

Bees and Wasps May Be Dangerous, but Who Is at Risk?

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Anybody, even a non-allergic individual, may die of a supraglottic bee or wasp sting. Fortunately, this is a rare event. Allergic patients, however, are at considerably higher risk. In the United States alone, insect sting allergies cause an estimated 50 fatal reactions every year, and this figure is most likely an underestimation of the actual frequency [1]. In up to 7.5% of the adult population, a systemic anaphylactic sting reaction has been reported [2]. Most allergists, and even more general practitioners, consider diagnostic procedures for insect venom allergy to be highly accurate [3]. However, the Insect Committee of the American Academy of Allergy, Asthma and Immunology recently acknowledged the fact that *we need revised guidelines for diagnosing insect sting allergies* [4]. Ideally, a diagnostic test with optimal sensitivity combined with high specificity is required. Currently, negative venom skin tests in patients with a positive history appear to be more common than previously supposed. Regarding specific IgE, a large group of patients with high concentrations of specific IgE do not react when re-stung [5]. In contrast, a proportion of patients with a history of severe reaction(s) have low IgE levels [6], indicating that factors beyond venom-specific serum IgE may modulate the reaction to insect venom in sensitized patients.

Several risk factors are associated with the occurrence and severity of a systemic reaction [2]: the time interval between stings and the number of stings, venom sensi-

zation, the severity of the preceding reaction, age, a history of cardiovascular disease and β -blocker treatment, the insect itself, elevated serum tryptase levels and mastocytosis. Recently, serum platelet-activating factor levels were found to be directly correlated with the severity of anaphylaxis, while an inverse correlation was noted for serum platelet-activating factor acetylhydrolase activity [7]. However, none of these risk factors helps to reliably predict the severity of a future sting reaction in a sensitized patient. Total IgE levels are one of the factors involved in asymptomatic sensitization [5]; specific antibodies are frequently seen in individuals with high total IgE levels, but appear to be largely irrelevant in clinical terms. A further reason for unexpectedly severe reactions in combination with low or even missing sensitization may be a smoldering mastocytosis [8].

The last decade has witnessed an embrace of genomic and personalized medicine that should permit more precise prediction and treatment for the individual patient [9]. In the 90s, several studies on Hymenoptera venom allergy (conducted at a single laboratory) indicated that a dysfunction in the renin-angiotensin system may result in more severe allergic responses to Hymenoptera venom [10]. Therefore, Niedozytko et al. [11] determined the prevalence of an angiotensin *AGT* MM M235T variant and angiotensin-converting enzyme *ACE* I/D, I/I, D/D gene polymorphisms in insect-venom-allergic patients, and tried to relate the presence of these gene variants to

the course of the disease and the safety of treatment. Indeed, the frequency of the *AGT* MM M235T variant was significantly higher in insect-venom-allergic patients than in controls. Besides, the presence of the MM M235T genotype increased the risk of a grade IV anaphylactic reaction. The authors concluded that the *AGT* MM M235T variant may be responsible for severe anaphylactic reactions to insect venom allergens experienced by some patients. The frequency of 29.9% in allergic patients compared with the 17.7% in controls may be statistically significant ($p = 0.02$), but is it clinically relevant? An odds ratio of 2.5 and a 95% confidence interval of 1.04–6.08 for grade IV reactions appears to be convincing, but how re-

liable is it in view of the small number of patients investigated? As the authors summarize in their article, pharmacogenetics is one of the most promising fields of allergy management. However, their conclusion that this approach will lead to safer and more effective treatment options remains to be proven. It may serve to explain the current discrepancy between the patients' individual history, ambiguous test reactions and the unpredictable outcome of the next sting. Such studies may also lead to a comprehensive approach that will identify individual risks and guide clinical management as well as decision-making. However, currently we appear to be far from such clinical applicability.

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