The prevalence of reported asthma is independent of exposure in house dust mite-sensitized children


ABSTRACT: In areas with low house dust mite (HDM) allergen exposure, both mite sensitization and asthma prevalence are low. In most other areas, HDM allergen exposure is higher than the threshold for sensitization. In this setting, is HDM allergen exposure a factor which is causally related to the development of asthma in HDM-sensitive individuals?

To answer this question, the cumulative prevalence of asthma was evaluated in a group of 157 schoolchildren, aged 10 and 11 yrs, who were allergic to HDM allergen, and compared it with HDM allergen exposure and atopic status, using univariate and multivariate analysis. HDM allergen levels were measured in mattress dust using an enzyme-linked immunosorbent assay (ELISA) method. Of mattress dust samples, 94% had an HDM allergen level >2 μg dust−1. Atopy was evaluated by means of skin prick tests using five common allergens.

Among the predictive variables studied by means of univariate analysis, only the number of positive skin tests and male sex correlated with asthma prevalence, but not HDM allergen exposure. Logistic regression analysis also demonstrated that the number of positive skin tests correlated with asthma prevalence (odds ratio (OR)=1.38, p=0.05), whereas the OR for HDM allergen exposure was 1.0.

This survey suggests that, in a geographical area with high HDM allergen exposure, asthma prevalence is not linked with HDM allergen levels.


It has been stated that house dust mite (HDM) allergen exposure is the dominant environmental cause of asthma fulfilling Bradford-Hill’s criteria for causality [1, 2]. A few studies have demonstrated a lower prevalence of asthma in areas with low HDM allergen levels [2–4] and avoidance has been shown, in some studies [5], to be useful as a primary prevention method. It is noteworthy that these areas have very particular climatic conditions (cold and/or dry), which are responsible for the very low level of mite infestation. Thus a low prevalence of asthma is associated with a low prevalence of HDM allergy. In contrast, in most other parts of the developed world, HDM allergen levels are quite high [6], leading to a high percentage of HDM allergy in the general population [7, 8]. In this setting, it is questioned whether HDM exposure could also be a factor which is causally related to the subsequent development of asthma in mite-sensitive individuals, or whether asthma is mainly linked to the atopic status. To answer this question, the cumulative prevalence of asthma was evaluated with respect to mite allergen levels and atopic status by questioning the parents of a group of schoolchildren allergic to mites.

Material

The study group included a group of 157 children, allergic to HDMs, who provided a mattress dust sample.

Protocol

These children were part of a cross-sectional epidemiological survey, performed from January to April 1993 in the Fos-L’Etang de Berre area, which is an industrial area located west of Marseilles, France. It included all the 4th and 5th grade children (mean±SD age: 10.7±0.7 yrs) from the state schools of the towns in this area, which has a mild temperate climate. The mean (±SD) annual temperature between 1985 and 1993 was 14.9±0.4 °C, and the mean (±SD) annual relative humidity (RH) was 73.0±5.0%.

The protocol included a questionnaire, which was filled in by the parents or guardians, skin tests to common allergens and measurement of mite allergens in house dust.
collected from the children’s mattresses. A bronchial challenge test to measure nonspecific bronchial reactivity, was not performed. The questionnaire, derived from the 1978 American Thoracic Society Questionnaire for children (ATS-DLD-78-C) [9], asked about socio-economic status (low, medium or high), medical history, passive smoking, divided into 3 categories (none, <10 cigarettes smoked at home when child present or >10 cigarettes daily), and asthma. Asthma was defined by a positive answer to the question: "Has your child ever had asthma?". Information on implementation of mite-avoidance procedures was not collected, apart from the possession of anti-allergic mattress covers, which were not used on any of the children’s beds. Skin prick tests were performed using a multitest device (Stallerkit®). Disposable paper bags were collected and stored at 4°C. A 7-mm diameter weal, in a group of patients sensitized to house dust mite-1 because 2 and 10 µg dust-1) have been suggested as the thresholds for sensitization to mite allergens and for the triggering of symptoms in sensitized patients, respectively [12]. Finally, logistic regression analysis was performed using the cumulative prevalence of asthma as a dependent variable, and log of HDM allergen levels, number of positive tests and sex as independent variables.

Results

The study group included 167 HDM-allergic children, whose parents provided a sample of mattress dust. However, 10 samples did not contain enough dust. Thus, 157 children were included in this study (table 1). It was noteworthy that the prevalence of asthma was similar in the children whose parents granted permission for skin testing and in those whose parents refused permission (9.0% and 10.4%, respectively). Similarly, the prevalence of asthma was similar in HDM-allergic children who provided house dust and in those who did not (23.8% and 21.8%, respectively).

Variables potentially predictive of asthma apart from house dust mite-exposure

Table 1. – Characteristics of the study group

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects n (%)</td>
<td>98 (62)</td>
<td>59 (38)</td>
</tr>
<tr>
<td>Mean (±sd) age yrs</td>
<td>10.7±0.6</td>
<td>10.7±0.8</td>
</tr>
<tr>
<td>Asthma prevalence %</td>
<td>31.5±4.7</td>
<td>12.1±4.2</td>
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</table>
of asthma apart from the number of positive skin tests (p=0.004). The mean (±SD) weal diameter of the skin reactions was 1.39±0.9 mm in the nonasthmatic children and 1.9±1.3 mm in the asthmatic children (p=0.01). The mean (±SD) weal diameters using HDM allergens were 1.64±2.06 mm and 2.76±2.43 mm, respectively.

### The influence of house dust mite-exposure

The group I allergen level varied from 0.1 (threshold) to 185.1 µg g dust$^{-1}$, with a geometric mean of 14.3 (median 19). Of note was that 94% of samples had a group I allergen level of >2 µg (fig. 1). Table 2 displays the cumulative prevalence of asthma according to HDM allergen levels. No association was found (p=0.03) between the two variables. Among the children with a history of asthma, 91.4% had an HDM allergen level >2 µg. This exposure was 94.6% in the nonasthmatic children. Linear logistic regression analysis using the cumulative prevalence of asthma as the dependent variable once again demonstrated that HDM exposure did not correlate with the cumulative prevalence of asthma (table 3). The odds ratio (OR) for the prevalence of asthma with respect to the number of positive skin tests (1 or 2 positive tests compared with ≥3 positive tests) was 1.38 (p=0.05), whereas the OR with respect to HDM allergen levels was 1.0 (p=0.44).

### Discussion

This cross-sectional epidemiological study strongly suggests that atopic status is the major risk factor for the occurrence of asthma, as opposed to mite allergen exposure. In the present data, an increased risk of asthma, according to the number of positive skin tests found, was marginally significant. This is because the study group only included children allergic to mites, and because mite allergens are known, amongst all common aeroallergens, as those which are predictive for the occurrence of asthma [14]. In other surveys including children both sensitized and nonsensitized to mites, this association is stronger [14]. In this latter study, the percentage of asthma symptoms increased, in a dose-dependent manner, from 34.3% in nonatopic children to 90% in children sensitized to seven or more allergens.

The new finding emerging from this survey is that mite allergen exposure was not a risk factor for the occurrence of asthma among children already sensitized to mite allergens. Dust sampling was performed by the parents. The percentage of samples containing <100 mg dust was only 17%, indicating that sampling was performed correctly in most cases. In this cross-sectional study, cumulative asthma was compared with a single mite allergen measurement performed at the time of the study. However, mattresses can be considered as allergogenic reservoirs, thus providing an index reflecting cumulative exposure. Few studies show that mite allergen exposure is a risk factor for the occurrence of asthma. The study of Sporik et al. [15] did not find any difference in mite allergen exposure levels among the subgroups "no history of wheezing", "history of wheezing", "active wheezing and bronchial hyperreactivity" and "receiving medication". There was no relationship between exposure to mite allergens at the age of 1 yr and current symptoms. Such a relationship was demonstrated only in atopic children, but it could be argued [16] that the children who developed asthma were also those who were most atopic. In addition to the study of Sporik et al. [15], mentioned above, another larger prospective study was conducted in schoolchildren aged 7–10 yrs [17]. It concluded that the occurrence of asthma in mite-sensitized children was not dependent upon mite exposure. Another important study, performed in a large group of Australian schoolchildren [2], convincingly demonstrated a close correlation between risk of current asthma in HDM-sensitized children and HDM allergen levels. However, in this latter study, HDM allergen levels were very high in some communities and very low in others. The other available evidence for a causal relationship between mite exposure and the occurrence of asthma comes from studies performed at high altitude. A significantly lower prevalence of asthma could be demonstrated in adults [18], with a similar trend exhibited in children [3]. In populations living at high altitude, exposure to mite allergens is approximately 50-times less than that at sea level [3]. Such low exposure levels lead to a low prevalence of mite allergen-sensitization [19, 20], which

<table>
<thead>
<tr>
<th>Subject*</th>
<th>Asthma prevalence %</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Socio-economic status Low 38 27.5</td>
<td></td>
</tr>
<tr>
<td>Medium 52 37.7</td>
<td></td>
</tr>
<tr>
<td>High 48 34.8</td>
<td></td>
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<tr>
<td>Passive smoking* Absent 71 22.6</td>
<td></td>
</tr>
<tr>
<td>Moderate 43 27.9</td>
<td></td>
</tr>
<tr>
<td>High 19 36.8</td>
<td></td>
</tr>
<tr>
<td>No. positive 1 or 2 99 17.1</td>
<td></td>
</tr>
<tr>
<td>skin tests ≥3 41 43.9**</td>
<td></td>
</tr>
<tr>
<td>Group I mite allergen µg g$^{-1}$ &lt;2 µg 9 33.3</td>
<td></td>
</tr>
<tr>
<td>2-10 µg 31 19.4</td>
<td></td>
</tr>
<tr>
<td>&gt;10 µg 100 26.0</td>
<td></td>
</tr>
</tbody>
</table>

* Some values missing. -: absent; none; moderate: <10 cigarettes daily; high: >10 cigarettes daily. **: p<0.01.

![Fig. 1. Relative cumulative frequency distribution of group I allergen concentrations in mattresses.](image-url)
is in turn responsible for a lower prevalence of atopic diseases. Such differences in mite allergen-exposure are unlikely to be commonly found within the same geographical area [21, 22]. Therefore mite-sensitization occurs in all genetically predisposed individuals, irrespective of the magnitude of the exposure. This is due to the ubiquitous nature of these antigens. In like manner, the presence of pets inside the house does not influence the development of atopy in children [23, 24] because these allergens can be detected at significant levels even in houses without pets. Recent experimental and epidemiological investigations strongly suggest that the threshold for allergic sensitization to HDMs might be well below 2 μg·g dust⁻¹ [25]. IRE and ZETTERSTROM [26] performed bronchial allergen challenges once a day over 7 consecutive working days in a group of asthmatic subjects. No immediate symptoms were recorded. Interestingly, non-specific bronchial hyperreactivity, as measured by bronchial histamine provocation tests, increased significantly after the allergen challenge period in comparison with that found beforehand. The specific challenge consisted of inhalation of 1 ng of a major allergen for a few minutes per day. PRICE et al. [27] suggested a lower threshold (0.5 μg·g dust⁻¹) for sensitization, based on the results of a retrospective study in infants. WARNER et al. [28] compared current HDM allergen-exposure at home, in 124 children with perennial asthma living in Sweden, with skin reactivity and specific serum immunoglobulin E directed against mites. There were 45 houses with HDM allergen concentrations of 0.016–2 μg·g dust⁻¹. Fifteen of the children living there were sensitized to HDMs. Statistical analysis revealed that the HDM-exposure level was associated with sensitivity, even at the low range of allergen concentrations found. There was also a strong correlation between HDM-exposure and serum mite-specific immunoglobulin E levels, even for HDM levels well below 2 μg·g dust⁻¹.

In conclusion, the risk of the occurrence of asthma in sensitized individuals depends on the degree of atopy (number of positive skin tests). Mite allergen exposure was not predictive of the occurrence of asthma. The authors’ hypothesis is that house dust mite-exposure is so ubiquitous in the area studied that virtually all genetically-predisposed individuals become sensitized to mites, whatever the HDM allergen level, which were in most cases far above the threshold for sensitization.

Acknowledgements. The authors would like to thank the staff of the schools (medical director: F. Brisse) who helped in organizing data collection, and the children and their families who participated in the study.

Table 3. – Logistic regression analysis relating cumulative asthma prevalence to predicting variable (group I allergen level is omitted because it is not predictive)

<table>
<thead>
<tr>
<th>Variable</th>
<th>b</th>
<th>SEM</th>
<th>Wald</th>
<th>df</th>
<th>p-value</th>
<th>r</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. positive skin tests</td>
<td>0.4779</td>
<td>0.1826</td>
<td>6.8474</td>
<td>1</td>
<td>0.0089</td>
<td>0.1859</td>
<td>1.62 (1.13–2.31)</td>
</tr>
<tr>
<td>Sex (male:female)</td>
<td>1.3350</td>
<td>0.4916</td>
<td>7.3735</td>
<td>1</td>
<td>0.0066</td>
<td>0.1958</td>
<td>3.80 (1.45–9.96)</td>
</tr>
</tbody>
</table>

df: degrees of freedom; OR: odds ratio; CI: confidence interval.

References


