

Prevalence, severity, and natural history of jack jumper ant venom allergy in Tasmania

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Background: The jack jumper ant (*Myrmecia pilosula*) is responsible for greater than 90% of Australian ant venom allergy. However, deaths have only been recorded in the island of Tasmania.

Objectives: We sought to determine the prevalence, clinical features, natural history, and predictors of severity of *M pilosula* sting allergy in Tasmania.

Methods: We performed a random telephone survey supported by serum venom-specific IgE analysis, review of emergency department presentations, and follow-up of allergic volunteers.

Results: *M pilosula*, honeybee (*Apis mellifera*), and yellow jacket wasp (*Vespula germanica*) sting allergy prevalences were 2.7%, 1.4%, and 0.6% compared with annual sting exposure rates of 12%, 7%, and 2%, respectively. Similarly, emergency department presentations with anaphylaxis to *M pilosula* were double those for honeybee. *M pilosula* allergy prevalence increased with age of 35 years or greater (odds ratio [OR], 2.4) and bee sting allergy (OR, 16.9). Patients 35 years of age or older had a greater risk of hypotensive reactions (OR, 2.9). Mueller reaction grades correlated well with adrenaline use. During follow-up, 79 (70%) of 113 jack jumper stings caused anaphylaxis. Prior worst reaction severity predicted the likelihood and severity of follow-up reactions; only 3 subjects had more severe reactions. Venom-specific IgE levels and other clinical features, including comorbidities, were not predictive of severity.

Conclusions: Sting allergy prevalence is determined by age and exposure rate. *M pilosula* sting exposure in Tasmania is excessive compared with that found in mainland Australia, and there is a high systemic reaction risk in allergic people on re-sting. Prior worst reaction severity (Mueller grade) and age predict reaction severity and might be used to guide management. (J Allergy Clin Immunol 2003;111:187-92.)

Serologic data suggest that the jack jumper ant *Myrmecia pilosula* (Figs 1 and 2) causes greater than 90% of ant venom anaphylaxis in Australia.¹ Although allergy is common in southeastern mainland Australia,² deaths have only been reported from the island of Tas-

Abbreviations used

ED: Emergency department

OR: Odds ratio

mania,³ despite its relatively small population of 459,659.⁴ A national mortality database search covering 20 years failed to identify a single death elsewhere.⁵ Other stinging insects commonly encountered in Tasmania are *Myrmecia forficata*, known locally as the inchman ant because of its larger (20 mm) size³; the honeybee (*Apis mellifera*); and the yellow jacket wasp (*Vespula germanica*). Hornets (*Vespa* species) and paper wasps (*Polistes* species) are not found in Tasmania.

Published clinical studies have been limited to case reports³ and surveys without venom-specific IgE analysis.^{2,6,7} Our aims were to compare sting exposure and allergy prevalences among local Hymenoptera, to describe the clinical features and natural history of *M pilosula* sting allergy, and to identify predictors of reaction severity. The Royal Hobart Hospital Ethics Committee approved the study.

METHODS

Population sting exposure and allergy prevalence

In 1998, households were randomly selected from Tasmanian telephone directories with the aim of securing data from 1000 subjects. Structured telephone interviews by a market research company collected demographic and sting exposure data for the best-known local insects (jack jumper, honeybee, and wasp). Respondents reporting allergic symptoms after a sting were referred to the clinical research team for further assessment, as follows.

Emergency department presentations

Royal Hobart Hospital emergency department (ED) presentations with sting anaphylaxis for an 8-year period to September 1998 were identified from a computerized tracking system; data on reaction severity and causation were extracted for analysis.

Allergic volunteers

Volunteers with *M pilosula* venom allergy were recruited from the ED database, population survey, local doctors, and media coverage from September 1998 onward. Structured interviews recorded demographics, cardiovascular comorbidity (ie, hypertension, ischemic heart disease, or heart failure), airways disease (ie, asthma or chronic airflow limitation), and, for each insect type causing a reaction, age at first systemic reaction, number of reactions requir-

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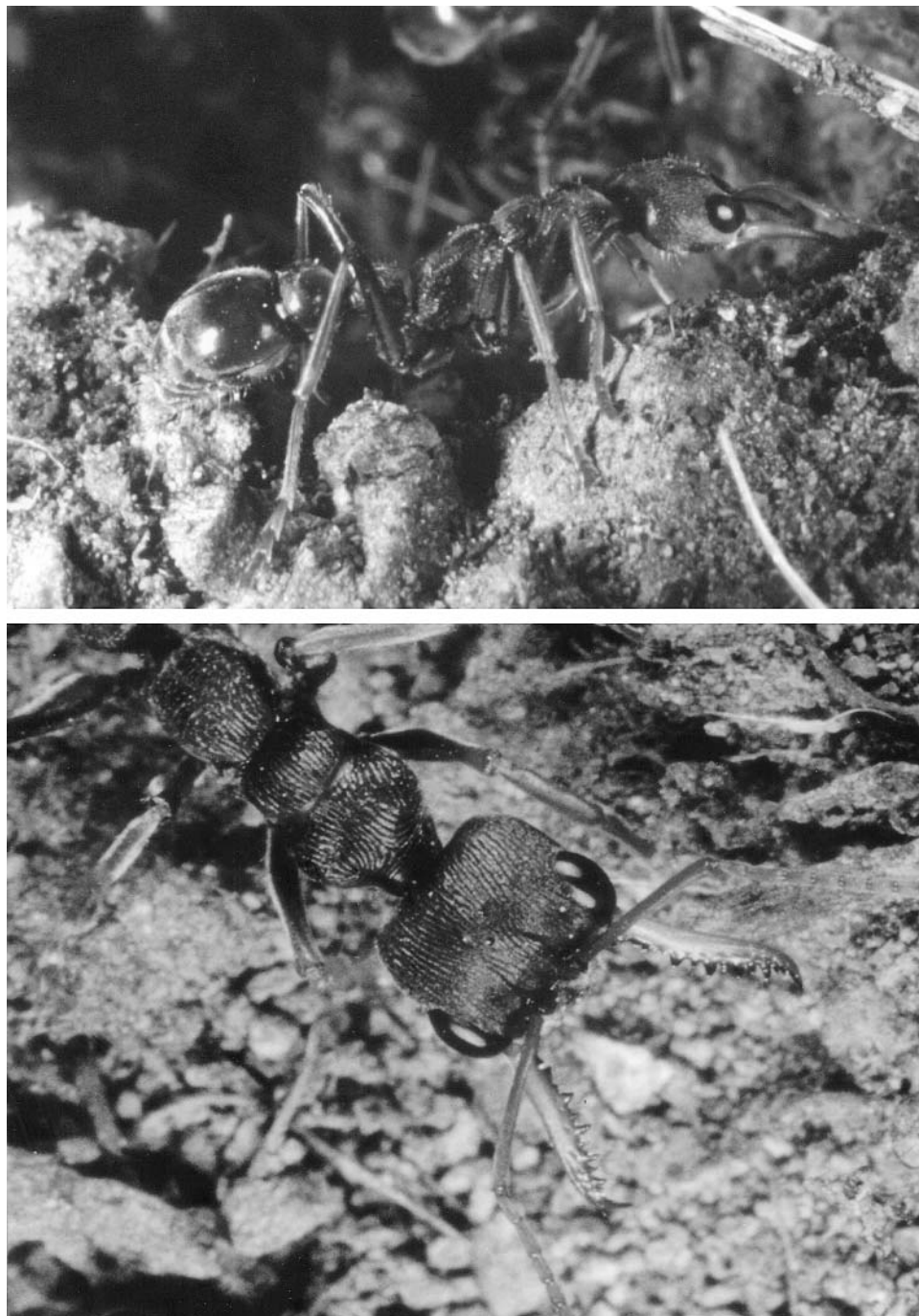


FIG 1. The jack jumper ant, *M pilosula*, 10-12 mm long and jet-black except for yellow-orange mandibles and leg tips, is attracted to movement and moves in short jumps (leading to the name *jack jumper*, after similarly sized "jumping jack" firecrackers). Grasping its victim with its strong mandibles, the ant delivers venom with an abdominal stinger. Like a wasp, a single ant can deliver multiple stings.

ing medical care, number of reactions treated with adrenaline, severity of worst reaction according to the Mueller system (Table I),⁸ and a detailed description for the most recent sting. Interview results were checked against available medical records.

Serum IgE analysis was performed; results were expressed as the percentage of uptake of anti-IgE to serum IgE bound to venom on a solid phase.¹ Venoms used were *M pilosula*, *A mellifera*, *V germanica*, and a panel of *gulosa* species group⁹ venoms closely related to

M forficata: *Myrmecia gulosa*, *Myrmecia pyriformis*, *Myrmecia tarsata*, and *Myrmecia simillima*. One hundred forty-nine control sera taken from nonallergic patients attending the ED and requiring blood to be taken for unrelated reasons were tested for IgE reactivity against *M pilosula* venom.

Data sheets and reply-paid envelopes were provided to monitor subsequent stings. Regular telephone calls were made to detect unreported stings. Termination of follow-up was defined by the last

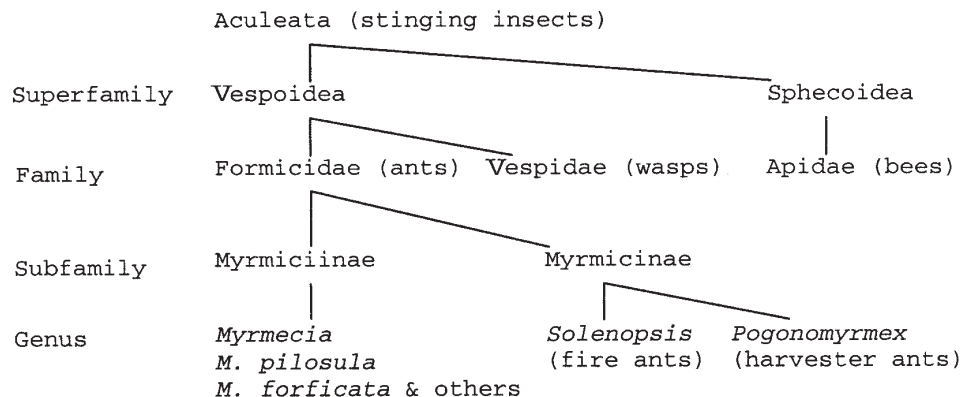


FIG 2. Phylogenetic relationships of *M pilosula* to other common stinging insects.¹ The subfamily Myrmecinae, considered one of the most primitive of the 16 living ant subfamilies, contains a single genus—*Myrmecia*, which includes 89 recognized species native only to Australia (88) and New Caledonia (1).⁹

successful telephone contact or entry into our venom immunotherapy trial in 2001.

Analysis

Proportions and CIs were determined by using the binomial test. Fisher exact tests with odds ratios (OR), Spearman correlation tests, and Mann-Whitney *U* tests were used to examine associations between reaction occurrence or severity and dichotomous, ordinal, and continuous variables, respectively. Statistical analyses were performed with SPSS software version 11 and Analyse-it version 1.61 for Microsoft Excel.

RESULTS

Population sting exposure and allergy prevalence

Four hundred seven (73%) of 560 households consented to participate. One thousand eleven interviews (2.5 interviews per household) were performed. Fifty-two percent of respondents were male, and the median age was 37 years, which is comparable with 1996 Tasmanian census data.⁴ Sting exposure rates are presented in Table II; there were no detectable sex differences in sting exposure.

Forty-six individuals reported systemic sting reactions (prevalence, 4.5%; 95% CI, 3.5-6.0). Of 30 persons reporting a systemic reaction after an ant sting (3.0%; 95% CI, 2.0-4.2), 27 were attributed to *M pilosula* (2.7%; 95% CI, 1.8-3.9) and 3 to *M forficata* (0.3%; 95% CI, 0.1-0.9). Honeybees and wasps were reported as causes in 14 (1.4%; 95% CI, 0.8-2.3) and 6 (0.6%; 95% CI, 0.2-1.3) subjects, respectively. Six subjects reported reactions to multiple insect species.

For subjects with *M pilosula* allergy, the median age was 56 years (range, 6-84 years), and 52% were male. Twenty-four clearly identified *M pilosula* as a cause, and in another 3, serum venom-specific IgE analysis implicated *M pilosula* with measured uptakes of 17% to 26% but insignificant uptakes to other venoms. Ten experienced a grade III or IV reaction, resulting in a prevalence of 1.0% (95% CI, 0.5-1.8) for severe allergy. *M pilosula* allergy prevalence was not affected by sex but increased

TABLE I. Grading of systemic allergic reactions according to the Mueller method⁸

I	Generalized urticaria (includes periorbital edema), itching, malaise, anxiety
II	Angioedema or 2 or more of the following: chest or throat tightness, nausea, vomiting, diarrhea, abdominal pain, dizziness
III	Dyspnea, wheezing, or stridor or 2 or more of the following: dysphagia, dysarthria, hoarseness, weakness, confusion, feeling of impending disaster
IV	Hypotension, collapse, loss of consciousness, incontinence of urine or feces, cyanosis

with age (1.5% and 3.6% in the <35- and ≥35-year age groups, respectively; OR, 2.44; 95% CI, 1.02-5.8; *P* = .05) and the presence of bee sting allergy (OR, 16.9; 95% CI, 4.9-58.0; *P* < .001). Although bee sting exposure increased the risk of jack jumper sting exposure (OR, 3.1; 95% CI, 1.7-5.4; *P* < .001), it was not significantly associated with an increased risk of jack jumper sting allergy (OR, 1.06; 95% CI, 0.2-4.6).

ED presentations

From the ED database, 264 Mueller grade I to IV reactions in 246 individuals were identified and attributed to jack jumper (43%; 95% CI, 37%-49%), honeybee (23%; 95% CI, 18%-29%), wasp (5%; 95% CI, 2.6%-8.3%), inchman (3%; 95% CI, 1.6%-6.4%), and unidentified (25%) stings. These proportions were unchanged when repeat sting reactions in the same individuals were excluded. For 114 jack jumper sting reactions occurring in 105 individuals, the median age at presentation was 29 years (range, 1-78 years), and 60% of subjects stung were male (95% CI, 50-69). Thirty-six percent and 20% of cases were of grade III and IV severity, respectively. Prior known jack jumper sting allergy was recorded in 54 (47%) presentations. Patients with grade IV reactions tended to be older than those with less severe reactions (median age, 44 vs 24 years; *P* = .047) but ranged in age from 1 to 78 years (5 were <15 years of age).

TABLE II. Population sting exposure

Insect	Lifetime exposure, % (95% CI)	Previous 12-mo exposure, % exposed (95% CI)	Average no. of stings per person exposed per year
Any insect	72% (69-75)	25% (22-28)	2.9
Any ant	53% (50-56)	16% (13-18)	2.3
Jack jumper	40% (37-43)*	12% (10-14)	1.9
Honeybee	54% (51-57)*	7% (6-9)	1.3
Wasp	14% (12-16)	2% (1-3)	1.2

*Greater lifetime exposure to honeybee compared with jack jumper stings was repeated across all age groups. Thus a larger proportion of the Tasmanian population is exposed to bee stings over a lifetime (possibly because of the greater range of flying insects), but jack jumper stings occur more frequently in areas where the ant is encountered.

Allergic volunteers

Initial assessment. Three hundred eighty-eight volunteers were recruited, with a median age of 51 years (range, 2-90 years). Fifty percent were male, and 26% reported a cardiovascular comorbidity: 85 had hypertension, 32 had ischemic heart disease, and 9 had heart failure. Sixty-one (16%) had airways disease. Three hundred eighty-one reported a systemic reaction after a clearly identified *M pilosula* sting, and in a further 7 who could not identify the causative insect, serum venom-specific IgE analysis implicated *M pilosula* as the cause, with tracer uptakes of 3% to 26% but insignificant uptakes to other insect species. Fifty percent reported systemic reactions on more than one occasion. Thirty (7.7%) provided a history of multiple sting allergies (honeybee, 20; wasp, 7; inchman, 5).

In those experiencing a systemic reaction when last stung, the proportion of grade IV reactions was 9% (10/116) for those aged younger than 35 years versus 22% (47/217) for those 35 years or older (OR, 2.9; 95% CI, 1.4-6.0; $P = .002$). Risk of a grade IV reaction was not significantly influenced by sex, comorbidities, or number of prior reactions. The proportion of grade III reactions was not influenced by age, sex, or comorbidities; however, the presence of respiratory disease increased the risk of bronchospasm (OR, 2.1; 95% CI, 1.02-4.45; $P = .05$).

Two hundred seventy-five allergic volunteers provided blood samples. Ninety-three percent were reactive ($>0.3\%$ tracer uptake) to *M pilosula* venom versus 22% of 149 nonallergic control sera tested (sensitivity, 0.93; specificity, 0.78). By using 1% and 2% tracer uptake cut-offs, sensitivities and specificities were 0.79 and 0.85 and 0.62 and 0.92, respectively. Fifty-four subjects in the nonallergic control group could not recall any exposure to *M pilosula* or any other ant; IgE reactivity was 0.0% in all except 2. Testing against all available venoms was done for the first 183 allergic volunteers. In sera from subjects with *M pilosula* allergy, 1.0% or greater tracer uptake against gulosa group, bee, and wasp venoms was apparent in 46 (25%), 30 (16.4%), and 21 (11.5%) subjects, respectively. In 27 subjects who had no recollection of honeybee or wasp sting exposure, reactivity to honeybee venom was identified in 1 subject, and reactivity to wasp venom was identified in 2 subjects.

Field stings during the follow-up period. Twenty subjects were lost to follow-up, leaving 368 for analysis. The

mean follow-up interval was 2.3 years. Eighty-seven volunteers experienced 113 clearly identified jack jumper stings, causing 79 systemic reactions in 60 subjects, a reaction rate of 70% (95% CI, 61%-78%). The median age of those stung was 59 years (range, 3-86 years), 42% were male (95% CI, 32-51), and 31% reported cardiovascular comorbidity: 23 had hypertension, 8 had ischemic heart disease, and 2 had heart failure. Twelve had airways disease. Systemic reactions were more common in women (OR, 3.7; 95% CI, 1.4-9.7; $P = .01$), subjects treated with adrenaline for their most recent sting (OR, 5.7; 95% CI, 1.5-21.1; $P = .006$), and those with a history of severe reactions (Tables III and IV). Prior reaction severity was the only significant predictor of subsequent reaction severity; worst reaction severity was a better predictor than recent reaction severity (Tables III and IV). Only 3 subjects experienced a reaction during follow-up that was more severe than the worst prior reaction at the time of study entry. Although sex correlated with reaction occurrence, it was not predictive of severity. Serum venom-specific IgE levels, duration of known allergy, number of reactions, time elapsed since the last sting, and comorbidities did not predict either occurrence or severity of reactions.

Pooled descriptive analysis of sting episodes. Details from 414 reactions (ie, those occurring with the most recent sting episodes at study entry and during the follow-up period) are presented in Table V. Reactions occurred to single stings in 76%. The maximum number of simultaneous stings was 35. Adrenaline, steroids, and antihistamines were administered in 41%, 20%, and 63%, respectively. Reaction severity correlated significantly with adrenaline use: 14.6%, 39.8%, 48.7%, and 69.2% for grades I through IV, respectively (Spearman correlation coefficient = 0.36, $P < .0001$). There were 5 (1.2%) delayed-phase reactions: 3 episodes of urticaria, 1 episode of dyspnea-cough, and 1 episode of generalized edema, aches, and pains for several days after 10 simultaneous stings.

DISCUSSION

Our ability to compare allergy to different insects was facilitated by the main species being easily distinguished from one another (a bee, a wasp, and a very distinctive ant). Even so, in 25% of subjects presenting to the ED, in the absence of venom-specific IgE analysis, a causative insect was not identified.

TABLE III. Worst reaction during follow-up period versus severity of most recent reaction

Most recent sting at time of first interview	No. exposed after first interview	Systemic reaction (%)*	Grade of worst reaction during follow-up†			
			I	II	III	IV
No reaction	13	6 (66)	3		1	2
Grade I	21	16 (69)	8	3	4	1
Grade II	15	9 (69)	5	4		
Grade III	26	19 (73)	7	3	9	
Grade IV	12	10 (83)		1	6	3

* $P = .06$.

†Spearman correlation coefficient = 0.28 ($P < .01$).

TABLE IV. Worst reaction during follow-up period versus severity of worst prior reaction

Worst prior reaction at time of first interview	No. exposed after first interview	Systemic reaction (%)*	Grade of worst reaction during follow-up†			
			I	II	III	IV
Grade I	12	7 (57)	5	1	1	
Grade II	16	9 (57)	6	3		
Grade III	40	28 (70)	10	5	12	1
Grade IV	19	16 (84)	2	2	7	5

* $P = .04$.

†Spearman correlation coefficient = 0.42 ($P < .0001$).

M pilosula sting systemic reactions are IgE mediated; solitary stings precipitate most reactions, and despite the low sensitivity of serum IgE analysis compared with skin testing,¹⁰ 93% of allergic volunteers had detectable venom-specific IgE reactivity compared with 22% of non-allergic control subjects. The latter finding is typical for asymptomatic sensitization,^{11,12} resulting in a poor positive predictive value (approximately 0.1) if the test is applied to the general population. In subjects with a history of sting anaphylaxis, a high pretest probability provides a high positive predictive value (≥ 0.9) for venom-specific IgE reactivity predicting the likely causative insect. This enabled us to accurately determine the causative insect in a number of cases with unclear histories.

Even though we included city dwellers and children, the prevalence of *M pilosula* sting exposure more than doubled that reported for adults in rural southeastern mainland Australia,² and the prevalence of allergy was higher (2.7% vs 1.9%). Tasmania's climate, which is cooler than that of mainland Australia, probably favors proliferation of and exposure to *M pilosula*. As previously reported,¹³ we found that sting allergy prevalence increased with age. Allergy prevalence also correlated with annual sting exposure rates but not with lifetime exposure prevalence. Presumably these observations are due to an increasing cumulative probability of encountering a T_H2 -type response with repeated exposure.

Honeybee sting allergy risk increased the risk of allergy to *M pilosula*, supporting the existence of individual predisposition toward sting allergy in general. Although antibody cross-reactivity might explain this finding, bee and wasp venom IgE reactivity in nonexposed subjects with *M pilosula* allergy was minimal. Cross-reactivity with more closely related gulosa group venoms has been noted previously.¹

TABLE V. Reaction features for 414 *M pilosula* sting-induced anaphylaxis episodes in allergic volunteers grouped according to Mueller grade

I	Urticaria, 45.2%; periorbital edema, 22.5%; itch, 56.8%; malaise, 18.8%; anxiety, 24.4%; 80% reported one or more skin features; urticaria, itch, periorbital edema, or angioedema
II	Angioedema, 41.5%; chest tightness, 26.6%; throat tightness, 30.4%; nausea, 16.4%; vomiting, 11.4%; diarrhea, 5.1%; abdominal pain, 6.8%; dizziness, 20.5%
III	Dyspnea, 39.1%; wheezing, 12.1%; stridor, 1.7%; dysphagia, 12.8%; speech difficulties, 15.5%; weakness, 15.0%; confusion, 4.6%; feeling of impending disaster, 12.6%
IV	Documented hypotension, 8.7%; collapse, 9.2%; loss of consciousness, 6.0%; incontinence of urine or feces, 1.7%; cyanosis, 0.7%
Grade I, 103 (24.9%); grade II, 88 (21.3%); grade III, 158 (38.2%); grade IV, 65 (15.7%)	

Consistent with previous studies,¹⁴ our initial assessment and ED data indicated a 3-fold greater risk of grade IV reaction severity with age 35 years or older, the age group in which most deaths occur.^{3,15-17} The lack of an apparent effect of age on reaction severity during follow-up was probably caused by lower sensitivity because of the small numbers of younger people. Age effects might be due to the development of comorbidities and changes in homeostatic mechanisms, such as the renin-aldosterone system.^{18,19}

We found no relationship between grade IV reactions and cardiovascular comorbidity, despite the previously observed association between such comorbidities and death.^{3,15-17} Although lacking power because of a low prevalence of heart failure, possible underrecognition of vascular disease, and incomplete data regarding medications, our results suggest that cardiovascular comorbidi-

ties (and thus antihypertensive medications) are not primary determinants of reaction severity. Instead, comorbidities and medications might contribute to death when a grade IV reaction occurs.

M pilosula stings are potent allergenic stimuli; our 70% follow-up reaction rate exceeds the 27% to 57% reaction rates reported for bee and wasp allergies.^{14,20-24} Low reaction rates for other insects have led to the suggestion that provocation tests be used to determine eligibility for immunotherapy.¹⁴ Such an approach appears unnecessary for jack jumper allergy.

The strong correlation between adrenaline use and the Mueller grading system indicates this to be a good measure of reaction severity. As demonstrated by means of cross-tabulation of last reaction severity with subsequent reactions, severity fluctuates significantly, possibly related to the variable amount of venom delivered,²⁵ as well as changes in patient sensitivity. Prior worst reaction grade is the most important predictor of subsequent reaction grade, with the vast majority of patients having similar or less severe reactions when stung again. In contrast to data reported from 324 provocation tests finding no reaction to be more severe than the previous worst reaction,¹⁴ we identified cases in which subsequent reaction severity exceeded that of the previous worst reaction. Nevertheless, reserving immunotherapy for people with a history of grade III or IV reactions should protect the majority of those at risk of a lethal reaction.

Sting allergy prevalence is determined by age and exposure rate. *M pilosula* sting exposure in Tasmania is excessive compared with that found in mainland Australia, and there is a high systemic reaction risk in allergic people on resting. Prior worst reaction severity (Mueller grade) and age predict reaction severity and might be used to guide management.

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REFERENCES

- Street MD, Donovan GR, Baldo BA, Sutherland S. Immediate allergic reactions to *Myrmecia* ant stings: immunochemical analysis of *Myrmecia* venoms. *Clin Exp Allergy* 1994;24:590-7.
- Douglas R, Weiner J, Abrahamson M, O'Hehir R. Prevalence of severe ant venom allergy in southeastern Australia. *J Allergy Clin Immunol* 1998;101:129-31.
- Brown SG, Wu QX, Kelsall GR, Heddle RJ, Baldo BA. Fatal anaphylaxis is following jack jumper ant sting in southern Tasmania. *Med J Aust* 2001;175:644-7.
- Australian Bureau of Statistics. Census of population and housing, State of Tasmania. Canberra, Australia: Australian Bureau of Statistics; 1996.
- McGain F, Winkel KD. Ant sting mortality in Australia. *Toxicon* 2002;40:1095-100.
- Clarke PS. The natural history of sensitivity to jack jumper ants (Hymenoptera formicidae *Myrmecia pilosula*) in Tasmania. *Med J Aust* 1986;145:564-6.
- Weiner JM, Baldo BA, Donovan GR, Sutherland SK. Allergy to jumper ant (*Myrmecia pilosula*) stings in south-eastern Australia. *Ann Allergy Asthma Immunol* 1995;74:60.
- Mueller UR. Insect sting allergy: clinical picture, diagnosis and treatment. New York: Gustav Fischer Verlag; 1990.
- Ogata K, Taylor RW. Ants of the genus *Myrmecia fabricius* a preliminary review and key to the named species (Hymenoptera: Formicidae: Myrmeciinae). *J Nat History* 1991;25:1623-73.
- Sobotka AK, Adkinson NF Jr, Valentine MD, Lichtenstein LM. Allergy to insect stings. IV. Diagnosis by radioallergosorbent test (R.A.S.T.). *J Immunol* 1978;121:2477-84.
- Fernandez J, Blanca M, Soriano V, Sanchez J, Juarez C. Epidemiological study of the prevalence of allergic reactions to Hymenoptera in a rural population in the Mediterranean area. *Clin Exp Allergy* 1999;29:1069-74.
- Golden DB, Marsh DG, Kagey-Sobotka A, et al. Epidemiology of insect venom sensitivity. *JAMA* 1989;262:240-4.
- Settipane GA, Boyd GK. Natural history of insect sting allergy: the Rhode Island experience. *Allergy Proc* 1989;10:109-13.
- van der Linden PW, Hack CE, Struyvenberg A, van der Zwan JK. Insect-sting challenge in 324 subjects with a previous anaphylactic reaction: current criteria for insect-venom hypersensitivity do not predict the occurrence and the severity of anaphylaxis. *J Allergy Clin Immunol* 1994;94:151-9.
- Barnard JH. Studies of 400 Hymenoptera sting deaths in the United States. *J Allergy Clin Immunol* 1973;52:259-64.
- Harvey P, Sperber S, Kette F, Heddle RJ, Roberts-Thomson PJ. Bee-sting mortality in Australia. *Med J Aust* 1984;140:209-11.
- Sasvary T, Muller U. [Fatalities from insect stings in Switzerland 1978 to 1987]. *Schweiz Med Wochenschr* 1994;124:1887-94.
- Hermann K, Ring J. The renin angiotensin system and hymenoptera venom anaphylaxis. *Clin Exp Allergy* 1993;23:762-9.
- Bauer JH. Age-related changes in the renin-aldosterone system. Physiological effects and clinical implications. *Drugs Aging* 1993;3:238-45.
- Reisman RE, Dvorin DJ, Randolph CC, Georgitis JW. Stinging insect allergy: natural history and modification with venom immunotherapy. *J Allergy Clin Immunol* 1985;75:735-40.
- Hunt KJ, Valentine MD, Sobotka AK, Benton AW, Amodio FJ, Lichtenstein LM. A controlled trial of immunotherapy in insect hypersensitivity. *N Engl J Med* 1978;299:157-61.
- Parker JL, Santrach PJ, Dahlberg MJ, Yunginger JW. Evaluation of Hymenoptera-sting sensitivity with deliberate sting challenges: inadequacy of present diagnostic methods. *J Allergy Clin Immunol* 1982;69:200-7.
- Blaauw PJ, Smithuis LO. The evaluation of the common diagnostic methods of hypersensitivity for bee and yellow jacket venom by means of an in-hospital insect sting. *J Allergy Clin Immunol* 1985;75:556-62.
- Kampelmacher MJ, van der Zwan JC. Provocation test with a living insect as a diagnostic tool in systemic reactions to bee and wasp venom: a prospective study with emphasis on the clinical aspects. *Clin Allergy* 1987;17:317-27.
- Schumacher MJ, Tveten MS, Egen NB. Rate and quantity of delivery of venom from honeybee stings. *J Allergy Clin Immunol* 1994;93:831-5.