

Modern Prevalence of Insect Sensitization in Rural Asthma and Allergic Rhinitis Patients

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ABSTRACT

Inhalant allergy to insects other than cockroaches and dust mites was described in the 1950s, but little attention has been paid to these findings. Sensitization rates for many allergens have increased since then. In this rural population, we describe the current prevalence of sensitization to commonly found insects. We evaluated 200 patients (38 adults and 162 children), for immunoglobulin E (IgE)-mediated sensitization to the caddis fly, mayfly, moth, carpenter ant, and housefly using the prick technique and commercially available whole-body extracts. All had symptoms consistent with asthma and/or allergic rhinitis. They also were tested to indoor and outdoor aeroantigens. Of the 200 patients, 60 patients (30%) tested positive to at least one of the five insects. The most prevalent positive skin test was to the mayfly (37/60), followed by the housefly (36/60), caddis fly (27/60), moth (14/60), and ant (10/60). Of the 60 patients positive for insects, 35 patients (58%) also tested positive to at least one species of mite, 36 patients (60%) tested positive to the cockroach. Twelve of the 60 patients (20%) with positive insect testing did not react to either cockroaches or mites. In our patients, the immunoglobulin E-mediated sensitization rate to insects excluding cockroaches is 30%. Many patients also were sensitized to mites and/or cockroaches. These insects are all present in the indoor/outdoor environment of this rural population. Cross-reactivity with mites and cockroaches

(insect panallergy) may partially explain our results. The presence of skin test sensitivity in the absence of cockroach or mite allergy suggests possible true insect sensitization. (Allergy and Asthma Proc 26:356–360, 2005)

Immunoglobulin E (IgE)-mediated sensitivity to indoor insects, particularly dust mites and cockroaches, has become increasingly appreciated as a cause of asthma and allergic rhinitis and has been documented in both urban and rural populations.^{1,2} Although cockroach and mite allergies have received considerable attention in recent years, little awareness has been paid to other ubiquitously prevalent insects such as the housefly, moth, carpenter ant, mayfly, and caddis fly. A variety of publications in the 1950s showed that many people were sensitized to these insects and they were felt to be a contributing factor in both asthma and allergic rhinitis.^{3–5} Since then, the incidence of atopy has increased greatly.⁶ For example, Bernton and Brown⁷ skin tested allergic children to cockroach allergen in 1967 and found no child <4 years of age with a positive skin test. By 1999, 28% of wheezing infants ≤3 years of age had a positive skin test to this allergen.¹

Several studies have suggested that dust mite avoidance measures are less effective in improving allergic symptoms than previously thought. This may be because of other allergens present in the patient's home environment. For example, we previously determined that sensitization to mouse allergen is present in rural children at a frequency of 12%.⁸ Observation of many homes in rural West Virginia revealed that these insects are commonly found inside. In this study, we prospectively studied the prevalence rate of sensitization to the housefly, moth, carpenter ant, mayfly, and caddis fly in our rural population. These data further suggest that other insects besides cockroaches and dust

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mites may be hidden triggers contributing to allergic disease.

METHODS

All new patients presenting to the West Virginia University Allergy/Immunology clinics with allergic complaints between July 2003 and January 2004 were evaluated. There were no excluded patients. Data on age, insurance status, dwelling, and environmental histories were collected on all patients. Each subject underwent standard allergy testing supervised by a physician. Skin testing was performed using the prick-puncture method using the Greer Dermapik (Greer Laboratories, Lenoir, NC)¹ with saline and histamine controls. Patients were skin tested to a standard panel including dust mites, cats, dogs, mice, cockroaches, molds, weeds, trees, and grasses indigenous to the region (supplied by Alk-Abello, Inc., Round Rock, TX). In addition, five skin tests using whole-body flying insect extracts from Greer also were performed using the caddis fly (*Trichoptera*), mayfly (*Ephemeroptera*), carpenter ant (*Camponotus pennsylvanicus*), moth (*Heterocera*), and housefly (*Musca domestica*). A positive skin test was defined as a wheal at least one-half the size of the histamine control or 5 mm greater than the saline control and a flare at least twice the size of the wheal. Chi-square analysis was performed using the InStat Statistics program (Graphpad, San Diego, CA). The Institutional Review Board of West Virginia University approved this study.

RESULTS

During the 6-month period, 200 patients (38 adults and 162 children) were prospectively evaluated. Demographic data on the patients are presented in Table I. Average age for the adults was 38 years (± 13 years) and for children was 7 years (± 3.7 years). The majority of patients presenting to the clinic had symptoms of rhinitis, asthma, or sinusitis. Seventy-seven percent of the patients lived in a rural environment. The remainder of patients lived in suburban areas. Thirty-nine percent of children and 29% of adults were exposed to tobacco smoke. Socioeconomic status was determined using the presence of insurance or Medicaid as a marker. Three adults and 75 (46%) of the children in our study had Medicaid as their primary insurance.

Skin testing results are shown in Table II. Of the 200 patients skin tested, the most prevalent positive result was dust mites (*Dermatophagoides pteronyssinus* and *D. farinae*) followed by cockroaches. For pediatric patients, cockroaches were the most common sensitizing allergen followed by dust mites. Overall, sensitivity to flying insects was the third most prevalent positive test (30%) and was equal to grass pollen sensitization.

Of the 200 patients, 60 patients (30%) skin tested positive to at least one of the five insects. The most prevalent positive skin test was to the mayfly (37/60), followed by the

TABLE I

Demographic Data		
	Adults	Children
Number ($n = 200$)	38	162
Mean age (yr) + SD	38 (SD 13)	7 (SD 3.7)
Diagnosis		
Allergic rhinitis	22	124
Asthma	18	101
Sinusitis	3	16
Vasomotor rhinitis	7	12
Urticaria/angioedema	4	6
Atopic dermatitis	2	7
Dwelling		
Suburban	19	45
Rural	17	109
Not available	2	8
Animal exposure		
Cat	18	63
Dog	18	83
Other	3	29
Smoking exposure (%)	23	39
Medicaid/not insured	3	75

TABLE II

Skin Test Results			
	Number of Positives		
	Adults	Children	Total (%)
Total Number in Study	38	162	
Dust mites	18 (29%)	60 (37%)	39%
Cockroach	12 (19%)	62 (38%)	37%
Cat	11 (17%)	33 (20%)	22%
Dog	5 (8%)	14 (8.6%)	9.5%
Grass	14 (22.5%)	46 (28%)	30%
Weed	11 (17.7%)	25 (15%)	18%
Tree	8 (12.9%)	43 (26.5%)	25.5%
Mold	5 (8%)	11 (6.7%)	8.0%
Total insects	9 (14.5%)	51 (31%)	30%
Caddis fly	7 (11%)	20 (12%)	13.5%
Ant	4 (6%)	6 (3.7%)	5.0%
Housefly	4 (6%)	32 (19.75%)	18.0%
Moth	4 (6%)	10 (6%)	7.0%
Mayfly	6 (9.6%)	31 (19%)	18.5%

housefly (36/60), caddis fly (27/60), moth (14/60), and carpenter ant (10/60). Of the 60 patients with positive flying insect skin tests, 25 patients were positive to only one insect, 17 patients were positive to two insects, 10 patients were positive to three of the insects, 6 patients were positive to four of the insects, and only 2 patients were positive to all five flying insects tested. Of the 60 patients with positive skin test results to flying insects, 35 patients (58%) also

tested positive to at least one species of dust mite ($p < 0.001$, chi-square) and 36 patients (60%) also tested positive to cockroaches ($p < 0.001$). Twelve of the 60 patients (20%) with positive flying insect skin tests did not react to either cockroaches or dust mites ($p < 0.001$). This pattern of sensitivities to multiple types of insects was only seen in the pediatric population, because there were no adults who were negative to both cockroaches and mites but positive to flying insects.

DISCUSSION

Occupational and environmental exposure to insects and their subsequent allergic responses such as bronchospasm or rhinitis has been periodically described in the literature since the 1930s.^{9,10} Although considerable attention is being paid to the effects of cockroaches and dust mites on asthma and other allergic diseases, the role of other commonly found insects has been ignored. We performed this preliminary study evaluating the current prevalence of insect sensitization other than cockroaches and dust mites in our patient population to determine if sensitization rates to insects had changed since their initial description. In our population, we found a prevalence rate of 30% positive skin tests for these insects. This rate is equal to the rate of grass sensitization in our patients, indicating that these insects may be a significant but underappreciated cause of allergic symptoms in our population.

In 1956, Feinberg *et al.*⁴ skin tested allergic patients to a variety of insect allergens and found that 69% were positive to the mayfly, 65% were positive to ant eggs, and 49% were positive to the housefly. The IgE-mediated nature of these reactions was verified by passive transfer technique. Hellreich,⁵ in 1962, studied adults with allergic rhinitis and found that 14/63 (22%) had moderate to marked intradermal skin test reactions to ants, 7/60 (11%) had moderate to marked intradermal skin test reactions to grasshoppers, and 15/60 (25%) had moderate to marked intradermal skin test reactions to the housefly compared with 15/60 (25%) for cockroaches. Wiseman *et al.*³ found a total insect reactivity rate of 36/328 (11%) in adults with allergic symptoms. Osgood¹¹ described his experience with caddis fly allergy in Buffalo, NY. He reported on a series of 623 adults and children living in the Niagara area who were skin tested to the caddis fly. Thirty-four percent of his patients had positive skin tests by intradermal testing and presented with typical allergic symptoms. Osgood concluded that in the appropriate environmental exposure and typical symptoms, skin testing to the caddis fly is warranted. In addition, Lierl *et al.*¹² described insect allergy in asthmatic children in a Midwestern urban population. They concluded that moth, cricket, grasshopper, housefly, and ant antigens might be important aeroallergens and required additional study.

Kino *et al.*¹³ also studied insect allergy to various insects indigenous to Japan, which included the moth, butterfly, caddis fly, and chironomid (a species of fly). Positive skin

tests to moths and butterflies occurred with an equal frequency as house dust and *Candida sp.* In addition, they performed nonblinded inhalation provocation testing with these insects and showed airway hyperresponsiveness. Quantification of butterfly and moth exposure in the patient's environment also was performed and found to correlate with specific IgE levels to specific insects.¹⁴ Kino's group concluded that insects besides cockroaches and dust mites are capable of causing allergic symptoms in a nonoccupational setting and raised the question that exposure to these insects may be as common as cockroaches, dust mites, and even pollen, which has received greater attention from allergists over the years. Cases describing patients suffering from allergic respiratory symptoms such as rhinitis and asthma related to exposure to the Asian ladybeetle *Harmoinia axyridis* have been described.¹⁵ These patients have positive skin-prick tests with ladybug extract as well as IgE immunoblotting with the sera showing at least two distinct allergenic proteins.

Baldo and Panzani¹⁶ also have concluded that these insects are commonly involved in allergic sensitization. They studied their Australian population by performing a radioallergosorbent test to detect the presence of IgE antibodies to various insects (housefly, blowfly, moth, cockroach, carpet beetle, and silverfish). They reported that 38 of 41 patients had IgE antibodies to the insects tested. They also noted that the majority of subjects had antibodies to three or more insects. This led them to hypothesize that a "panallergy" syndrome may be present whereby cross-reactivity to similar proteins present in all species may account for the multiple insect-positive skin and radioallergosorbent test results as opposed to unique exposures causing sensitization.

Tropomyosin has been proposed as the protein responsible for insect panallergy.⁹ Common proteins in the 34- to 40-kDa range, corresponding to tropomyosin, have been identified as relevant allergens in shrimp with significant cross-reactivity to other crustaceans as well as the fruit fly and dust mites.¹⁶⁻¹⁸ Witteman *et al.*¹⁹ performed a study using a monoclonal antibody to tropomyosin and described cross-reactivity between *Dermatophagoides* and shrimp supporting this hypothesis. Panzani hypothesized that this panallergy extends across the class Arthropoda to include mites, crustaceans (*i.e.*, shrimp), and cockroaches and may even extend to mollusks and nematodes.⁹ In contrast, Martinez *et al.*²⁰ also showed cross-reactivity with insects and various other species including seafood and parasites, but their data did not indicate the presence of tropomyosin in *Dermatophagoides* by immunoblotting. Clearly, the exact nature of insect cross-reactivity and allergy requires additional study.

The specific insects included for testing in our study were chosen for their ubiquitous presence in the indoor environment of West Virginia (houseflies, carpenter ants, and moths), their potential for causing allergic symptoms (caddis fly and mayfly), and their commercial availability as

TABLE III			
Insect Summary Data			
	Adult	Children	Total
Total Positives	9	51	60
Insect Positive			
Caddis fly	7	20	45%
Carpenter ant	4	6	16%
Housefly	4	32	60%
Moth	4	10	23%
Mayfly	6	31	62%
Cockroach (+)	8	28	60%
Dust mites (+)	7	28	58%
Cockroach (-)/mite (-)	0	12	20%

whole-body extract. The common housefly (*Musca domestica*) is one of the most common household pests in the world. Caddis flies and mayflies are lesser-known flying insects found near freshwater bodies including lakes, rivers, and streams. West Virginia and its surrounding regions have numerous freshwater sources, making it possible that our population has encountered them in the ambient environment. Although direct quantification of flying insect antigen has not been reported, it seems reasonable that our population may have significant exposure resulting in sensitization levels similar to the patients in other studies.^{10,13}

In our rural study population, insect-positive skin tests were the third most common positive skin test result after dust mites and cockroaches. Overall, 30% of the study population tested positive to at least one flying insect and this sensitization rate equaled that of the grass pollens. This degree of sensitization to these insects suggests that these allergens might be an underappreciated trigger of allergic rhinitis and asthma. The most common flying insect sensitization was to mayflies followed by the ubiquitously present housefly. Because of differences in study design and patient populations, it is difficult to compare our results directly with the previous studies done in the 1950s and 1960s but these results are certainly consistent with their findings. During these previous investigations, 11–34% of patients were noted to have IgE-mediated sensitization to insects.

In our study, 60% of patients with positive skin tests to flying insects also had positive tests to cockroaches and 58 to at least one species of *Dermatophagoides*. It is possible that this is due to cross-reactivity. However, of the patients with positive skin tests to flying insects, 20% were negative to both cockroaches and dust mites (see Table III). Although it is uncertain if these flying insect sensitivities are the result of cross-reacting allergens or represent true sensitivities secondary to true exposures, the lack of positive skin tests to cockroaches or dust mites in this subpopulation suggests that true sensitivity may be present. In addition, of the 60 patients with positive flying insect testing, only 8 patients were allergic to four or more insects. One might expect that

if cross-reactivity were the sole reason for positive skin testing and extended across the entire insect order, our data would have shown more patients with panallergy to more than just one or two flying insects.

Currently, there is little information on insect allergen levels in our patients' homes or their outdoor environment, making it difficult to correlate exposure with symptoms. However, we do have a significant number of patients sensitized to flying insects that needs further evaluation. It is possible that for some populations, flying insect allergy may be as common as grass pollen or dust-mite allergy, but it remains unrecognized. Additional studies in this population could include direct quantification of indoor flying insect exposure by ambient air sampling, in addition to nasal or bronchial provocation challenges. In addition, studies in an urban population for ubiquitous flying insects such as the housefly and moth would be interesting. Identification of these patients with true flying insect allergy is important because it may lead to targeted interventions such as avoidance measures or other medical treatment.

We conclude that sensitization to insects other than cockroaches and dust mites is relatively prevalent in our U.S. rural population and is consistent with previously described studies. Our data suggest that true sensitization to flying insects may be present rather than cross-reactivity with cockroaches or dust mites because of the panallergy syndrome. Skin testing to common flying insects may provide insight into otherwise underappreciated triggers of asthma and rhinitis. Given the high prevalence of flying insect sensitization found in our population, additional studies of antigen levels of these insects in the home and local outdoor environment are warranted.

REFERENCES

1. Wilson NW, Robinson NP, and Hogan MB. Cockroach and other inhalant allergies in infantile asthma. *Ann Allergy Asthma Immunol* 83:27–30, 1999.
2. Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 336:1356–1363, 1997.
3. Wiseman RD, Woodin WG, Miller HC, and Myers MA. Insect allergy as a possible cause of inhalant sensitivity. *J Allergy* 30:191–197, 1959.
4. Feinberg AR, Feinberg SM, and Benaim-Pinto C. Asthma and rhinitis from insect allergens. *J Allergy* 27:437–444, 1956.
5. Hellreich E. Evaluation of skin tests with insect extracts in various allergic diseases. *Ann Allergy* 20:805–808, 1962.
6. Barbee RA, Kaltenborn N, Lebowitz MD, and Burrows B. Longitudinal changes in allergen skin test reactivity in a community population sample. *J Allergy Clin Immunol* 294:16–24, 1987.
7. Bernton HS, and Brown H. Cockroach allergy: Age of onset of skin reactivity. *Ann Allergy* 28:420–422, 1970.
8. Welch JE, Hogan MB, and Wilson NW. Mouse allergy among asthmatic children from rural Appalachia. *Ann Allergy Asthma Immunol* 90:223–225, 2003.
9. Panzani RC, and Ariano R. Arthropods and invertebrates allergy (with the exclusion of mites): The concept of panallergy. *Allergy* 56(suppl 69):1–22, 2001.

10. Parlato SJ. Studies of hypersensitiveness to the emanations of caddis flies. JAMA 102:910–912, 1934.
11. Osgood H. Allergy to caddisfly (*Trichoptera*). J Allergy 28:292–300, 1957.
12. Lierl MB, Riordan MM, and Fischer TJ. Prevalence of insect allergen-specific IgE in allergic asthmatic children in Cincinnati, Ohio. Ann Allergy 72:42–50, 1994.
13. Kino T, and Oshima S. Allergy to insects in Japan. I. The reaginic sensitivity to moth and butterfly in patients with bronchial asthma. J Allergy Clin Immunol 61:10–16, 1978.
14. Kino T, Chihara J, Fukuda K, et al. Allergy to insects in Japan. III. High frequency of IgE antibody responses to insects (moth, butterfly, caddisfly, and chironomid) in patients with bronchial asthma and immunochemical quantitation of the insect-related airborne particles smaller than 10 microns in diameter. J Allergy Clin Immunol 79:857–866, 1987.
15. Ray JN, and Pence HL. Ladybug hypersensitivity: Report of a case and review of literature. Allergy Asthma Proc 25:133–136, 2004.
16. Baldo BA, and Panzani RC. Detection of IgE Antibodies to a wide range of insect species in subjects with suspected inhalant allergies to insects. Int Arch Allergy Appl Immunol 85:278–287, 1988.
17. Shanti KN, Martin BM, Nagpal S, et al. Identification of tropomyosin as the major shrimp allergen and characterization of its IgE-binding epitopes. J Immunol 151:5354–5363, 1993.
18. Witterman AM, van den Oudenrijn S, van Leeuwen, et al. IgE antibodies reactive with Silverfish, cockroach, and chironomid are frequently found in mite allergic patients. Int Arch Allergy Immunol 108:165–169, 1995.
19. Witterman AM, Akkerdaas JH, van Leeuwen J, et al. Identification of a cross-reactive allergen (presumably tropomyosin) in shrimp, mite and insects. Int Arch Allergy Immunol 105:56–61, 1994.
20. Martinez A, Martinez J, Palacios R, et al. Importance of tropomyosin in the allergy to household arthropods. Cross-reactivity with other invertebrate extracts. Allergol Immunopathol (Madr) 25:118–126, 1997. □

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