

Allergy to honeybee body components: distinction from bee venom sensitivity

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Two patients with inhalant allergy to whole bee body components are described, documented by positive skin tests to whole bee body extract and the presence of serum bee body-specific IgE. Both had evidence of mild sensitivity to bee venom. RAST inhibition studies indicated that the IgE antibodies directed at whole bee body components and bee venom were distinct. These observations suggest that venom allergy from insect stings and bee body inhalant allergy are caused by different antigens. (J ALLERGY CLIN IMMUNOL 71:18, 1983.)

In recent years there has been considerable progress in understanding the pathogenesis of stinging insect allergy.¹⁻³ The major allergens responsible for allergic reactions are present in venom and are not found in the insect body.⁴⁻⁶ These basic studies along with clinical observations⁷ have suggested that whole-body extracts are unreliable for diagnosis and treatment of allergy due to insect stings. Despite these findings, inappropriate use of whole-body extracts has continued.

This article addresses the issue of venom and body component allergenicity from the other direction. Two patients who developed inhalant allergy to bee body components in the course of their occupation are described. Both patients also had immunologic evidence of concomitant bee venom sensitivity. RAST inhibition studies indicated that the specificity of the IgE antibody activity directed at bee body components and bee venom is distinct, suggesting that the major allergens in these preparations do not cross-react.

MATERIALS AND METHODS

Immunologic evaluation

Intradermal direct skin tests were performed with commercial whole bee body extracts and bee venom. RASTs

were performed as previously described.⁷ Discs were coupled with either bee venom (100 μ g/disc) or whole bee body extract (22 μ g of protein/disc). Results were expressed in percent of net binding of a serum pool from ragweed-sensitive patients to ragweed-coupled discs. The net binding to the bee venom or whole bee body discs greater than 5% was regarded as significant. The binding of the ragweed standard was about 12% of total activity added. Background activity bound when normal human serum was assayed was about 1% of the total activity added.

RAST inhibition studies were performed as previously described.⁶ In brief, 100 μ l of serial threefold dilutions of bee venom, starting at 625 μ g of venom protein/ml or whole bee body extract at 625 μ g of protein/ml, were used for absorption of 100 μ l of serum from two patients with elevated levels of IgE antibodies. All tests were performed in duplicate. Fifty percent RAST inhibition was determined on the basis of a sigmoid curve calculated from individual values by a microcomputer program.

CASE HISTORIES

Patient 1

R. S., a 27-yr-old man, had been exposed to large numbers of honeybees for many years because his family was in the honey production business. Since childhood he had been aware of burning of the eyes, shortness of breath, and wheezing when exposed to honeybees or even to the clothes of those individuals who had been working about the hives. At age 6 yr, after multiple bee stings, he had an acute allergic reaction with dyspnea and generalized edema, requiring emergency medical therapy. At age 9 yr, after a single bee sting, he became unconscious and again required emergency care. There have been no further bee stings since that time. One wasp sting has been tolerated with no difficulty.

Allergy injections with whole bee body extract were given from ages 12 to 15 yr, with no apparent benefit.

He was evaluated on two occasions, in May 1980 and

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Abbreviation used

RAST: Radioallergosorbent test

June 1981, with similar results (Table I). Direct intradermal tests with whole bee body extract, 1:1,000,000 (Whole Bee Body Extract; Hollister-Stier Laboratories, Spokane, Wash.) resulted in a marked immediate reaction with pseudopods (4+). A positive reaction (2+) was found with bee venom at a concentration of 0.01 $\mu\text{g/ml}$.

The results of RASTs performed on both occasions were identical. Borderline reactions (5% and 6%) were found with bee venom and elevated levels (16%) were seen with whole bee body extract.

RAST inhibition studies were done with whole bee body extract as the coupling antigen. Whole bee body extract did inhibit this reaction; 0.17 μg of protein caused 50% inhibition. Bee venom had no effect. These results are shown in Fig. 1. Because of the low titer of bee venom-specific IgE in direct RAST, RAST inhibition studies with bee venom as the coupling antigen could not be done.

Patient 2

About 2 mo after starting to work in a honey-producing plant, D. H., a 29-yr-old man, noted the onset of coughing, which became more persistent and seemed worse at night. When he was away from the honey farm for 2 wk, the cough completely cleared. Approximately 24 hr after his return, the symptoms recurred.

He had been stung a number of times by bees in early childhood, with no significant reactions. While working at the honey farm, he was stung on the average of once a week, with only mild reactions. No anaphylactic reactions occurred. As time went on, the local reactions became less intense.

Intradermal skin tests with whole bee body extracts showed a very marked reaction at a dilution of 1:500. An immediate reaction was found with bee venom only at a concentration of 10 $\mu\text{g/ml}$. Elevated RAST titers of 22% with whole bee body extract and 16% with bee venom were found (Table I).

RAST inhibition studies were done with discs coupled with whole bee body extract and bee venom (Figs. 1 and 2). With whole bee body-coupled discs, inhibition was found with whole bee body extract (50% inhibition, 29.5 μg of protein). No inhibition was found with bee venom. With bee venom-coupled discs, only bee venom inhibited the RAST reaction (50% inhibition, 52.3 μg of protein) and no inhibition was found with whole bee body extract.

DISCUSSION

Inhalant allergy due to bee body components was initially described by Benson and Semenov⁹ and in more detail by Ellis and Ahrens.¹⁰ In the latter study, two individuals were reported, both of whom also had allergic reactions after bee stings. Both patients had positive skin tests with whole bee body extract and

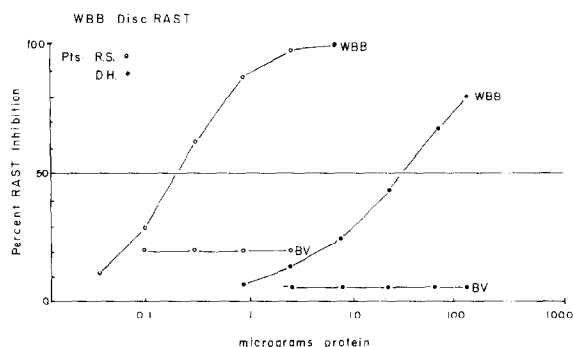


FIG. 1. Whole bee body extract RAST inhibition. Inhibition of the RAST reaction between sera of patients 1 (R. S.) and 2 (D. H.) and discs coupled with whole bee body (WBB) extract by whole bee body extract and bee venom (BV). Inhibition was found only with the homologous antigen, whole bee body extract.

TABLE I. Summary of immunologic results

	Patient 1 (R.S.)	Patient 2 (D.H.)
Positive intradermal skin tests		
Whole bee body extract (w/v dilution)	1:100,000	1:500
Bee venom ($\mu\text{g/ml}$)	0.01	10
Direct RAST (% standard)		
Whole bee body extract	16	22
Bee venom	5	17
50% RAST inhibition (μg protein)		
Bee venom disc		
Whole bee body extract	ND	0
Bee venom	ND	52.3
Whole bee body extract disc		
Whole bee body extract	0.17	29.5
Bee venom	0	0

ND = not done.

serum IgE antibodies were demonstrated by passive transfer test. Subsequently, numerous other observations have been made of beekeepers with inhalant allergy to bee body components.^{8, 11, 12}

This article describes two individuals with inhalant sensitivity to whole bee body protein components, documented by positive immediate skin-test reactions to whole bee body extracts and by the demonstration of serum bee body-specific IgE. Both patients also had mild sensitivity to bee venom. Patient 1 had a positive bee venom skin test and borderline levels of serum bee venom-specific IgE; patient 2 had serum IgE antibodies but a positive skin test only to a high bee venom concentration. RAST inhibition studies indicated that the antibodies directed at body components and at bee venom were distinct. The reaction of

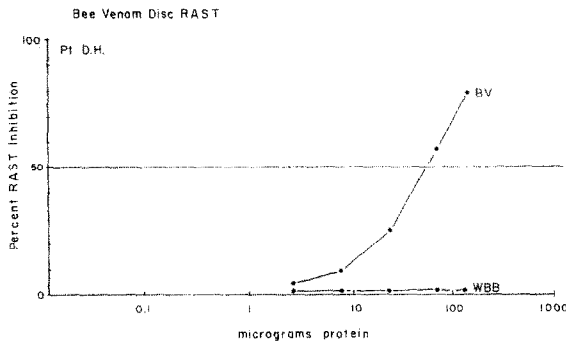


FIG. 2. Bee venom RAST inhibition. Inhibition of the RAST reaction between the serum of patient 2 (D. H.) and discs coupled with bee venom (BV) by whole bee body (WBB) extract and bee venom. Inhibition was found only with the homologous antigen, bee venom.

both sera with discs coupled with whole bee body extract could be inhibited only by the homologous antigen; venom failed to inhibit this RAST reaction. With one serum, it was possible to do the opposite test—couple discs with bee venom and inhibit the whole bee body extract and bee venom. In this situation, only the bee venom caused inhibition.

Other observations have suggested that bee body and bee venom antigens are distinct. Phospholipase A, the major allergen in bee venom, cannot be demonstrated in commercial whole bee body extracts.⁶ Testing with venom and body extracts by either skin test or RAST in bee-allergic patients and beekeepers has shown discordant results. For example, Light et al.⁸ found that of 17 bee sting-allergic patients with positive venom skin tests, only nine had positive reactions to whole bee body extracts. Sequential studies of serum IgE antibodies in two beekeepers revealed that after a sting reaction, only the bee venom-specific IgE rose, and the whole body extract-specific IgE remained unchanged. Similarly, serum bee venom-specific IgE may rise after bee venom therapy but is not influenced by whole bee body extract therapy.¹³

Highest levels of whole bee body extract-specific IgE have been described in beekeepers who have inhalant allergy.¹¹ Occasionally these patients do not have detectable venom-specific IgE. For example, Müller (personal communication, 1982) observed nine beekeepers with histories suggestive of inhalant allergy. Seven had positive skin tests with whole bee body extract and only three had venom-specific IgE.

We have described one patient who had IgE antibodies reacting with yellow-jacket body components and not with yellow-jacket venom, probably as a result of unusual inhalant exposure.¹⁴

In this article, two patients are described who have typical whole bee body inhalant sensitivity. For these individuals, whole bee body extracts are helpful in diagnostic studies and may be useful in immunotherapy. Such extracts should therefore remain available for this purpose. However, these results suggest once again that whole-body extracts and venom are antigenically distinct and that each has a specific place for diagnosis and therapy.

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