

Antivenoms for the Treatment of Spider Envenomation[†]

Graham M. Nicholson^{1,*} and Andis Graudins^{1,2}

¹Neurotoxin Research Group, Department of Health Sciences, University of Technology, Sydney,
New South Wales, Australia

²Departments of Emergency Medicine and Clinical Toxicology, Westmead Hospital, Westmead,
New South Wales, Australia

*Correspondence: Graham M. Nicholson, Ph.D., Director, Neurotoxin Research Group,
Department of Health Sciences, University of Technology, Sydney, P.O. Box 123, Broadway,
NSW, 2007, Australia; Fax: 61-2-9514-2228; E-mail: Graham. Nicholson@uts.edu.au.

[†]This review is dedicated to the memory of Dr. Struan Sutherland who's pioneering work on the development of a funnel-web spider antivenom and pressure immobilisation first aid technique for the treatment of funnel-web spider and Australian snake bites will remain a long standing and life-saving legacy for the Australian community.

ABSTRACT

There are several groups of medically important araneomorph and mygalomorph spiders responsible for serious systemic envenomation. These include spiders from the genus *Latrodectus* (family Theridiidae), *Phoneutria* (family Ctenidae) and the subfamily Atracinae (genera *Atrax* and *Hadronyche*). The venom of these spiders contains potent neurotoxins that cause excessive neurotransmitter release via vesicle exocytosis or modulation of voltage-gated sodium channels. In addition, spiders of the genus *Loxosceles* (family Loxoscelidae) are responsible for significant local reactions resulting in necrotic cutaneous lesions. This results from sphingomyelinase D activity and possibly other compounds. A number of antivenoms are currently available to treat envenomation resulting from the bite of these spiders. Particularly efficacious antivenoms are available for *Latrodectus* and *Atrax/Hadronyche* species, with extensive cross-reactivity within each genera. In the case of *Latrodectus* antivenoms this is of considerable importance in countries where antivenom is unavailable or where certain antivenoms are associated with an unacceptably high risk of adverse reactions. Moreover, *Latrodectus* and *Atrax* antivenoms appear to be effective in the treatment of envenomation by closely related *Steatoda* spiders (family Theridiidae) or the un-related spider *Missulena bradleyi* (family Actinopodidae), respectively. The effectiveness of *Loxosceles* antivenom in the treatment of the necrotic arachnidism resulting from the bite of recluse spiders is less clear mainly due to late presentation of victims. Antivenom is also available for *Phoneutria* envenomation but is reserved only for severe cases.

Key Words: Envenomation; Spiders; Antivenom; *Latrodectus*; *Phoneutria*; *Steatoda*; *Atrax*; *Hadronyche*; *Missulena*; *Loxosceles*.

INTRODUCTION

Although most cases of spider bite result in minimal if any significant clinical consequences, there are a small number of spiders that may produce either serious systemic clinical envenomation syndromes or significant local reactions. The true incidence of spider bite, spider envenomation and death resulting from spider bite in humans world-wide is unknown and more than likely under-represented due to the voluntary nature of most reporting processes. This review will discuss the role and effectiveness of spider antivenoms for treatment of envenomation by medically important spiders of the genera *Latrodectus*, *Loxosceles*, *Phoneutria* and the subfamily Atracinae (genera *Atrax* and *Hadronyche*).

HUMAN ENVENOMATION BY THERIDIID SPIDERS

Distribution of *Latrodectus* Species

Arguably the most clinically significant group of spiders are the widow spiders (Araneae: Araneomorphae: Theridiidae), of the genus *Latrodectus*. This genus is comprised of multiple species found on all continents excluding Antarctica (Bucherl, 1971) (see Figure 1). Little is known about the true incidence of envenomation following the bite of Widow spiders due to a lack of organized data collection in most regions of the world. In Australia, an estimate of two to three thousand *L. hasselti* (Red-back spider) bites per year has been made. Clinically significant Red-back spider envenomation requiring antivenom therapy occurs in around 20% of these cases (Jelinek et al., 1989; White, 1998). In the United States, reports to the American Association of Poison Control Centers in 1997 revealed 2757 cases of Widow spider bite, but with only 0.004% defined as having a 'major outcome' (Litovitz et al., 1998).

Latrodectism

Although rarely fatal, envenomation by *Latrodectus* spp. may result in an incapacitating syndrome of severe local, regional, or systemic pain and autonomic features called 'latrodectism' which, if left untreated, may last for several days or weeks (Maretic, 1983; White et al., 1995). The syndrome may vary in severity depending on the species and size of the spider, the season of the year, and the amount of venom injected but appears to be similar regardless of the geographic location of the spider (Bogen, 1926; Keegan et al., 1960; Maretic, 1983; McCrone, 1964; Moss and Binder, 1987; Muller, 1993; Sutherland and Trinca, 1978; Wiener, 1961a; Zukowski, 1993).

The initial bite of a Widow spider is often described as initially feeling like a bee sting (Bogen, 1926; Ingram and Musgrave, 1933; Maretic, 1983; Sutherland and Trinca, 1978). Most commonly local pain, sweating, erythema, and piloerection are noted at the bite site within 1 hour of exposure (Maretic, 1983; Muller, 1993; Sutherland and Trinca, 1978; Zukowski, 1993). Clinical features may remain isolated to the site of the bite or less commonly progress to become regional or systemic (see Table 1). Progression to systemic toxicity may occur at a variable rate either rapidly or over a few hours (Clark et al., 1992; Jelinek et al., 1989; Maretic, 1983; Timms and Gibbons, 1986; White et al., 1995). The risk of systemic toxicity is greater in the very young, the very old, and those with any premorbid chronic medical illnesses. The natural progression of envenomation is a gradual diminution of symptoms and signs over several days to weeks although, uncommonly, features of envenomation may persist for months. Fortunately, however, there have been no reports of death from widow spider envenomation in the medical literature in the last 40 years. This is probably related to both an improvement in medical supportive and resuscitative therapies as well as the development of specific antivenom therapies (see Treatment and Management of Latrodectism).

Table 1. Summary of the local, regional, and systemic features of latrodectism.

Signs and symptoms	
Local and	<ul style="list-style-type: none">• Pain• Erythema at bite site

regional ^a effects	<ul style="list-style-type: none"> • Piloerection • Sweating • Regional sweating to limb or specific region of body 	<ul style="list-style-type: none"> • Muscle fasciculation • Regional lymphadenopathy and tenderness
Systemic effects	<ul style="list-style-type: none"> • Generalized muscle pain • Abdominal pain mimicking acute abdomen • Muscle fasciculation and tremor • Generalized sweating • Tachycardia • Hypertension • Nausea • Priapism 	<ul style="list-style-type: none"> • Vomiting • Insomnia • Dizziness • Dyspnea • Restlessness • Mild pyrexia • Paresthesia • Pavor mortis^b • Facies latroductismica^c

^aIncludes bitten limb and can also occur in contralateral limb.

^bFeeling of impending doom.

^cAn unusual pattern of facial muscle grimacing, trismus, blepharoconjunctivitis, and facial flushing.

Data taken from: Bogen, (1926), Jelinek et al. (1989), Maretic, (1983), Muller, (1993), Russell, (1962), Sutherland and Trinca, (1978), Timms and Gibbons, (1986), White, (1985), White et al., (1995), Zukowski, (1993).

The venoms of all *Latrodectus* species are thought to contain similar toxic components. This assertion is based on two significant observations. 1) Envenomation resulting from the bite of any Widow spider results in a similar clinical picture regardless of the species of spider. 2) Widow spider antivenoms produced using the venoms of specific *Latrodectus* species reverse the effects of envenomation from other *Latrodectus* spiders both in experimental animal models and in the clinical setting (see Antivenom Cross-Reactivity with Other *Latrodectus* Venoms). The toxin believed to be responsible is the vertebrate-specific, α -latrotoxin (α -LTx), a 120 kDa toxin that acts selectively on presynaptic nerve endings causing massive release of neurotransmitters by synaptic vesicle exocytosis (for a review see Sudhof (2001)).

Treatment and Management of Latrosectism

Treatment with locally produced species-specific antivenom is regarded as the principal therapy in countries where antivenom is available. Specific antivenoms raised against the venoms of various *Latrodectus* species have been developed in many regions of the world (Theakston and Warrell, 1991) (see Table 2). Nevertheless, there are large areas where no local antivenom is available. These include Central Asia, the Middle East, northern Africa and Southeast Asia, and also Europe where antivenom production ceased with the outbreak of the Balkan conflict in the 1990s.

Antivenom Effectiveness

Antivenom therapy is considered the most effective treatment for the symptoms and signs of latrosectism (Bogen, 1926; Clark et al., 1992; Russell et al., 1979; Sutherland and Trinca, 1978; Wiener, 1956; Wiener, 1961a). Patients receiving antivenom therapy are more likely to be discharged home directly from emergency departments and have much shorter hospital stays than those receiving supportive measures alone (Clark et al., 1992). Additionally, relief of symptoms usually occurs within 1 to 2 hours of antivenom administration with all available antivenoms (Clark et al., 1992; Maretic, 1983; Muller, 1993; Sutherland and Trinca, 1978).

Table 2. Cross reactivity of *Latrodectus* antivenoms.

Venom that antivenom is raised against	Source	Composition	Cross-neutralization of venom/toxin	
			Clinically	Mice (in vivo)
<i>L. mactans</i>	Merck & Co., Inc., West Point PA, USA Instituto Nacional de Microbiologia, Buenos Aires, Argentina Instituto Bioclon, Calzada de Telalpan, Mexico D.F.	Equine IgG Equine IgG Polyvalent Equine F(ab)2 IgG	<i>L. hesperus</i> ^a <i>L. variolus</i> ^a <i>L. bishopi</i> ^a	–
<i>L. indistinctus</i>	South African Institute for Medical Research, Rietfontein, Edenvale, Transvaal, South Africa	Equine IgG	<i>L. geometricus</i> ^a	–
<i>L. hasselti</i>	Commonwealth Serum Laboratories, Melbourne, Australia	Equine F(ab)2 IgG fragment	<i>L. katipo</i> ^a <i>L. tredecimguttatus</i> ^c <i>Steatoda grossa</i> ^{g,h}	<i>L. mactans</i> ^{d,e} <i>L. hesperus</i> ^{d,e} <i>L. tredecimguttatus</i> ^d <i>L. lugubris</i> ^d α -LTx ^d

				<i>Steatoda grossa</i> ^g
<i>L. tredecimguttatus</i>	Institute of Immunology, Zagreb, Croatia ^b	Ovine IgG		<i>L. mactans</i> ^f <i>L. hasselti</i> ^f

^aNormal clinical indication for usage.

^bNo longer available.

^cData taken from: Wiener (1961a).

^dData taken from: Graudins et al. (2001).

^eData taken from: Daly et al. (2001).

^fData taken from: Keegan (1955).

^gData taken from: Graudins et al. (2002a).

^hData taken from: South et al. (1998).

Generally, the dose of Widow spider antivenom required to treat envenomation is reported as one to two ampoules of antivenom for most formulations (Clark et al., 1992; Jelinek et al., 1989; Maretic, 1983; Sutherland and Trinca, 1978; Wiener, 1956; Wiener, 1961a). Uncommonly, some patients have required up to 8 vials of Australian red-back spider antivenom to reverse the features of *L. hasselti* envenomation (Graudins et al., 1999). Importantly antivenom may reverse envenomation presenting to hospital many days or even weeks after exposure (Allen and Norris, 1995; Banham et al., 1994; Wiener, 1956).

Antivenom Side-Effects

The incidence of severe anaphylactic reactions occurring with different antivenom formulations appears to vary. This has resulted in an inconsistency in the threshold for use of antivenom from region to region. In the United States, there appears to be the greatest reluctance by physicians to use specific immunotherapy. This is most likely due to isolated case reports of death following administration of North American widow spider antivenom (Clark et al., 1992) and an extrapolated risk of anaphylaxis calculated from the use of crotalid polyvalent snake antivenom (Spaite et al., 1988). Clark et al. observed an 8% incidence of allergic reactions (urticaria and bronchospasm) with North American widow spider antivenom use (Clark et al., 1992). This has resulted in alternative therapies being employed however large case studies have shown that these are not as effective as antivenom therapy (Clark et al., 1992). Manufacturer recommendations for the use of this

antivenom suggest that it should be reserved for 'severe cases' of envenomation or those occurring at the extremes of age. However, these recommendations are conservative and could result in a significant number of patients suffering from prolonged envenomation if left untreated.

In Australia, on the other hand, Red-back spider antivenom, an equine derive F(ab)₂ fragment, is the most commonly used antivenom in the country (Ho et al., 1999; Sutherland and Trinca, 1978; White, 1998). Clinicians will commonly administer antivenom to any patient with persisting local features of envenomation, regional symptoms or signs and any case of systemic envenomation. Mild allergic reactions are reported to occur in 0.54% of cases (half of these were the result of administration of undiluted antivenom intravenously), with a 1.4% incidence of serum sickness (Sutherland and Trinca, 1978). Severe anaphylaxis or death has not been reported following Red-back spider antivenom use. The reported incidence of allergic reactions is probably over-represented with this antivenom as it is based on voluntary reporting of antivenom use to the manufacturer (Ho et al., 1999).

Antivenoms in general contain a significant amount of protein with anti-complement activity that may result in anaphylactoid reactions if infused rapidly (Sutherland, 1977). This activity is reported to be reduced in trypsin-digested antivenoms such as Red-back spider antivenom. It may be much greater in antivenoms produced as crude hyperimmune equine sera, such as North American widow spider antivenom (Sutherland, 1977). Little is documented about the use of antivenom and the incidence of adverse reactions with antivenom formulations in other parts of the world.

Antivenom Cross-Reactivity with Other *Latrodectus* Venoms

Widow spider antivenoms are commonly produced from animals exposed to one specific *Latrodectus* venom. Nevertheless, it has been observed that species-specific antivenoms

are capable of treating envenomation from more than one kind of Widow spider. Indeed clinical observations of antivenom use around the world and *in vivo* studies in mice suggest that it may be possible to use antivenom raised to the venom of related widow spiders, from other continents, to treat widow spider envenomation (see Table 2). These observations suggest that all Widow spider antivenoms may be capable of reversing clinical envenomation by any other *Latrodectus* species worldwide. This is supported by the observation that *L. hasselti* antivenom can neutralize the toxicity of α -LTx derived from *L. tredecimguttatus* venom (Graudins et al., 2001).

Use of Widow Spider Antivenom in the Treatment of Envenomation by Related Theridiid Spiders

The ‘Cupboard’, ‘Brown house’, or ‘False widow’ spider are all descriptive terms used to encompass various species of Steatoda (Araneae: Araneomorphae: Theridiidae), close relatives of widow spiders. They are found worldwide and are endemic to most continents (Cavalieri et al., 1987; Korszniak and Story, 1994; Main, 1984; Rutherford and Sutherland, 1989; South et al., 1998; Warrell et al., 1991). In general, bites from Steatoda spp. result in minor local symptoms not requiring any specific intervention. However, they have been implicated in a small number of cases of systemic envenomation in humans, also called ‘steatodism’ (Graudins et al., 2002a; Rutherford and Sutherland, 1989; South et al., 1998; Warrell et al., 1991). The envenomation syndrome observed in these severe cases is similar to that of latrodectism adding further support to *in vitro* observations of an α -LTx-like effect by *Steatoda* venom (Einhorn and Hamilton, 1973; Einhorn and Hamilton, 1974; Frontali et al., 1976; Gorio et al., 1978; Graudins et al., 2002a; Korszniak and Story, 1994). Red-back spider antivenom has been successfully administered in two cases of systemic steatodism with resolution of all features of envenomation (Graudins et al., 2002a; South et al., 1998). *In vitro* toxicity data supports this clinical observation, and suggests that *S. grossa* venom is immunogenically and

chromatographically similar to *Latrodectus* venoms (Graudins et al., 2002a).

HUMAN ENVENOMATION BY AUSTRALIAN FUNNEL-WEB SPIDERS

Distribution of *Atrax* and *Hadronyche* Species

Australian funnel-web spider venom probably represents one of the most toxic spider venoms known to affect humans. Australian funnel-web spiders (Araneae: Mygalomorphae: Hexathelidae: Atracinae) are a relatively large group of spiders that include the genera *Atrax* and *Hadronyche*. These genera comprise of over 35 different species of that are mainly located along the southeastern seaboard of continental Australia and Tasmania (Gray, 1987; White et al., 1995) (see Figure 2).

Clinical Features of Envenomation by *Atrax* and *Hadronyche* Species

The medical literature contains numerous reports describing severe male *Atrax robustus* envenomation and death in humans (Sutherland, 1983a; Torda et al., 1980; Wiener, 1961b). Life-threatening envenomation indistinguishable to that of *A. robustus* resulting from the bite of *Hadronyche* species has also been observed and appears to be becoming more common due to rapid population spread (Dieckman et al., 1989; Harrington et al., 1999; Miller et al., 2000). These reports suggest that the envenomation syndrome is similar between species and all Funnel-web spiders are thought to have venom potentially toxic to primates and man (White et al., 1995). Despite this, Funnel-web envenomation remains an uncommon phenomenon. An estimate of envenomation occurring in one out of ten bites has been made and that there are approximately 30 to 40 funnel-web bites with 3 to 4 cases of envenomation per year (White et al., 1995).

Systemic envenomation, while rare, may develop extremely rapidly and has been reported as quickly as 10 minutes following a bite (White et al., 1995; Sutherland, 1983a).

Children may deteriorate rapidly and death may result in 1 to 2 hours if left untreated

(Sutherland, 1983a). Death usually results from progressive, irreversible hypotension, or possibly raised intracranial pressure resulting from cerebral edema (Fisher et al., 1980; Torda et al., 1980) (see Table 3).

The envenomation syndrome is due to the presence of δ -atracotoxins (formerly robustoxin and versutoxin) that are 4–5 kDa peptide neurotoxins found in Funnel-web spider venoms (Brown et al., 1988; Sheumack et al., 1985; Szeto et al., 2000). These all act by slowing sodium current inactivation (Nicholson et al., 1994, 1996, 1998; Szeto et al., 2000) resulting in spontaneous repetitive firing of action potentials (Grolleau et al., 2001). Ultimately, excessive neurotransmitter release results in muscle fasciculation and autonomic effects on the cardiovascular system and exocrine glands.

Table 3. Summary of clinical features of funnel-web spider envenomation.

Local effects	<ul style="list-style-type: none"> • pain • piloerection 	<ul style="list-style-type: none"> • sweating • muscle fasciculation
Systemic effects	<ul style="list-style-type: none"> • circumoral paresthesia • tongue fasciculation • salivation • lachrymation • sweating • nausea • vomiting • generalized muscle fasciculation and weakness 	<ul style="list-style-type: none"> • tachycardia • hypertension • non-cardiogenic pulmonary edema • dyspnea • confusion • coma • cerebral edema • metabolic acidemia.
Late effects¹	<ul style="list-style-type: none"> • persistent hypotension • unremitting coma • coagulopathy 	<ul style="list-style-type: none"> • disseminated intravascular coagulation • rhabdomyolysis

^aCommonly not seen in patients receiving early treatment with antivenom.

Data taken from Fisher et al. (1980), Sutherland (1983a), Torda et al. (1980).

Treatment and Management of *Atrax* and *Hadronyche* Envenomation

First-aid for Funnel-web spider bite may be a life saving maneuver in patients who will require transport to hospital. Application of a pressure immobilization bandage inhibits the development of envenomation and has been proven to be clinically effective in the prevention of Funnel-web spider envenomation (Sutherland and Duncan, 1980; Sutherland et al., 1980). Prolonged application of a pressure immobilization bandage for up to 24 hours may result in apparent local neutralization of venom (Sutherland et al., 1980). It is hypothesized that the venom is slowly inactivated in the tissues, possibly by hydrolysis (Sutherland et al., 1980).

Antivenom Effectiveness

In view of the life-threatening envenomation syndrome that may result from the bite of Funnel-web spiders, a purified rabbit IgG antibody to the venom of the male *A. robustus* was developed in 1980 by Commonwealth Serum Laboratories in Melbourne, Australia (Fisher et al., 1981; Hartman and Sutherland, 1984; Sutherland, 1980; Sutherland et al., 1981). Antivenom therapy has markedly shortened the course of envenomation and resulted in reduced hospital stay as well as reduced the morbidity and mortality from funnel-web spider envenomation (Fisher et al., 1981; Sutherland, 1983a). Antivenom treated patients are commonly discharged from hospital within 1 to 3 days of antivenom treatment. Prior to antivenom availability the average length of hospital stay for severe, non-fatal cases of envenomation was 14 days (Torda et al., 1980).

The antivenom has also been reported to be effective in reversing envenomation from other species of Funnel-web spider including *H. formidabilis*, *H. infensa*, *H. species 14*, *H. cerbera* and *H. versuta* (Dieckman et al., 1989; Harrington et al., 1999; Miller et al., 2000). More recently, Graudins et al. (2002b) have shown that Funnel-web spider antivenom can neutralize the toxicity of a number of other *Hadronyche* and *Atrax* spp. venoms from both male and female spiders in vitro.

Antivenom Side-Effects

Although figures are unavailable, the incidence of allergic reactions to funnel-web antivenom appears to be low. Only one case of delayed serum sickness has been documented one week following treatment with Funnel-web spider antivenom (Miller et al., 1999).

Use of Funnel-Web Spider Antivenom for the Treatment of Envenomation by Mouse Spiders (Genus *Missulena*)

There are currently 11 recognized species of mouse spider in the genus *Missulena* (Araneae: Mygalomorphae: Actinopodidae) with a wide-spread distribution over mainland Australia (Faulder, 1995; Main, 1985; Main, 1996). Envenomation is uncommon but may resemble systemic funnel web spider envenomation in severe cases (Faulder, 1993). Funnel-web spider antivenom has been used to successfully treat an envenomation syndrome from the bite of a male Eastern mouse spider (*Missulena bradleyi*, see Figure 3) (Underhill, 1987). Subsequently a δ -atracotoxin-like action of the venom to slow sodium channel inactivation has been identified and the action of antivenom to neutralize the venom confirmed in isolated nerve-muscle preparations (Rash et al., 2000).

HUMAN ENVENOMATION BY LOXOSCELES SPIDERS

The second most medically important group of spiders are from the genus *Loxosceles* (Araneae: Araneomorphae: Loxoscelidae) otherwise known as ‘recluse’, ‘violin’ or ‘gaucho’ spiders. These spiders can cause necrotic arachnidism, otherwise known as loxoscelism, a form of necrotic cutaneous lesion. Less commonly they can cause a systemic illness that is sometimes fatal.

Distribution of *Loxosceles* Species

They are distributed in the southern states of North America, as well as Central and South America, Europe, southern Africa, Middle East and parts of Asia and have been

accidentally introduced into Australia and some other countries (see Figure 4). Although there are over 50 species only a few have been implicated in loxoscelism.

Loxoscelism

There are two basic forms of loxoscelism: cutaneous (the more frequent form) and viscerocutaneous which is relatively uncommon to rare (see Table 4). Diagnosis of envenomation is usually based on clinical presentation since the spider is not usually available for identification. Despite this enzyme immunoassay ELISAs have been successful in detecting *Loxosceles* venom in necrotic skin lesions (Cardoso et al., 1990) and specific IgG antibodies in patients (Barbaro et al., 1992a) although the latter has not proved effective so far. In addition a passive haemagglutination inhibition assay for *L. reclusa* venom appears to show promise for the confirmation of loxoscelism (Barrett et al., 1993).

Sequelae of the cutaneous form include disfiguring scars (Schenone et al., 1989), persistent damage to underlying nerves, hyalinizing panniculitis and myonecrosis (Bascur et al., 1992), pseudoepitheliomatous hyperplasia and pyoderma gangrenosum (Ingber et al., 1991). In the rare cases of lethal envenomation, typically in children, death is associated with acute renal failure mainly due to hemolysis (Futrell, 1992).

Table 4. Summary of the clinical features of cutaneous and viscerocutaneous loxoscelism.

Form of loxoscelism	Signs and Symptoms	
Cutaneous	<ul style="list-style-type: none"> • painless bite with pain intensifying (probably due to ischemia) • itching and tenderness • nonspecific erythema • local edema 	<ul style="list-style-type: none"> • hemorrhagic mottling areas with regions of ischemia • fever • dry necrosis with underlying ulceration
Viscerocutaneous	As above plus:	<ul style="list-style-type: none"> • intravascular hemolysis

-
- | | |
|------------|--|
| • weakness | • thrombocytopenia |
| • nausea | • disseminated intravascular coagulation |
| • vomiting | • acute renal failure |
-

Taken from Bascur et al. (1992), Futrell, (1992), Schenone et al. (1989).

The dermonecrotic, platelet aggregative and intravascular hemolytic activity of *Loxosceles* spp. venom is due to the presence of 31–35 kDa sphingomyelinase D that can account for death of laboratory animals (Babcock et al., 1981; Barbaro et al., 1992b; Futrell, 1992; Kurpiewski et al., 1981; Tambourgi et al., 1998). Polymorphonuclear leucocytes are also important in the development of the necrotic lesions (Smith and Micks, 1979; Young and Pin, 1988) and appear to be related to the presence of circulating complement (Ward and Cochrane, 1965) although the extent of complement pathway involvement is still uncertain (see Futrell (1992)).

Treatment and Management of Loxoscelism

The Instituto Butantan (Sao Paulo, Brazil) has developed a specific antivenom to *L. reclusa* (soro-antiloxxoscelico) that is used routinely in patients with acute cutaneous lesions and/or signs of systemic toxicity. Nevertheless the antivenom has shown limited success in reversing symptoms, mainly due to late presentation of victims (Futrell, 1992). However, a recent study employing polyclonal anti-*Loxosceles* Fab fragments indicated that administration of antivenom within 4 hours reduced *Loxosceles*-induced dermonecrotic lesions in rabbits (Gomez et al., 1999). This maybe why the effectiveness of the antivenom is poor clinically. A polyvalent antivenom (soro-antiarachnidico polyvalente) is also available for bites of other species of *Loxosceles* found in Brazil including the three most common and clinically important species *L. intermedia*, *L. gaucho* and *L. laeta* (Braz et al., 1999; Mota et al., 1995). However antivenom is not available in most regions where these spiders are found.


To date the treatment for envenomation consists of general wound management and documentation of the extent of the lesion. Blood and urine tests are also performed to exclude viscerocutaneous involvement that requires supportive measures including blood transfusion and systemic antibiotics. Occasionally antihistamines, dapson, hyperbaric oxygen and even cautious use of surgical excision have been tried. However systemic corticosteroids are now generally not recommended (for a review see White et al. (1995)).

ENVENOMATION AND TREATMENT OF PHONEUTRIA BITES

Distribution of Phoneutria Species and Clinical Features of Envenomation

The 'Banana' or 'armed' spiders of the genus *Phoneutria* (Araneae: Araneomorphae: Ctenidae) are mainly confined to the eastern areas of Central and South America. In particular they represent the most common cause of spider bites presenting to hospitals in Brazil (White et al., 1995). The venom appears to contain many neurotoxins some of which are capable of causing a slowing of inactivation and a hyperpolarizing shift in the voltage dependence of activation of voltage-gated sodium channels (for a review see Cordeiro et al. (1995)). This is thought to result in an increased release of peripheral neurotransmitters, particularly acetylcholine and catecholamines. Pain is the most common symptom of envenomation but autonomic features also predominate (see Table 5).

Table 5. Summary of the clinical features of Phoneutria envenomation.

Local features	<ul style="list-style-type: none"> • pain • swelling • localized vasodilatation • profuse sweating 	
Systemic features	<ul style="list-style-type: none"> • agitation • tachycardia • arterial hypertension • vomiting • excessive salivation • profuse sweating • priapism • bradycardia • hypotension • diarrhea • acute pulmonary edema • shock 	<p>mild</p>  <p>severe</p>

Data adapted from White et al., 1995.

Treatment and Management of Phoneutria Envenomation

Treatment is based on the severity of envenomation with symptomatic treatment involving the use of a local anesthetic block to relieve pain. An equine antivenom is available (soro-antiaracnidico polyvalente, Instituto Butantan, Sao Paulo, Brazil) which contains an anti-*Phoneutria* fraction. However it is reserved only for moderate to severe cases. Therefore in Hospital Vital Brazil in Sao Paulo it is used in less than 5% of patients, being mainly children under the age of 7 and elderly patients (White et al., 1995). Since the antivenom is administered intravenously there is also a high risk of immediate hypersensitivity reactions.

CONCLUSIONS

Antivenoms are available and particularly effective for the treatment of bites from

Latrodectus and *Atrax/Hadronyche* spp. and most likely *Steatoda* and *Missulena* envenomation. The cross-reactivity of certain *Latrodectus* antivenoms is of particular importance especially where antivenoms are unavailable or associated with high risk of adverse reactions. The role of antivenom therapy in the treatment of *Loxosceles* envenomation, however, is less clear typically due to the late presentation of victims nevertheless it can be useful in severe *Phoneutria* envenomation.

ACKNOWLEDGMENT

We gratefully acknowledge the financial support of the Australian Rotary Health Research Fund.

REFERENCES

Allen, R. C., Norris, R. L. (1995). Delayed use of widow spider antivenin. *Ann. Emerg. Med.* 26:393,394.

Anderson, P. C. (1982). Necrotizing spider bites. *Am. Fam. Phys.* 26:198 – 203.

Babcock, J. L., Civello, D. J., Geren, C. R. (1981). Purification and characterization of a toxin from brown recluse spider (*Loxosceles reclusa*) venom gland extracts. *Toxicon* 19:677–689.

Banham, N. D., Jelinek, G. A., Finch, P. M. (1994). Late treatment with antivenom in prolonged Red-back spider envenomation. *Med. J. Aust.* 161:379 – 381.

Barbaro, K. C., Cardoso, J. L. C., Eickstedt, V. R. D., Mota, I. (1992a). IgG antibodies to *Loxosceles* sp. spider venom in human envenoming. *Toxicon* 30:1117–1121.

Barbaro, K. C., Cardoso, J. L. C., Eickstedt, V. R. D., Mota, I. (1992b). Dermonecrotic and lethal components of *Loxosceles gaucho* spider venom. *Toxicon* 30:331–338.

Barrett, S. M., Romine-Jenkins, M., Blick, K. E. (1993). Passive haemagglutination

inhibition test for diagnosis of brown recluse spider bite envenomation. *Clin. Chem.* 39:2104–2107.

Bascur, L., Yevenes, I., Barja, P. (1992). Effects of *Loxosceles laeta* spider venom on blood coagulation. *Toxicon* 20:795,796.

Berger, R. S. (1973). The unremarkable brown recluse spider bite. *JAMA* 225:1109 – 1111.

Bogen, E. (1926). Arachnism. *Arch. Intern. Med.* 38:623–632.

Braz, A., Minozzo, J., Abreu, J. C., Gubert, I. C., Chávez-Olórtegui, C. (1999). Development and evaluation of the neutralizing capacity of horse antivenom against the Brazilian spider *Loxosceles intermedia*. *Toxicon* 37:1323–1328.

Brown, M. R., Sheumack, D. D., Tyler, M. I., Howden, M. E. H. (1988). Amino acid sequence of versutoxin, a lethal neurotoxin from the venom of the funnel-web spider *Atrax versutus*. *Biochem. J.* 250:401–405.

Bucherl, W. (1971). Venomous animals and their venoms. In: Bucherl, W., Buckley, E. E., eds. *Venomous Invertebrates*. Vol. 3. London: Academic Press, pp. 197–277.

Cardoso, J. L. C., Fan, H. W., Franca, F. O. S., Warrell, D. A., Theakston, R. D. G. (1990). Detection by enzyme immunoassay of *Loxosceles gaucho* venom in necrotic skin lesions caused by spider bites in Brazil. *Trans. R. Soc. Trop. Med. Hyg.* 84:608,609.

Cavalieri, M., D'Urso, D., Lassa, A., Pierdominici, E., Robello, M., Grasso, A. (1987). Characterization and some properties of the venom gland extract of a theridiid spider (*Steatoda paykulliana*) frequently mistaken for black widow spider (*Latrodectus tredecimguttatus*). *Toxicon* 25: 965 – 974.

Clark, R. F., Wethern-Kestner, S., Vance, M. V., Gerkin, R. (1992). Clinical presentation and treatment of black widow spider envenomation: a review of 163 cases. *Ann. Emerg.*

Med. 21:782–787.

Cordeiro, M. D. N., Richardson, M., Gilroy, J., De Figueiredo, S. G., Beirao, P. S. L., Diniz, C. R. (1995). Properties of the venom from the South American ‘armed’ spider *Phoneutria nigriventer* (Keyserling, 1891). *J. Toxicol., Toxin Rev.* 14:309–326.

Daly, F. F., Hill, R. E., Bogdan, G. M., Dart, R. C. (2001). Neutralization of *Latrodectus mactans* and *L. hesperus* venom by redback spider (*L. hasselti*) antivenom. *J. Toxicol., Clin. Toxicol.* 39:119–123.

Dieckman, J., Prebble, J., McDonogh, A., Sara, A., Fisher, M. M. (1989). Efficacy of funnel web spider antivenom in human envenomation by *Hadronyche* species. *Med. J. Aust.* 151:706,707.

Einhorn, V. F., Hamilton, R. (1973). Transmitter release by red back spider venom. *J. Pharm. Pharmacol.* 25:824–826.

Einhorn, V. F., Hamilton, R. C. (1974). Red back spider venom and inhibitory transmission. *J. Pharm. Pharmacol.* 26:748–750.

Faulder, R. (1993). Records of bites by *Missulena* species. *Aust. Arachnol.* 46:4,5.

Faulder, R. (1995). Two new species of the Australian spider genus *Missulena* Walkenaer (Araneae: Actinopodidae). *Rec. West. Aust. Mus. Suppl.* 52:73–78.

Fisher, M. M., Carr, G. A., McGuinness, R. T., Warden, J. C. (1980). *Atrax robustus* envenomation. *Anaesth. Intensive Care* 8:410–420.

Fisher, M. M., Raftos, J., McGuinness, R. T., Dicks, I. T., Wong, J. S., Burgess, K. R., Sutherland, S. K. (1981). Funnel-web spider (*Atrax robustus*) antivenom. 2. Early clinical experience. *Med. J. Aust.* 2:525– 526.

Frontali, N., Ceccarelli, B., Gorio, A., Mauro, A., Siekaevitz, P., Tzeng, M.-C., Hurlbut,

W. P. (1976). Purification from black widow spider venom of a protein factor causing the depletion of synaptic vesicles at neuromuscular junctions. *J. Cell Biol.* 68:462–479.

Futrell, J. M. (1992). Loxoscelism. *Am. J. Med. Sci.* 304:261–267. Gajardo-Tobar, R. (1966). Personal experience with loxoscelism. *Mem. Inst. Butantan* 33:689–698.

Gomez, H. F., Miller, M. J., Trachy, J. W., Marks, R. M., Warren, J. S. (1999). Intradermal anti-loxosceles Fab fragments attenuate dermonecrotic arachnidism. *Acad. Emerg. Med.* 6:1195–1202.

Gorio, A., Rubin, L. L., Mauro, A. (1978). Double mode of action of black widow spider venom on frog neuromuscular junction. *J. Neurocytol.* 7:193 – 205.

Graudins, A., Vassiliadis, J., Dowsett, R. P. (1999). Red-back spider (*Latrodectus mactans hasselti*) envenomation requiring ‘high dose’ antivenom therapy (abstract). *J. Toxicol., Clin. Toxicol.* 37:615.

Graudins, A., Padula, M., Broady, K. W., Nicholson, G. M. (2001). Red-back spider (*Latrodectus hasselti*) antivenom prevents the toxicity of widow spider venoms. *Ann. Emerg. Med.* 37:154–160.

Graudins, A., Gunja, N., Broady, K. W., Nicholson, G. M. (2002a). Clinical and in vitro evidence for the efficacy of Australian red-back spider (*Latrodectus hasselti*) antivenom in the treatment of Brown cupboard spider (*Steatoda grossa*) envenomation. *Toxicon* 40:767–775.

Graudins, A., Wilson, D., Alewood, P. F., Broady, K. W., Nicholson, G. M. (2002b). Cross-reactivity of Sydney funnel-web spider antivenom: neutralization of the in vitro toxicity of other Australian funnel-web (*Atrax* and *Hadronyche*) spider venoms. *Toxicon* 40:259–266.

Gray, M. R. Distribution of the funnel web spiders. In: Covacevich, J., Davie, P., Pearn, J.,

eds. Toxic Plants and Animals: a Guide for Australian Animal Toxin, Brisbane: Queensland Museum, pp. 1987. 313–321.

Grolleau, F., Stankiewicz, M., Birinyi-Strachan, L. C., Wang, X.-H., Nicholson, G. M., Pelhate, M., Lapied, B. (2001). Electrophysiological analysis of the neurotoxic action of a funnel-web spider toxin, δ -atractotoxin-Hv1a, on insect voltage-gated Na⁺ channels. *J. Exp. Biol.* 204:711 – 721.

Harrington, A. P., Raven, R. J., Bowe, P. C., Hawdon, G. M., Winkel, K. D. (1999). Funnel-web spider (*Hadronyche infensa*) envenomations in coastal south-east Queensland. *Med. J. Aust.* 171:651–653.

Hartman, L. J., Sutherland, S. K. (1984). Funnel-web spider (*Atrax robustus*) antivenom in the treatment of human envenomation. *Med. J. Aust.* 141:796 – 799.

Ho, J., White, J., Staples, A., Hobbs, P. (1999). An analysis of antivenom use in Australia, based on reports of use, 1995–1999. In: Fifth Asia-Pacific Congress on Animal, Plant and Microbial Toxins. Pattaya, Thailand: International Society of Toxinology, p. 128.

Ingber, A., Trattner, A., Cleper, R., Sandbank, M. (1991). Morbidity of brown recluse spider bites: clinical picture, treatment and prognosis. *Acta Derm. Venereol. Stokh.* 71:337–340.

Ingram, W. W., Musgrave, A. (1933). Spider bite (arachnidism): a survey of its occurrence in Australia, with case histories. *Med. J. Aust.* 2:10–15.

Jelinek, G. A., Banham, N. D., Dunjey, S. J. (1989). Red-back spider-bites at Fremantle Hospital, 1982–1987. *Med. J. Aust.* 150:693–695.

Keegan, H. L. (1955). Effectiveness of *Latrodectus tredecimguttatus* antivenin in protecting laboratory mice against effects of intraperitoneal injections of *Latrodectus mactans*. *Am. J. Trop. Med. Hyg.* 4:762–764.

Keegan, H. L., Hedeem, R. A., Whittemore, F. W. (1960). Seasonal variation in venom of black widow spiders. *Am. J. Trop. Med. Hyg.* 10:477–479.

Korszniak, N. V., Story, D. F. (1994). Effects of the venom of the Theridiid spider *Steatoda capensis* Hann, on autonomic transmission in rat isolated atria and caudal artery. *Toxicon* 32:85–96.

Kurpiewski, G., Forrester, L. J., Barrett, J. T., Campell, B. T. (1981). Platelet aggregation and sphingomyelinase D activity of a purified toxin from the venom of *Loxosceles reclusa*. *Biochim. Biophys. Acta* 678:467–476.

Litovitz, T. L., Klein-Schwartz, W., Dyer, K. S., Shannon, M., Lee, S., Powers, M. (1998). 1997 Annual reports of the American Association of Poison Control Centers toxic exposure surveillance system. *Am. J. Emerg. Med.* 16:443–497.

Lucas, S. (1988). Spiders in Brazil. *Toxicon* 26:759–772.
Sydney: Collins.

Main, B. Y. (1996).

Main, B. Y. (1996).

Catalogue. Vol. III. Canberra: Australian Government Publishing Service, pp. 1–48.

Main, B. Y. (1996). Biosystematics of Australian mygalomorph spiders: description of a new species of *Missulena* from southwestern Australia (Araneae: Mygalomorphae: Actinopodidae). *Rec. West. Aust. Mus* 17: 355 – 359.

Maretic, Z. (1978). Venoms of Theridiidae, genus *Latrodectus*, B. epidemiology of envenomation, symptomatology, pathology, and treatment. In: Bettini, S., ed. *Arthropod Venoms*. Vol. 48. *Handb. Exp. Pharmacol.*, Berlin: Springer-Verlag, pp. 185–212.

Maretic, Z. (1983). Latrodectism: variations in clinical manifestations provoked by *Latrodectus* species of spiders. *Toxicon* 21:457–466.

McCrone, J. D. (1964). Comparative lethality of several *Latrodectus* venoms. *Toxicon* 2:201–203.

Miller, M. K., Whyte, I. M., Dawson, A. H. (1999). Serum sickness from funnelweb spider antivenom. *Med. J. Aust.* 171:54.

Miller, M. K., Whyte, I. M., White, J., Keir, P. M. (2000). Clinical features and management of *Hadronyche* envenomation in man. *Toxicon* 38: 409 – 427.

Moss, H. S., Binder, L. S. (1987). A retrospective review of black widow spider envenomation. *Ann. Emerg. Med.* 16:188–192.

Mota, I., Barbaro, K. C. (1995). Biological and biochemical properties of venoms from medically important *Loxosceles* (Araneae) species in Brazil. *J. Toxicol., Toxin Rev.* 14:402–421.

Muller, G. J. (1993). Black and brown widow spider bites in South Africa. A series of 45 cases. *S. Afr. Med. J.* 83:399–405.

Newlands, G., Atkinson, P. (1988). Review of southern African spiders of medical importance, with notes on the signs and symptoms of envenomation. *S. Afr. Med. J.* 73:235–239.

Newlands, G., Atkinson, P. (1990). A key for the clinical diagnosis of araneism in Africa south of the equator. *S. Afr. Med. J.* 77:96,97.

Nicholson, G. M., Willow, M., Howden, M. E. H., Narahashi, T. (1994). Modification of sodium channel gating and kinetics by versutoxin from the Australian funnel-web spider *Hadronyche versuta*. *Pflügers Arch. (Eur. J. Phys.)* 428:400–409.

Nicholson, G. M., Little, M. J., Tyler, M., Narahashi, T. (1996). Selective alteration of sodium channel gating by Australian funnel-web spider toxins. *Toxicon* 34:1443–1453.

Nicholson, G. M., Walsh, R., Little, M. J., Tyler, M. I. (1998). Characterisation of the effects of robustoxin, the lethal neurotoxin from the Sydney funnel-web spider *Atrax robustus*, on sodium channel activation and inactivation. *Pflügers Arch. (Eur. J. Phys.)*

436:117– 126.

Platnick, N. (1990). *Advances in Spider Taxonomy, 1981 – 1987*. A supplement to Brignoli's 'A Catalogue of the Araneae Described between 1940–1981. Manchester: Manchester University Press.

Rash, L. D., Birinyi-Strachan, L. C., Nicholson, G. M., Hodgson, W. C. (2000).

Neurotoxic activity of venom from the Australian eastern

mouse spider (*Missulena bradleyi*) involves modulation of sodium channel gating. *Br. J. Pharmacol.* 130:1817–1824.

Rees, R., Campbell, D., Rieger, E., King, L. E. (1987). The diagnosis and treatment of brown recluse spider bites. *Ann. Emerg. Med.* 16:945–949.

Russell, F. E. (1962). Muscle relaxants in black widow spider (*Latrodectus mactans*) poisoning. *Am. J. Med. Sci.* 1:159–161.

Russell, F. E., Marcus, P., Streng, J. A. (1979). Black widow spider envenomation during pregnancy. Report of a case. *Toxicon* 17:188,189.

Rutherford, A. M., Sutherland, S. K. (1989). Large blister formation after a bite by the common cupboard spider, genus *Steatoda*. *Med. J. Aust.*

151:542.

Schenone, H., S

Bettini, S., ed. *Arthropod Venoms*. Vol. 48. *Handb. Exp. Pharmacol.*, Berlin: Springer-Verlag.

Schenone, H., Rubio, S., Villarroel, F., Rojas, A. (1975). Epidemiology and clinical course of loxoscelism. A study of 133 cases caused by the bite of the corner spider (*Loxosceles laeta*)(author's transl). *Bol. Chil. Parasitol.* 30:6–17.

Schenone, H., Savedra, T., Rojas, A., Vilaroel, F. (1989). *Loxoscelismo en Chile:*

estudios epidemiológicos clínicos y experimentales. *Rev. Inst. Med. Trop. Sao Paulo* 36:403–415.

Sheumack, D. D., Claassens, R., Whiteley, N. M., Howden, M. E. H. (1985). Complete amino acid sequence of a new type of lethal neurotoxin from the venom of the funnel-web spider *Atrax robustus*. *FEBS Lett.* 181: 154 – 156.

Smith, C. W., Micks, D. W. (1979). The role of polymorphonuclear leukocytes in the lesion caused by the venom of the brown spider, *Loxosceles reclusa*. *Lab. Invest.* 22:90–93.

South, M., Wirth, P., Winkel, K. D. (1998). Redback spider antivenom used to treat envenomation by a juvenile *Steatoda* spider. *Med. J. Aust.* 169:642.

Southcott, R. V. (1976). Arachnidism and allied syndromes in the Australian region. *Rec. Adel. Child. Hosp.* 1:97–186.

Spaite, D. W., Dart, R. C., Hurlbut, K., McNally, J. T. (1988). Skin testing: implications in the management of pit viper envenomation. *Ann. Emerg. Med.* 17:152.

Sudhof, T. C. (2001). α -Latrotoxin and its receptors: neurexins and CIRL/ latrophilins. *Annu. Rev. Neurosci.* 24:933–962.

Sutherland, S. K. (1977). Serum reactions: an analysis of commercial antivenoms and the possible role of anticomplementary activity in de-novo reactions to antivenoms and antitoxins. *Med. J. Aust.* 1:613–615.

Sutherland, S. K. (1980). Antivenom to the venom of the male Sydney funnel-web spider *Atrax robustus*. Preliminary report. *Med. J. Aust.* 2:437 – 441.

Sutherland, S. K. (1983a). Genus *Atrax* Cambridge, the funnel-web spiders. In: Sutherland, S. K., ed. *Australian Animal Toxins*. Melbourne: Oxford University Press, pp. 255–298.

Sutherland, S. K. (1983b). *Latrodectus mactans hasselti*, the Australian red-back or jockey spider. In: Sutherland, S. K., ed. Australian Animal Toxins. Melbourne: Oxford University Press, pp. 242–254.

Sutherland, S. K., Duncan, A. W. (1980). New first-aid measures for envenomation: with special reference to bites by the Sydney funnel-web spider *Atrax robustus*. Med. J. Aust. 1:378–379.

Sutherland, S. K., Trinca, J. C. (1978). Survey of 2144 cases of red-back spider bites. Med. J. Aust. 2:620–623.

Sutherland, S. K., Duncan, A. W., Tibballs, J. (1980). Local inactivation of funnel-web spider (*Atrax robustus*) venom by first-aid measures: potentially lifesaving part of treatment. Med. J. Aust. 2:435–437.

Sutherland, S. K., Tibballs, J., Duncan, A. W. (1981). Funnel-web spider (*Atrax robustus*) antivenom. 1. Preparation and laboratory testing. Med. J. Aust. 2:522–525.

Szeto, T. H., Birinyi-Strachan, L. C., Wang, X. -H., Smith, R., Connor, M., Christie, M. J., King, G. F., Nicholson, G. M. (2000). Isolation and pharmacological characterisation of δ -atracotoxin-Hv1b, a vertebrate-selective sodium channel toxin. FEBS Lett. 470:293–299.

Tambourgi, D. V., Magnoli, F. C., Van den Berg, C. W., Morgan, B. P., De Araujo, P. S., Alves, E. W., Da Silva, W. D. (1998). Sphingomyelinases in the venom of the spider *Loxosceles intermedia* are responsible for both dermonecrosis and complement-dependent hemolysis. Biochem. Biophys. Res. Commun. 251:366–373.

Theakston, R. D. G., Warrell, D. A. (1991). Antivenoms: a list of hyperimmune sera currently available for the treatment of envenoming by bites and stings. Toxicol. 29:1419.

Timms, P. K., Gibbons, R. B. (1986). Latrodectism-effects of the Black widow spider.

West. J. Med. 144:315–317.

Torda, T. A., Loong, E., Greaves, I. (1980). Severe lung oedema and fatal consumption coagulopathy after funnel-web bite. *Med. J. Aust.* 2:442–444.

Underhill, D. (1987). Unwelcome stranger. In: Sutherland, S. K., ed. *Australia's Dangerous Creatures*. Sydney: Readers Digest Services, p. 175.

Ward, P. A., Cochrane, C. G. (1965). Bound complement and immunologic injury of blood vessels. *J. Exp. Med.* 121:215–234.

Warrell, D. A., Shaheen, J., Hillyard, P. D., Jones, D. (1991). Neurotoxic envenoming by an immigrant spider (*Steatoda nobilis*) in southern England. *Toxicon* 29:1263–1265.

Wasserman, G. S., Anderson, P. C. (1983). Loxoscelism and necrotic arachnidism. *J. Toxicol., Clin. Toxicol.* 21:451–472.

White, J. (1985). Latrodectism as a mimic (letter). *Med. J. Aust.* 142:75. White, J. (1998). Envenoming and antivenom use in Australia. *Toxicon* 36:1483 – 1492.

White, J., Carduso, J. L., Fan, H. W. (1995). Clinical toxicology of spiderbites. In: Meier, J., White, J., eds. *Handbook of Clinical Toxicology of Animal Venoms and Poisons*. New York: CRC Press, pp. 259–329.

Wiener, S. (1956). The Australian red back spider *Latrodectus hasselti*: I. Preparation of antiserum by the use of venom absorbed on aluminium phosphate. *Med. J. Aust.* 1:739–742.

Wiener, S. (1961a). Red back spider antivenene. *Med. J. Aust.* 2:41–44.

Wiener, S. (1961b). Observations on the venom of the Sydney funnel-webspider (*Atrax robustus*). *Med. J. Aust.* 2:693–699.

Young, V. L., Pin, P. (1988). The brown recluse spider bite. *Ann. Plast. Surg.* 20:447 –

452.

Zukowski, C. W. (1993). Black widow spider bite. *J. Am. Board Fam. Pract.* 6:279 – 281.

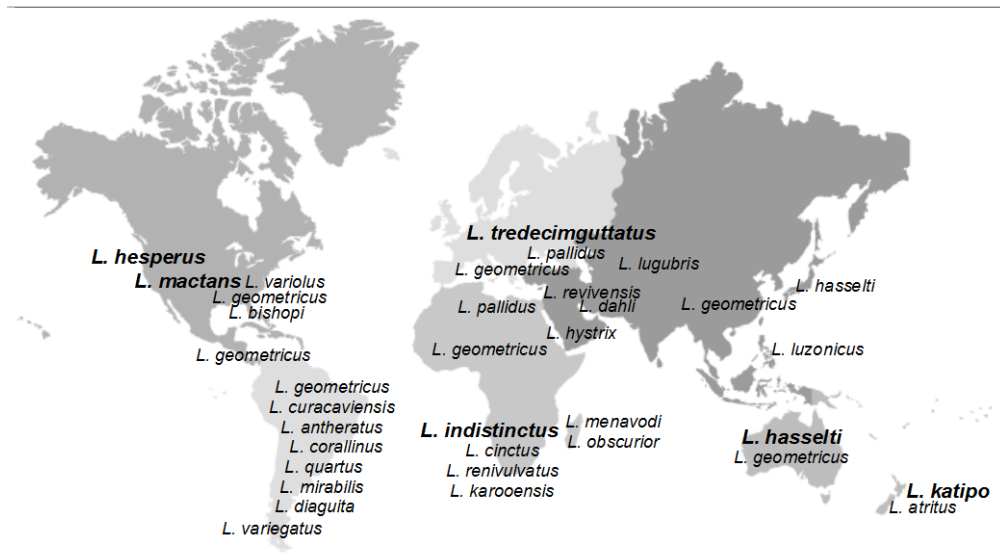


Figure 1. Worldwide distribution of some species of *Latrodectus*. Medically important species are highlighted in bold text. Data from Bucherl (1971), Lucas (1988), Maretic (1978), Newlands and Atkinson (1988), Platnick (1990), Sutherland (1983b).

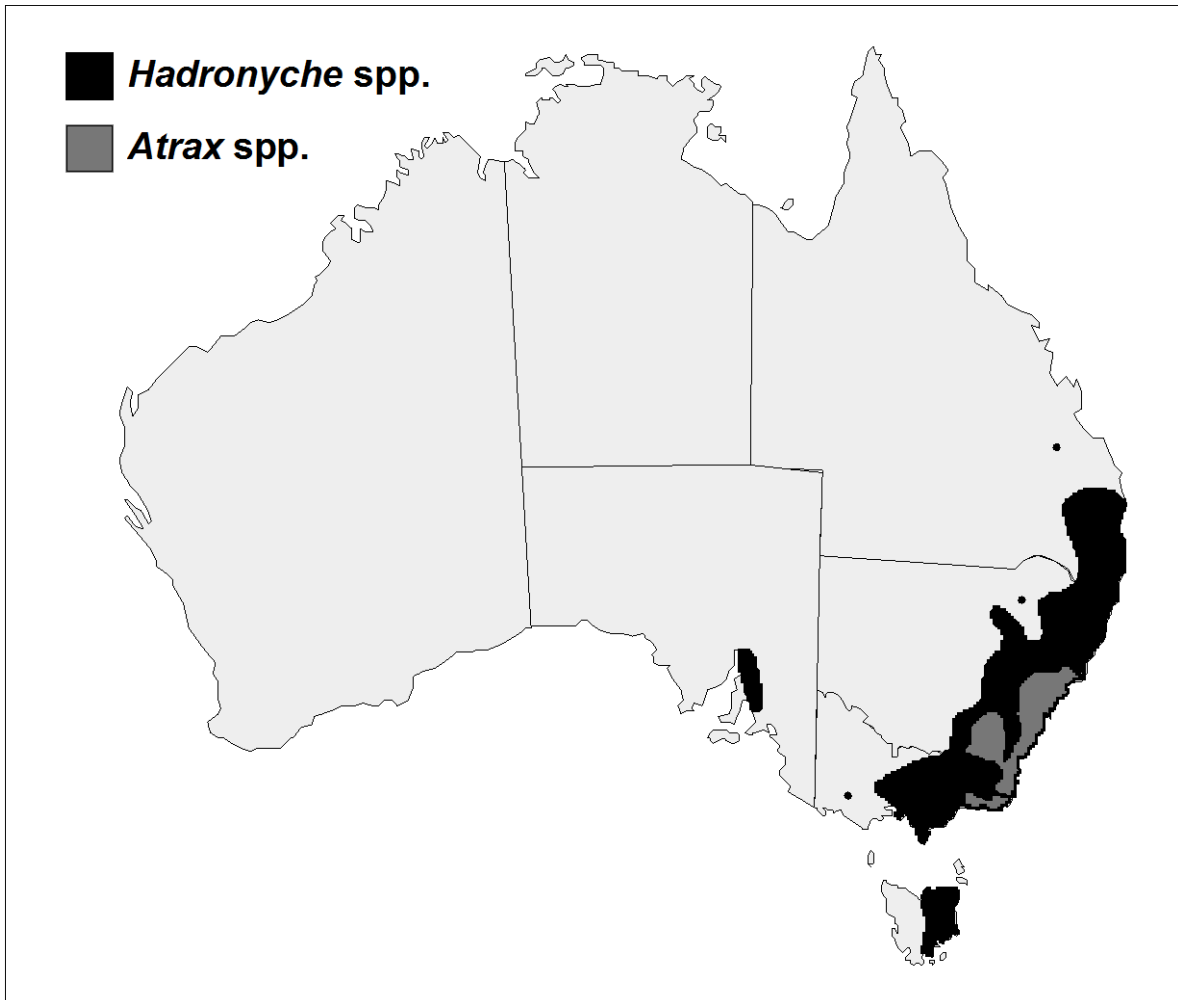


Figure 2. Distribution of Australian funnel-web spiders (*Atrax* and *Hadronyche*). Data from Gray (1987).

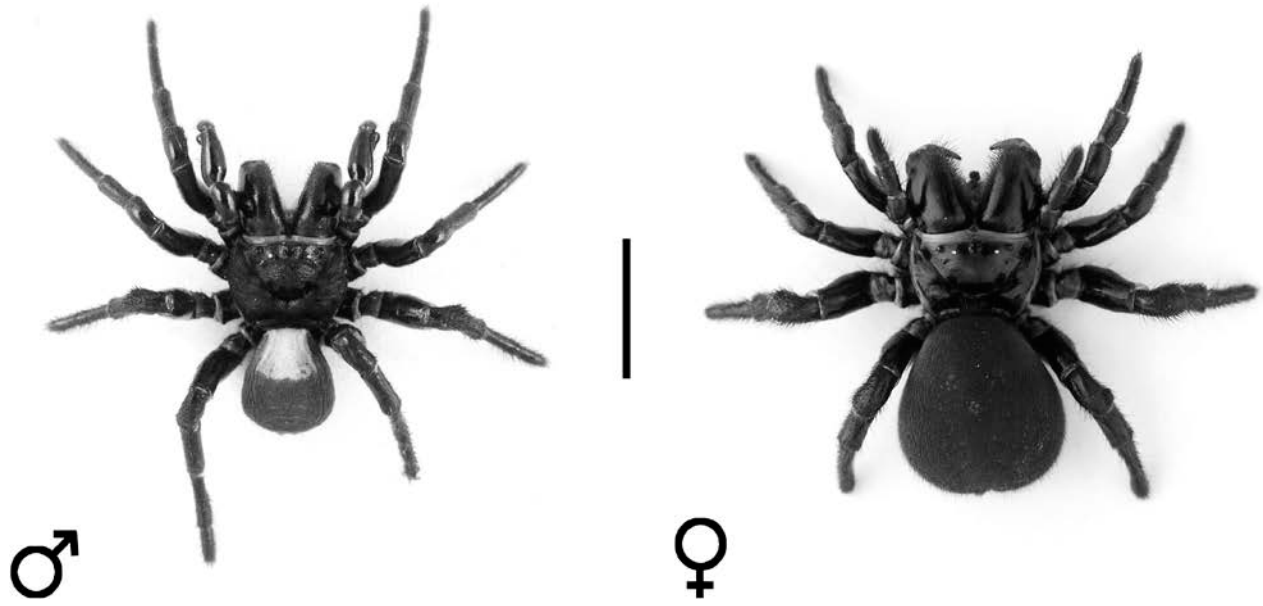


Figure 3. The male (left) and female (right) Eastern mouse spider (*Missulena bradleyi*). Scale bar represents 1 cm. Photo courtesy of David Humfrey.

