

Editorial

Skin tests to insects: reliable markers of sensitization?

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Positive skin tests to natural allergen extracts are the hallmark of immediate hypersensitivity and play a key role in allergy diagnosis. Even today, most allergy diagnosis is based on skin tests, rather than *in vitro* measurements of allergen-specific immunoglobulin (Ig)E. Skin tests have been extensively used to assess sensitization in epidemiological studies, especially in children, where they allow sensitization to be measured quickly and relatively painlessly, without the need to draw blood. Skin tests are sensitive and show greater specificity with quality allergen extracts (mites, pollens, animal danders). Cross-reactivity between IgE antibodies to allergens can complicate skin test results (reviewed in 1), especially in epidemiological studies where there may be little clinical follow-up. These problems may be exacerbated with less well-defined extracts such as those derived from insects, fungi or foods, which are unstandardized and may contain allergens that cross-react with mites or pollens.

A short communication by Lødrup Carlsen and colleagues in this issue of the Journal describes a high prevalence of cockroach (CR) sensitization among asthmatic children and their parents in Norway (2). Of 100 families (426 subjects) enrolled in the Genetics of Asthma International Network (GAIN) study, and who were skin tested with common inhaled allergens, 7.5% (31 subjects) were sensitized to CR as assessed by skin-prick testing (SPT) (>3 mm wheal) or serum IgE antibodies. Among sensitized subjects with at least one positive skin test, 14% were CR sensitive. However, only three of the CR-sensitized subjects gave a >3 mm skin test and had detectable serum IgE ab ($>$ class 2).

These findings are unexpected because there has neither been previous reports of CR allergy in

Scandinavia, nor of CR allergens in housing. At issue is whether these observations reflect true sensitization to CR allergens, or reflect IgE cross-reactivity with other environmental allergens to which the subjects may have been exposed. The lack of a correlation between skin tests and serum IgE ab responses suggests either that the patients were weakly sensitive to CR or that the skin-test results might reflect cross-reactivity to other allergens. The results do not seem to fit the pattern of responses seen in CR allergic patients in the US, for example, who show positive skin tests to CR, have high levels of serum IgE ab (CAP class 3–6) and usually live in CR-infested houses or apartments (3–6). Similar CR allergic asthma patients, living in low cost public housing in Strasbourg, France, gave positive skin tests to CR extracts and were exposed to high levels of Bla g 1 and Bla g 2, both in dust and airborne in their apartments (7). Other cross-sectional surveys in Europe have reported an apparently high prevalence (12–25%) of positive skin tests to CR (reviewed in 6), but the exposure to CR was not studied.

Lødrup Carlsen and colleagues investigated whether cross-reactivity could be a factor in their study but found only three cases where the subjects also had serum IgE ab to shrimps, which might be explained by cross-reactive antibodies to tropomyosin. The tropomyosin allergens from shrimp, mite and CR show $\sim 80\%$ amino acid sequence homology and tropomyosin should be considered as a potential cross-reacting allergen in cases of household insect allergy (5). Other cross-reactive allergens found in insects, mites and crustacea include paramyosin and glutathione S transferase (1, 5). Curiously, in this study, CR sensitization was most strongly associated with grass-

pollen reactivity (60%), rather than dust mite (42%), raising the question as to whether cross-reacting IgE antibodies to grass pollen proteins or carbohydrates and CR may occur. Analyzing the data according to which allergens gave the strongest reactivity on skin testing might have given further insights into potential sources of cross-reactivity. Other interesting candidates for potentially cross-reactive allergens are the recently described families of 40 kDa arginine kinase pan-allergens identified in indianmeal moths and found in mites, CR and crustacea (lobster, prawn, and mussels) (8).

The results of this study of cockroach sensitization in Norway are tantalizing and the authors were wise to leave open the clinical implications of their findings. The missing link is whether the subjects were exposed to CR allergens in their homes. In the US, visible CR infestation was observed in 80% of the homes of CR

allergic patients admitted to the Emergency Room with asthma (3). High levels of CR allergens have been reported in inner city asthma studies (3–7). Environmental exposure assessments using CR traps or dust analysis for CR allergens would have made it much easier to interpret the skin-test data. Similar measures should be used to augment and verify relevant exposures to any potential insect allergen found in the home.

The results of the GAIN epidemiology study in Norway highlight difficulties that can arise in assessing allergen sensitization based on diagnostic criteria alone. They confirm that it is unwise to make assumptions about allergen exposure (9). A combination of skin tests, serum IgE ab measurements and exposure assessment is needed to clearly ascertain the importance of allergen sensitization (10) in epidemiologic studies of asthma.

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