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Letter to the Editor

Do spiders vector bacteria during bites? The evidence indicates otherwise

The history of clinical spider bite toxinology is filled with speculative associations and misattributions of some clinical findings to presumptive but unproven "spider bites". This is particularly true for necrotic arachnidism worldwide, loxoscelism in North America and "white tailed spider bite" in Australia and New Zealand (Swanson and Vetter, 2005; Vetter and Isbister, 2008; White and Weinstein, 2014). One common attribution is a purported association between spider bites and secondary infection.

Medical care providers frequently treat patients exhibiting cutaneous infections. Patients may offer histories of antecedent trauma to the skin as the source, but often there is no obvious cause. Occasionally, patients or their physicians speculate that a bite, especially a spider bite, is the etiology of the infection (Soe et al., 1987; Dominguez, 2004; Moran et al., 2006; Vetter et al., 2006a; El Fakih et al., 2008; Arora and Raza, 2011; Suchard, 2011). However, this speculation begs the question of whether spiders are capable of vectoring human pathogens or even can provoke an infection through a break in the skin. Although experimental work has suggested that this is tenable, extrapolations from those observations to validate clinical diagnoses of infection appear to be putting the proverbial cart before the horse. We present here a discussion of the evidence regarding the association between human bacterial pathogens and spider bites, and the likelihood that bacterial infections are spider-vectored. We show that the evidence for spider-vectored infection is meager, and the mere presence of bacteria on spider fangs or mouthparts does not predicate spiders as vectors.

Clostridium spp. were reported in the venom and on the mouthparts of a small percentage of South American recluse (*Loxosceles*) spiders (Monteiro et al., 2002; Catalán et al., 2010). Subsequently, *Clostridium perfringens* acted as a synergist, increasing dermonecrotic lesion size when concomitantly injected with *Loxosceles* venom into experimental rabbits (Catalán et al., 2010). Although a mechanism is suggested where *Loxosceles* bites could vector these bacteria, there is no proof that *Clostridium* actually enhances clinical dermonecrotic manifestations of cutaneous loxoscelism in humans nor has been isolated from such lesions.

Likewise, conjecture circulated that *Mycobacterium ulcerans* played a contributory role in necrotic arachnidism in Australia because of clinical similarity to infection. However, this was demonstrated to be highly improbable because the bacterium does not readily survive on purposefully contaminated spider fangs and mouthparts and is not readily transferred in simulated bites (Atkinson et al., 1995). A more likely scenario is that *M. ulcerans* infection, contracted in a more conventional way and presenting as local ulceration, was misdiagnosed as necrotic arachnidism when this spurious diagnosis was popular amongst both medical professionals and the media (Harvey and Raven, 1991; Hayman and Smith, 1991). Spider bite is not currently listed as a vector for *M. ulcerans* infection (Merritt et al., 2010).

Ahrens and Crocker (2011) surveyed black widow (*Latrodectus*) fangs for bacteria and generated a list of potential pathogens. The authors postulated that widow envenomation could lead to necrotic arachnidism through a mechanism of cutaneous infection by bacteria. However, in overwhelming contradiction, published documentations of 3245 *Latrodectus* bite diagnoses worldwide show little evidence of bacterial infection as part of widow envenomation syndrome (Table 1) nor have *Latrodectus* spiders *ever* been associated with necrotic arachnidism.

Mascarelli et al. (2013) attempted to associate woodlouse spiders, *Dysdera crocata*, with *Bartonella henselae* infection in a mother and two children. The authors readily admitted that 1) no spiders were seen inflicting bites and were merely implicated by their presence, 2) the presumptive bites may have had nothing to do with the infection, and 3) finding *Bartonella* DNA in the spider may have only been coincidental. Also mentioned is that the family dog, albeit seronegative, had a flea infestation and slept on the mother's bed. Multiple patients in the same family showing the same medical malady is an indicator that spiders are not involved (Vetter et al., 2006a) and that a hematophagous arthropod or infectious etiology should be considered instead. The wounds shown in the article are typical blood sucking injuries.

If infection were part of spider bite syndrome, it should be obvious, common and a routinely reported manifestation of envenomation. Publications describing clinical spider bites are plentiful in the medical literature, and include large case series documenting the spectrum of signs and symptoms in humans. Such series involve medically important spiders of the genera *Latrodectus* (widow spiders), *Loxosceles* (recluse spiders), *Phoneutria* (Brazilian wandering or armed spiders), *Atrax/Hadronyche* (Australian funnel web spiders) as well as general spider envenomations encompassing a plethora of species, and four studies exonerating specific genera as etiologies of necrotic arachnidism (Table 1). Nineteen studies documented in Table 1 involving 2358 bite diagnoses and verified bites give no mention of infections. These include one study of 167 verified bites of red-back spiders (*Latrodectus hasselti*) listing 41 non-infectious clinical features (Wiener, 1961), a second study involving 45 verified South African *Latrodectus* bites or strong

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Table 1
Studies of series of spider bite diagnoses and its association, or lack thereof, with bacterial infections. Some studies were performed retrospectively and, hence, the most appropriate designation is "bite diagnoses" rather than "spider bite" as these could have been misdiagnoses with non-spider etiologies. DX = diagnoses.

Spider (genus)	# of DX	Country	Comment	Reference
Widow (*Latrodectus*)	2144	Australia	infection uncommon	Sutherland and Trinca 1978
Widow (*Latrodectus*)	167	Australia	no mention of infection	Wiener 1961
Widow (*Latrodectus*)	56[a,b]	Australia	no mention of infection	Isbister and Gray 2002
Widow (*Latrodectus*)	163	USA	no mention of infection	Clark et al., 1992
Widow (*Latrodectus*)	52	USA	no mention of infection	Frawley and Ginsburg 1935
Widow (*Latrodectus*)	42	USA	no mention of infection	Ginsburg 1937
Widow (*Latrodectus*)	25	USA	no mention of infection	Kirby-Smith 1942
Widow (*Latrodectus*)	463	Uzbekistan	no mention of infection	Krasnonos et al., 1989
Widow (*Latrodectus*)	56	Iran	no mention of infection	Afshari et al., 2009
Widow (*Latrodectus*)	32	Croatia	no mention of infection	Dzelalija and Medic, 2003
Widow (*Latrodectus*)	45	South Africa	no mention of infection	Müller 1993
Recluse (*Loxosceles*)	359	Brazil	3% mild local infection	Málaque et al., 2002
Recluse (*Loxosceles*)	267	Brazil	18% secondary infection	Sezerino et al., 1998
Recluse (*Loxosceles*)	111[c]	USA	1 case of cellulitis mentioned	Wright et al., 1997
Recluse (*Loxosceles*)	19[b]	USA	no mention of infection	Sams et al., 2001
Armed (*Phoneutria*)	422	Brazil	no mention of infection	Bucaretchi et al., 2000
Wolf (*Scaptocosa*)	515	Brazil	no mention of infection	Ribeiro et al., 1990
Australian Funnel Web (*Atrax/Hadronyche*)	198	Australia	no mention of infection	Isbister et al., 2005
Yellow sac			(*Cheiracanthium*)	20[b,d]
USA/Australia	no	cases of confirmed infection		Vetter et al., 2006b
General (many species)	36[b]	Australia	no mention of infection	White et al., 1989
General (many species)	14[b]	Switzerland	no mention of infection	Nentwig et al., 2013
General (many species)	33[b]	USA	no mention of infection	McKeown et al., 2014
General (many species)	750[b]	Australia	7 patients with infection (redness, pain, no mention of pus)	Isbister and Gray 2002
White-tail (*Lampona*)	130[e]	Australia	no cases of confirmed infection	Isbister and Gray 2003
Black house (*Badumna*)	25[e]	Australia	no cases of confirmed infection	Isbister and Gray 2004

[a] A subset of the 750 verified Australian bite series recorded by Isbister and Gray 2002.
[b] Verified bite reports with offending spider identified by an arachnologist or knowledgable physician.
[c] The authors mention that some of their presumptive *Loxosceles* diagnoses are undoubtedly incorrect.
[d] Ten of these *Cheiracanthium* bites were a subset from the 750 verified Australian bite series.
[e] Bites from white-tail and black house spiders were part of the 750 Australian bite series but they are repeated here because these spiders were wrongly implicated in necrotic skin lesions.

pathognomonic latrodectism cases (*L. indistinctus*, *L. geometricus*) listing 22 non-infectious signs and symptoms (Müller, 1993) and another of 19 verified brown recluse spider bites (Sams et al., 2001). Isbister and Gray (2002) reported an infection rate of 0.9% in 750 verified bites, although the infections were non-confirmed and based on nonspecific findings of redness, swelling and pain. Málaque et al. (2002) simply reported that infection is rare (3%) and mild in loxoscelism. The study by Sezerino et al. (1998) involved retrospective analysis of loxoscelism cases and stated nothing more instructive than "18% secondary infections" listed as a line in a table; a spider was verified in only 2.6% of the cases, making this outlier result difficult to interpret, as well as loxoscelism being historically fraught with many misdiagnoses (Anderson, 1998; Vetter, 2008).

The late Phillip Anderson, American dermatologist and loxoscelism expert in the latter portion of the 20th Century, stated that he and his colleagues treated about 1000 credible loxoscelism cases, mostly referrals (i.e., the more extreme cases), and "never encountered an infected bite, even in unmedicated patients." He further noted that recluse bites are "not exudative" (Anderson, 1998). Rader et al. (2012) recently offered a diagnostic algorithm where "pus observed in lesion" is the first negative exam feature that removes recluse spider bite from the prioritized differential diagnosis.

MRSA (methicillin-resistant *Staphylococcus aureus*) has become a worldwide pandemic in recent years, and has been frequently misdiagnosed as spider bite (Dominguez, 2004; Miller and Spellberg, 2004; Moran et al., 2006; Vetter et al., 2006a; Cohen, 2007; El Fakih et al., 2008; Arora and Raza, 2011). It has also been speculated, without supportive evidence, to be spider-vectored (Fagan et al., 2003); this speculation was soundly criticized (Miller and Spellberg, 2004; Suchard, 2011). Baxtrom et al. (2006) sampled 100 common household spiders from Illinois (USA). From cultures of external and internal microbial fauna, they detected 11 taxa of bacteria, none being MRSA, and only one human pathogen: *Aeromonas* spp., a primarily gastrointestinal pathogen which may occasionally cause soft tissue infection, most often after trauma and exposure to a contaminated aquatic source (Janda and Abbott, 2010; SAW pers. obs.) but has no clinical or basic biomedical association with spider bites. In the Pacific Northwest of North America, hobo spiders (*Eratigena* (=*Tegenaria*) *agrestis*) were originally implicated in necrotic skin lesions, but currently their venom toxicity is in question (Binford, 2001; Vetter and Isbister, 2004; McKeown et al., 2014). A recent study investigating the possibility of bacterial synergism in hobo spider bites documented eight strains of external and internal microbial fauna, none being pathogenic (Gaver-Wainwright et al., 2011). Furthermore, when hobo spiders were exposed to MRSA in petri dishes for 5 min, no MRSA bacteria were found on the spiders afterward nor did they transfer MRSA to clean surfaces upon which they were placed (Gaver-Wainwright et al., 2011).

A spider bite with its infusion of venom is not analogous to a contaminated break in human epidermis from a random cut or abrasion antecedent to infection. In fact, spider venoms (and venoms from other animals, i.e., snakes, bees, wasps, scorpions) are known to have antibacterial properties (Stocker and Traynor, 1986; Talan et al., 1991; Yan and Adams, 1998; Haeberli et al., 2000; Corzo et al., 2001, 2002; Kuhn-Nentwig et al., 2002; Budnik et al., 2004; Kozlov et al., 2006; Benli and Yigit, 2008; Harrison et al., 2014; Jalaei et al., 2014) and were subject to investigation in hope of discovering novel antibacterial therapeutics. Venom from two spiders inhibited growth of *S. aureus* (Corzo et al., 2002; Benli and Yigit, 2008). Kozlov et al. (2006) calculated that a bite from the spider *Lachesana tarabaevi* introduced sufficient venom into a prey to clear all potential bacterial contaminants. Speculation

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