

Reactions to Insect Allergens

The Incidence of Response to Testing Among Allergic And Nonallergic Persons

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FOR CENTURIES it has been known that in some persons the bites or stings of insects will produce dramatic or fatal reactions. Since reactions of this kind are out of proportion to the amount of insect material injected, it is now recognized that they are allergic rather than toxic, and that there must have been previous sensitizing exposures.

Not until recent times, however, was there recognition that allergic disease of the respiratory tract was sometimes caused by inhalation of insect particles. Since Wilson's paper on sensitization to May flies in 1913,¹³ cases of asthma and hay fever have been reported from time to time due to emanations of such insects as sand flies,⁷ mosquitoes,¹ bees,² house flies,⁵ moths,¹¹ beetles,⁹ aphids,⁴ and weevils.³ In most cases specific sensitivity to the particular insect has been shown by direct or passive transfer testing.

Because of the emphasis usually given to such well recognized sensitizers as household dusts, animal danders, grass pollens or food proteins, the possibility seems often to have been overlooked that sensitivity to inhaled insect particles may be an important cause of clinical disease. Feinberg and co-workers³ in 1956 noted that as many as 65 per cent of a group of patients with seasonal asthma that could not be explained by sensitivity to the usual antigens had positive reactions to tests with such materials as ant eggs, house flies, bees and mosquitoes. Desensitization with the appropriate insect extracts brought relief to 19 of 26 patients.

Weisman and coworkers,¹² after testing allergic patients with extracts of insects of ten orders, concluded that "insect allergy may be a significant cause of seasonal clinical allergy." Perlman⁸ reported that half of patients he had observed with asthma and allergic rhinitis, reacted to standardized insect antigens.

• Positive reactions to skin tests with extracts of various insects were found to be significantly higher in 200 patients with allergic disease than in 150 nonallergic controls.

Forty-seven per cent of the allergic group had positive reaction to bee, 46 per cent to house fly, 39.5 per cent to moth, 29.5 to ant and 28.5 to aphid. Ant and house fly extract caused the greatest number of severe reactions (4+), with moth second and bee third.

Because extracts of nonstinging insects caused reaction almost as often and as strong as stinging insects, it may be inferred that sensitization is due to inhaled insect particles. There appeared to be no necessary connection between a history of having been stung and a strong skin test reaction to bee protein.

Testing for insect sensitivity appears a good way to get diagnostic information that can enhance the effectiveness of treatment.

If insect emanations can be important allergens in those parts of the country where they are present only in the warmer months, they should be even more significant in the central and southern areas of California where insects can grow during almost the entire year. The number of insects that go through a life cycle each season is astronomical. It has been estimated¹⁰ that the number present at any one time in the topsoil of cultivated land runs from one hundred to two hundred million per acre and as they die and fragment they become a source of airborne insect debris.

Because of the lack of published data on this point for the Los Angeles area, we have undertaken to find the incidence of positive reactions to skin tests with insect extracts in a group of patients with allergic disease and in a comparable control group of persons free of any known allergic symptoms. We believed that a significantly higher incidence of reactions in the patients would indicate that these extracts may be used to detect specific sensitivity to insects, and could be used in treatment according to the classical methods of desensitization.

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MATERIALS AND METHODS

The group with allergic disease was made up of 200 clinic and private patients. The control group was 150 persons with no known symptoms of allergic sensitivity. They were selected to resemble as closely as possible the allergic group. The majority in both groups were between 30 and 49 years of age. Female subjects predominated over male in the ratio of 1.6:1 for patients and 2.6:1 for controls.

Among the 200 patients there were 123 cases of asthma, 107 of nasal allergic diseases, ten of eczema and three of miscellaneous disorders.

Routine tests on the patients (Table 1) showed that 95 per cent reacted to "environmental allergens" such as house dust, animal dander, cotton lint, gums, insecticides and mold spores. Eighty-one per cent were reactive to pollens and 65 per cent to foods. Every patient reacted to at least one of the allergens in the categories named.

The insects used were ants, aphides, bees, house flies, mosquitoes, moths, wasps, and yellow jackets. This selection was dictated partly by availability of material and partly by the frequency of occurrence in the area. Wasps are not as commonly encountered

as the others but were included for comparison with the other stinging insects.

Test extracts were prepared from whole insects, as it has been shown by our own work with desensitization to bee anaphylaxis that the allergenic material is found throughout the insect. After defatting with ether, maceration and thorough drying, the weighed powdered materials were soaked for 48 hours in buffered saline solution containing 50 per cent glycerine as a preservative. The extracts were sterilized by Seitz filtration.

Intradermal testing was carried out in the usual manner, using dilutions of 1:5000, and 1:500 of the insect extracts. Reactions were read as one plus to four plus, but, for purposes of recording, only the two plus, three plus or four plus reactions were considered significant.

RESULTS

The proportions of nonreacting patients and controls and the proportions with two plus, three plus or four plus to each insect extract are given in Table 2.

Among the patients, bee extract produced the greatest number of positive reactions (47 per cent) and house fly extract was second (46 per cent). However, there were more four plus reactions to house fly. The positive reactions to each insect extract among the controls paralleled the incidence among the patients, although at a much lower level.

There were no four plus reactions in the control group to extracts of ant, aphid, fly, mosquito or yellow jacket, and only one each to bee, moth and wasp. The greatest numbers of reactions among controls were to bee and fly. One hundred and twenty-eight (86.4 per cent) of the controls did not

TABLE 1.—Results of Allergen Testing of 200 Patients with Allergic Disease

Class of Allergen	Positive Reactions		Negative Reactions	
	No.	Per Cent	No.	Per Cent
Environmentals (dust, animals, molds, etc.)	190	95	10	5
Pollens (grass, weed, tree)	162	91	38	19
Foods	130	65	70	35
Insects*	142	71	58	29

*Bee, house fly, moth, ant, aphid, yellow jacket, mosquito, wasp.

TABLE 2.—Reaction of 200 Allergic Patients and 150 Controls to Intradermal Tests with Insect Extracts

Insect		PROPORTION WITH VARIOUS DEGREES OF REACTION			
		(Negative)	(2 Plus)	(3 Plus)	Total Positive
Bee	Patients	53.0%	19.0%	18.5%	47.0%
	Controls	86.0%	12.0%	1.3%	14.0%
Fly	Patients	54.0%	15.5%	16.0%	46.0%
	Controls	86.4%	9.3%	3.3%	13.6%
Moth	Patients	60.5%	13.5%	14.5%	39.5%
	Controls	91.3%	6.0%	2.0%	8.7%
Ant	Patients	70.5%	12.5%	12.5%	29.5%
	Controls	91.8%	7.5%	0.7%	8.2%
Aphid	Patients	71.5%	9.5%	13.5%	28.5%
	Controls	90.5%	6.8%	2.7%	9.5%
Yellow jacket	Patients	74.0%	8.0%	11.5%	26.0%
	Controls	87.3%	10.0%	2.7%	12.7%
Mosquito	Patients	77.5%	9.0%	10.0%	22.5%
	Controls	93.3%	5.4%	1.3%	6.7%
Wasp	Patients	78.0%	9.5%	8.0%	22.0%
	Controls	91.3%	6.7%	1.3%	8.7%

react to any insect extract, whereas 58 (29 per cent) of the allergic patients showed no reactions. Statistical analysis confirmed that the difference between the patients and the controls was highly significant in every instance. It may be concluded therefore that a positive reaction to a test with these insect extracts is a reliable indication of some degree of sensitivity.

Eleven of the patients had previously had general reactions to bee or yellow jacket stings. Nine of the eleven reacted strongly to extract of the same kind of insect that had stung them, but two did not. Among the controls two had experienced such reactions and both had positive reaction to testing with the extract. The incidence of sting sensitivity appeared to be significantly higher among persons with allergic disease.

A substantial majority of both patients and controls could recall one or more stings by bees. Many more were not sure, but thought they must have been stung at least once. It appeared impossible to find any close correlation between having been stung and a positive reaction to bee extract. Many non-reactors had been stung repeatedly.

The fact that insect extracts do cause reaction in some presumably nonallergic people could indicate either that the extracts contain nonspecific whealing agents for some persons, or that these subjects have skin sensitizing antibodies. Since five-sixths of the controls who reacted strongly belonged to families in which there were members who had allergic sensitivity, the latter possibility seems the more likely. (Seeking proof on this point was beyond the scope of the present study.)

The method of natural sensitization to these insect proteins can only be inferred from our results. Unless the patient had never been stung, the high incidence of bee sensitivity might be due partly to the introduction of protein along with the venom. In the case of the house fly the sensitivity might result from the insect's saliva released when probing the pores of the skin. However, in the case of the moth, which presumably rarely breaks the skin, the apparently most logical postulation is inhalant sensitization from the wing scales and other parts of the

dried insect. Since sensitivity to moth among our patients was almost as common as to bee and house fly, it is tempting to assume (provided that moth protein is not a much more potent sensitizer) that the greater part of bee and fly sensitivity is also acquired by inhalation.

The results here reported are indicative that sensitivity to insects is present in a large proportion of allergic persons in the Los Angeles area. Because of the extended season when insect particles are in the air, both indoors and out, testing with these materials should be part of the standard procedure for dealing with persons with symptoms of allergic disease. When sensitivity is found it should be treated if it appears to be clinically significant. Furthermore, patients who are not doing well and who have not been tested for sensitivity to insect extracts might well benefit if so tested.

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