

Ant allergy in Asia and Australia

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Purpose of review

Anaphylaxis due to ant sting is increasingly being recognized as a significant problem. Severe allergic reactions to ants are well described in the south-eastern United States, but have only been recognized in recent years as being important in other parts of the world. There are many different ant species and their distribution around the world varies. The purpose of this review is to familiarize the reader with the epidemiology and clinical characteristics of ant allergy in Asia and Australia.

Recent findings

In Korea, allergy to *Pachycondyla chinensis* (subfamily *Ponerinae*) has been well described. In an ant-endemic area, sensitization was 23%, with about 1% having anaphylactic reactions. There were at least eight IgE-binding proteins in *P. chinensis* venom, with 1 major allergen binding 85% of patient sera. *P. chinensis* venom was also found to be possibly crossreactive with bee venom, but not with imported-fire-ant venom. In Australia, anaphylactic reactions to ant stings are usually caused by the 'jack jumper' ant (*Myrmecia pilosula*) or the bull ant (*Myrmecia pyriformis*). A recent study showed promising results for immunotherapy with *M. pilosula* venom. There have been reports of stings by other ant species in Asia and Australia, but these reports are few and sporadic.

Summary

The study of ant allergy in Asia is in its infancy. Clinicians in Asia need to be aware of ant stings as a cause of severe allergic reactions. Certain species that cause allergic reactions are unique to Asia and Australia and deserve further research. The allergens in the venom of the different ant species need to be identified. We should aim for improved understanding of the epidemiology of ant-sting anaphylaxis, formulation of better diagnostic tests and possibly the introduction of immunotherapeutic strategies.

Keywords

anaphylaxis, ant allergy, Asia, Australia, *Pachycondyla chinensis*

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Introduction

Ant stings are increasingly being recognized as an important cause of severe allergic reactions, including anaphylaxis. Ants belong to the order Hymenoptera and the family Formicidae. About 8800 species have been described; all bite, some sting, but few cause allergic reactions. In the United States, the imported fire ants (*Solenopsis invicta* and *Solenopsis richteri*) are responsible for most of the serious anaphylactic reactions. In Australia, the usual culprits are the 'jack jumper' ant (*Myrmecia pilosula*) and the bull ant (*Myrmecia pyriformis*) [1]. Even though ant stings on the whole are an uncommon cause of fatal allergic reactions, they may be the most common cause of anaphylaxis in an ant-endemic area [2]. To date, there is scant information regarding ant allergy in Asia. However, recent work, particularly from Korea, has revealed that ant allergy is likely to be a significant problem in some parts of the region.

Ants can live in nearly every terrestrial habitat and environment, including in soil, deserts, beaches and walls. Geographical boundaries of ant habitation can change, and the entry of imported fire ants into the United States from South America is a good example of this. These ants have invaded the south-east USA and are now endemic there [3]. Physicians need to be aware of the different ant species causing disease worldwide, because there is the possibility of transfer of ants across continents and expansion into non-native habitats. It is interesting to note that a high number of transfers are from Asia and the tropics [4].

Epidemiology of ant allergy in Asia

The ant fauna of Asia is large and varied [5]. There are many different climates in Asia, including arid regions, cold temperate areas and wet tropical jungles. Asia also contains the most species-rich community of ants, in Kinabalu National Park, Sabah, Malaysia. This park contains the world's highest ant diversity: 642 species of ants from 82 genera and eight subfamilies have been collected within a few hectares (see <http://www.antbase.de/HomeFrameset.htm> and [6]). Due to this wide variety, different species have been described to cause allergic disease in Asia. We will review a few of them here.

Pachycondyla species

Ant allergy in Asia has been best studied in Korea. Over the last few years, there have been increasing reports of allergic reactions to *Pachycondyla chinensis*. This species

belongs to the subfamily *Ponerinae* (Fig. 1). They are winged ants that form small colonies and are found near woodlands, in rotten wood and in old wooden houses [7]. This species exists in most East Asian countries. Sensitization rates in an ant-endemic area of Korea were found to be about 23%, which were comparable to sensitization rates in fire-ant-endemic areas in the USA [8]. Around 2.1% of adults residing in this area had immediate-type allergic responses to ant stings [9••]. Out of these, about half also had anaphylactic reactions. These patients had positive skin tests and higher serum-specific IgE to *P. chinensis* extract than other residents in the same area. Interestingly, the authors also reported that sensitization to bee venom as shown by skin tests was higher in ant-allergic subjects. They suggested possible crossreactivity between bee venom and *P. chinensis* venom. There are also reports of *P. chinensis* causing anaphylaxis in neighboring Japan [7].

A study of the allergens found in *P. chinensis* venom revealed the presence of eight IgE-binding proteins and one major allergen (12 kDa) which bound 85% of patient sera tested [10]. There was evidence of crossreactivity with yellow jacket venom from ELISA inhibition studies. However, the possibility of crossreactivity between imported fire ants and *P. chinensis* was low because there was no evidence of inhibition by fire-ant protein [10,11]. Thus, patients allergic to *P. chinensis* are unlikely to benefit from immunotherapy with fire-ant extract. More work needs to be done in this field, including elucidating the natural history of *P. chinensis* allergy and developing specific immunotherapy.

The sting of *Pachycondyla sennaarensis*, commonly called the Samsun ant, is responsible for allergic reactions in

the United Arab Emirates [12]. This ant is found in the African tropics and the Arabian Peninsula. Its sting is extremely painful but leaves no scarring. It was responsible for a significant number of anaphylactic reactions, including four fatalities within 4 years. Skin tests to *P. sennaarensis* whole-body extract and measurement of *P. sennaarensis*-specific IgE were both found to be sensitive methods of identifying patients with anaphylactic reactions.

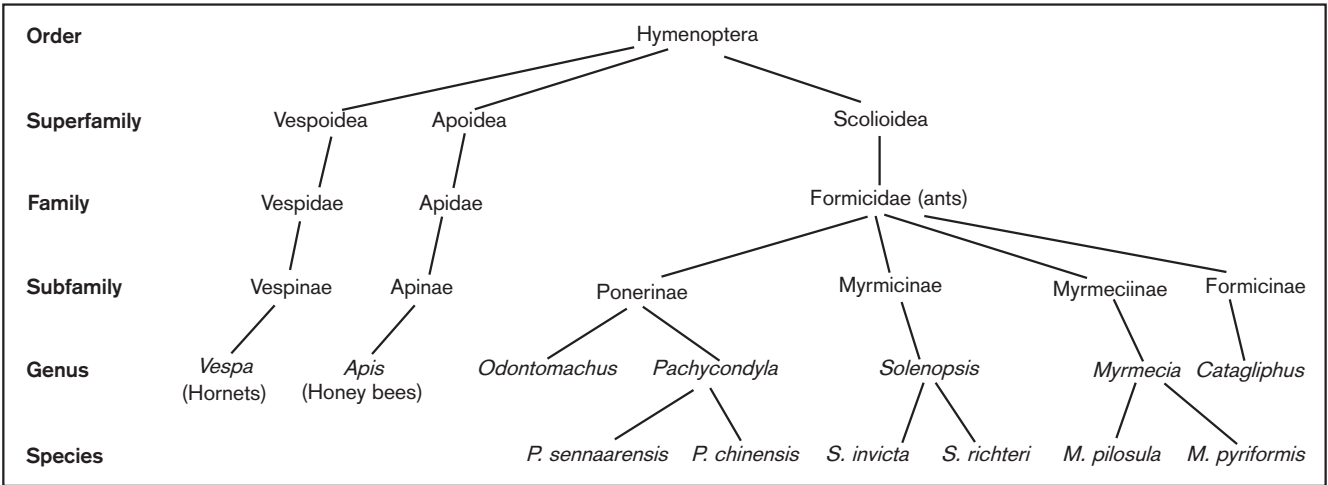
Solenopsis species

The red fire ant (*S. invicta*) and the black fire ant (*S. richteri*) are also found in Asia. A retrospective review over 2 years of cases admitted to Najran General Hospital, Saudi Arabia, identified 10 cases of anaphylaxis due to the sting of *S. richteri* [13]. The majority of these patients presented with typical symptoms of generalized urticaria, dyspnoea and hypotension. No fatalities were reported. Many more patients had large local reactions. We could find no reports of *S. invicta* causing allergic reaction in Asia. However, these ants have found their way across the ocean from their native South America and have invaded Australia. Colonies have been established in Brisbane, and anaphylaxis as a result of *S. invicta* stings has been reported there. If the habitat of *S. invicta* continues to expand in Australia, it is estimated that this ant will occupy much of the country and be responsible for up to 3000 anaphylactic reactions per year by 2030 [14•].

Myrmecia species

To the south of Asia, Australia boasts almost 3000 known species and subspecies of ants [15]. Of these, the two of importance to the allergist are the jack jumper ant (*M. pilosula*) and the bull ant (*M. pyriformis*). Fatalities are

Figure 1. Taxonomy of Hymenoptera, including ants that cause allergic reactions in Asia



Common names are included in parentheses.

rare, with a reported mean national annual incidence of 0.02 deaths per million population per year from 1980 to 1999 [1•]. In Tasmania, more than double the cases of anaphylaxis requiring adrenaline were due to *M. pilosula* stings compared with honey bee stings [16]. Unlike the massive ant attacks typical of imported fire ants, single or few stings were sufficient to cause anaphylaxis. Initial trials of immunotherapy with whole-body extracts of *M. pilosula* were disappointing, but a recent double-blind, placebo-controlled, crossover study has showed promising results [17••]. In this study, patients in the placebo arm had a high rate of severe reaction with sting challenge (72%), compared to none in the initial group treated with venom immunotherapy.

Other species of ants causing allergic reactions

Around the world, other species of ants have been reported to rarely cause allergic reactions. These include *Odontomachus bauri* in Venezuela [18] and *Cataglyphis bicolor* in Egypt [19]. These genera are present in Asia and may possibly cause allergic reactions in the region, though there have been no other reports in the scientific literature.

Nature and severity of reactions

Ant-sting reactions to the various species in Asia range from painful, small reactions to large local reactions and even fatal anaphylaxis. Around 1.6% of subjects in a *P. chinensis*-endemic area had large local reactions after stings, 2.1% (seven out of 327) had systemic immediate-type reactions, and four out of these seven had anaphylaxis [9••]. No fatalities were reported. The clinical manifestations of anaphylaxis are similar to those seen with other stings, consisting of generalized urticaria, flushing, shortness of breath and hypotension with cardiovascular collapse [13]. Even though there are few published reports in Asia of death due to ant stings, it is probable that it is under-recognized and under-reported. Apart from IgE-mediated immediate-type reactions, delayed hypersensitivity reactions also occur. These include local dermatitis and necrosis, serum sickness and acute tubular necrosis. However, there is very little data regarding this in Asia.

Diagnosis

If an allergic or anaphylactic reaction to ant sting is suspected, efforts should be made to identify the offending arthropod. Circumstances around the incident should be ascertained; for example, what the patient was doing at the time of the sting, where it occurred and the nature of insect activity in the area. Patients should bring the insect, dead or alive, to the physician for identification.

Ant-sting provocation has been used to confirm *P. chinensis* as the cause of anaphylaxis [20]. However, it

has not been used extensively because of the fear of provoking severe reactions and poor reproducibility of the test. Using skin-prick tests, all patients with anaphylaxis had positive reactions (defined as a *P. chinensis* extract/histamine wheal ratio of >2 , or the presence of a wheal with erythema >21 mm) compared to 23.3% of asymptomatic residents in that area [9••]. Specific IgE levels to *P. chinensis* extract were also significantly higher than in patients with large local reactions or asymptomatic individuals. In another study, 100% of patients (seven out of seven) with *P. chinensis*-induced anaphylaxis had IgE antibodies to two protein bands (12 and 30 kDa) [10]. It remains to be seen if the use of these diagnostic tools can identify all patients with *P. chinensis*-induced anaphylaxis without the need for sting challenge. An interesting point in some of the patients with anaphylaxis to *P. chinensis* was the detection of raised IgG₄ levels to the crude extract [10,21]. IgG₄ levels are known to increase after allergen immunotherapy, but none of these patients had received such treatment. The relevance of this finding remains to be ascertained.

Management

In many areas of Asia, ant immunotherapy is not available because of insufficient data on its efficacy, unavailability of extracts and lack of physician expertise [13]. Regarding general measures, patients need to be educated on the importance of avoiding re-sting. This would involve not disturbing ant nests, the use of insecticides and the avoidance of walking barefoot outdoors. Guidelines on the general measures that can be taken have been published elsewhere [22] and will not be described here. It is worthwhile to note that, in Asia, the majority of stings occurred around the home [9••,13]. Proper pest control and elimination of ant nests from homes should be advised to families in our region. Patients should also be advised to avoid stings by other insects because of the possibility of crossreactivity between *P. chinensis* and bee venom.

Emergency treatment for anaphylaxis should follow standard guidelines with adrenaline and fluid resuscitation as the mainstay of treatment for anaphylactic shock. A recent paper has suggested that carefully titrated adrenaline infusion in the hospital is effective and may prevent deterioration compared to giving only one dose of adrenaline [23••]. This study involved patients who were undergoing sting challenge after being in a placebo-controlled trial of venom immunotherapy. All patients who developed significant symptoms of anaphylaxis were started on resuscitative treatment which included adrenaline infusion. Symptoms improved consistently after starting therapy but recurred in some when the infusion was stopped. In clinical practice, most anaphylactic reactions to ant sting occur outside the

hospital. Carrying an adrenaline auto-injector should be recommended for those with severe reactions especially during outdoor activities. Unfortunately, these auto-injectors are relatively costly and still not available in many parts of Asia.

Conclusion

Much is still unknown about ant allergy in Asia. In view of the abundance and diversity of ant species in this region, it is possible that ant allergy is under-recognized, and therefore deserves further evaluation. For a start, clinicians need to consider ant stings as a possible cause of anaphylaxis and educate patients accordingly. Life-saving measures such as immediate access to medical care and adrenaline auto-injectors should be available. The identity of the allergens in many of these different ant species is still unknown and needs to be elucidated. We can then aim for better diagnostic tests and specific immunotherapy.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

- 1 McGain F, Winkel KD. Ant sting mortality in Australia. *Toxicon* 2002; 40:1095–1100.
A study of ant-sting mortality over a 20-year period in Australia, including detailed clinical analysis of each case.
- 2 Freeman TM. Hymenoptera hypersensitivity in an imported fire ant endemic area. *Ann Allergy Asthma Immunol* 1997; 78:369–372.
- 3 Kemp SF, deShazo RD, Moffitt JE, et al. Expanding habitat of the imported fire ant (*Solenopsis invicta*): a public health concern. *J Allergy Clin Immunol* 2000; 105:683–691.
- 4 McGlynn TP. The worldwide transfer of ants: geographical distribution and ecological invasions. *J Biogeog* 1999; 26:535–548.
- 5 Bolton B. A taxonomic and zoogeographical census of the extant ant taxa (Hymenoptera, Formicidae). *J Nat Hist* 1995; 29:1037–1056.
- 6 Bruhl CA, Gunsalam G, Linsenmair KE. Stratification of ants (Hymenoptera, Formicidae) in a primary rain forest in Sabah, Borneo. *J Trop Ecol* 1998; 14:285–297.
- 7 Fukuzawa M, Arakura F, Yamazaki Y, et al. Urticaria and anaphylaxis due to sting by an ant (*Brachyponera chinensis*). *Acta Derm Venereol* 2002; 82:59.
- 8 Hoffman DR, Dove DE, Moffitt JE, Stafford CT. Allergens in Hymenoptera venom. XXI. Cross-reactivity and multiple reactivity between fire ant venom and bee and wasp venoms. *J Allergy Clin Immunol* 1988; 82:828–834.
- 9 Cho YS, Lee YM, Lee CK, et al. Prevalence of *Pachycondyla chinensis* venom allergy in an ant-infested area in Korea. *J Allergy Clin Immunol* 2002; 110:54–57.
This study described the prevalence of *P. chinensis* allergy in an ant-endemic area of Korea. It showed that the incidence of sensitization in this area was high even among asymptomatic individuals.
- 10 Kim SS, Park HS, Kim HY, et al. Anaphylaxis caused by the new ant, *Pachycondyla chinensis*: demonstration of specific IgE and IgE-binding components. *J Allergy Clin Immunol* 2001; 107:1095–1099.
- 11 Yun YY, Ko SH, Park JW, Hong CS. Anaphylaxis to venom of the *Pachycondyla* species ant. *J Allergy Clin Immunol* 1999; 104:879–882.
- 12 Dib G, Guerin B, Banks WA, Leynadier F. Systemic reactions to the Samsun ant: an IgE-mediated hypersensitivity. *J Allergy Clin Immunol* 1995; 96:465–472.
- 13 Khan SA, Shelleh HH, Latief AK, Shah H. Black fire ant (*Solenopsis richteri*) sting producing anaphylaxis: A report of 10 cases from Najran. *Ann Saudi Med* 1999; 19:462–464.
- 14 Solley GO, Vanderwoude C, Knight GK. Anaphylaxis due to Red Imported Fire Ant sting. *Med J Aust* 2002; 176:521–523.
This paper describes the first reported case of anaphylaxis due to imported fire ants in Australia.
- 15 Shattuck SO. Australian ants: their biology and identification. Collingwood, Victoria: CSIRO Publishing; 2000.
- 16 Brown SG, Franks RW, Baldo BA, Heddle RJ. Prevalence, severity, and natural history of jack jumper ant venom allergy in Tasmania. *J Allergy Clin Immunol* 2003; 111:187–192.
- 17 Brown SG, Wiese MD, Blackman KE, Heddle RJ. Ant venom immunotherapy: a double-blind, placebo-controlled, crossover trial. *Lancet* 2003; 361:1001–1006.
An excellent clinical study on the efficacy of venom immunotherapy for *M. pilosula* allergy. The design of the trial (double-blind, placebo-controlled, crossover) gave strong support to the claim that venom immunotherapy confers protection in cases of anaphylaxis due to *M. pilosula*.
- 18 Rodriguez-Acosta A, Reyes-Lugo M. Severe human urticaria produced by ant (*Odontomachus bauri*, Emery 1892) (Hymenoptera: Formicidae) venom. *Int J Dermatol* 2002; 41:801–803.
- 19 Sanad EM, Helmy AZ, Morsy TA. Ant allergy in Benha District Qalubia Governorate, Egypt. *J Egypt Soc Parasitol* 2002; 32:901–906.
- 20 Kang SY, Chang SI, Min KU, et al. A case of systemic reaction induced by ant venom allergy [in Korean]. *Kor J Allergy* 1985; 5:183–189.
- 21 Kim SC, Hong CS. A case of anaphylaxis by ant (*Ectomomyrmex* spp.) venom and measurements of specific IgE and IgG subclasses. *Yonsei Med J* 1992; 33:281–287.
- 22 Portnoy JM, Moffitt JE, Golden DB, et al. Stinging insect hypersensitivity: A practice parameter. *J Allergy Clin Immunol* 1999; 103:963–980.
- 23 Brown SG, Blackman KE, Stenlake V, Heddle RJ. Insect sting anaphylaxis; prospective evaluation of treatment with intravenous adrenaline and volume resuscitation. *Emerg Med J* 2004; 21:149–154.
This study was carried out in the context of the clinical trial described in [17••]. The results of this study are consistent with the clinical experience that one dose of adrenaline may not be enough in severe anaphylaxis.