

Reactions to insect bites and stings: what about the orphan insects?

The article in this issue, *Stinging and Biting Insect Allergy: An Australian Experience*, by Solley summarizes clinical data from 1,762 patients who were evaluated for local and systemic reactions to insect bites and stings in a Queensland clinic during a 17-year period from 1980 until 1997.¹ Honeybees and wasps are the predominant culprit insects in the study, but stings and bites from ants, flies, and ticks (noninsect arthropods) also caused many reactions. *Vespula* and hornets are not found in that area. The analysis is retrospective and uses a tabular analytic approach without application of formal statistical methods. A host of clinical features were evaluated. These features include insect type, time to onset of symptoms, spectrum of symptoms and signs, the relationship between most recent and any previous reaction, the relationship between sting site and type of reaction, the association of insect reactions with other allergic problems, the presence of asthma, reactions after multiple stings, the relationship of the reaction to allergy testing results, first sting reactions, and medication use.

The author drew several conclusions based on the analysis; some of these conclusions can be summarized as follows. Clinical symptoms and signs of anaphylactic reactions to these insects are similar to those induced by exposure to other allergens. Stings on the head or neck do not seem more likely to cause life-threatening reactions than stings elsewhere on the body. A lesser sting or bite reaction will not necessarily lead to a more serious reaction from a future sting. Although most patients with insect allergy do not have atopic disease, asthmatic patients are prone to wheeze with insect anaphylaxis. Anaphylaxis is usually confined to a particular insect species for an individual patient. Patients who have had multiple stings at one time may have experienced true anaphylaxis rather than a toxic response. Patients who have had anaphylaxis from other exposures are at no greater risk than the general population of insect sting or bite anaphylaxis. Many patients had reactions to stings for which no effective diagnostic or treatment agent is available.

The findings of this study are generally consistent with previous studies on insect allergy and anaphylaxis.¹⁻⁵ Several aspects of the article are worthy of note, not the least of which is the tremendous amount of data collected for more than 17 years. Reactions to insect stings typically have a rapid onset. In this study, 45% of all reactions (including local ones) began within 5 minutes following the sting or bite. An additional 19% of reactions had their onset between 5 and 10 minutes, and another 16% occurred within 30 minutes fol-

lowing the sting or bite. Thus, 80% of all reactions began within 30 minutes of the sting or bite. Perhaps more notably, 81% of anaphylactic reactions with respiratory or cardiovascular symptoms or changes in consciousness had begun within 10 minutes, and only 1.6% of these reactions began after 30 minutes of the sting or bite. Only 9% of all reactions began after 2 hours, and 89% of them were limited to local swelling only.

Urticaria and/or angioedema are extremely common features of allergic reactions; 257 patients had reactions limited to urticaria and/or angioedema, and 775 of 1,194 patients with reactions featuring airway or cardiovascular symptoms had urticaria and/or angioedema as a component of the reactions. Thus, urticaria and/or angioedema occurred in 1,032 (71%) of 1,451 patients believed to have experienced generalized type 1 hypersensitivity reactions.

The study included 8 patients with more than 40 stings occurring at one time. Seven of these 8 patients experienced cardiovascular or respiratory symptoms. Six of these were tested for venom specific IgE, and test results were positive in 5. These findings remind us that type 1 hypersensitivity is responsible for many reactions that involve large numbers of insect stings and that testing for venom hypersensitivity in patients thought to have toxic reactions should not be overlooked when clinically relevant.

The author also found that serious allergic reactions were not necessarily preceded by milder ones and that most patients who present with reactions with respiratory or cardiovascular features or alterations of consciousness had no prior history of generalized allergic reactions to insect stings or bites. At the same time, 37 children were reported to have experienced a progression of initial isolated cutaneous reactions to more severe subsequent ones. Care must be exercised to properly interpret these findings because of the study design and the method of data collection, since this study was not designed to allow specific quantification of the risk for more severe reactions to future stings or bites. Previous studies such as those by Valentine et al⁶ and Schuberth et al⁷ were prospective in nature and were designed to evaluate the risk for future reaction faced by these children. In the study by Valentine et al, which was the larger of these 2 studies by overlapping investigators, 86 untreated children with histories of isolated cutaneous reactions experienced 196 stings and 18 (9.2%) of the stings caused reactions. None of the reactions were more serious than the patient's original reac-

tion. The findings of these studies resulted in the recommendation that immunotherapy is not required for children with isolated cutaneous reactions, a practice that is still in place today.⁸ A recent long-term follow-up study by Golden et al⁹ found that 12 (13%) of 89 untreated patients who experienced isolated cutaneous reactions as children had reactions to subsequent stings when followed up for many years. Six (7%) had similar isolated cutaneous reactions and 6 (7%) had moderate systemic allergic reactions that "usually included signs and symptoms of a cutaneous reaction as well as discomfort in the throat or chest, mild symptoms of airway obstruction, lightheadedness, and dizziness or mild hypotension."⁹ None had more severe reactions of greater severity than moderate ones.

The management of insect sting allergy is a success story in the field of allergy and immunology.¹⁰⁻¹⁵ Most of the basic principles worked out by investigators in the late 1970s and early 1980s are still in place. The diagnosis is usually uncomplicated, and treatment is highly effective, with a success rate of approximately 95% to 97%. There are few examples in all of medicine with greater treatment efficacy. Because there is so much agreement on the basic management of insect sting allergy, the dilemmas we face for most common types of Hymenoptera sting allergy revolve around isolated issues, such as the evaluation of the patient with a negative skin or in vitro test result despite a history strongly suggestive of an allergic reaction, the decision of whether to include all cross-reactive venoms that yield positive test results in the immunotherapy prescription, and the identification of patients who may need indefinite continuation of immunotherapy. Unfortunately, the same degree of certainty does not exist about diagnosis and treatment for patients who have experienced allergic reactions to insect bites or stings of Hymenoptera insects where quality diagnostic and treatment reagents are unavailable. For these patients, specialists in allergy and immunology are generally limited to prescribing epinephrine for emergency self-administration and dispensing advice about insect avoidance measures. This article reminds us that patients often experience reactions to bites or stings from these other insects whose specific allergens are poorly understood.

Solley reports that 24% (140/678) of patients seen for reactions to wasp stings had negative test results for venom specific IgE compared with only 3.7% of those who reacted to honeybee stings and had negative test results. He attributes this to the limited shared allergenicity in the venoms of wasps found in Australia and commercially available wasp venom. The article also reports that 111 patients or 6% of all patients were seen for reactions to ant stings and 1.2% to March fly bites; ticks, which are noninsect arthropods, caused reactions in 27 patients or 1.4% of the total. There are many reports in the medical literature that describe anaphylactic reactions to bites or stings of lesser known or "orphan" insects. With rare exceptions, most are case reports or describe a small number of patients.¹⁶⁻²⁴ This article expands our knowledge by including a larger number of patients and presenting them in

relation to the total number of anaphylactic reactions to all types of insects. Despite some recent advances such as those in mosquito allergy and the identification of a *Triatoma* allergen, our knowledge about allergy to "orphan" insect bites or stings is limited and requires expansion in the future.^{19,24} The lack of effective commercially available products for patients with allergic reactions to the stings or bites of these insects severely affects their quality of care and quality of life. The time has come to better understand the immunopathogenesis of reactions to these orphan insects.

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