Necrotic Spider or Tick Bite? Warning Against Dermal Therapies Using Heat or Other Vasodilator

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Spider bites and tick bites need careful diagnostic differentiation in clinical and forensic investigation, particularly if associated with severe systemic illness. This article, continuing part I of the Winter 2007 issue of *The Forensic Examiner,* compares envenomation by brown spiders (Sicariidae), six-eyed crab spiders (Sicariidae), and sac spiders (Clubionidae) to tick-transmitted or other zoonotic illnesses, including babesiosis (with notes on Rocky Mountain spotted fever), Lyme disease, tularemia, Ebola hemorrhagic fever, and African tick-bite fever. Spider bites, compared to tick bites, are more readily necrotic and present sooner with systemic symptoms. Vasodilation therapies, facilitating the venom's entry into the blood at bite sites, are warned against.

Sicariidae, Genus Loxosceles

Recent reviews from the United States (Hogan, Barbaro, & Winkel, 2004; Swanson & Vetter, 2005; Wendell, 2003) and Brazil (da Silva et al., 2004), as well as recent clinical and epidemiological studies from Tennessee, United States (Sams et al., 2001), and Santa Catarina, Brazil (Sezerino et al., 1998), have addressed the public health threat of necrotic and systemic loxoscelism, with yet some uncertainties and controversies regarding therapies.

Within the United States, the web-weaving brown recluse spider, *Loxosceles reclusa* (Gertsch & Mulaik, 1940) of the Sicariidae, inhabits mainly the south-central region, roughly reaching from a northern line of demarcation (southeastern Nebraska to southern Ohio) south to the Gulf of Mexico, excepting Florida and southwestern Texas (Swanson & Vetter, 2005; Vetter 2000, 2005). From bordering regions, suspected bites have been reported from the Chicago area (Erickson, Hryhorczuk, Lipscomb, Burda, & Greenberg, 1990), Montana (Lee, Buker, & Petersen, 1969), and Idaho (Wand, 1972).

The spider's brown body, marked by a sunken cephalothorax, reaches about 10 mm in length in the female; males are somewhat smaller. Immobilized at temperatures around 5°C, the species retreats in a silken tube during winter and appears most active in summer and early fall (Hite, Gladney, Lancaster, & Whitcomb, 1966). It may enter homes seeking dark, secluded places. For correct identification, the six eyes are important, occurring as pairs in the 100 *Loxosceles* species worldwide and contrasting with the eight eyes of most spiders (Swanson & Vetter, 2005).

Loxosceles laeta of South America is the larger species. It is known to cause, more frequently than *L. reclusa,* bites with severe systemic reactions (viscerocutaneous loxoscelism) (Hogan et al., 2004). These reactions have been described as "unfailingly" lethal unless rapidly treated. The spider, imported into the United States, prefers old houses and is drawn to furniture, clothing, and cracks in walls (Schenone & Prats, 1961). It appears in circumscribed urban areas of Los Angeles County, as in the towns of Alhambra, Sierra Madre (reviewed in Schenone, Rojas, Reyes, Villarroel, & Suarez, 1970), and San Gabriel (Vetter, 2005). Presently, the spider is thriving in commercial basements and steam tunnels (Vetter, Cushing, Crawford, & Royce, 2003), with no known confirmed bites. Yet, one amputation and one death have been associated with loxoscelism in California (Vetter et al., 2003).

Additionally, a few native *Loxosceles* species are found in the dry, relatively unpopulated southwestern regions of the United States: *L. deserta, L. arizonica, L. apachea, L. blanda,* and *L. devia,* in that order, claim specific regions from southern California to southwestern Texas (Swanson & Vetter, 2005). *L. rufescens* is found scattered throughout the United States, with no known cases of verified envenoming (Vetter, 2005). It has been

noted in Chicago (Vetter & Bush, 2004), California, and is present in other countries, as in the Mediterranean Sea countries and Japan (Madon & Hall, 1970).

Symptom Analysis

In 19 documented *L. reclusa* bites, local erythema and local pain were most commonly encountered. Eleven patients developed necrosis, with a mean healing period of 5.6 weeks. Only a few patients suffered systemic symptoms (Sams et al., 2001). Such symptoms may appear 1 day post-bite and include fever, chills, malaise, nausea, vomiting, and arthralgia. In some systemic cases, a hemolytic anemia is observed as late as on the third day post-bite, often with hemoglobinuria and possibly causing fatal renal failure. Serious manifestations also include hematuria, anuria, dehydration, raised white blood cell count, thrombocytopenia, disseminated intravascular coagulation (DIC), liver injury (Wasserman & Anderson, 1984), and jaundice (Nance, 1961). Coma may occur and appears closely associated with the anuria, possibly progressing to death (Anderson, 1982). Rhabdomyolysis may contribute to renal failure (Hogan et al., 2004).

Wilson and King (1990) described the typical initial discoloration of severe *L. reclusa* bites as blue (centralized thrombosis leading to necrosis), white (halo around lesion due to vasoconstriction), and red (large area of erythema). Bite sites may present with edema, induration, pain, pruritus, and blisters. According to Anderson (1982), strong local pain due to infarction of the outer skin layer and a gradual sinking of the expanding blue area below the level of the normal skin signal impending necrosis. Auer and Hershey (1974) observed: The blistered epidermis of the necrotizing area sloughs during the second week post-bite, revealing an ulcerous, gangrenous cavity. The remaining dead skin may function as dry eschar, but, with continuation of the necrosis, can be lost weeks later. The necrosis is severe and particularly indolent in fatty areas of the body.

In the more serious *L. laeta* envenomation, the diagnostic information from confirmed and probable cases revealed that the violet-black, blistered then dried, and parchment-like skin is sloughed usually during the second week post-bite, sometimes revealing even the underlying muscles and aponeuroses. During the hours or days post-bite, victims suffer local edema (which increasingly recedes from the violet area) and particularly strong, insomnia-causing local pains not alleviated by pain medication (Macchiavello, 1947). Schenone and Prats (1961) noted painful local edema developing within 1 hour post-bite, spreading extensively from the bite site and gradually deepening in color.

Systemic signs and symptoms associated with *L. laeta* envenomation have included fever, restlessness, nervousness, insomnia, and, infrequently, darkened urine or hematuria (Macchiavello, 1947; Schenone & Prats, 1961). As observed in a clinic, the urinary changes tend to develop within 24 hours post-bite, often accompanied by a steep rise in temperature and leading to jaundice, cyanosis, dyspnea, anuria, coma, and sometimes death. For example, of 40 patients treated, four suffered viscerocutaneous loxoscelism and one died, showing gastric erosion (postmortem). Thirty-one of the cases had occurred in spring and summer in Chile (Schenone & Prats, 1961).

A study by Sezerino et al. (1998) including proven bites by *L. laeta* or *Loxosceles intermedia* noted that the percentage of cases with viscerocutaneous (sometimes fatal) involvement was highest in those regions of South America where *L. laeta* was prominent, as in Chile, or near prominent, as in the Brazilian state of Santa Catarina; in contrast, some reports of Brazilian regions with a prevalence of either *Loxosceles gaucho* or *L. intermedia* had shown zero deaths.

Compared to *L. reclusa* and *L. laeta,* the species *L. rufescens* is linked with relatively mild symptoms. Bite victims in Israel suffered local pain and blistering, nonserious necrosis with eschar formation, fever, weakness, joint and

muscle pain, lymphadenopathy, pharyngitis, and generalized papular erythematous rash. One case in 21 showed transient microscopic hematuria (Borkan, Gross, Lubin, & Oryan, 1995).

Detection Tests, Antivenom, and Homeopathic Therapies

Loxosceles envenoming detection tests and other diagnostic laboratory aids are available (Hogan et al., 2004). For example, an enzyme-linked immunosorbent assay (ELISA) detects venom recovered from bite sites by aspirate, biopsy, or hair sample for at least 7 days post-bite (in mammals) (Gomez, Krywko, & Stoecker, 2002). Immunity detection by use of a lymphocyte transformation test identifies a brown recluse bite in humans as early as 4–6 weeks post-bite (Berger, Millikan, & Conway, 1973).

Antivenom therapies, already practiced in South America (Hogan et al., 2004; Sezerino et al., 1998; da Silva et al., 2004), have been investigated in the United States (reviewed in Erickson et al., 1990; Swanson & Vetter, 2005). The Instituto Butantan in São Paulo, Brazil produces effective polyvalent (*Loxosceles, Phoneutria, Tityus*) and *Loxosceles* antivenoms. Some patients, such as 6.5% of 125 victims treated intravenously with *Loxosceles* antivenom, have developed side effects including urticaria, nausea, and bronchospasms (Sezerino et al., 1998). A potential vaccine derived from *L. intermedia* venom by use of a nontoxic recombinant protein, of interest for public health measures in *Loxosceles*-infested regions, has been tested in rodents in South America (reviewed in da Silva et al., 2004; Swanson & Vetter, 2005). Alternative medicine recommends a homeopathic prophylaxis and treatment (Richardson-Boedler, 1998, 2002).

Prevention Measures of Systemic Loxoscelism

Anderson (1977) noted that hemolysis in loxoscelism is caused by the direct destructive action of the venom on cell walls and aggravated by mechanical injury to erythrocytes present at the bite site due to vascular coagulation. The advice given is to rest the part bitten, apply padding over the bite site, and splint, if a limb is involved, to prevent further trauma (Anderson, 1982). Rest, ice compresses, and elevation (RICE) are commonly prescribed (Erickson et al., 1990; Sams et al., 2001; Wilson & King, 1990). Applied heat has been observed to increase the severity of the lesion and was suggested to activate the necrotizing lipase, sphingomyelinase D (King, 1985). Strenuous exercise is not recommended (King & Rees, 1986).

Richardson-Boedler (1998) suggested: A severe systemic reaction in loxoscelism is facilitated by local (vasodilating) treatment with heat or alcohol (also alcohol consumption) and local trauma received at the moment of the bite, such as hitting the biting spider (and one's body). Severe systemic loxoscelism has been viewed as caused by the absorption rather than intradermal (extravascular) presence of the venom (Macchiavello, 1947; Wasserman & Anderson, 1984; Wilson & King, 1990). Machiavello's (1947) early suggestion that the viscerocutaneous arachnidism was caused by the direct entry of the venom into a blood vessel was later verified by laboratory evidence (Denny, Dillaha, & Morgan, 1964; Rees, O'Leary, & King, 1983).

Public guidelines posted at the hospital Vital Brazil in São Paulo, Brazil, recommend to avoid alcohol intake in snake envenomation; yet, in spider bites (including *Loxosceles* bite) or scorpion stings, the public is admonished to apply warm compresses to alleviate local pain before seeking medical aid (Museu Instituto Butantan, 2001a, b; personal visit of January 11, 2005). In a Brazilian review, however, ice, elevation, rest, and avoidance of heat are named as established therapeutic prescriptions in loxoscelism (da Silva et al., 2004).

In the Pacific Northwest (see Part 1), local heat application has been prescribed for suspected spider bite, such as to alleviate a local swelling or the numbness of a limb bitten; moreover, the sympatholytic agent Regitine (phentolamine), applied subcutaneously, is one of the medicines routinely chosen (see Akre & Myhre, 1991).

Regitine is known to counteract necrosis and trigger vasodilation but has not proven effective in loxoscelism (Fardon, Wingo, Robinson, & Masters, 1967; Wasserman & Anderson, 1984).

Topical nitroglycerin, used by physicians in the form of patches to prevent necrosis from *L. reclusa* bites, has been tested in rabbits inoculated with *Loxosceles* venom. Applied as paste to the skin lesion every 6 hours for 3 days, it did not prevent necrosis. However, compared to untreated inoculated controls, it caused heightened inflammation score and a twofold increase in creatine phosphokinase levels. Vasodilation, caused by topical nitroglycerin and viewed as aiding in the removal of toxins from envenomation sites and in the prevention of thrombosis, was suggested to increase, however, the risk of systemic toxicity (Lowry, Bradfield, Carroll, Brewer, & Meggs, 2001).

As reported, heat has been applied in suspected *L. reclusa* bites to the entire limb affected (2 days post-bite) (Lee et al., 1969), directly to the lesion (3 days post-bite) (Erickson et al., 1990), or to the excised area (Vetter & Bush, 2002). Vasodilators and nitroglycerin are listed as specific therapies in loxoscelism (Swanson & Vetter, 2005), among antivenom, hyperbaric oxygen, dapsone, antihistamines, antibiotics, dextran, glucocorticoids, heparin, curettage, surgical excision, and electric shock. The collaborators recommended to subject therapies to controlled, randomized trials, as some may be toxic.

Locally or systemically applied measures that increase the blood flow to the affected area should be detrimental in any form of envenomation associated with a potential hematological severity.

Babesiosis (With Notes on Rocky Mountain Spotted Fever)

Clinical symptoms similar to those of severe systemic loxoscelism (and those of malaria) are caused by the zoonotic hematological illness of babesiosis, triggered in humans and animals by a tick-borne protozoal parasite (genus *Babesia*) that attacks erythrocytes. Cases of babesiosis, caused by *Babesia microti,* found transmitted by (nymphal) *Ixodes dammini* ticks (Dammin, Spielman, Benach, & Piesman, 1981; Spielman, Clifford, Piesman, & Corwin, 1979), have been reported particularly from the northeastern United States (Gombert et al., 1982; Meldrum, Birkhead, White, Benach, & Morse, 1992) and also from Wisconsin (Iacopino & Earnhart, 1990; Steketee et al., 1985).

The first case documented in the United States was triggered by an unknown *Babesia* species in 1966 in northern California (Scholtens, Braff, Healy, & Gleason, 1968). The disease occurs more readily in the elderly (Benach & Habicht, 1981; Gombert et al., 1982). A characteristic skin lesion at the site of inoculation is not noted (Dammin et al., 1981).

The incubation time for babesiosis, which is treated with clindamycin and quinine in combination, is ca. 1 to 2 weeks (Anonymous, 1986). Babesiosis can be asymptomatic or, in the other extreme, fatal. Symptoms include fever, shaking chills, headache, dark urine due to hemolytic anemia, and thrombocytopenia. Splenectomized patients are at risk of a fatal outcome (Gombert et al., 1982). With severe hemolytic anemia, jaundice, respiratory distress syndrome, and hepatomegaly have also been observed (Iacopino & Earnhart, 1990).

Comparably, in Rocky Mountain spotted fever, *Rickettsia rickettsii* pathogens attack small blood vessels, multiplying in damaged endothelial cells. The illness, at times fatal, may progress to diffuse generalized systemic vasculitis, affecting internal organs; the incubation time is 5 to 7 days. Tick vectors are *Dermacentor andersoni* in the west, *Dermacentor variabilis* in the east and south (Anonymous, 1986). Initial symptoms include fever (high at night), headache, myalgia, nausea, vomiting, and maculopapular, later petechial and ecchymotic rash worse warmth and first on extremities (Fischer, 1990).

Lyme Disease

First noted in the northeastern United States in 1975, Lyme disease has spread through most parts of the country. Caused by *Borrelia burgdorferi* (spirochete),mostly *Ixodes*-transmitted, it is initially treated with tetracycline. The incubation time is usually 1 to 2 weeks, when the local erythema chronicum migrans (often also smaller secondary lesions) and systemic symptoms appear, including malaise, headache, fever, myalgia, arthralgia, and lymphadenopathy. Weeks later, a second stage of illness manifests with neurological and cardiac symptoms, followed weeks or years later by arthritis (third stage) (Anonymous, 1986).

In contrast to the main lesion, which forms a growing circular area (red on the outer border, clearing in center), secondary lesions are smaller, less prone to expand, and may form several days after onset of the main lesion (Anonymous, 1986).

In some patients with Lyme disease, the erythema chronicum migrans may develop within hours or days of the bite and have a vesicular or necrotic center and bluish discoloration. Malaise, fever, and arthralgia may also commence during the days following the bite, thus moving the manifestations closer to those of local and (mild) systemic loxoscelism. Yet, atypical for systemic loxoscelism, the clinical course in the two reported cases, such as in regard to the arthralgic pains, was prolonged (Osterhoudt, Zaoutis, & Zorc, 2002; Rosenstein & Kramer, 1987). In regions endemic for *I. dammini,* but nonendemic for *Loxosceles* spiders, Lyme disease should be suspected before brown recluse bite (Rosenstein & Kramer, 1987).

Tularemia

Transmitted by rodents (“rabbit fever”) and most hard ticks, tularemia is caused by the coccobacillus *Francisella (Pasteurella) tularensis* and treated with streptomycin. The incubation time is 5 to 10 days (Anonymous, 1986). It has ranged from 1 to 21 days, with a mean of 4.2 days, in 30 documented cases (Sanders & Hahn, 1968).

Along with influenza-like symptoms, such as fever, chills, malaise, headache, vomiting, and diarrhea, four types of tularemia were encountered among 106 cases: [1] ulceroglandular in 74 cases, [2] typhoidal in 16 cases, [3] glandular in 15 cases, and [4] oculoglandular in 1 case. Renal failure preceded death in 2 cases. The illness, first noted in rodent-exposed humans in 1914 in California, can also be transmitted by cats (Sanders & Hahn, 1968).

The ulcers of tularemia are known to resemble a necrotizing spider bite (Bennett & Vetter, 2004; Swanson & Vetter, 2005). Developing at the site of inoculation, the ulcer is indolent, usually infected, and may not resolve for several weeks (Evans, 1969). It may be as small as 4x4 mm; moreover, in glandular tularemia, the lymphadenopathy may not abate for several months (Sanders & Hahn, 1968). By 1970, most cases of tularemia in the United States had been reported in Arkansas, Illinois, Tennessee, and Missouri (Brooks & Buchanan, 1970). These states are also endemic for *L. reclusa,* which triggers some similar symptoms; yet, the dermal lesion in loxoscelism is clearly necrotic and may enlarge aggressively, and systemic symptoms appear sooner following inoculation.

Sicariidae, Genus Sicarius

Next to the genus *Loxosceles,* the genus *Sicarius* (Sicariidae), six-eyed crab spiders,is associated with severe local necrosis and fatal intravascular complications, mainly in South Africa. It is indigenous also to South and Central America, but not North America (Newlands, 1982).

In South Africa, *Sicarius* species, such as *Sicarius testaceus* (Purcell, 1908), tend to appear in arid and semi-arid regions. Buried in sand, they do not readily contact humans, are nonaggressive, and do not make webs. They

reach a body length of 15 mm, are yellowish, reddish-brown in color, and have a tough outer skin with small spines (Newlands & Atkinson, 1988). Of this genus, *Sicarius spatulatus* is the smallest species and the only species of South Africa not found in arid regions. It appears in populated regions of the southeastern Cape Province (Newlands, 1982).

In South America, the genus *Sicarius tropicus,* found in northeastern Brazil, is known to cause necrotic symptoms similar to those of *Loxosceles* spiders (Lucas, 1988; Lucas, Cirelli, Knysak, & Zveibil, 1978/79). *Loxosceles* serumtherapy cures; the reddish spiders show soil on their bodies (Lucas et al., 1978/79). However, in 1998, they were still not known as a major health problem (Sezerino et al., 1998). *Sicarius ruoepes* of Chile has once been considered a possible cause of necrotic arachnidism, which was later ascribed to *L. laeta* (Macchiavello, 1947).

Symptom Analysis

Public health concerns in South Africa have led to the formulation of key symptoms learned from suspected *Sicarius* bites: A severely necrotic lesion, visible 6 to 8 hours post-bite, develops surrounded by a hemorrhagic ecchymotic region; an eschar forms 1 to 3 days post-bite; and minimal local edema or inflammation occurs. Systemically, the bite causes DIC as early as 1 to 3 days post-bite, a generalized edema 7 to 10 days post-bite, and massive local tissue destruction (Newlands & Atkinson, 1990a). Death in humans is known to occur (Newlands & Atkinson, 1990a, b). The necrosis may spread aggressively, having caused the loss of an arm in a victim with a presumptive *S. spatulatus* bite(Newlands, 1982).

Sicarius albospinosus, collected in the Namib Desert, was confirmed to carry proteolytic venom. Rabbits bitten suffered symptoms that suggested the venom's strong virulence in man: Local necrosis with hemorrhage and tissue destruction present ca. 2 to 3 hours post-bite, with black eschar by 5 hours post-bite; systemic petechial hemorrhaging present ca. 5 hours post-bite, affecting visceral organs (liver, kidney, lungs, spleen, alimentary canal, mesenteries, and heart); no local edema or erythema (though present in surviving rabbits); ecchymotic zone surrounding necrosis; DIC (diagnosed), with thrombocytopenia and deactivation of the clotting factor VIII (platelet cofactor); but no hemoglobinuria (Newlands, 1982).

S. testaceus bites in rabbits produced the following symptoms: subcutaneous hemorrhage within 1–3 hours post-bite, tissue necrosis, inflammatory infiltration (muscle and adipose tissue), permeable blood vessels near the bite site, and petechial visceral bleeding (liver, kidney, lungs, and duodenum). *S. testaceus* was suggested as potentially harmful to humans and associated with thrombocytopenia, in contrast to loxoscelism, which causes thrombocytopenia in combination with hemolysis (Van Aswegen et al., 1997).

Ebola Hemorrhagic Fever

The infective agent of Ebola hemorrhagic fever is a thread-like negative-strand RNA virus (Filoviridae) marked by a secretory and a surface glycoprotein; the latter's binding to endothelial cells, which facilitates the replication of the virus, has been suggested to trigger DIC. The actual illness has occurred in monkeys and humans only and is transmitted mainly through body fluids, possibly also through the air or by skin contact (reviewed in Mwanatambwe et al., 2001).

A comparative review (Richardson-Boedler, 1999) has noted systemic similarities in experimental mammals between symptoms of *Sicarius* envenomation (Newlands, 1982) and those of Ebola hemorrhagic fever (Fisher-Hoch et al., 1985). Both conditions are marked by a decline of factor VIII in the plasma previous to DIC, whereby the Ebola virus causes a decline of factor VII as well. Newlands (1982) had proposed the decline of factor VIII, known as rare in DIC, as uniquely leading to DIC in *Sicarius* envenomation.

In humans, DIC can occur within 1 to 3 days following a suspected *Sicarius* bite. In contrast, the incubation time for Ebola hemorrhagic fever (central Africa) is 5 to 10 days. Symptoms include high fever, headache, myalgia, diarrhea, and mental changes. These symptoms are followed during the second week of illness by a generalized hemorrhage with hematological manifestations, including DIC, thrombocytopenia, and lymphopenia (Sodhi, 1996).

Morvan, Nakouné, Deubel, & Colyn (2000), studying at localities in the Central African Republic, identified three dominant small mammals—two rodent species, *Mus setulosus* and *Praomys* species, and one shrew species, *Sylvisorex ollula*—as healthy hosts of traces of the virus, the first of nonprimate mammals. Zoonotic transmission in central Africa, such as of the Ebola virus and of the simian (SIV)—leading to human (HIV)—immunodeficiency virus, is associated with human contact with body fluids of primates via hunting, preparing, and eating (Wolfe et al., 2004); notably, rodents were commonly eaten. Fruit bats, also consumed by humans in central Africa, are newly revealed carriers of Ebola gene sequences and antibodies against the virus (Choi, 2006).

Clubionidae, Genus Cheiracanthium

Sac spiders, genus *Cheiracanthium* (Clubionidae), retreat in a silken sac during the day and activate and hunt at night. They thenfrequently come in contact with humans and cause painful bites and some systemic effects. As reported by Gorham and Rheney (1968), *Cheiracanthium inclusum* (Hentz, 1875) is a species present in the United States with an average body length of 7.5 mm. Hentz (1875) had observed the species in North and South Carolina and described it as livid white or pale yellow, with a dusky longitudinal abdominal line.

Cheiracanthium mildei, a species imported from Europe, is present in North America next to the indigenous *C. inclusum* (Spielman & Levi, 1970). Associated with local necrosis in some reports, the necrotizing potential of *Cheiracanthium* bites has recently been discredited (Isbister et al., 2005; Vetter, Isbister, Bush, & Boutin, 2006). It was concluded that, only rarely, a mild necrosis may occur (Vetter et al., 2006). Worldwide, spiders of the genus *Cheiracanthium* causing local and systemic effects also include *C. punctorium* of Europe, *C. diversum* (syn.: *C. mordax*) of the central and southwest Pacific region, *C. japonicum* of Japan,and *C. lawrencei* of South Africa.

Symptom Analysis

Mostly from August to October, probable *C. mildei* bites occurring indoors near Boston, Massachusetts, produced sharp pain, a red wheal, and soon a slough. Local necrosis is also present 2 or 3 days post-bite, lasting from 1.5 to 8 weeks, reaching up to 30 mm in diameter, and often surrounded by a zone of induration. A voluntary, mildly pricking bite received from an immature *C. mildei* caused local itching, erythema, and induration (3 mm in diameter); the lesion was absent by the next day (Spielman & Levi, 1970). Local induration present for a few weeks followed a painful bite by a female *C. mildei,* inflicted indoors in June in Connecticut (Krinsky, 1987).In Indiana, an adult female *C. mildei,* present indoors during December, caused an immediate stinging sensation and a red wheal (ca. 20x10 mm). After a few days post-bite, a 50x70 mm zone of erythema and nodular induration with small petechiae developed, healing within 3 weeks (Minton, 1972). The three reports noted no systemic symptoms.

C. inclusum has caused immediate local pain, which intensified and gradually involved the part bitten, but no necrosis (Fuhrman & Reeves, 1957; Gorham & Rheney, 1968). Nausea and ineffectual vomiting were present as early as 15 minutes post-bite. The culprit species was a female *C. inclusum,* found in August in Georgia (indoors) (Gorham & Rheney, 1968). *C. inclusum* adhered to the bite site after injection of the venom; it was later identified as an immature male, found indoors in California (Fuhrman & Reeves,1957).

Local pain, a necrotic lesion nearly pea-sized (in diameter) and visible hours after the bite, and the acute systemic symptoms of chest constriction, chills, malaise, and swollen regional lymph nodes were caused by a

verified nocturnal *C. punctorium* bite (in the left axilla) in August in Yugoslavia. Three other victims, who had also brought the spider in for identification, showed similar symptoms; one victim had an additional light fever (Maretic´, 1962). In Germany, bites are most common in August, when the female *C. punctorium* guards her eggs in a silken structure that is built with plant parts and reaches, in some cases, the size of a chicken egg. All of the victims observed suffered repeated chills and chest constriction (Habermehl, 1974). In addition, a local bluish-red swelling with burning pains, later yielding to itching and rarely suppurating, as well as headache, nausea, vomiting, circulatory collapse, have been caused by this species known as the only venomous spider present in Germany (Habermehl, 1974, 1976).

C. diversum, found in the central and southwest Pacific region, is known to cause moderate to grave symptoms (Fuhrman & Reeves, 1957). The spider has apparently triggered, compared to the other species of this genus, more serious systemic effects that result in hospitalization. The species is even suspected of having elicited a coma in a female Hawaiian resident that occurred 4 hours post-bite and culminated in a fatal brain hemorrhage 4 days later (during January) (Baerg, 1959). Another victim of the Hawaiian Islands, a 4-year-old girl, was bitten on the finger by *C. diversum*, resulting in immediate severe local pain that rapidly affected her whole arm. The pain subsided after treatment, but her hand remained swollen (Anonymous, 1962).

C. japonicum of Japan is contacting humans, often during the night, between May and August. Male spiders in particular were found to infest houses. Victims bitten suffered (locally) continuous pain, edema, erythema, and petechiae, often with systemic manifestations such as nausea, vomiting, and headache (Ori, 1975).

In the Pretoria-Witwatersrand area of South Africa, *Cheiracanthium* bites are considered the most common, followed by *Loxosceles* and *Latrodectus* bites (Newlands & Atkinson, 1988). South African tick-bite fever has been a differential diagnosis for the dermal and systemic symptoms of suspected *C. lawrencei* bite. Bites by both *C. lawrencei* and infected ticks are associated with local necrosis. Ascribed to the spider bite are local edema, erythema, pain, and necrosis (two initial necrotic areas from fang entry points merge, becoming yellowish), which heals after ca. 10 days. Systemic symptoms (fever, headache, and rash) resembling tick-bite fever occur within 3 days of the spider bite or on the third day post-bite—a shorter incubation time than noted for South African tick-bite fever—and do not respond to tetracycline normally given for the latter condition; therefore, a rickettsial infection, which is also distinguished by a black eschar at the bite site, could not be suspected in the cases observed (Newlands & Atkinson, 1990a). The spider's role as vector of the infective agent was found unlikely (Newlands & Atkinson, 1988).

Initially, suspected *C. lawrencei* bites are painless and do not interfere in the victim's sleep if they occur at night (Newlands, Martindale, Berson, & Rippey, 1980). Instead, the local pain intensifies gradually (Newlands & Atkinson, 1988). In some victims, and also in experimental rabbits (Newlands et al., 1980), a bruise-like secondary lesion is visible ca. 14 days post-bite (Newlands & Atkinson, 1988, 1990a).

Compared to suspected *C. lawrencei* bites, the local pains triggered by, at least, *C. inclusum, C. punctorium,* and *C. diversum* are marked by a more rapid onset, as are the systemic symptoms caused by, at least, *C. inclusum* and *C. punctorium.*

African Tick-bite Fever

African tick-bite fever, caused by *Rickettsia africae,* causes rather mild symptoms and a late development of specific antibodies. The illness, encountered in sub-Saharan Africa, was formerly attributed to *Rickettsia conorii,* the agent of the more serious Mediterranean spotted fever, which causes a faster immune response than *R. africae* (Fournier, Jensenius, Laferl, Vene, & Raoult, 2002).African tick-bite fever, transmitted by *Amblyomma*

ticks (parasites of cattle and game), tends to occur in clusters, often affecting groups of travelers. A victim may have several inoculation eschars. The incubation time is 6 to 7 days, and fever or an influenza-like syndrome, regional lymphadenopathy, and rash (maculopapular or vesicular, seldom purpuric) are encountered (Raoult et al., 2001).

Conclusion

In geographical regions where public health issues focus on serious manifestations from both spider and tick bites, or due to travel of thus affected humans from endemic to nonendemic areas, the differential diagnosis is of importance in clinical and forensic investigation. As a rule, dermal symptoms are potentially more prolonged and serious in spider bites (two lesions from fangs), especially in bites by a member of the Sicariidae, than in infective bites (usually one lesion). Also, systemic symptoms of spider bites tend to develop sooner following inoculation than those of a similar zoonotic hematological illness. Heat or other locally applied vasodilators in necrotic arachnidism, also in tick bite with brief attachment, are warned against.

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