

VERIFIED BITES BY YELLOW SAC SPIDERS (GENUS *CHEIRACANTHIUM*) IN THE UNITED STATES AND AUSTRALIA: WHERE IS THE NECROSIS?

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Abstract. Spiders of the genus *Cheiracanthium* are frequently reported in review articles and medical references to be a definitive cause of dermonecrosis or necrotic arachnidism in humans. We provide 20 cases of verified bites by *Cheiracanthium* spiders from the United States and Australia, none with necrosis. A review of the international literature on 39 verified *Cheiracanthium* bites found only one case of mild necrosis in the European species *C. puncturium*. The basis for the suggestion that this spider genus causes dermonecrosis seems to be mostly inference from venom experiments in rabbits and guinea pigs, circumstantial spider involvement in human skin lesions, and repetitive citation of non-definitive reports in the medical literature. We discuss factors that lead to the erroneous elevation of virtually innocuous spiders to that of significant medical concern, which is a recurring problem in the medical community.

INTRODUCTION

Yellow sac spiders (genus *Cheiracanthium*) have been implicated in cases of necrotic arachnidism (i.e., dermonecrotic skin lesions) in North America,¹ Europe,² and South Africa.^{3–6} The association between bites by this spider genus and necrosis has been repeatedly cited in review articles, medical textbooks, and correspondence in medical journals,^{7–12} where the lesions are often described as being similar or less virulent than that of the brown recluse spider *Loxosceles reclusa*. The medical and toxinology literature contains numerous examples where spider species have been elevated to medical significance through reports of presumptive bites, poorly conducted clinical studies, and extrapolation from animal experiments. This is exacerbated by historical prejudice of both the medical community and the general public to blame spiders for causing idiopathic lesions.^{13,14}

Newly emerging research has investigated whether many of these implicated spiders cause necrosis. Several spider taxa have been exonerated by studies involving verified bites in humans with expert identification of the alleged culprit: in South America wolf spiders¹⁵ and in Australia wolf spiders,¹⁶ white-tail spiders, *Lampona cylindrata/murina* complex,¹⁷ and *Badumna* spp.¹⁸ Similar lack of definitive proof has caused the hobo spider *Tegenaria agrestis* in North America to come under scrutiny as wrongly incriminated in dermonecrosis.^{19,20}

Most of the basis for incriminating *Cheiracanthium* spiders as dermonecrotic agents is extrapolation from animal models where experimentally induced envenomations in rabbits and guinea pigs produced manifestations similar to idiopathic lesions in humans.^{1,3} However, differential toxicity between humans and various other mammals exists for venom of recluse spiders (*Loxosceles* spp.),²¹ Australian funnel-web spiders (*Atrax* and *Hadroncyhe* spp.),²² and Australian theraphosids.²³ In an amusing but demonstrative case, a harmless South African wandering spider *Palystes natalius* (Sparassidae) was incorrectly deemed potentially dangerous to hu-

mans because the experimental bite by a live spider to the nose of one guinea pig caused death; in subsequent research using anesthetized and conscious guinea pigs, researchers concluded that death was probably due to fright, not venom toxicity.²⁴ Thus, although extrapolations from animal models are useful, they can also be misleading if misinterpreted. Foradori and others²⁵ showed that *Cheiracanthium mildei* does not contain sphingomyelinase D, the enzyme in *Loxosceles* venom purported to cause dermonecrotic lesions. Also, using rabbit models, they could not induce dermonecrosis with *Cheiracanthium* venom gland homogenate compared with venom gland homogenate of *Loxosceles* spiders, which did cause dermonecrosis.

There are nearly 200 species of *Cheiracanthium* spiders restricted to Europe, Asia, Africa, Australasia, and several Pacific Islands.²⁶ Two species (*C. inclusum* and *C. mildei*) are present in continental North America. The Australian *Cheiracanthium* spiders are poorly known and need taxonomic attention. Despite the large number of *Cheiracanthium* species, less than 10 have been implicated in human envenomations,²⁷ which may be a greater reflection of the synanthropic behavioral propensity of a few species to interact with humans rather than deleterious venom toxicity.

To accurately determine the risk of envenomation of any spider taxon in humans, a prospective series of verified bites, including those causing minor injury, is required to demonstrate the full spectrum of clinical effects. Although spiders are sometimes killed or collected after a bite, rarely is the verified culprit submitted for identification to someone with sufficient arachnologic skills. We present a series of 20 verified bites by *Cheiracanthium* spp. to investigate the dermonecrotic potential of this spider genus in North America and Australia, as well as a systematic review of the international literature on verified *Cheiracanthium* bites.

MATERIALS AND METHODS

Since data collection was performed simultaneously but separately by researchers in the United States and Australia, the information gathered by each group differs slightly. In the United States, six verified *Cheiracanthium* bites were generated by bite victims who sought out one of us (RSV) for

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identification of the offending spider and knowledge as to the possible consequences of its bite. Thorough questioning of the bite victim ensured that the incident was indeed a verified bite, i.e., spider collected immediately at the bite site after the person was bitten. Information procured included demographics, bite history and locality, medical history, initial clinical effects and progression of the effects until resolution. Four additional retrospective incidents involved arachnologists or entomologists (with proficient arachnologic skills) as bite victims such that their identification of the spiders to genus was deemed sufficient for inclusion in the study.

In Australia from February 1999 to April 2001, 10 verified *Cheiracanthium* bites were included from a prospective study of 750 spider bites recruited from three of the four major Poison Information Centers in Australia (New South Wales, Western Australia, and Queensland) or three tertiary emergency departments. The methodology for the spider bite study in Australia has been described elsewhere.^{28,29} Ethical approval was obtained from all institutions involved. Cases were included if there was a definite history of spider bite and the spider was collected at the time of the incident. All patients were contacted within 24 hours of the bite, and followed-up by telephone for at least one week. Only cases of bites by *Cheiracanthium* spiders are included here. The following information was recorded using a standardized format for each case: demographics, circumstances, bite site, local and systemic effects, and treatment. Spiders were identified to genus by one of us (LJB). The taxonomy of Australian *Cheiracanthium* is in need of revision; therefore, either near species (nr. *C. stratioticum*) or no species was designated.

Medline from 1966 to May 2005 and Premedline, Oldmedline, and Embase from 1980 to May 2005 were searched using the following terms: *Cheiracanthium*, *Chiracanthium*, *Clubionidae*, sac spiders, and running spiders. Additional articles were included from reference lists, review articles, and major textbook chapters on spider bite and clinical toxicology. Abstracts were initially reviewed and reports of unverifiable bites or bites from other spiders were excluded. Full text was obtained for the remainder and translations were undertaken for articles in German, Russian, French, and Italian. We only include reports of verified bites in the data analysis where a spider was definitively associated with the bite and mentioned in some manner in the report (i.e., spider described in some

taxonomic sense [e.g., sex, length], identified by a well-known arachnologic authority).

RESULTS

During a 50-month period in the United States, 10 definite *Cheiracanthium* spider bites (four retrospective) were reported. Nine bites occurred in female patients; these patients had an age range of 4–61 years (median = 39, interquartile range [IQR] = 39–48). There was one pediatric case (four years of age). Bites were more common in warmer months and all bites occurred indoors.

During a 27-month period in Australia, 10 definite bites by *Cheiracanthium* spp. were reported. There were six male and four female bite victims (age range = 2–55 years, median = 35, IQR = 30–42). There were two pediatric cases (two and three years of age). Australian bites occurred from September to May, and not in winter (Southern Hemisphere). Seven (70%) bites occurred outdoors.

The clinical effects for bites from both continents are listed in Table 1. Bites occurred on various parts of the body, with four on distal limbs (finger or thumb), five on a proximal limb, and one on the ear. Pain or discomfort occurred in all cases and had a median duration of 1 hour and 45 minutes (IQR = 45 minutes–18 hours) and two patients had pain for 36 hours and 48 hours. Systemic effects occurred in two bites, including headache in one patient and nausea and vomiting in another. There were no cases of necrotic lesions or ulcers. There were no cases of confirmed infection or allergic reactions. The characteristics of bites by American spiders versus Australian spiders were similar except that most of the bites in Australia occurred outdoors and itchiness was reported more commonly in spider bites in the United States.

Review of the literature identified 39 verified bites by *Cheiracanthium* species,^{1,2,27,30–44} which are listed in Table 2 with brief details of their effects including one intentional bite.¹ An additional 64 reports^{1,5,33,45–55} were excluded because they did not meet the inclusion criteria: 1) the cases were clearly presumptive, based on symptomatology without spider presence, 2) cases may have been definite bites but the reports were incomplete, or 3) papers cited under verified bites^{1,33} listed additional unverified cases.

TABLE 1
Clinical effects of bites by yellow sac spiders (*Cheiracanthium* spp.)

Clinical effects	Australia <i>Cheiracanthium</i> spp.		United States <i>C. mildei</i> and <i>C. inclusum</i>	
	N = 10	% or time	N = 10	% or time
Severe pain	7	40%	6	60%
Median duration of pain		105 minutes		90 minutes
Fang marks	1	10%	1	10%
Redness/red mark	8	80%	9	90%
Swelling	3	30%	3	30%
Itchiness	1	10%	5*	50%
Systemic effect	2	20%	1	10%
Circumstances				
Outdoors	7	70%	0	0%
Night (6:00 PM to 6:00 AM)	2	20%	3	30%
Winter	1	10%	3	30%
Bite region: distal limb bite	4	40%	4	40%

* Itchiness continued for five days in one patient and was delayed and persistent in another patient with associated redness.

TABLE 2
Cheiracanthium spider bites reported in the literature*

Species (sex of spider if listed)	Reference	Patient (age)	Location	Clinical effects
<i>C. inclusum</i> (M)	Furman 1957 (30)	Adult	California	Severe pain for 12 hours
<i>C. inclusum</i> (F)	Gorham 1968 (31)	M (22)	Georgia	Severe pain, radiating pain lasting for three days, initial nausea and red mark
<i>C. inclusum</i> (F)	Leech 1994 (32)	F (30s)	Alberta, Canada	Pain for 36 hours associated with puncture marks and a raised red area lasting for 8 hours
<i>C. japonicum</i> (15 M, 1 F)	Ori 1984 (33)	16 cases	Japan	Male spiders caused local pain and redness, and occasionally non-specific systemic features. Female spider caused local pain and redness. No cases of necrosis.
<i>C. mildei</i> (immature)†	Spielman 1970 (1)	Adult	United States	Deliberate envenomation causing mild pricking sensation, immediate itching lasting 90 minutes, 15-mm erythematous wheal with 3-mm indurated central wheal, no eschar and resolution by the next day
<i>C. mildei</i>	Minton 1972 (34)	M (51)	United States	Sudden severe pain, with local erythema that settled over 24 hours
<i>C. mildei</i> (F)	Allred 1980 (35)	M adult	Utah	Severe pain for 4 hours and radiating pain
<i>C. mildei</i> (F)	Krinsky 1987 (36)	M (19)	Connecticut	Pain and a local red raised area that subsided over 1 hour. An indurated area lasted for a few weeks.
<i>C. mordax</i>	Anonymous 1950 (37)	F adult	Hawaii	Bite on eyelid, severe local pain and local redness and swelling that lasted approximately 24 hours. Nausea for 24 hours.
<i>C. mordax</i> (M)	Anonymous 1953 (38)	M (3)	Hawaii	Severe local pain lasting 30 minutes, and then irritability and discomfort for 12 hours.
<i>C. mordax</i>	Anonymous 1959 (39)	F adult	Hawaii	Severe local pain lasting approximately 24 hours.
<i>C. mordax</i>	Anonymous 1963 (40)	M adult	Hawaii	Localised pain for 2 hours and swelling for 12 hours.
<i>C. punctatorium</i>	Forel 1876 (41)	M adult	Europe	Four bites: one patient developed severe pain but nothing else. There were three additional bites in one patient that caused severe pain but nothing else.
<i>C. punctatorium</i>	Bertkau 1891 (42)	M adult	Germany	Three bites on fingers. Severe pain lasting 12 hours, with radiation of the pain, followed by itchiness the next day.
<i>C. punctatorium</i> (M)	Spasskii 1957 (43)	F adult	Russia	Bite on finger causing severe initial pain and swelling
<i>C. punctatorium</i>	Maretic 1962 (2)	M (48)	Germany	Transient pain, local redness and small local necrosis.
<i>C. punctatorium</i>	de Haro et al. 1997 (44)	M (67) and F (59)	France	Man: Painful bite with local inflammation and numbness lasting 3 days. Woman: Painful and inflamed region lasting for 10 days.
<i>C. punctatorium</i> (F)	Stingeni et al. 1998 (27)	F (28)	Italy	Severe local pain with local blistering over the eyelid, erythema and urticaria over head associated with lethargy and excitability. Lasted 10 days‡

* With regard to references on species in the older literature, *C. nutrix* is now considered to be *C. punctatorium* and *C. diversum* is now considered to be *C. mordax*.

† Immature *Cheiracanthium* spiders cannot be identified to species; however, this spider was collected in a region that produced only mature *C. mildei* specimens.

‡ Report states subsequent necrosis; however, no description of this is provided and it resolved over 10 days.

DISCUSSION

None of the 20 verified bites of *Cheiracanthium* spiders reported here from Australia or the United States resulted in a dermonecrotic lesion (Table 1). A consistent sign was an initial sharp, painful bite equivalent to that of a bee sting. Bites frequently occurred while sleeping or putting on clothes. Typically, the effects were minor and self-limiting, including erythema, mild swelling, and pruritus. This was sup-

ported by our systematic review of the literature where we could identify only one case of minor necrosis from the 39 definite *Cheiracanthium* bites, most of which caused only minor effects. There were many suspected but non-verifiable reports that attributed a spider bite diagnosis to necrotic ulcers. In the literature, the effects of *Cheiracanthium* bites are reported as severe or grave^{30,37,53,56,57} when the manifestations are relatively minor, generalized symptoms in comparison to the extensive, medically significant envenomations

from widow spiders, Brazilian armed spiders, or Australian funnel-web spiders. Effects of *Cheiracanthium* envenomation should be referred to as mild or moderate, leaving the term severe for more dramatic systemic manifestations.

In Japan, many victims were bitten while collecting the spider, resulting in a preponderance of hand injuries;⁵⁷ similarly, the injuries to Bertkau⁴² occurred during purposeful collection. Sleeping victims were awakened by the painful bite in Europe^{2,27} and the United States^{30,36} as well as one case from this study. One of our American bite victims had episodes of recurrent pruritus of variable severity over a period of five days; latent pruritis after being asymptomatic occurred in at least one *Cheiracanthium* bite in the literature.³⁴

There is one verified bite in the medical literature involving European *C. punctatorum* causing a pea-sized necrotic lesion on the victim's shoulder.² Eleven additional European bites by this species show no necrosis.^{2,27,41-44} Regarding verified *Cheiracanthium* bites elsewhere, there was no necrosis in 17 bites in continental North America,^{1,30-32,34-36} (including this study), 10 in Australia (all from this study), 4 in Hawaii,³⁷⁻⁴⁰ and 16 in Japan.³³ Owri⁵⁷ summarized the effects of 50 bites in Japan (some of which were verified case histories previously published) and does not list necrosis as a manifestation. It seems more judicial to conclude that 1) most *Cheiracanthium* envenomations result in virtually harmless bites with mild, self-limiting effects and 2) dermonecrosis is a rare event and mild at best.

The often cited dermonecrotic capability of *Cheiracanthium* spider bites is predominantly due to presumptive case histories or comparison of idiopathic skin lesions in humans to verified bites in rabbits or guinea pigs. In South Africa, several papers³⁻⁵ incriminate *C. lawrencei* in necrotic arachnidism. However, in a summary paper,⁵ all 19 bites are clearly reported as suspected. Matthews correctly stated in a subsequent paper⁶ that the findings of Newlands and others³⁻⁵ have "not been accurately or reliably validated in humans," and then presented additional circumstantial data to corroborate this incrimination, yet inexplicably not one case involves a verified bite with an expertly identified spider of any species.

There are inconsistencies between the South African reports and those found elsewhere. The South African *Cheiracanthium* spider bite is stated to be relatively painless,³⁻⁵ whereas a sharp, initial pain was a very common finding in definite bites reported in this study as well as in published cases in North America,^{30,32,34-36} Japan,⁵⁷ and Europe.^{2,27,41,42} A second discrepancy is that the characteristic bite gap for suspected envenomation of *C. lawrencei* spiders is listed as 4-8 mm³ and then later as 6-8 mm.⁴ On the basis of the report by Newlands and others,³ an anterior view of a female spider biting a rabbit allowed us to estimate that the female (based on the 11-mm body length spider in an accompanying dorsal image) has a fang gap of approximately 3 mm, which is less than the minimum distance of the alleged characteristic bite gap. Electronic images provided by Leon Lotz (National Museum, Bloemfontein, South Africa) allowed one of us (RSV) to estimate the length of the disarticulated fang-chelicera of a mature female *C. lawrencei* as 4 mm and that of the mature male as 3.5 mm; *C. lawrencei* spiders have a maximum body length of 14 mm.⁴ Therefore, for this species to have a characteristic bite gap of 6-8 mm, it would have to spread its chelicerae in complete opposition approximately

half of its body length, which is 1) anatomically impossible and 2) even if anatomically possible, would leave the spider with an extremely obtuse angle of cheliceral splay, making it mechanically impossible to contract its musculature to effect an envenomation. Until verified proof is presented that South African *Cheiracanthium* spiders cause a relatively painless bite in humans with a 6-8-mm gap between fang marks, it seems prudent to question the legitimacy of this spider's involvement in dermonecrosis.

In the United States, Spielman and Levi¹ incriminated *Cheiracanthium* spiders by forcing envenomations in guinea pigs with necrotic results and by associating people with necrotic lesions with the circumstantial presence of ubiquitous *C. mildei* spiders in their homes. The five human victims who developed necrotic lesions (the largest being 12 cm in diameter with a 3-cm diameter necrotic center) did feel a painful initial event yet no spiders were recovered in any of the incidents. Included in this study was one additional intentional, experimental bite that resulted in minor manifestation, no necrosis, and resolved within 24 hours (Table 2). This paper¹ is frequently cited by those touting the dermonecrotic capabilities of *Cheiracanthium* spiders. However, the first word of the title is "Probable" and the last sentence of the paper states "The evidence, however, remains circumstantial." Foradori et al.²⁵ showed that *C. mildei* lacks sphingomyelinase D, which is the main dermonecrotic enzyme known in spider venoms and that venom gland homogenate of *C. mildei* does not cause dermonecrosis in rabbits. Although this venom challenge technique differs from that of Spielman and Levi,¹ who effected envenomations by pushing spiders into shaved guinea pig flesh, these contrary results along with the lack of necrosis in the 17 verified North American *Cheiracanthium* bites mentioned here demonstrate that the definitive toxicologic analysis of its bite still needs to be performed. Nonetheless, in no case of a verified *Cheiracanthium* bite of any species worldwide is there expressed the 3-cm necrosis as that described for the circumstantially alleged bite described in the original paper.

Another inconsistency involves the painful bite. Many medically important spiders (*Latrodectus* and *Loxosceles*) have painless bites and, therefore, the culprit is not collected at the time of the bite. Spider association is often made by clinical examination of bite symptoms; in regard to *Loxosceles* spiders, this leads to many disease states being misdiagnosed as spider bites.^{14,58-60} In contrast, almost all *Cheiracanthium* bites hurt similar to bee stings and thus similar to algogenic scorpion stings, the victim typically locates the culprit at the injury site moments after puncture. We find it difficult to accept that idiopathic necrotic lesions without painful origin can be realistically attributed to *Cheiracanthium* spiders.

If *Cheiracanthium* spiders actually can cause necrosis in a small proportion of cases, this may not be detected in the sample size we have reported. Foradori and others²⁵ screened the venom of 45 spider species for hemolysis-inducing capability. Hemolysis was caused only by *Loxosceles reclusa* (by the dermonecrotic enzyme sphingomyelinase D) and *C. mildei* (by the non-dermonecrotic enzyme phospholipase A₂). Nonetheless, as our data currently demonstrate, 20 verified *Cheiracanthium* bites on two continents did not cause necrosis, and a review of the literature revealed 39 verified bites with only one case of mild necrosis involving *C. punctatorum*. Until *Cheiracanthium* spiders of any species are definitively

shown to be common dermonecrotic agents and prospective studies confirm the involvement of *C. punctatorium* bites in necrotic lesions, the association between *Cheiracanthium* bites and necrosis is flimsy at best. *Cheiracanthium* spiders should not be considered a differential diagnosis of necrotic ulcers without a history of a definite bite and a spider collected and identified.

Unfortunately, circumstantial evidence presented in the spider bite literature often evolves into conventional (and incorrect) medical wisdom. It is disconcerting to repeatedly see an almost predictable misconception where a medically inclined audience reads reports that clearly state “suspected”, “probable,” or “reported” in alleged bite incidents, yet will transform this non-definitive data into conclusive proof of spider involvement. We see a strong predilection to blame spiders in idiopathic lesions when spider involvement is almost uniformly non-existent.^{61–64} Health care would improve if future investigators did not refer to *Cheiracanthium* spiders as potentially dermonecrotic. Instead, health care workers need to focus on other dermonecrosis-inducing conditions,^{60,65} which are far more probable. These conditions can sometimes be far more serious than spider bites where delayed or inappropriate treatment could lead to serious consequences. The aspects incriminating spiders as medical scapegoats are partly due to human psychology of placing blame on a readily recognizable source and partly are a reflection of medical consensus where repetitive citation leads to widespread acceptance of a spider species as a dermonecrotic agent without proof.^{13,14,20,66} An examination of the false elevation of *Cheiracanthium* and other previously mentioned spiders to medically significant status gives insight as to how information, for better or worse, becomes accepted knowledge in the medical field.

Finally, two spellings exist for this spider genus in the literature. The original spelling *Cheiracanthium* reflects one convention in transliterating from Greek to Latin, but later other arachnological purists preferred a different convention of latinization, and amended it to *Chiracanthium*.⁶⁷ Although the latter spelling has been frequently cited, currently *Cheiracanthium* is the accepted genus name.

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