

Ant sting mortality in Australia

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Abstract

We investigated ant sting related fatalities in Australia over the period 1980–1999. Data was obtained from the Australian Bureau of Statistics and state coronial authorities. Six ant sting-related fatalities were identified, five in Tasmania and one in New South Wales. All were males aged between 40 and 80-years-of-age and most (5/6) had prior histories of jumper or bull ant (*Myrmecia* spp.) venom allergy. However, none of the deceased carried injectable adrenaline and most died within 20 min of a single sting. Significant cardiopulmonary co-morbidities were identified in all cases and, in addition, moderate–severe laryngeal oedema and coronary atherosclerosis was observed in most (4/6) cases at autopsy. Where ascertained, *Myrmecia* ant venom specific immunoglobulin E antibodies levels were always elevated and fell into two distinct patterns of immunoreactivity. Adult Tasmanian males with a prior history of ant venom allergy and cardiopulmonary co-morbidities are therefore at highest risk of a fatal outcome from ant stings. Deaths may be avoided by the early recognition of anaphylaxis and self-treatment with adrenaline as well as by the development of purified *Myrmecia* ant venom immunotherapy. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Ants are widespread Hymenopteran insects of the family Formicidae with approximately 8800 species described worldwide. Australia is richly endowed with 2750 known species and subspecies (Shattuck, 1999). However, despite this diversity there are relatively few species of medical importance and those can be divided into two major groups, distinguished by the extent of development of a venom injection apparatus. The first type has no effective apparatus while the second group has a clearly recognisable sting.

The former type, exemplified by the ‘meat’ ant, *Iridomyrmex* spp., can cause irritating bites that they spray with secretions from their abdominal glands (Southcott, 1988). The second group, typified by the *Myrmecia* ants, subfamily Myrmeciinae, are notable for their painful true stings and allergenic venom. Known as ‘jumper’ or ‘bull-dog’ ants they are widely distributed in, and virtually endemic to, Australia. Amongst the at least 89 *Myrmecia* species

identified so far, only two are well known; the small (10 mm long), jack jumper (*Myrmecia pilosula*), which is black with yellow mandibles, and the larger (15–20 mm long), bull ant (*Myrmecia pyriformis*) that is a duller brown in colour.

Both species are widely found throughout much of south-east Australia, including Tasmania. *M. pilosula* is also found in the south-west tip of Western Australia and much of South Australia (Sutherland and Tibballs, 2001). Other stinging ants, such as the IFA (*Solenopsis* spp.) and the primitive genus *Rhytidoponera*, are also found in Australia (Southcott, 1988). However, to date only four minimally documented ant sting fatalities are recorded in the Australian medical literature. In 1931, Cleland recorded three ant sting related fatalities, two adults and an infant, all from NSW. One fatality, a middle aged woman, was recorded from Tasmania in 1963 (Trinca, 1964; Lee, 1975).

Detailed analysis of fatalities can provide an important source of information on the determinants of severe morbidity for the purposes of injury prevention. Therefore, as part of a study of Hymenopteran fatalities in Australia (Levick et al., 1997, 2000; McGain et al., 2000, 2001), we undertook an analysis of ant sting related fatalities that occurred in Australia over the last two decades. We discuss

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the cases identified and make prevention and treatment recommendations.

2. Methods

In the absence of national coronial data for the study period, we proceeded through the national statistical database through to individual state-based coronial systems and, where necessary, individual clinicians. Specifically we searched, with their approval, the Australian Bureau of Statistics (ABS) mortality dataset for ant sting related fatalities that occurred during the period 1 January 1980–31 December 1999. With the consent of the relevant state and territory registrar—generals of births, deaths and marriages, the death registration number was provided in each case so identified. This number allowed us to obtain the names of the deceased from said registrars.

This then allowed the tracing of the individual cases via the Coroners and local hospitals for details of the ant sting locality, circumstances of death, autopsy results and any prior history of hymenoptera sting allergy and its management. Post-mortem immunological assay results, described later, were obtained from the Molecular Immunology Laboratory, Kolling Institute of Medical Research, Royal North Shore Hospital, Sydney, NSW. This project was undertaken with the approval of the University of Melbourne Health Sciences human ethics subcommittee.

2.1. Trypsin assays

Serum mast cell trypsin levels were initially determined by commercial radioimmunoassay (Pharmacia, Uppsala, Sweden), now discontinued, and the results expressed in $\mu\text{g/l}$ (<2 considered negative, whilst a level of 5 is considered slightly elevated) (Enander et al., 1991). More recent assays were performed by fluoroimmunoassay (Unicap Trypsin, Pharmacia and Upjohn, Uppsala, Sweden). The results of this latter assay are also expressed in $\mu\text{g/l}$ but due to a greater sensitivity <13 is considered a negative (Ludolph-Hauser et al., 2001). Trypsin levels are elevated 3–6 h after anaphylactic reaction and return to normal within 14 h (Schwartz et al., 1989).

2.2. Antibody determination

Venom specific Immunoglobulin E (IgE) levels were determined for serum collected at post-mortem, as previously described (Street et al., 1994). Briefly this involved incubating aliquots of patient sera with nitrocellulose discs coated with standardised quantities of venom from a panel of *Myrmecia* species. Bound antibodies were detected by ^{125}I -anti-human IgE and the results presented as the percentage uptake of radioactive label using human cord serum as an IgE 'free' control. An uptake of $>2\%$ of the radioactive label was considered a positive result (Street et al., 1994).

3. Results

We identified six fatalities that equates to a mean national annual incidence rate of 0.02 deaths per million population per year during the 20-year period. The fatalities were marked temporally skewed such that most (5/6) occurred in the second 10-year period and all of the cases occurred within an 11-year period. All of the deceased were men living in either NSW (1/6) or Tasmania (5/6). The average age of death was 58 years, with the range being from 40 to 80 years. All fatalities occurred between September and March (one in each month in this period except for February) with most deaths occurring during the day (5/6 occurred between 11.30 a.m. and 4.30 p.m.); one death occurred at 7 p.m.

A concise summary of each case is given in Table 1. For those cases where it was available, the serum trypsin and venom specific IgE levels are also presented (Table 2).

4. Discussion

This study confirms the lesser importance of ant stings, compared with snakebite, and bee and wasp sting fatalities, in Australia (Harvey et al., 1984; Sutherland, 1992; Sutherland and Leonard, 1995; Levick et al., 2000; McGain et al., 2000, 2001). This national mortality ranking is similar to that recorded in the USA (Barnard, 1973; Langley and Morrow, 1997; Prahlow and Barnard, 1998) with both countries reporting a near-identical fatality rate for ant stings (Langley and Morrow, 1997).

There are, however, clear regional variations in the relative importance of each type of venomous bite and sting reflecting the distribution of different stinging Hymenoptera. Australian wasp sting fatalities, for example, have mostly been reported in the warmer northeast state of Queensland (Cleland, 1913; Lee, 1975; McGain et al., 2000, 2001). In contrast, the ant sting related deaths, identified in this and earlier studies, mostly occurred in temperate Tasmania (Cleland, 1931; Lee, 1975).

The absence of formal identification of the responsible ant species in the cases reported here, a problem in Hymenoptera mortality studies generally (Prahlow and Barnard, 1998; McGain et al., 2000, 2001), makes attribution to a particular species difficult. However, combining historical and IgE results, it seems that cases three and six were probably due to *M. pilosula* whilst case five was likely due to *M. pyriformis*. Case four could have been either *M. pilosula* or *M. pyriformis* or a related species, whilst cases one and two were more likely due to *M. pilosula*. The jumper ant, *M. pilosula*, would therefore, appear to be responsible for most ant sting fatalities in Australia.

The low number of stings, rapidity of onset of symptoms of anaphylaxis (most arrested within 20 min), and overrepresentation of middle aged males seen here is generally consistent with previous analyses of Hymenoptera sting

Table 1

A summary of the circumstances and features of ant sting related fatalities in Australia occurring during the period January 1980–December 1999

Case number	Medical history	Allergy treatment	Circumstances	Autopsy results
1	Hypertension treated with Enalapril	Known jumper ant venom allergy (degree unspecified). Carried antihistamines in case of stings	Witnessed ant sting to the forearm whilst woodcutting in thick forest with workmates. Initially uncompromised and given antihistamines. However, became dyspnoeic and unresponsive within 20 min	Autopsy showed minimal coronary atherosclerosis and mild laryngeal oedema
2	Mild asthma treated with salbutamol	No allergies specified in the coronial record	Witnessed sting by a 'jack-jumper' to the hand whilst in the garden. Became unresponsive within 5 min	Post-mortem revealed laryngeal oedema and moderate coronary atherosclerosis
3	Not recorded in the coronial report	No allergies specified in the coronial record	Stung on the forearm by a jack-jumper ant whilst at a reservoir recreation area. Rapidly became dyspnoeic, collapsed and died within 20 min	Post-mortem showed gross facial, pharyngeal and laryngeal oedema, with moderate coronary atherosclerosis, myocardial fibrosis and left ventricular hypertrophy
4	Alcoholism and sleep apnoea	Increasingly severe ant venom allergy. He carried antihistamines and adrenaline inhaler	Stung on the foot by an ant whilst inebriated in the garden one evening. Became increasingly drowsy and was put to bed. Found deceased several hours later	Autopsy found minimal laryngeal oedema and coronary atherosclerosis
5	Depression	Known history of systemic allergic reactions to ant stings, but apparently had not sought medical advice	Whilst gardening with his son he was stung on the hand by a bull ant to which he remarked "I suppose that my lips will turn blue again" and died within 5 min	Post-mortem revealed laryngeal oedema with moderate coronary atherosclerosis
6	Atrial fibrillation, repaired patent foramen ovale, cardiac failure, drug treatment included warfarin, digoxin, bumetanide, carvedilol and fosinopril	Had been treated with whole ant extract 20 years previously after systemic allergic reactions. He did not carry adrenaline	Whilst gardening cried out to his wife that he had been stung by a jack-jumper ant. Collapsed and died within 20 min	Post-mortem revealed marked laryngeal oedema with moderate coronary atherosclerosis

mortality (Harvey et al., 1984; Rhoades et al., 1989; Prahlow and Barnard, 1998; Levick et al., 2000; McGain et al., 2000, 2001). Unlike recent US IFA infestations (deShazo et al., 1999), no cases of massive ant attacks were identified amongst these fatalities. Indeed the coronial records suggest that single stings were recorded in all cases.

Underlying cardiac or respiratory disease has been proposed to explain the increased risk of severe anaphylaxis in males >40-years-old suffering Hymenoptera stings (Reisman, 1995). Consistent with this possibility a high rate of underlying cardiovascular disease was seen in this series. In addition, those cases with only minimal coronary atherosclerosis (one and four) had other significant co-morbidities such as hypertension, alcoholism and sleep apnoea.

Research in the importance of non-immunological factors

in determining the outcome of anaphylaxis has focussed attention on the role of cardiovascularly active mediators such as the renin–angiotensin system (Hermann and Ring, 1993). Significantly reduced components of that system have been reported amongst patients with a history of Hymenoptera venom-induced anaphylaxis (Hermann and Ring, 1993; Herman et al., 1994). The use of angiotensin converting enzyme inhibitors (ACE) has also been associated with anaphylaxis in those undergoing Hymenoptera venom immunotherapy (Tunon-de-Lara et al., 1992). In this context it is interesting that at least two of the deceased (cases one and six) were being treated with ACE inhibitors. The latter patient was particularly at risk due to the concurrent use of a β -blocker (Sutherland and Tibballs, 2001). Clearly such 'high risk' patients should be counselled to be particularly careful about sting prevention and the

Table 2
Post-mortem tryptase and ant venom specific IgE assay results

		Case number			
		3	4	5	6
Tryptase ($\mu\text{g/l}$)		2.73 ^a	2.72 ^a	38.3 ^b	51.6 ^b
Specific	<i>M. pilosula</i>	–	31.7	0.8	10.1
IgE	<i>M. nigrocinta</i>	–	24.5	0.7	0.3
(% Uptake) ^c	<i>M. pyriformis</i>	–	39.6	3.9	0.3
	<i>M. tarsata</i>	–	42.1	5.2	0.3
	<i>M. similima</i>	–	39.8	1.9	0.3
	<i>M. gulosa</i>	–	37.0	3.1	0.3

^a Pharmacia radioimmunoassay.

^b Pharmacia Unicap fluoroenzymeimmunoassay.

^c Ant venom specific IgE: ¹²⁵I-anti-human IgE for specific IgE expressed as a percentage of total labelled IgE. Case three was assayed but the result was not available in the coronial record.

emergency management of anaphylaxis. Constitutively elevated mast cell tryptase levels have also been proposed as a risk factor for severe allergic reactions to Hymenoptera venom (Ludolph-Hauser et al., 2001).

Both bulldog and jumper ant venoms are rich in the enzymes phospholipase A₂ and B, hyaluronidase, and acid and alkaline phosphatase as well as in histamine itself (Matusek et al., 1992, 1994). They also contain multiple IgE-binding components, including (in *M. pilosula*) the dominant allergens Myr p 1 and Myr p2 (Donovan et al., 1993; Street et al., 1996). The proteinaceous nature of the *Myrmecia* venom contrasts with the uniquely low protein but high piperidine alkaloid content of IFA venom (Stafford, 1996). The preservative action of the alkaloids may be why the IFA whole ant body extract (WBE) compares favourably with pure venom for diagnostic and immunotherapy purposes (Strom et al., 1983; Freeman et al., 1992).

Immunotherapy with jumper and bull WBE, prepared at the former Commonwealth Serum Laboratories (now CSL Limited), was provided to scores of patients from the 1960s onwards (Trinca, 1964; Clarke, 1986; Sutherland and Tibballs, 2001). Despite initial optimism (Trinca, 1964), and in contrast to the continuing US experience with ant WBE (Freeman et al., 1992; Duplantier et al., 1998), only a slight reduction in the severity of subsequent reactions of patients thus treated was observed (Sutherland and Tibballs, 2001). Consequently the value of this preparation was questioned (Clarke, 1986; Solley, 1990) and its production ceased in the late 1980s. The unfortunate outcome of case six appears to validate this decision. Although progress has been made in the definition of the key *Myrmecia* venom allergens (Donovan et al., 1993; Street et al., 1994, 1996) and preparation of purified venom standards (Sutherland and Tibballs, 2001), no commercial immunotherapy product is yet available. Clearly the ongoing occurrence of ant sting fatalities adds impetus to the need for purified ant venom immunotherapy.

The pattern of *Myrmecia* venom specific IgEs detected

amongst the deceased raises several issues. Firstly, patients allergic to jumper or bulldog ants may not necessarily be allergic to all other *Myrmecia* species. Conversely, as discussed later, allergy may exist to multiple *Myrmecia* species not previously encountered. Therefore patients should be advised to avoid all such ants and to be aware that lack of severe reactions to one sting does not imply the absence of continuing risk of life-threatening reactions to other or subsequent stings. It appears that such a misunderstanding arose in patient six, who mistakenly believed he was no longer allergic to *Myrmecia* stings.

Secondly, we confirm the two IgE reactivity patterns previously seen amongst *Myrmecia* ant venom allergic patients (Street et al., 1994): sera that reacts with a single venom (mostly *M. pilosula*) and sera that reacts with multiple venoms. In our series the strength of reactivity seen in the latter group tended to vary along established taxonomic relationships; *M. gulosa*, *M. pyriformis*, *M. similima* and *M. tarsata* compared with *M. pilosula* and *M. nigrocinta* (Ogata and Taylor, 1991). Presumably these patterns reflect cross-reactivity between shared antigenic determinants (Street et al., 1994).

Case five, who had *M. pyriformis* but not *M. pilosula* specific IgE, is a particularly important example of patients reactive with multiple *Myrmecia* spp. venoms. His IgE pattern implies that purified *M. pilosula* venom alone may be insufficient as immunotherapy for all Australian *Myrmecia* allergic patients. A combination of *M. pilosula* and *M. pyriformis* venoms, analogous to the venom mixes available for *Vespula* and *Polistes* wasp sting allergies (Solley, 1990; McGain et al., 2000), would appear most appropriate.

As documented for wasp sting fatalities in Australia (McGain et al., 2000), most of the deceased reported here had a clear prior history of significant ant venom allergy. Despite this, none carried injectable adrenaline, a key component in the emergency self-management of anaphylaxis (O'Hehir and Douglass, 1999). Such potentially preventable cases emphasise the need for a specific immunotherapy and, in the meantime, patient education about sting avoidance and early treatment with adrenaline.

As noted in previous investigations of Hymenoptera mortality (McGain et al., 2000), dependence upon a single data set is likely to lead to an underestimation of the total injury burden. It is possible that additional ant sting related deaths occurred during the study period but were unrecorded due to mis-certification, mis-identification of ant deaths as bee deaths or due to inadequate recording methods. It is hoped that the new national coronial information system will greatly enhance the quality and accessibility of Australian mortality data to facilitate future studies (McGain et al., 2001).

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