

# Latrodectism: a prospective cohort study of bites by formally identified redback spiders

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REDBACK SPIDERS, *Latrodectus hasselti*, are widow spiders,<sup>1</sup> arguably the most medically significant spiders in the world, and certainly in Australia.<sup>2-5</sup> Two major issues relating to redback spider bite remain unresolved. The first is the proportion of bites causing severe effects, and the second is the indications for antivenom and its route of administration.<sup>6</sup> Many doctors in Australia believe that most redback spider bites (80%) cause minor effects,<sup>7,8</sup> and, although a safe and effective intramuscular antivenom exists, doctors are reluctant to use it unless there is severe or systemic envenomation.<sup>9,10</sup> Severe pain is often not regarded as an indication for administering the antivenom.

Redback spider antivenom is usually given intramuscularly, which remains the recommendation of CSL Ltd.<sup>11</sup> However, redback spider antivenom was introduced without controlled studies to demonstrate efficacy or safety. Its introduction was based on a retrospective collection of 167 cases reported by Australian doctors suggesting it was effective.<sup>12</sup>

Here we report an analysis of the subset of bites by *L. hasselti* from a larger prospective cohort of 750 spider bites in Australia<sup>4</sup> to better describe the clinical features, proportion of severe cases, and outcomes of redback spider bite. We also address two further issues: the effect of intramuscular antivenom in a smaller cohort of patients presenting to hospital and the diagnostic utility of early features of bites by *L. hasselti* which distinguish them from other spider bites.

## ABSTRACT

**Objective:** To determine the spectrum of severity and early diagnostic predictors of redback spider bites (*Latrodectus hasselti*), and to examine the effect of intramuscular redback antivenom.

**Design and setting:** Prospective cohort study of calls to New South Wales, Queensland and Western Australian poisons information centres and presentations to Royal Prince Alfred Hospital and Royal Darwin Hospital emergency departments.

**Patients:** 68 people with definite redback spider bites in which the spider was immediately collected and expertly identified (1 February 1999 to 30 April 2002).

**Interventions:** Intramuscular redback spider antivenom in a smaller cohort of hospitalised patients.

**Main outcome measures:** Pain severity and duration, local effects and systemic envenomation (effects, prevalence, and persistence > 24 hours).

**Results:** The median duration of effects was 48 hours (interquartile range, 24–96 hours). Pain occurred after all bites and was severe in 42 (62%). Forty-five patients (66%) had pain lasting longer than 24 hours, and 22 (32%) were unable to sleep because of pain. Systemic effects occurred in 24 (35%). Increasing pain over one hour occurred in 37 cases (54%), and local/regional diaphoresis in 23 (34%); both these features were highly predictive of *L. hasselti* bites compared with bites of other spiders. One of six patients treated with intramuscular antivenom (17%) had no pain at 24 hours, compared with two of 17 untreated patients (12%) (difference, 5%; 95% CI, –36% to +64%;  $P=0.95$ ). There was no difference in duration of systemic effects with antivenom administration.

**Conclusions:** Most redback spider bites cause severe and persistent effects. Intramuscular antivenom appears to be less effective than previously thought and its use by this route needs review.

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## METHODS

### Case collection

Subjects were recruited prospectively over 39 months from 1 February 1999 to 30 April 2002. Most were a subgroup of a large, prospective study of all spider bites in Australia, conducted from 1 February 1999 to 30 April 2001.<sup>4</sup> In the following 12 months, the same method-

ology was used, but only including redback spiders (this study), white-tail spiders,<sup>13</sup> and mygalomorph spiders (unpublished).

Patients were recruited from Royal Prince Alfred Hospital and Royal Darwin Hospital emergency departments and from calls to New South Wales, Queensland and Western Australia poisons information centres. Cases were only included if a definite history of spider bite was obtained and the spider was collected at the time of the bite. All patients were seen or contacted within 24 hours of the bite, and then followed up by telephone after 1 week or until the clinical features resolved. Verbal and written consent for the study was obtained from all patients.

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Spiders were either collected directly from the patient or mailed to the authors. Spiders were identified (species, sex and maturity) by an expert arachnologist (MG).

### Details of bites

For each spider bite, we recorded patient demographics, circumstances of the bite (location, time, activity, season), bite site, local and systemic effects, and management (hospital attendance, antivenom). Severe pain was defined as pain greater than a bee sting or equivalent, and "increasing pain" as pain that increased within the first hour.

### Effect of antivenom

A subgroup of patients who presented to an emergency department with definite *L. hasselti* bites was used to examine the effect of redback spider antivenom by intramuscular administration. Treatment was defined as receipt of intramuscular antivenom within 6 hours of the bite. The primary outcome was the proportion of patients with no pain at 24 hours. Where systemic effects occurred, a further outcome was the proportion of patients in which these lasted beyond 24 hours. Adverse reactions to antivenom were recorded.

### Utility of bite features in identifying spider as redback

The utility of the initial features of *L. hasselti* bite (circumstances and early clinical features), versus all other spider bites (obtained from the large prospective study for comparison<sup>4</sup>), to predict whether the spider was *L. hasselti* was tested using the final taxonomic identification as a gold standard. The initial features we investigated were the person's activity at the time of the bite (dressing, putting on shoes) and the initial clinical effects ("increasing pain", local diaphoresis, severe pain, radiating pain).

### Ethics approval

Ethics approval was obtained from the Central Sydney Area Health Service Ethics Review Committee (RPAH Zone), the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Men-

### 1: Geographical distribution of redback spider bites



The map includes only the 56 cases collected in the study of all spider bites between 1 February 1999 and 30 April 2001.<sup>4</sup> The 12 cases collected later are not included because the recruitment site differed, so the first 56 bites provide a more accurate geographical representation.

zies School of Health Research, and the Ethics Committee of Royal Children's Hospital and District, Brisbane, to cover all institutions involved.

### Statistics

For descriptive statistics, median and interquartile ranges (IQR) were used for data not normally distributed. Fischer's exact test was used for comparison of proportions and the Mann-Whitney test for comparing medians. Confidence intervals were calculated using StatMate.<sup>14</sup> All statistical analysis was done using GraphPad InStat<sup>15</sup> except for the treatment analysis, for which exact methods in StatXact<sup>16</sup> were used for the small numbers.

## RESULTS

### Details of bites

Sixty-eight definite bites by redback spiders were recorded during the 39 months (27 male and 41 female subjects; age range, 5–83 years; median age, 35 years [IQR, 28–47 years]). Redback spider bites occurred across Australia (Box 1). Most bites occurred in the warmer months between December and April, and 90% occurred between 0800 and 2400 hours.

Bites occurred to all parts of the body. The median duration of all effects was 48 hours (IQR, 24–96 hours). Pain

### 2: Clinical effects and circumstances of 68 redback spider bites

Features of bites	No.	Percentage (95% CI)
<b>Pain</b>		
Severe pain	42	62% (49%–73%)
Pain > 24 hours	45	66% (54%–77%)
Severe pain > 24 hours	38	56% (43%–68%)
Unable to sleep for first 24 hours	22	32% (22%–45%)
Increasing pain in first hour	37	54% (42%–67%)
Radiating pain (proximal limb)	26	38% (27%–51%)
Abdominal/chest pain*	8	12% (5%–22%)
<b>Other local/regional effects</b>		
Local or regional diaphoresis	23	34% (23%–46%)
Redness/red area	50	74% (61%–83%)
Swelling	5	7% (2%–16%)
Puncture marks	4	6% (2%–14%)
<b>Systemic effects†</b>		
Nausea	16	24% (14%–35%)
Vomiting	3	4% (1%–12%)
Headache	7	10% (4%–20%)
Malaise	7	10% (4%–20%)
Lethargy	7	10% (4%–20%)
Generalised diaphoresis	3	4% (1%–12%)
<b>Bite site</b>		
Distal extremity	31	46% (33%–58%)
Proximal limb	18	26% (17%–39%)
Trunk	14	21% (12%–32%)
Head/neck	5	7% (2%–16%)
<b>Circumstances of bite</b>		
Putting on shoe	19	28% (18%–40%)
Dressing	7	10% (4%–20%)

\* Includes pain radiating to groin/abdomen and chest/breast. † Less common systemic effects included anorexia, dizziness, generalised myalgia and hypertension.

occurred in all bites and was severe in 42 (62%) (Box 2). The median duration of pain was 36 hours (IQR, 11–48 hours). Systemic effects occurred in 35% of redback spider bites (Box 2). The median duration of systemic effects was 1 day (IQR, 1–2 days).

Sixty-six bites were by female spiders (adult and juvenile), one was by an adult male spider and one by a juvenile (sub-

**3: Characteristics of hospital patients who were and were not treated with intramuscular antivenom, and comparison with non-hospital patients**

Characteristics	Hospital patients				Non-hospital patients (n=40)	
	Not treated with antivenom (n=17)		Treated with antivenom (n=6)			
	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)
Males	6	35% (14%–62%)	1	17% (0–64%)	17	43% (27%–59%)
Median (IQR) age (years)	34 (28–44)		41 (31–52)		39 (28–48)	
Distal bite region	9	53% (28%–77%)	2	33% (4%–78%)	16	40% (25%–57%)
Severe pain	12	71% (44%–90%)	5	83% (36%–100%)	21	53% (36%–69%)
Initial systemic features	8	47% (23%–72%)	4	67% (22%–96%)	9	23% (11%–38%)
Median (IQR) pain duration (hours)	48 (33–72)		48 (48–66)		24 (3–48)	
Unable to sleep because of pain	7	41% (18%–67%)	2	33% (4%–78%)	10	25% (13%–41%)
No pain at 24 hours	2	12% (1%–36%)	1	17% (0–64%)	18	45% (39%–71%)
Systemic effects > 24 hours	8	47% (23%–72%)	4	67% (22%–96%)	9	23% (11%–38%)

**4: Diagnostic utility of circumstances and early clinical effects of spider bites in differentiating bites by redback spiders, *L. hasselti* (68 cases), from all other types of biting spiders in Australia\***

Diagnostic feature	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	LR	P
<b>Circumstances</b>						
Dressing	—	—	—	—	—	0.291
Putting on shoes	28% (18%–40%)	95% (93%–96%)	0.35 (0.22–0.49)	0.93 (0.91–0.95)	5.4	< 0.0001
<b>Early clinical effects</b>						
"Increasing pain" over first hour	54% (42%–67%)	98% (97%–99%)	0.74 (0.60–0.85)	0.96 (0.94–0.97)	29	< 0.0001
Diaphoresis (local or regional)	34% (23%–46%)	99.7% (99%–100%)	0.92 (0.74–0.99)	0.94 (0.92–0.96)	117	< 0.0001
Pain radiating	38% (27%–51%)	96% (94%–97%)	0.46 (0.33–0.60)	0.94 (0.92–0.96)	8.8	< 0.0001
Severe pain	62% (49%–73%)	75% (72%–78%)	0.20 (0.14–0.26)	0.95 (0.93–0.97)	2.5	< 0.0001

\* Included from a previous study (694 cases).<sup>4</sup> LR = Likelihood ratio.

adult) male spider. There was no significant difference between the effects of bites by juvenile and adult females. The adult male caused short-lived, mild pain only. The subadult male caused severe pain for 12 hours, but no systemic effects.

Of the 28 hospitalised patients, two received a combination of intravenous and intramuscular antivenom, two received intramuscular antivenom after 6 hours (16 hours and 24 hours), and six received intramuscular antivenom within 6 hours. The pain had resolved before presentation in one of the 18 patients not receiving antivenom; this patient was excluded from the analysis of antivenom effectiveness.

**Effect of antivenom**

The six patients treated with intramuscular antivenom within 6 hours were compared with 17 patients not receiving antivenom. Baseline characteristics for

these two groups were similar (Box 3). One of six treated patients (17%) had no pain at 24 hours, compared with two of 17 untreated patients (12%), which was not significantly different (+5%; 95% CI, -36% to +64%;  $P = 0.95$ ) (Box 3). In all 12 patients with systemic effects, these lasted for 24 hours or longer.

Three of the six treated patients received repeated doses of antivenom. One patient who received six ampoules of antivenom had mild serum sickness with malaise, myalgia, rash and pruritus, which resolved over 5 days, and another developed a localised itchy rash after receiving two ampoules of antivenom. These were the only adverse reactions to antivenom, including the four patients not included in this analysis.

**Identifying spider from bite features**

Box 4 shows the diagnostic value of the initial features investigated in this study

for predicting bites of redback spiders versus all other biting spider types.

**DISCUSSION**

Currently, it is believed that many redback spider bites cause minor effects and require neither treatment nor hospital assessment.<sup>7,8</sup> Although redback spider antivenom is believed to be effective, doctors are reluctant to use it unless there is severe systemic envenomation.

Two studies of hospitalised patients, involving 150 adults and 156 children with definite redback spider bites, demonstrated that 29% and 22%, respectively, had systemic envenomation; 21% of subjects in both studies received antivenom.<sup>10,17</sup> In a small prospective study of nine patients with redback spider bites, more than half had severe effects, and eight received antivenom.<sup>18</sup>

These three studies, based on emergency department presentations, suffer from sample bias, and patients were not followed up. The largest study, of 2144 cases,<sup>19</sup> consisted of reports to the antivenom manufacturer, and did not define the true spectrum of definite redback spider bite.

Our study shows that, when only definite cases are included, a much higher proportion of redback spider bites causes severe and ongoing effects than previously reported.<sup>10,17</sup> Two-thirds of patients had pain persisting beyond 24 hours and, in 32%, pain was severe enough to prevent sleep in the first 24 hours. Thirty-five per cent of patients had systemic effects, similar to the proportion in previous studies, but our study showed that these lasted 1–2 days (earlier studies had not examined duration of systemic effects). Our study demonstrates that the severity of envenomation is related not only to the severity of pain and systemic features, but also to the duration of these effects.

Recently, the intramuscular use of redback spider antivenom has been questioned. One series of four patients demonstrated that intramuscular antivenom was ineffective, but intravenous antivenom administered after failure of intramuscular antivenom was effective.<sup>6</sup> In our study, intramuscular antivenom was no better than no treatment when all patients were followed up over a week.

Because of the small number of patients in our cohort, the study lacked power to definitively demonstrate no difference between intramuscular antivenom and no treatment. However, we believe that an acceptable treatment effect would be that 80%–90% of patients are pain-free at 24 hours. We found that this is not occurring, with 17% (95% CI, 0–64%) pain-free at 24 hours. This is a poor treatment effect for any antivenom, as they usually have dramatic effects. There are considerable implications of this finding, and the use of intramuscular antivenom<sup>9</sup> needs review. A randomised controlled trial of intravenous versus intramuscular antivenom would now be appropriate.

Previous bite reports have invariably involved female redback spiders, and it was widely believed that male spiders are too small to bite and envenom

humans.<sup>8,9</sup> This article includes the first report of bites by male redback spiders, one causing severe pain. Our study confirms that bites by male spiders are rare compared with bites by females. This is probably due to the small size of males (3–4 mm body length, indicative of smaller jaws, compared with females, measuring up to 14 mm), rather than the male spider being incapable of delivering an effective bite or lacking venom of similar potency to females.

Our study has some limitations, including whether the sample truly represents all patients with redback spider bites. However, there was clear case definition with expert identification of spiders, and the prospective nature and follow-up of all patients were superior to previous studies. Bites were included from poisons information centre calls and from emergency department presentations. As these populations may differ, it is important to include both. Spider bites for which the patient did not seek any medical attention were not included, and this may have biased the study to more severe bites.

Our study demonstrates that, in many patients, early referral to hospital for assessment of severe pain is appropriate. We believe antivenom should be administered in most cases for pain relief alone, although the smaller cohort analysis challenges the current practice of using intramuscular antivenom, which is based on anecdotal experience. Controlled trials are required to compare the efficacy and safety of intramuscular and intravenous antivenom, because it may be more appropriate to use the latter. It will be a challenge, particularly for primary care physicians and poisons information centre specialists, in identifying cases of redback spider bite and in determining which patients should be advised to seek further treatment. However, we have demonstrated that early features of bites can be used to assess whether the spider is a redback (Box 4).

## COMPETING INTERESTS

None identified.

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