

Exposure to indoor inhalant allergens

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S. Lau

Berlin, Germany

S. Lau, University Children's Hospital, Rudolf H. Virchow, Augustenburger Platz, D-13353 Berlin, Germany

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Exposure and sensitization to inhalant allergens precedes the onset of respiratory disease in childhood. Epidemiological studies indicate that the prevalence of allergic airway disease has been increasing during the last decades, especially in countries with so called "western lifestyle". We now spend 95% or more of our time in tightly sealed, overheated buildings, an environment where allergen sources like house dust mite find a favourable climate to grow - one factor why indoor allergen exposure increased. Many studies suggested a causal relationship between exposure to indoor allergens, sensitization and asthma. Several cross-sectional studies in older children indicate that specific sensitization to house dust mites is related to dust mite allergen concentrations in mattress dust (1, 2). Exposure threshold levels for several indoor allergens have been proposed, but individuals vary widely in their susceptibility to levels of exposure, and no absolute value has been identified which could generally ensure minimum risk.

Assessment of the relationship between indoor allergen exposure, sensitization and allergic airway disease. Major allergens of house dust mite *Dermatophagoides* species (*Der p* 1, *Der f* 1), cat (*Fel d* 1) and dog (*Can f* 1) have been identified and can be measured in immunoassays.

When studying exposure of indoor allergen, sensitization and asthma, the setting of the study will decide if we will get an useful answer to our question. If we study a population where no allergen is present because of climatic conditions (for example, Los Alamos, New Mexico, with a low presence of mite allergen (3)) we will find a low prevalence of sensitization and will face difficulties in studying symptoms. In areas with a very high prevalence of allergen, we will find similar exposure in houses of asthmatic sensitized, asthmatic non-sensitized and nonasthmatic control patients (Marks & Tovey (4) in Sydney, Australia failed to find a relationship between exposure and allergic disease).

Other areas showed different results: Korsgaard (5) reported that asthmatic patients with mite allergy lived in houses with higher levels of allergen than random control subjects. In Marseille, Vervloet et al (6) observed a dose-response relationship between mite allergen concentration in dust and severity of asthma symptoms among individuals with mite allergy. In Sweden, where house dust mites are found in homes relatively infrequently, the presence of mite allergens has been reported to relate to asthmatic symptoms (7). For older children a dose response relationship effect between exposure and asthmatic symptoms has been difficult to demonstrate because many factors may simultaneously influence the severity of asthma (8). Sporik (9) in his birth control study was able to demonstrate that the onset of wheezing in later childhood is related to the amount of *Der p* 1 in mattress dust samples in infancy. However, the evidence for a dose-response effect between mite allergen exposure and disease severity was indirect and largely circumstantial. Our group was not able to show a relationship between wheezing during the first two years of life and allergic sensitization or a positive family history of atopy.

Threshold levels?

A cross-sectional study on children demonstrated that an exposure of greater than 2 µg of group 1 mite allergen per gram of dust in homes represents a risk for developing positive skin test responses and serum IgE antibodies (1). Much of these data apply to genetically predisposed individuals. In a prospective study on 1802 children, Kühr et al (2) were able to demonstrate a dose-response relationship between the concentration of mite allergen on bedding and sensitization of atopic school children (with pre-existing other inhalant allergies). Increased risk for sensitization became significant at approximately 2 µg/g of group 1 allergen per gram. In contrast, the data showed that sensitization of children who did

not have a pre-existing positive skin test response to an inhalant allergen other than mite (nonatopic) required exposure to concentrations of mite allergen as high as 89 µg/gm. For cat and dog allergen no consistent data on threshold levels have been reported (3). There does not seem to be just a simple dose-response relationship between quantitative exposure to indoor allergens and sensitization or symptoms, even if there was one, the variability between individuals would obscure it. Furthermore, we always face methodological problems, i.e., we never know how reliable the measurement of allergen is. Airborne measurements are good for animal-derived allergens, but in an undisturbed room they are not good for mite allergen measurements, where we prefer solid dust samples, although this method does not represent the amount of allergen entering the patient's lung. We assume that the amount of allergen is closely related to the degree of inflammation and that the degree of inflammation is related to the severity of disease (10). We get indirect evidence by studies showing a decrease in bronchial hyperreactivity while reducing mite antigen in the environment of sensitized asthmatic children.

Longitudinal investigations

A German multicenter atopy study, which is now evaluated up to the age of 3 years, analyzed the exposure of mite and cat (*Der p 1*, *Der f 1*, *Fel d 1*) as measured in carpet dust samples (12). Exposure varied over a large range (median *Der p 1*+*Der f 1* appr. 200 ng/g; median *Fel d 1* 160 ng/g). Relating mite allergen exposure to the sensitization status of children at 12, 24 and 36 months (specific serum IgE), the median allergen exposure levels were higher for sensitized than non-sensitized children. In children who had been found to be sensitized at least once to house dust mite, the median carpet dust concentrations were significantly higher than for the non-sensitized group (median allergen concentrations: 868 ng/g versus 210 ng/g dust; $p < 0.001$). Similar results were found for children sensitized to cats regarding sensitization status till three years of age; the median cat allergen concentrations in the group of sensitized children were significantly higher than in the group of non-sensitized children (median allergen concentrations: 150 ng/g versus 64 ng/g dust). However, for cat allergen the difference in allergen exposure is not that clear. In homes with very low (<25th percentile) carpet dust concentrations, the risk of sensitization to mite or cat allergens during the first three years of life is 1.6% or 2.0% respectively, increasing to values above 6% if the domestic major allergen exposure is above the 75th percentile, which is 1200 ng/g for *Der p 1*+*Der f 1* and 220 ng/g for the major cat al-

lergen *Fel d 1*. If stratified by atopic family history, the relationship between sensitization and allergen exposure shows different patterns. In the group with a positive family history, a mite allergen exposure below 750 ng/g is sufficient to result in a 3% sensitization rate. In contrast, an exposure up to 25,000 ng/g dust is necessary to achieve a sensitization rate of 3% in the group of children with a negative family history. Similar dose-response relationships were found for cat allergen exposure and sensitization rates cumulated over exposure levels in the two subgroups. Logistic regression analysis shows that the risk of sensitization to mite allergens increases significantly with age (odds ratio 5.2 for 2nd, 8.8 for 3rd versus first year; $p < 0.0001$). In contrast, the risk of sensitization to cat allergens remains the same ($p = 0.37$) in the second and third year when compared with the already high risk in the first year. There are indications that the increase in sensitization risk at low allergen levels is more pronounced in cat allergy than in mite allergy. Probably exposure in other places than the domestic environment may have led to specific IgE responses. Munir et al (13) have reported higher levels of *Fel d 1* in dust samples of Swedish day care centers than in family apartments.

Conclusion and intervention strategies

Since specific sensitization to mites and pets appears to be especially important among the various environmental risk factors for childhood asthma, intervention strategies have been developed in order to reduce allergen exposure. In most studies, strategies have been investigated in established diseases, where sensitization has already occurred (secondary prevention). There is only one study in the literature (14) investigating attempts to prevent or delay mite sensitization of infants at risk for atopic disease. Intervention in this study included both reduction of indoor allergen exposure as well as avoidance of exposure to food allergens in infancy. Early avoidance of even low concentrations of inhalant indoor allergens seems to be mandatory as primary prevention. If we think of allergen elimination we should take into consideration that significant allergen concentration can also be found in houses without a cat and that significant concentrations of *Fel d 1* can be found months after the removal of a cat. Cat allergens remain airborne over a long period, so their elimination may have to include air filtration. Mite allergen reduction should concentrate on mattresses (encasings), carpets (removal) and indoor humidity (optimal ventilation).

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