<sup>71</sup> and conservative wound management<sup>10,12,72</sup> (ice packs, immobilization, symptomatic treatment); however, none of these has been proved effective in controlled trials with humans. Dapsone, which can have dangerous side effects, has shown some mixed success when treatment is begun before the more serious dermatologic sequelae begin to appear; corticosteroids are generally advocated for aggressive treatment of systemic symptoms.

A number of case reviews have been published,<sup>11,44,47,50,65,66,69,70,73,71,74-77</sup> but only Fardon and colleagues<sup>69</sup> made an attempt to gather information about brown recluse bite management by groups of clinicians. They surveyed 30 physicians in Kansas regarding their experience with brown recluse envenomation. More than 80% of the physicians responded, and only 6 (20%) reported no experience with the problem. Twelve reported having seen 1 to 10 cases; 4 reported 10 to 30 cases; 1 reported 100 cases; and 1 reported 200 cases. No time frame was given, so it is impossible to estimate the frequency of contact, and no information was presented about bite characteristics. One clinical trial<sup>78</sup> with humans compared dapsone, dapsone plus antivenom, and antivenom alone. No difference in healing rate or complications was found between the groups.

Questions remain regarding characteristics of lesions thought by family physicians to be brown recluse bites, the average healing time of those lesions, the probabilities of complications and scarring, and the spectrum of treatment approaches being used. To better characterize the problems these bites pose to family physicians in Oklahoma, we conducted a prospective study involving physician members of the Oklahoma Physicians Research Network (OKPRN). OKPRN is a practice-based research network consisting of 25 practices and 33 members. The practices are dispersed throughout Oklahoma with 5 located in rural settings, 8 urban, and 11 in medium-sized cities. All OKPRN physicians are members of the Oklahoma Academy of Family Physicians and are residency trained and board certified.

FIGURE 2

Early brown recluse bite.

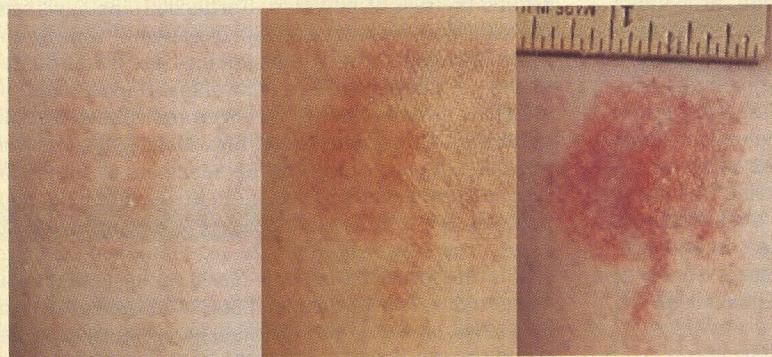


Photo courtesy of John Ronck, MD (victim) and Michael Pontious, MD (photographer).



FIGURE 3

## Late brown recluse bite.



Photo courtesy of John Ronck, MD (victim) and Michael Pontious, MD (photographer).

## METHODS

We conducted a literature search, and an annotated bibliography of pertinent articles was prepared and circulated to all OKPRN members. Cards were designed, and a protocol for the study was prepared. The members reviewed the proposed cards and protocol, and a few modifications were made. The study was approved by the members, and data collection began as soon as they returned to their practices.

Data for this study were recorded by 27 physicians from 19 OKPRN practices on 2 preprinted, postage paid cards. The first was completed when the physician encountered a patient with a suspected brown recluse bite, and the second was used to follow the progress of the lesion until healed. Beginning in May 1995, physicians were asked to fill out a card on every lesion that they thought might be a brown recluse spider bite, using whatever criteria they usually used to make that assessment. On the card were questions about the time and place of the bite, whether the spider was identified, patient characteristics, severity of the bite, probability that it was a brown recluse bite, symptoms, signs, treatment provided, and whether the patient required hospitalization. They were then asked to see or make telephone contact with the patient weekly until the lesion had healed (epithelialization and resolution of edema and induration) and complete the second card documenting the date of healing, whether [or not] scarring was likely, and their retrospective estimate of the likelihood that the lesion had been a brown recluse bite. In addition, data were collected from the Poison Control Center of Oklahoma on every call regarding a suspected brown recluse bite beginning in May 1996.

Data were entered into a computer database and analyzed using Microsoft Excel (Microsoft Corporation, Redmond, Washington).

## RESULTS

Between April 11, 1996, and August 1, 1998, the members of OKPRN reported 149 possible brown recluse bites. Follow-up data were obtained on 112 of these. On the basis of initial probability assessments, 33% were possible brown recluse spider bites; 51% were probable; and 13% were felt to be definite. In retrospect, 11% of the lesions were rated "not a brown recluse bite," 22% as possible, 40% as probable, and 9% as definite. Thirty-nine percent of the bite victims were men, 59% were women, 2% had no gender recorded on their cards. Patients younger than 21 years accounted for 17% of the cases, 74% were aged 21 to 65 years, and 4% were older than 65 years.

Table 1 presents a summary of the data collected. For cases reporting necrosis, the average diameter was 1.00 cm (range = 0.1 to 5 cm). Erythema averaged 5.84 centimeters (range = 0.5 to 37 cm). Reported induration averaged 3.71 cm (range = 0.02 to 42 cm). The average delay in seeking treatment was 3.31 days (range = 0 [same day] to 38 days). The average time from treatment to healing was 15.25 days (range = 0 to 78 days).

The card used for data collection provided a space for the physician to write down any systemic signs or symptoms noted during the patient's visit. (Table 2). As indicated in Table 1, 27% of the bites had at least 1 systemic symptom, and 14% had at least 1 systemic sign.

During the visit, the patient was asked what he or she was doing when bitten. The majority of the patients' responses (84 cases, 56%) were either "asleep" (41 cases) or "unknown" (43 cases). The rest reported activities that would predict a high probability of an encounter with a brown recluse spider, such as working in or cleaning out storage areas, garages, and other low-traffic areas (14 cases); putting on clothing (6 cases); and working or playing outside (20 cases). A summary of the treatments used is provided in Table 3.

Conservative wound management is mainly directed at reducing swelling and the spread of venom (eg, in the use of ice packs) and cleansing to reduce the risk of infection. Systemic and topical antibiotics are used to reduce the risk of infection. Corticosteroids have been used for their protective effects in systemic, topical, and local injection form. Antihistamines are administered mainly to relieve pruritis and swelling. Dapsone may be effective in ameliorating the necrotic effects of PMN infiltration subsequent to the bite. Meat tenderizer was suggested by one of the OKPRN members as something that might break down the venom toxins into innocuous peptides. HVDC refers to the use of "stun gun" treatment as advocated by Osborn.<sup>65,66</sup> The use of topical nitroglycerin in the form of a patch is based on anecdotal data<sup>71</sup> suggested by one of the members; some scientific basis for its use, however, may be found in literature exploring the beneficial role of nitric oxide in tissues.<sup>79</sup>

An arrangement was made with the Oklahoma Poison Control Center to use a modified form of the OKPRN card



TABLE 1

Data Summary for Patients with Suspected Brown Recluse Spider Bites

Variable	Cases, %
Location when bitten	
Indoors	58
Outside	19
Unknown	22
Patient felt bite	14
Bite position	
Arm or hand	25
Leg or foot	42
Trunk	19
Face or head	13
Spider identified	15
Brown recluse seen in area	54
Bitten before	13
Systemic symptoms	27
Systemic signs	14
Erythema	97
Induration	72
Pain at site of bite	60
Itch	59
Necrosis	40
Blisters or vesicles	28
Drainage	9
Delay in seeking help ≤2 days	54
Delay in seeking help >2 days	44
Time to heal >2 weeks	57
Time to heal <2 weeks	43
Scar after healing	13

to collect data from telephone calls if the victim was suspected to have been bitten by a brown recluse spider. The Poison Control Center logged a total of 293 suspected brown recluse bites from April 1996 through December 1997. These data agree with OKPRN data that the bite of the brown recluse is primarily a warm-weather phenomenon, and are roughly similar to the OKPRN data reported in Table 1.

## DISCUSSION

The purpose of this study was to describe the characteristics of suspected brown recluse spider bites seen by family physician members of OKPRN and to examine the treatment and management provided by these physicians. The brown recluse bite appears to be a common problem for physicians in Oklahoma.

TABLE 2

Systemic Signs and Symptoms of Patients with Suspected Brown Recluse Spider Bites

Sign or Symptom	Cases, %
Nausea	7
Rash	5
Fever, fatigue	3
Headaches, myalgia, pain	2
Arthralgia, chill, itch, malaise, red streaks	1
Muscle aches, joint aches, adenopathy, leg cramps, lightheadedness, lymphangitis, nausea or vomiting, chest pain, side pain, unconsciousness, swelling	<1

TABLE 3

Treatments for Suspected Brown Recluse Spider Bites

Treatments	All Cases (N = 149)	
	n	%
Conservative*	83	56
Systemic antibiotics	98	66
Systemic steroids	46	31
Antihistamines	35	23
Dapsone	25	17
Topical antibiotics	24	16
Local injection steroids	9	6
Topical steroids	8	5
Meat tenderizer	4	3
HVDC†	3	2
Nitroglycerine patch	3	2

\*Conservative treatment refers to cleansing, immobilization, ice packs, and symptomatic treatment.

†HVDC denotes high-voltage direct current, the "stun gun" treatment thought by some to have a denaturing effect on the brown recluse venom.

Three previous studies<sup>45,70,80</sup> provided patient characteristics that are roughly comparable to those from our study (Table 4). Those studies all took place in hospital settings, and patients were mostly referrals or emergency room visits. Most of the bites in those studies appear to have been in early stages and were not clearly severe at the time of presentation.

Case reports of bites tend to focus on more dramatic examples, those with severe necrosis, systemic reactions, even death; however, it is commonly noted that many if



TABLE 4

## Comparisons with Other Studies

Characteristic	Study			
	Rees et al <sup>45</sup> (N = 31)	Clowers <sup>80</sup> (N = 39)	Wright et al <sup>28</sup> (N = 111)	Current study (N = 149)
Age, years	16 - 72, average 33	3 - 68, majority 16 - 45	34 ±17	11 - 82, average 38, majority 21 - 65
Women, no. (%)	16 (52)	22 (56)	54 (49)	49 (55)
Treatment delay	0.5 to 9 days, average 2.4	Emergency treatment within 48 hours of bite	38 <24 hrs 38 24 - 72 hrs 35 >72 hrs	0 to 14 days, average 3.2 days, 6 same day 55 1 to 3 days
Pain, no. (%)	Not reported	27 (69)	Not reported	58 (65)
Bitten on extremity, no. of cases (%)	28 (90)	29 (74)	87 (78)	61 (69)
Erythema, no. (%)	31 (100)	37 (94.9)	Not reported	87 (98)
Erythema diameter, cm	1 - 22, average 7.4	<2.5 to >15	Not reported	0 - 37, average 6.2
Necrosis, no. (%)	31 (100)	Not reported	41 (37)	41 (46)
Necrosis diameter, cm	0 - 4 , average 1.2	Not reported	Not reported	0 - 3.75 average 0.48
Systemic signs or symptoms, no. (%)	Not reported	Fever in 17 (44)	18 (16), 16 systemically ill	42 (47)

not most brown recluse bites are unremarkable,<sup>17,49,59,70,77</sup> and the present study echoes that sentiment. To obtain a more unbiased picture of the true nature and magnitude of the health threat presented by the bite of the brown recluse, more studies with a wider scope are needed. It also appears that practice-based research on the brown recluse bite would benefit from more standardization and detail in the data reported.

The primary strength of our study is the inclusion of less dramatic bites and the collection of data from a larger group of physicians in practices ranging from urban to rural.

The most serious limitation to our study is the absence of a definitive laboratory test or standard diagnostic criteria for brown recluse spider bites. However, a comparison between bites felt to be "probable or definite" by practitioners differed very little except in severity from those felt to be "possible". Without such a test, the development of triage or diagnostic criteria is very difficult.

## CONCLUSIONS

In Oklahoma, the bite of the brown recluse spider seems to be a problem from May to October. None of the bites

logged as definite occurred outside that time period, and winter cases reported to the poison control center were most likely not brown recluse bites.

The data in Table 4 support some tentative conclusions. Most brown recluse spider bite victims are children older than 16 years and adults younger than 65 years. Slightly more victims are women. Most victims seek treatment within 3 days. Pain is fairly common but not a certainty. Most bites occur on the extremities. Erythema is virtually a certainty, but necrosis occurs in less than half.

Patients' responses to bites are usually limited to dermal reaction but are often accompanied by minor systemic symptoms. Hospitalizations are rare. Although classification schemes for assessing bite severity have been proposed,<sup>12,68</sup> and at least 1 attempt was made to develop a triage scheme,<sup>80</sup> there are no diagnostic criteria or commercial laboratory tests available.

## ACKNOWLEDGMENTS

This study was supported in part by the US Department of Health and Human Services, Public Health Service, Health Resources and Services Administration, Bureau of Health Professions, Division of Medicine 42 USC 293K Section 747(B) PHS Act, Grants for Establishment of Departments of Family Medicine grant #1 D32 PE10117-01; and in part by grant #G9708 from the Joint American Academy of Family Physicians Foundation/American Academy of



Family Physicians Grant Awards Council.

We are grateful for the contributions of Drs Mike Aaron, JoAnn Carpenter, Tony Drain, Mark Gregory, John Leatherman, Dan Woiwode, Dee Legako, Dale Peterson, Tim Siler, Jim Lynch, Keith Underhill, Jeffrey Spear, Ed Farrow, Christopher Sturch, Stan Jackson, Mark Cotton, Kurt Frantz, John Ronck, Mike Pontious, Joe Jamison, Bill Bondurant, Terry Truong, David Rogers, Paul Preslar, Helen Franklin, Kyle Waugh, Marcia Mathews, Stephen Cobb, Cary Fisher, John Pittman, James Carley, K. Ramakrishnan, David Hadley, Keith Conoway, Scott Stewart, Tina Cooper, Samantha Lewellen; and Gary Sharp, PA, MPH. We are also grateful to Lee McGoodwin, MS, RPH, clinical assistant professor and managing director of the Oklahoma Poison Control Center, and to the staff of the center.

## REFERENCES

- Allen C. Arachnid envenomations. *Emerg Med Clin North Am* 1992; 10:269-98.
- [No authors listed]. Necrotic arachnidism: Pacific Northwest, 1988-1996. *MMWR Morb Mortal Wkly Rep* 1996; 45:433-6.
- Hite JM, Gladney WJ, Lancaster JL, Whitcomb WH. Biology of the brown recluse spider. *Bulletin* 711. Fayetteville, Ark: Agricultural Experiment Station, Division of Agriculture, University of Arkansas, 1966.
- Hall RD, Anderson PC. Brown recluse spider bites: can they be prevented? *Mo Med* 1983; 78:243-4.
- Atkins JA, Curtis WW, Sodeman WW. Probable cause of necrotic spider bite in the midwest. *Science* 1957; 126:73.
- Wilson JT. Poisoning by the bite of the southern spider. *Tr South S Gynec* 1893; 5:406.
- Ginsberg CM, Weinberg AG. Hemolytic anemia and multiorgan failure associated with localized cutaneous lesion. *J Pediatr* 1988; 112:496-9.
- Lessenden C, Zimmer L. Brown spider bites: a survey of the current problem. *J Kans Med Soc* 1960; 379-85.
- Vorse H, Seccareccio P, Woodruff K, Humphrey GB. Disseminated intravascular coagulopathy following fatal brown spider bite (necrotic arachnidism). *J Pediatr* 1972; 80:1035-7.
- Anderson PC. Brown recluse spider bites: some immunologic aspects. *IMJ* 1978; 53:150-3.
- Anderson PC. Loxoscelism threatening pregnancy: five cases. *Am J Obstet Gynecol* 1991; 165:1454-6.
- Anderson PC. Necrotizing spider bites. *Am Fam Physician* 1982; 26:198-203.
- Gendron BP. *Loxosceles reclusa* envenomation. *Am J Emerg Med* 1990; 8:51-4.
- Rosenstein ED. Lyme disease misdiagnosed as a brown recluse spider bite. *Ann Intern Med* 1987; 107:782.
- Russell FE. Arachnid envenomations. *Emerg Med Ser* 1991; 20:16-47.
- Russell FE, Gertsch WJ. Last word on araneism. *Am Arach* 1982; 7:10.
- Blackman JR. Spider bites. *J Am Board Fam Pract* 1995; 8:288-94.
- Patel KD, Modur V, Zimmerman GA, Prescott SM, McIntyre TM. The necrotic venom of the brown recluse spider induces dysregulated endothelial cell-dependent neutrophil activation: differential induction of GM-CSF, IL-8, and E-selectin expression. *J Clin Invest* 1994; 94:631-42.
- Elgert KD, Ross MA, Campbell BJ, Barrett JT. Immunological studies of brown recluse spider venom. *Infect Immun* 1974; 10:1412-9.
- Babcock JL, Civello DJ, Geren CR. Purification and characterization of a toxin from brown recluse spider (*Loxosceles reclusa*) venom gland extracts. *Toxicon* 1981; 19:677-89.
- Forrester LJ, Barrett JT, Campbell BJ. Red blood cell lysis induced by the venom of the brown recluse spider: the role of sphingomyelinase D. *Arch Biochem Biophys* 1978; 187:355-65.
- Futrell JM, Morgan PN. Identification and neutralization of biological activities associated with venom from the brown recluse spider, *Loxosceles reclusa*. *Am J Trop Med Hyg* 1977; 26:1206-11.
- Gates CA, Rees RS. Serum amyloid P component: its role in platelet activation stimulated by sphingomyelinase D purified from the venom of the brown recluse spider (*Loxosceles reclusa*). *Toxicon* 1990; 28:1303-15.
- Gebel HM, Finke JH, Elgert KD, Cambell BJ, Barrett JT. Inactivation of complement by *Loxosceles reclusa* spider venom. *Am J Trop Med Hyg* 1979; 28:756-62.
- Geren CR, Chan TK, Howell DE, Odell GV. Partial characterization of the low molecular weight fractions of the extract of the venom apparatus of the brown recluse spider and of its hemolymph. *Toxicon* 1975; 13:233-8.
- Heitz JR, Norment BR. Characteristics of an alkaline phosphatase activity in brown recluse venom. *Toxicon* 1974; 12:181-7.
- Morgan PN. Preliminary studies on venom from the brown recluse spider *Loxosceles reclusa*. *Toxicon* 1969; 6:161-5.
- Wright RP, Elgert KD, Campbell BJ, Barrett JT. Hyaluronidase and esterase activities of the venom of the poisonous brown recluse spider. *Arch Biochem Biophys* 1973; 159:415-26.
- Futrell JM, Morgan PN. Inhibition of human complement components by *Loxosceles reclusa* venom. *Int Arch Allergy Appl Immunol* 1978; 57:275-8.
- Futrell JM, Morgan PN, Su SP, Roth SI. Location of brown recluse venom attachment sites on human erythrocytes by the ferritin-labeled antibody technique. *Am J Pathol* 1979; 95:675-82.
- Gates C, Rees RS. Platelet activation stimulated by the toxin of the brown recluse spider requires serum amyloid P component, not C-reactive protein. *Toxicon* 1989; 27:953-4.
- Hufford DC, Morgan PN. C-reactive protein as a mediator in the lysis of human erythrocytes sensitized by brown recluse spider venom. *Proc Soc Exp Biol Med* 1981; 167:493-7.
- Majeski JA, Stinnett JD, Alexander JW, Durst GG Sr. Action of venom from the brown recluse spider (*Loxosceles reclusa*) on human neutrophils. *Toxicon* 1977; 15:423-7.
- Morgan BB, Morgan PN, Bowling RE. Lysis of human erythrocytes by venom from the brown recluse spider, *Loxosceles reclusa*. *Toxicon* 1978; 16:85-8.
- Rees RS, O'Leary JP, King LE Jr. The pathogenesis of systemic loxoscelism following brown recluse spider bites. *J Surg Res* 1983; 35:1-10.
- Rees RS, Gates C, Timmons S, Des Prez RM, King LE Jr. Plasma components are required for platelet activation by the toxin of *Loxosceles reclusa*. *Toxicon* 1988; 26:1035-45.
- Smith CW, Micks DW. The role of polymorphonuclear leukocytes in the lesion caused by the venom of the brown spider, *Loxosceles reclusa*. *Lab Invest* 1970; 22:90-3.
- Forrester LJ, Barrett JT, Campbell BJ. Serodiagnostic test for *Loxosceles reclusa* bites. *Clin Tox* 1974; 7:375-82.
- Barrett SM, Romine-Jenkins M, Blick KE. Passive hemagglutination inhibition test for diagnosis of brown recluse spider bite envenomation. *Clin Chem* 1993; 39:2104-7.
- Berger RS, Millikan LE, Conway F. An in vitro test for *Loxosceles reclusa* spider bite. *Toxicon* 1973; 11:465-70.
- Cardoso J, Wen FH, Franca F, Warrell D, Theakston R. Detection by enzyme immunoassay of *Loxosceles gaucho* venom in necrotic skin lesions caused by spider bites in Brazil. *Tr Royal Soc Trop Med Hygiene* 1990; 84:608-9.
- Finke JH, Campbell BJ, Barrett JT. Serodiagnostic test for *Loxosceles reclusa* bites. *Clin Toxicol* 1974; 7:375-82.
- Beilman GJ, Winslow CL, Teslow TW. Experimental brown spider bite in the guinea pig: results of treatment with dapsone or hyperbaric oxygen. *J Wilderness Med* 1994; 5:287-94.
- DeLozier JB, Reaves L, King LE, Rees RS. Brown recluse spider bites of the upper extremity. *South Med J* 1988; 81:181-4.
- Rees RS, Altenbern DP, Lynch JB, King LE Jr. Brown recluse



- spider bites: a comparison of early surgical excision versus dapsone and delayed surgical excision. *Ann Surg* 1985; 202:659-63.
46. King LE Jr, Rees RS. Dapsone treatment of a brown recluse bite. *JAMA* 1983; 250:648.
  47. Michaud ME, Gibler WB. Hemolytic anemia and hemoglobinuria due to systemic loxoscelism: report of a case. *J Wilderness Med* 1991; 2:49-54.
  48. Phillips S, Kohn M, Baker D, et al. Therapy of brown spider envenomation: a controlled trial of hyperbaric oxygen, dapsone, and cyproheptadine. *Ann Emerg Med* 1995; 25:363-8.
  49. Mack RB. The bite of the spider woman: *Loxosceles reclusa* (the brown recluse). *N C Med J* 1992; 53:200-3.
  50. Dillaha CJ, Jansen GT, Honeycutt WM, Hayden CR. North American loxoscelism: necrotic bite of the brown recluse spider. *JAMA* 1964; 188:33-6.
  51. Jansen GT, Morgan PN, McQueen JN, Bennett WE. The brown recluse spider bite: controlled evaluation of treatment using the white rabbit as an animal model. *South Med J* 1971; 64:1194-202.
  52. Butz WC. Envenomation by the brown recluse spider (Aranae, Scytodidae) and related species: a public health problem in the United States. *Clin Toxicol* 1971; 4:515-24.
  53. Wasserman GS, Siegel C. Loxoscelism (brown recluse spider bites): a review of the literature. *Clin Toxicol* 1979; 14:353-8.
  54. Wasserman GS, Anderson PC. Loxoscelism and necrotic arachnidism. *J Toxicol Clin Toxicol* 1983-84; 21:451-72.
  55. Broughton G II. Management of the brown recluse spider bite to the glans penis. *Mil Med* 1996; 161:627-9.
  56. Holmes HS. Stings and bites: tips on coexisting comfortably with the insects. *Postgrad Med* 1990; 88:75-8.
  57. Binder LS. Acute arthropod envenomation: incidence, clinical features and management. *Med Toxicol Adverse Drug Exp* 1989; 4:163-73.
  58. Arnold RE. Brown recluse spider bites: five cases with a review of the literature. *JACEP* 1976; 5:262-4.
  59. Berger RS. The unremarkable brown recluse spider bite. *JAMA* 1973; 225:1109-11.
  60. Hobbs GD. Brown recluse spider envenomation: is hyperbaric oxygen the answer? *Acad Emerg Med* 1997; 4:165-6.
  61. Merchant ML, Hinton JF, Geren CR. Effect of hyperbaric oxygen on sphingomyelinase D activity of brown recluse spider (*Loxosceles reclusa*) venom as studied by <sup>31</sup>P nuclear magnetic resonance spectroscopy. *Am J Trop Med Hyg* 1997; 56:335-8.
  62. Strain GM, Snider TG, Tedford BL, Cohn GH. Hyperbaric oxygen effects on brown recluse spider (*Loxosceles reclusa*) envenomation in rabbits. *Toxicon* 1991; 29:989-96.
  63. Svendsen FJ. Treatment of clinically diagnosed brown recluse spider bites with hyperbaric oxygen: a clinical observation. *J Ark Med Soc* 1986; 83:199-204.
  64. Bucknall NC. Electrical treatment of venomous bites and stings. *Toxicon* 1991; 29:397-400.
  65. Osborn CD. Treatment of spider bites by high voltage direct current. *J Okla State Med Assoc* 1991; 84:257-60.
  66. Osborn CD. More on spider bites and stun guns. *J Okla State Med Assoc* 1993; 86:40.
  67. Barrett SM, Romine-Jenkins M, Fisher DE. Dapsone or electric shock therapy of brown recluse spider envenomation? *Ann Emerg Med* 1994; 24:21-5.
  68. Auer A, Hershey F. Proceedings: surgery for necrotic bites of the brown spider. *Arch Surg* 1974; 108:612-8.
  69. Fardon DW, Wingo CW, Robinson DW, Masters FW. The treatment of brown spider bite. *Plast Reconstr Surg* 1967; 40:482-8.
  70. Wright SW, Wrenn KD, Murray L, Seger D. Clinical presentation and outcome of brown recluse spider bite. *Ann Emerg Med* 1997; 30:28-32.
  71. Burton KG. Nitroglycerine patches for brown recluse spider bites. *Am Fam Physician* 1995; 51:1401.
  72. King LE. Brown recluse spider bites: stay cool. *JAMA* 1985; 254:2895-6.
  73. Duffey PH, Limbacher HP. Brown spider bites in Arizona. *Ariz Med* 1971; 28:89-95.
  74. Russell FE, Waldron WG, Madon MB. Bites by the brown spiders *Loxosceles unicolor* and *Loxosceles arizonica* in California and Arizona. *Toxicon* 1969; 7:109-17.
  75. Ingber A, Trattner A, Cleper R, Sandbank M. Morbidity of brown recluse spider bites: clinical picture, treatment and prognosis. *Acta Derm Venereol* 1991; 71:337-40.
  76. Sendovski U, Rothman MG, Fried M, Har-Zahav L. Brown spider bites [R]. *J Fam Pract* 1990; 31:417-20.
  77. Vest DK. Necrotic arachnidism in the Northwest United States and its probable relationship to *Tegenaria agrestis* (Walckenaer) spiders. *Toxicon* 1987; 25:175-84.
  78. Rees R, Campbell D, Rieger E, King LE. The diagnosis and treatment of brown recluse spider bites. *Ann Emerg Med* 1987; 16:945-9.
  79. Weller R. Nitric oxide: a newly discovered chemical transmitter in human skin. *Br J Dermatol* 1997; 137:665-72.
  80. Clowers TD. Wound assessment of the *Loxosceles reclusa* spider bite. *J Emerg Nurs* 1996; 22:283-7.