

Symptom in search of a toxin: muscle spasms following bites by Old World tarantula spiders (*Lampropelma nigerrimum*, *Pterinochilus murinus*, *Poecilotheria regalis*) with review

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Summary

Background: Tarantula spiders are widely kept and bred in captivity by both adults and children. Their bites are generally considered harmless.

Aim: To explore the effects of envenoming by Old World tarantulas.

Design and Methods: Clinical studies and review of conventional literature and hobbyist web sites.

Results: Two men bitten on their index fingers by pet Old World tarantula spiders, *Lampropelma nigerrimum* (Ornithoctoninae) and *Pterinochilus murinus* (Harpactirinae) in England, developed intense local pain, swelling and episodic, agonising, generalised muscle cramps. In one of them, cramps persisted for 7 days and serum creatine kinase concentration was mildly elevated. A third man bitten on a finger by *Poecilotheria regalis* (Poecilotheriinae), suffered persistent local cramps in the affected hand. Reports since 1803, including recent ones on hobbyist

web-sites, have been largely overlooked. They mentioned muscle spasms after bites by these and other genera of Old World tarantulas, including *Eumenophorus*, *Selenocosmia* and *Stromatopelma*. The severe muscle spasms seen in two of our patients were a challenge to medical treatment and might, under some circumstances, have been life threatening. They demand a toxinological explanation.

Conclusions: Bites by several genera of African, Asian and Australasian tarantulas can cause systemic neurotoxic envenoming. In the absence of available antivenom, severe persistent muscle spasms, reminiscent of latrodectism, pose a serious therapeutic challenge. Discovery of the toxin responsible would be of scientific and potential clinical benefit. Tarantula keepers should be warned of the danger of handling these animals incautiously.

Introduction

Once, in the interests of experimentation, I pricked my hand with a needle and then, after rubbing the same needle against a spider's fang, pricked my hand again in a different place. The site of envenoming puckered into a papule, becoming red, hot and

inflamed, as if to combat and suppress the noxious effects of the venom.

William Harvey (1651) (authors' translation).¹

In what has been cited as 'one of the earliest recorded examples of a controlled observation in toxicology',² William Harvey, the discoverer of the circulation of the blood, predicted the inflammatory effects of envenoming and set a trend for

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Figure 1. East/Central African king baboon spider (*Citharischius crawshayi*) showing the large downward pointing fangs typical of theraphosid spiders (courtesy: Peter Kirk).

self-experimentation that, in recent times, has persisted, not always intentionally, among keepers of pet tarantulas. Mygalomorph spiders of the family Theraphosidae are becoming increasingly popular pets, kept and bred by both children and adults in Western countries.³ Despite their very large size, tarantulas are generally perceived to be harmless. Bites are uncommon, but when they do occur, details rarely reach the toxicological literature, although they are sometimes reported on hobbyist web-sites, a valuable but neglected source of toxicological information. The defensive ejection of urticating abdominal setae by New World tarantulas can cause kerato-uveal injuries ('ophthalmia nodosa') and irritation of skin and pharyngeal and respiratory tracts.^{4,5} In birds, and mammals as large as dogs, tarantula bites may be lethal.⁶ In human victims, a strike by the large vertically-orientated fangs (Figure 1) may be traumatic (one penetrated a human finger nail) and may cause an allergic reaction, but envenoming by New World tarantula bites appears to be clinically trivial with the possible exception of a few genera such as *Sericopelma* (Theraphosinae).⁶⁻⁹ However, Old World tarantulas, which lack protective urticating hairs, are more ready to bite and commonly cause local pain, swelling and stiffness of the joints. Observation of persistent, generalised cramps in two men bitten by Old World tarantulas, and of persistent local cramps in a third, prompted us to explore a largely neglected literature.

Case reports

Case 1

In 2007, a previously healthy 33-year-old man was bitten on the left index finger by his pet female



Figure 2. Female Borneo black tarantula (*Lampropelma nigerrimum*) responsible for biting Case 1.

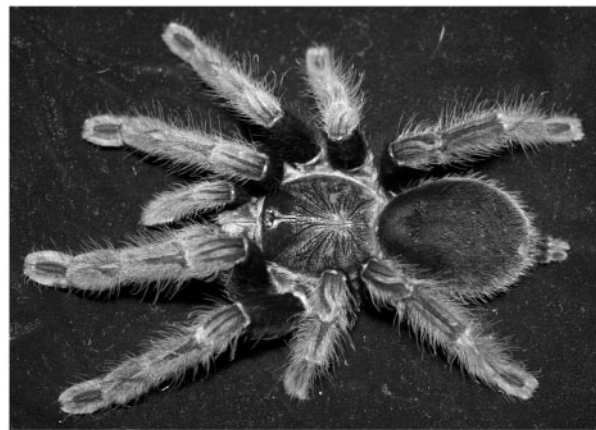


Figure 3. Borneo black tarantula (*Lampropelma nigerrimum*) (courtesy: Peter Kirk).

'Borneo black' tarantula spider (*Lampropelma nigerrimum*) (Ornithoctoninae) (Figures 2 and 3) just before midnight, 'after having a few beers'. At the age of 12 years, he had been bitten by a Mexican red-kneed tarantula (*Brachypelma smithi*) (Theraphosinae) but that was 'only like a bee sting'. Thirty seconds after the *L. nigerrimum* bite, his finger began to swell and, with the palm, became reddened. A severe burning throbbing pain spread up the forearm. It reached its maximum intensity after 2–3 min and began to decline after 2–3 h, following immersion of the arm in ice-cold water. He was free from pain after 5–6 h. He then went to sleep but was awoken after only 45 min by repeated intensely painful cramps of the left calf, each lasting 2–3 min. Over the next 48 h, agonisingly painful, visible cramps of gradually increasing intensity spread to involve virtually all his muscle groups: feet, legs, abdomen, chest, mouth and jaw.

They prevented his sleeping, eating or opening his bowels as they were provoked both by any movement and even by attempts to relax. Each spasm lasted from 30 s to 3–5 min. They occurred frequently, almost continuously. Forty-eight hours after the bite, he finally presented to hospital in desperation. Two faint puncture wounds 8 mm apart with surrounding erythema were visible on the radial aspect of the bitten finger which was swollen together with the whole of the left hand, restricting interphalangeal joint movements. The patient's skin was clammy to touch and he had a tachycardia of 125 beats per minute but a normal blood pressure. The muscle spasms were so severe that it proved impossible to give him an intramuscular injection of tetanus toxoid. He was admitted for observation, but trismus and generalized spasms continued to increase until ~4 days after the bite, after which they declined and had disappeared completely 7 days after the bite. There was no fever, chest pain or respiratory symptoms. Routine blood tests, including differential white blood count, were within normal limits, but the serum creatine kinase was 1062 iu/l (normal <195 iu/l), later falling to normal by the time he was discharged. Plasma electrolyte concentrations, including Na⁺ and Ca²⁺ were normal. The total Ca²⁺ concentration corrected for serum albumin was initially 2.28 mmol/l (normal 2.25–2.6 mmol/l) and subsequently ranged from 2.39 to 2.44 over the next 3 days. The admission electrocardiogram (ECG) confirmed a sinus tachycardia with a ventricular rate of 114 beats per minute. Subsequent traces showed no atrial or ventricular tachyarrhythmias. Serial troponin-I cardiac enzyme levels were not elevated. Oral diazepam and six hourly intravenous calcium gluconate injections were given in an attempt to relieve the spasms but the patient was not convinced that these treatments helped at all. A good diuresis was maintained with intravenous fluids supplemented by oral fluids. At follow-up 10 weeks later, he had recovered completely.

Case 2

In 1988, a previously healthy 35-year-old man was bitten on his right index finger by an 'African baboon tarantula' (*Pterinochilus murinus* Harpactirinae) (Figure 4) while he was drunk. In hospital 20 min later, he had pain, swelling and erythema that extended along the ulnar border of the bitten hand and forearm. Apart from a neutrophil leucocytosis (72% of $15.74 \times 10^9/l$), routine blood tests, including plasma electrolytes, and ECG were normal. Twenty-two hours later, he developed sudden intermittent cramps of the legs, abdomen



Figure 4. Male African baboon spider (*Pterinochilus murinus*) (red phase): the species responsible for biting Case 2 (courtesy: Richard Gallon).

and chest that caused him to grimace with pain. Unfortunately, he insisted on discharging himself from the hospital 2 h later despite continuing cramps and he was lost to follow up.

Case 3

In 2000, a middle-aged man was bitten on his finger by an Indian Ornamental Tarantula (*Poecilotheria regalis* Poecilotheriinae) whose body was 4 cm long. He developed local swelling and erythema of the hand, and severe local pain. At follow up, 8 days later, these symptoms had resolved but he still had a tight feeling and cramps in the bitten hand and vague generalized 'flu-like' myalgias.

Ethical considerations

Cases 1–3 were observed and treated as normal NHS patients. No special ethical considerations arose.

Discussion

Bites by *Pterinochilus* spp. (Africa)

The symptoms experienced by Case 2, bitten by an 'African baboon tarantula' (*Pterinochilus murinus* (Harpactirinae), recall one of the earliest published descriptions of a tarantula bite in Africa. In Sierra Leone in 1803, Thomas Winterbottom (discoverer of the eponymous sign in African sleeping sickness) observed that '*Aranea avicularia*' 'caused more violent pain than the sting of the scorpion and often produces cold sweats and fainting; but there is seldom much swelling of the part'.¹⁰ A 40-year-old

local woman bitten on the hand developed excruciating pain radiating up to her shoulder, with coldness and hyperaesthesia, generalized coldness and sweating with rigors, weak pulse, frequent fainting and tightness of the pectoral muscles. Her symptoms resolved within 24 h. The spiders involved were probably Sierra Leone mouse brown (*Eumenophorus clemensi*) or Sierra Leone greater mouse brown (*E. murphyorum*) tarantulas (Eumenophorinae).¹¹ A bite, said to be by '*Pterinochilus mammilatus*' but more probably by the red/orange colour phase of *P. murinus* (Figure 4), has been reported but without clinical details.¹² A bite by a *Pterinochilus* spp. in Tanzania caused only transient local pain and sweating.¹³ In Germany, a bite by a member of this genus caused severe pain lasting for only one hour.¹⁴

Bites by other *Harpactirinae* and *Stromatopelminae* (Africa)

The South African baboon spider, *Harpactira lightfooti* (Harpactirinae), can inflict a painful bite sometimes associated with symptoms of systemic envenoming such as vomiting and shock.^{15,16} In West Africa, 'pigeon spiders' of the genera *Stromatopelma* and *Heteroscodra* (Stromatopelminae) can inflict bites that cause agonising pain radiating up the bitten limb with involvement of local lymph nodes. A bite by *Stromatopelma* spp. caused electric shock-like pain in the bitten finger, followed by mild cramping that persisted for some weeks.¹⁷

Bites by *Lampropelma* spp. (Southeast Asia)

The Bornean black tarantula (also known as Borneo orange-fringed) (*Lampropelma nigerrimum*) (Ornithoconinae), the species responsible for biting Case 1, has caused much taxonomic confusion. Spiders of identical appearance displayed on the Internet have been described as *Cyriopagopus* spp. (<http://fugleedderkopper.blogspot.com/>). No bites by this taxon have been reported under any guise but, in Western Malaysia, the indigenous Orang Asli consider the bite of the Singapore violet or Malaysian blue femur tarantula (*L. violaceopes*) as potentially fatal.¹⁸ It can kill rodents and sparrows in a few minutes. A 22-year-old man bitten on the finger tip developed local redness and swelling with severe local and constricting chest pain followed by migratory myalgia and headache persisting for 72 h. There were no

laboratory abnormalities.¹⁸ In France, a 30-year-old woman bitten by this species developed pain, fever and local swelling, symptoms that required hospitalisation.³

Bites by other *Ornithoconinae*, *Poecilotheriinae* and *Selenocosmiinae* (Asia and Oceania)

Other members of the sub-families Ornithoconinae (Southeast Asian 'earth giants') and Poecilotheriinae (Indian/Sri Lankan tree spiders, known as 'pokies' in the pet trade—see below) have caused systemic envenoming. Songping Liang, who has worked for many years on the venom of the Chinese bird spider, earth tiger or golden earth tiger tarantula *Haplopelma huwenum* (formerly placed in the genera *Selenocosmia* and later *Ornithoconus*), observed that while female spiders could kill a mouse or sparrow in <2 min, no case of fatal human envenoming was known.¹⁹ Internet-propagated rumours that a species of this genus had killed a child in China are apocryphal. Songping Liang mentioned several bites that were very painful and produced severe local swelling. One man bitten on the index finger experienced immediate extreme pain and, within ~2 h, swelling involved the whole palm and part of the arm with increased sensitivity to pain which, together with weakness, took 2 days to recover. Two finger bites by 'cobalt blue tarantulas' (*Haplopelma lividum*) in Japan caused transient severe pain, inflammation and joint stiffness lasting for weeks in one case.²⁰ In Alice Springs in central Australia, a 35-year-old woman was bitten on the thigh by a 'Barking spider' (*Selenocosmia stirlingi* Selenocosmiinae) while she was asleep.²¹ She developed a painful erythematous local lesion, nausea, vomiting, severe retro-orbital headache, photophobia, urinary frequency, dysuria and a rigor. When admitted to the hospital 4 days later, the hot erythematous area at the bite-site had a vesiculated margin and covered almost two-thirds of her thigh. There was no evidence of urinary tract infection. She recovered completely. A bite by a closely related larger species (*S. crassipes*) near Darwin, was reported to have killed a 4.5 kg dog within two and a half hours.²² A review of Australian theraphosid bites included seven fatal bites inflicted on dogs by *Selenocosmia* and *Phlogiellus* spp. (Selenocosmiinae), but among the nine human victims, there was no hint of severe envenoming.⁶

Symptom in search of a toxin: muscle spasms following Old World tarantula bites

In Cases 1 and 2, the dominant symptom was agonising generalized and persisting tonic muscle spasms. There are a few published accounts of similar symptoms following Old World tarantula bites. A 39-year-old man who, like two of our patients, had been drinking alcohol, was bitten on his left little finger by a sub-adult, female Pedersen's ornamental tarantula (*Poecilotheria pedersenii*) from Sri Lanka.²³ There was almost immediate swelling, reddening and stiffness of the finger followed by painful paraesthesiae radiating up the arm. About 33 h after the bite, he noticed that his left axillary glands were painfully enlarged and, like our Case 3 who was bitten by *P. regalis*, he developed 'flu like' symptoms. Five days after the bite, intermittent twitching developed in the bitten finger and two days later he noticed cramps in his left lower leg and right foot which persisted for 4 days. A 35-year-old man seen in Marseille developed 'fever, myalgia, shivers, dysaesthesias, cramps and pain' after a bite by an Indian *Poecilotheria* spp. but recovered in 2 days.³ 'Trembling and convulsions' have also been attributed to these spiders, but without clinical details.¹² Two other cases of severe generalised cramps resulting from Indian ornamental (*P. regalis*) and Mysore ornamental (*P. striata*) tarantula bites have been posted on hobbyist web sites (e.g. <http://www.bighairyspiders.com/bites.shtml>). A 35-year-old man was bitten on his ring finger by a mature female Sri Lankan *P. fasciata*.¹⁴ After a delay of a few days, he developed cramps in the bitten and adjacent finger, like the localised cramps experienced by our Case 3 who was bitten by *P. regalis*. Another man bitten by this species experienced violent pain that radiated up the bitten arm into the axillary lymph nodes and persisted for 20 min. In Papua New Guinea, a tarantula spider, possibly *Selenocosmia* nr. *stirlingii*, bit a plantation manager on the palm of his hand. About 20 min later: 'he was seized with muscular spasms involving all the muscles of the body and lasting several minutes with intervals of relaxation in between. The spasms continued for 4 h followed by drenching sweatings and collapse'.²⁴ A woman bitten on the forearm by a male *Selenocosmia* spp. (initially believed to be *S. lanipes*) developed severe shooting pains of stinging quality and redness of the arm within 20 min which persisted with hypersensitivity to touch and spasms in the thumb and finger for 24 h.²⁵

The striking muscle spasms are reminiscent of those in classic latrodectism described in Europe

and the Americas,^{26–29} but they are not mentioned in patients envenomed by *L. hasselti* in Australia.³⁰ In latrodectism, spasms are associated with rigidity of the abdomen (simulating an acute abdomen), limbs and face with trismus. However, the many manifestations of autonomic nervous system activation and hypertension in classic latrodectism were not seen or reported in the cases of Old World tarantula bite reviewed here.

Tarantula venom

Studies of tarantula toxins have yielded many interesting findings, some relevant to interpreting the symptoms of envenomed humans.^{31,32} For example, the excruciating pain experienced by some tarantula bite victims may be attributable partly to 'vanillotoxins' (VaTxs), so far isolated from venoms of the Trinidad chevron tarantula (*Psalmopoeus cambridgei*) and *Haplopelma/Ornithoctonus huwenum*. These Inhibitory Cystine Knot (ICK) peptides specifically activate the noxious heat-sensing Transient Receptor Potentiating (TRP) V1 receptor that is also the target of capsaicin, the painful vanilloid toxin in 'hot' chilli peppers.³³ The combination of mechanical injury from the large fangs, low venom pH and effects of biogenic amines, adenosine and adenosine triphosphate may also contribute to local pain.³¹ Hanatoxin from the venom of the Chilean rose tarantula (*Grammostola spatulata*) and a growing number of related tarantula toxins inhibit activation of voltage-activated potassium (Kv) channels by interacting with their voltage-sensing domains.³² They might cause the disturbance of skeletal muscle excitability responsible for the tonic muscle spasms that have been described. Possibly most relevant to our case of *L. nigerrimum* envenoming is the toxinology of *Haplopelma huwenum* venom as this spider, shortly to be renamed *H. schmidtii*, is a member of the same sub-family, Ornithoctoninae. Its venom contains ~400 peptides or proteins. Neurotoxins (huwentoxins) inhibit voltage-gated Ca²⁺ and Na⁺ channels.^{19,34} Huwentoxin-I (HWTX-I) is a neuropeptide that has been shown to induce 'spastic' paralysis of the hind limbs in mice.¹⁹ It selectively blocks N-type voltage-sensitive calcium channels. Based on its similarity to ω -Conotoxin MVIIA from *Conus magus* venom, it is being developed as an analgesic drug. HWTX-VI and HWTX-IX induce reversible paralysis in mammals.

Pathophysiology and treatment of muscle spasms

Although the chemical properties of the toxins are becoming clearer, the mechanism of Old World

tarantula envenoming in human beings is unexplained. The mild increase in serum creatine kinase in Case 1 is of interest but is more likely to have reflected his frequent generalised muscle spasms than venom myotoxin activity. There may be a parallel with the action of crotamine from the venom of some populations of tropical rattlesnakes (*Crotalus durissus* subspp.).³⁵ It is conceivable that the tonic spasms were the result of a direct effect of venom neurotoxins acting on voltage-gated sodium and/or calcium channels in the victim's muscles. The admission total plasma Ca^{2+} concentration was towards the lower end of the normal range, hinting that Ca^{2+} might have entered the muscle fibres under the influence of the putative spasm-producing toxin.

It is not possible to assess the role of the palliative treatment given in an attempt to relieve our patients' muscle spasms. No antivenoms are available for any tarantula envenoming and, since tarantula bites are rare, it is inconceivable that any will be manufactured. Since the pathophysiology is obscure, treatment of such patients must remain symptomatic and empirical. Muscle relaxants such as diazepam and intravenous calcium gluconate have been used empirically to control muscle spasms in *Latrodectus* envenoming but there is no convincing evidence of their efficacy.^{36,37} By analogy with other medical conditions associated with severe muscle spasms; such as tetanus, malignant hyperthermia and neuroleptic malignant syndrome; larger doses of benzodiazepines might be tried. Our patients' spasms were extremely distressing, incapacitating and persistent but did not compromise respiration or circulation. However, in a child tarantula enthusiast, or even a debilitated elderly person, the severity of the symptoms we observed in these two healthy young men might well prove life threatening. Dantrolene depresses skeletal muscle excitation-contraction possibly by binding to the ryanodine receptor, the major calcium release channel of skeletal muscle sarcoplasmic reticulum, thus decreasing intracellular calcium concentration.³⁸ Dantrolene has proved effective in treating malignant hyperthermia, neuroleptic malignant syndrome, spasticity and ecstasy intoxication. Its use might be considered in benzodiazepine-refractory spasms caused by tarantula spider envenoming.

Conclusions

In the United Kingdom, keepers of dangerous venomous snakes are required by law to license them.³⁹ This is not demanded of those who keep tarantulas in captivity. CITES <http://www.cites.org/>

prohibits trade in only three endangered species of Theraphosidae, *Aphonopelma albiceps*, *Aphonopelma pallidum* and *Brachypelma* spp., none of them from the Old World. Therefore, the only feasible preventive strategy is to encourage pet traders and hobbyist clubs and societies to explain the potential dangers of too-intimate contact with these attractive exotic animals, especially to potential child buyers.

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