

Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma

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Summary

Background and objectives The determinants of variability in the clinical expression of atopy are still to be documented. The goals of this study were to determine, in subjects with a clinical diagnosis of symptomatic asthma or rhinitis, what is the possible contribution of different types of indoor and outdoor allergens to the development of their disease, by looking at the prevalence and degree of sensitization to these allergens according to age and gender.

Subjects and methods We analysed allergy skin prick tests to common airborne indoor and outdoor allergens in 3371 consecutive patients, grouped according to diagnosis of allergic asthma, rhinitis, or both. For each of these three groups, we calculated the prevalence of sensitization to indoor/outdoor allergens, the atopic index (AI), the number of positive responses to allergy skin prick test and the mean wheal diameter (MWD) of these responses.

Results The prevalence of atopy and the values of AI and MWD peaked in subjects aged 16 to 25 years, declining afterwards; in subjects ≥ 18 years old, atopic indices were slightly higher in men than in women. In atopic subjects, the prevalence of sensitization was, in decreasing order: housedust (84.2%), cat hair-epithelium (76.5%), dog hair-dander (63.0%), house dust mite (54.2%), grasses (51.9%), trees (47.2%) and ragweed pollens (44.9%) and finally, moulds (25.4%). Among subjects sensitized only to outdoor allergens ($n = 195$), 73.8% had a rhinitis, 11.8% had asthma and 14.4% had both diagnoses; for those sensitized only to indoor allergens ($n = 710$), these values were respectively 48.6, 24.5 and 26.9%, and for those sensitized to both indoor and outdoor allergens ($n = 1793$), the comparable values were 55.5, 14.6 and 29.9%.

Conclusion These data show that in our population of subjects with respiratory allergic symptoms, indoor allergen sensitization is strongly associated with asthma, while exclusive sensitization to pollens is associated primarily with rhinitis. Sensitization was more prevalent for indoor allergens than for outdoor allergens in all groups determined according to diagnosis or age. Indices of atopy were higher in men in the group ≥ 18 years old. Prevalence and degree of sensitization were shown to peak in young adults, regardless of the allergen, and to diminish with age. This study stresses the role of indoor allergens in the development of asthma and shows the variability of allergic manifestations according to the type of sensitization.

Keywords: asthma, rhinitis, atopy, indoor and outdoor allergens

Clinical and Experimental Allergy, Vol. 27, pp. 52–59. Submitted 24 October 1995; revised 31 May 1996; accepted 10 June 1996.

Introduction

Asthma and rhinitis of allergic origin are two common respiratory conditions in North America, and their prevalence and severity seem to have increased in industrialized countries over the last few years [1,2,3]. These diseases are believed to result from an allergen-induced inflammatory process of the upper or lower respiratory mucosa of sensitized subjects [4,5]. It is, however, unknown why some subjects develop only an allergic rhinitis while others develop asthma as well. Several factors are involved in determining the pattern of respiratory symptoms following exposure to allergens [6–9]. Subjects with allergic rhinitis and pulmonary symptoms, when compared with individuals with rhinitis alone, express a greater sensitivity to allergens both at skin and bronchial levels, higher specific IgE levels and increased mediator release during allergen challenge [10]. Additional factors may also be important in determining the pattern of respiratory symptoms after environmental exposure to allergens. These factors include the degree of bronchial lability, the type of allergen to which a subject becomes sensitized, the duration or intensity of sensitization and/or exposure and, possibly, the subject's genetically determined response to the allergic stimulus. However, the relative importance of the various factors remains to be documented.

A large proportion of asthmatic and rhinitic subjects are sensitized to common allergens of indoor or outdoor origin [11–13]. Sensitization to these allergens seems to be influenced by different factors, including genetic susceptibility, age at which the exposure begins and the degree and type of allergen exposure [13,14,15]. Recent improvements in the insulation of houses and buildings have led to increased awareness of the role of indoor allergens in the development of allergic respiratory diseases [16,17]. As most city dwellers spend the bulk of their time indoors, exposure to indoor allergens may have a strong influence on the development of allergic diseases.

This study was therefore undertaken to determine the comparative prevalence of sensitization to indoor and outdoor allergens in subjects who reside in the Quebec City metropolitan area, and to determine if the prevalence and degree of sensitization to these allergens was different in the presence of asthma, rhinitis or both diagnoses. The type and degree of sensitization according to age group and gender were also examined.

Subjects

Data were obtained from subjects referred to the asthma and allergy clinics of two university-affiliated hospitals, the Centre Hospitalier de l'Université Laval and Laval Hospital, Sainte-Foy, Quebec. A total of 3371 computerized data files

Table 1. Prevalence of sensitization to common allergens according to diagnosis

	Asthma (%)	Rhinitis + asthma (%)	Rhinitis (%)
<i>Indoor allergens</i>			
House dust	83.2	88.6	82.2
Cat hair-epithelium	75.4	86.0	72.1
Dog hair-dander	65.6	75.2	56.0
House dust mite	49.5	60.0	52.6
<i>Outdoor allergens</i>			
Grass pollen	36.2	54.5	55.5
Tree pollen	35.1	48.5	50.3
Ragweed pollen	29.9	45.2	49.3
<i>Indoor and outdoor allergens</i>			
Moulds (<i>Alternaria</i>)	20.9	27.4	25.8

of subjects with diagnoses of asthma and/or rhinitis were sufficiently complete to allow the present analysis (Table 1). Subjects included 1932 women (57.3%) and 1439 men (42.7%); 72.6% of the women and 56.2% of the men were >18 years old. Of those, 82.7% of the men and 78.1% of the women were atopic, as defined by at least one positive response to the allergens tested (mean wheal diameter of 3 mm or more, according to previously published guidelines [18,19]).

Inclusion criteria were: (a) a clinical diagnosis of allergic rhinitis and/or asthma made by the consulting allergist or chest physician, based on symptoms and pulmonary function tests (including methacholine challenge for some of the subjects); and (b) submission to a battery of allergy tests for various common airborne allergens, using the skin prick test technique.

Files of subjects with uncertain diagnoses were excluded, as were those of subjects who had a negative response to the histamine skin test control (wheal diameter <3 mm). Also excluded were subjects who had used antihistamines within a week (1 month for astemizole) of the allergy skin test.

Classification of subjects

The subjects were divided into three groups according to the diagnosis of asthma, rhinitis or both. All subjects were also sub-divided into three sub-groups according to their sensitization to exclusively indoor, exclusively outdoor or both indoor and outdoor allergens. Finally, data were analysed according to age group: 0–5 years, 6–15, 16–25, 26–45, 46–65, and over 66 years old [20].

Methods

Evaluation and definitions

The following parameters were obtained: age, sex, diagnosis, specialist-confirmed diagnosis of asthma or rhinitis (allergic or non-allergic) and results of allergy skin prick tests from a battery of eight airborne allergens. The atopy index (AI) represents the total number of allergens out of the eight tested to which the subject had a positive response. The mean wheal diameter (MWD) of responses was calculated. The data were obtained from two computerized databases using the program '4th dimension' (MacIntosh).

Allergy skin prick tests

The skin tests were done by the allergist or chest physician, using the prick test method, as described by Pepys [18]. Interpretation was according to current guidelines [19]. For all subjects, the wheal response was read at 10 min and reported as an absolute value in mm (mean of the largest diameter and the largest perpendicular to it). The response to the following eight allergens, grouped to reflect indoor and outdoor exposure, was noted. (a) Indoor allergens: house dust (weight/volume 1:10), cat hair-epithelium and dog hair-danders (both 1:10) and *Dermatophagoides farinae* (house dust mite; 30 000 PNU/ml). (b) Outdoor allergens: mixed grasses (1:20), mixed trees (1:20) or ragweed pollens (1:20). (c) Indoor/outdoor allergens: moulds (*Alternaria* 1:10). We obtained each specific from a consistent source, either Bencard (Montreal, Quebec) or Omega (Montreal, Quebec). Other allergens could have been tested in these subjects, but a subject was considered non-atopic only if the skin response to all allergens tested was negative. As allergens used for prick tests came from different batches over time, we regularly verified their potency by skin test end-point titration in a group of control atopic subjects.

Data analysis

Analysis has been done both including and excluding house dust, as it is an uncharacterized allergen extract which is likely to contain a mixture of both indoor and outdoor allergens. The atopic index has also been calculated both including and excluding house dust.

Values are given as mean $\pm$ one standard deviation. We used the chi-square test to compare the different percentages and *t*-tests to look at means. We compared the different groups and age classes using an analysis of variance (ANOVA) with a Tukey test to determine which groups were significantly different from each other ($P < 0.05$). For graphical representation of the data, results of representative measures

were expressed as mean values $\pm$ SEM. For Figure 2, the correspondence analysis [21] was used to represent graphically a contingency table (data matrix) of association between the type of allergen and diagnoses of asthma, rhinitis or both. This technique makes it possible to represent the frequency of sensitization to each type of allergen according to the diagnosis. When two points representing diagnosis are close, they must have similar proportions in types of allergen sensitization. In the same manner, if two points representing two types of allergen are close, they must have the same frequency distribution for diagnosis. When these two points are opposed along a straight line, that means they have opposite profiles. The origin of the axes corresponds to the average profile of diagnosis and type of allergen.

For Table 4, we used parametric analysis with no transformation on data, as the normality and homogeneity of variance assumptions were not rejected. We performed the Tukey's comparison technique to compare mean values.

Results

Prevalence of sensitization to common allergens in the studied population

Eighty per cent of the subjects included in the study were allergic, reflecting the fact that those subjects were referred to specialized asthma and respiratory allergy clinics.

Prevalence and degree of sensitization to indoor and outdoor allergens

The majority of allergic subjects were sensitized to indoor allergens (92.7%), but many (66.4%) were also sensitized to at least one outdoor allergen. Among the total population studied, 21.1% were sensitized exclusively to indoor allergens, 5.8% exclusively to outdoor allergens and 53.2% to both types of allergens.

In subjects sensitized to both indoor and outdoor allergens ($n = 1793$), the atopic index was significantly higher than in those sensitized exclusively to outdoor allergens ($n = 205$) or to indoor allergens ($n = 710$) (respectively 5.5 ± 1.5 , 1.7 ± 0.9 and 2.6 ± 1.0 , P value for the overall variation: <0.0001 , pair-wise value: <0.05). When house dust was excluded, leaving three different allergens in either the indoor or outdoor category, the mean atopic index was 1.9 ± 0.8 in subjects sensitized to indoor allergens only ($n = 656$), similar to the index measured in subjects sensitized to outdoor allergens only (1.80 ± 0.9 , $n = 272$, $P > 0.05$). The mean wheal diameter of the response to prick tests was significantly higher in the group of subjects sensitized to both types of allergens (3.9 ± 1.6 mm), followed by the group sensitized exclusively

to indoor allergens (2.7 ± 2.3 mm), and finally by the group sensitized to outdoor allergens alone (2.3 ± 1.4 mm, $P < 0.0001$); when house dust was excluded from the analysis, the Tukey comparison showed no significant difference between the mean wheal diameter of the groups sensitized exclusively to indoor or outdoor allergens (respectively 1.5 ± 0.9 and 1.5 ± 1.0 mm).

Prevalence and type of sensitization according to gender and age

Among allergic subjects, the atopic index was slightly higher in men than in women (4.6 ± 2.0 and 4.3 ± 2.0 , $P = 0.0003$), as was the mean wheal diameter (3.3 ± 1.8 and 3.1 ± 1.7 mm, $P = 0.002$). Looking at subjects $<$ and $>$ 18 years old separately, we found that all indexes were similar in men ($n = 511$) and women ($n = 418$) under 18 years old, while for those $\geq$ age 18, the atopic index was 4.76 in men and 4.30 in women, and the mean wheal diameter was 3.53 in men and 3.11 in women, with P values all < 0.0001 .

Distribution of subjects according to diagnosis

The 3371 subjects included 1403 with allergic ($n = 1214$) or non-allergic ($n = 189$) asthma. In all patients with asthma, 582 had no diagnosis of rhinitis (allergic = 459, non-allergic = 123). A total of 2789 subjects had a

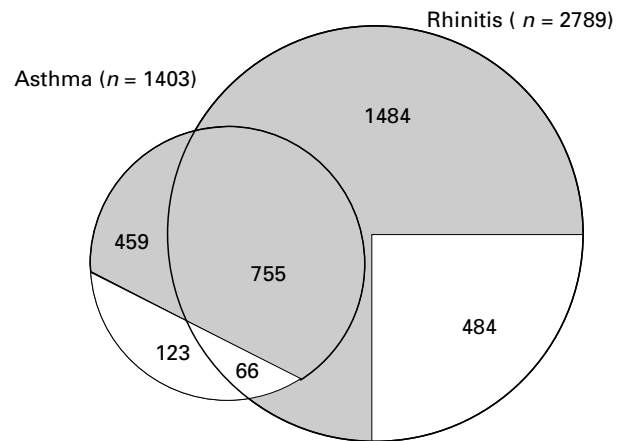


Fig. 1. Number of allergic and non-allergic subjects within groups of subjects with asthma and/or rhinitis. □ = non-allergic; ■ = allergic.

rhinitis, either allergic ($n = 2239$) or not ($n = 550$); 2068 of the subjects with rhinitis, either allergic ($n = 1484$) or not ($n = 484$), had no associated asthma (Figure 1).

Prevalence and degree of sensitization to allergens according to diagnosis

In atopic subjects, indoor allergens were the most significant source of sensitization. The overall prevalence of

Table 2. Number (n) and percentage (%) of allergic subjects sensitized to indoor, outdoor or both indoor and outdoor allergens

	Asthma	Rhinitis + asthma	Rhinitis	Total (100%)
<i>Indoor allergens</i>				
A	174	191	345	710
B	37.9%	25.3%	23.3%	
C	24.5%	26.9%	48.6%	
<i>Outdoor allergens</i>				
A	23	28	144	195
B	5.0%	3.7%	9.7%	
C	11.8%	14.4%	73.8%	
<i>Indoor and outdoor allergens</i>				
A	262	536	995	1793
B	57.1%	71.0%	67.0%	
C	14.6%	29.9%	55.5%	
Total (100%)	459	755	1484	2698

A = Number of subjects

B = Percentage of subjects from each group sensitized to indoor, outdoor or both indoor and outdoor allergens. Example: 37.9% (174/459) of asthmatic subjects were sensitized only to indoor allergens.

C = Percentage of subjects sensitized to indoor, outdoor or both indoor and outdoor allergens belonging to each group. Example: 24.5% (174/710) of subjects sensitized only to indoor allergens belong to the asthma group.

sensitization for this group was, in decreasing order: house dust (84.2%), cat hair-epithelium (76.5%), dog hair-dander (63.0%), house dust mite (54.2%), grasses (51.9%), trees (47.2%), ragweed pollens (44.9%) and finally, moulds (25.4%, Table 1).

The mean ages of allergic and non-allergic subjects in the groups with asthma and rhinitis were respectively: 25.18 ± 0.02 and 41.75 ± 0.31 years ($P < 0.0001$); in the group with asthma, they were 28.45 ± 0.04 and 46.95 ± 0.15 ($P < 0.0001$); and in the group with rhinitis, they were 26.68 ± 0.01 and 26.30 ± 0.04 ($P > 0.05$).

Of the 3371 subjects studied, the proportions sensitized to indoor and/or outdoor allergens were, respectively, 68.1/57.9% in non-asthmatic rhinitic subjects and 88.6/68.7 and 74.9/49.9% in asthmatic subjects with and without rhinitis. Among those subjects who were sensitized, the percentages sensitized exclusively to indoor allergens, exclusively to outdoor allergens, and to both are given in Table 2. As shown in Figure 2, asthma was strongly associated with indoor allergens and rhinitis with outdoor ones.

Among subjects sensitized only to outdoor allergens ($n = 195$), the incidence of rhinitis only was 73.8%, of asthma only 11.8%, and of both diagnoses 14.4%; among those sensitized only to indoor allergens ($n = 710$), these values were 48.6, 24.5 and 26.9%; for those sensitized to both types ($n = 1793$), they were 55.5, 14.6 and 29.9%.

The atopic index was significantly higher in the group with both asthma and rhinitis (4.8 ± 2.0) than in those with

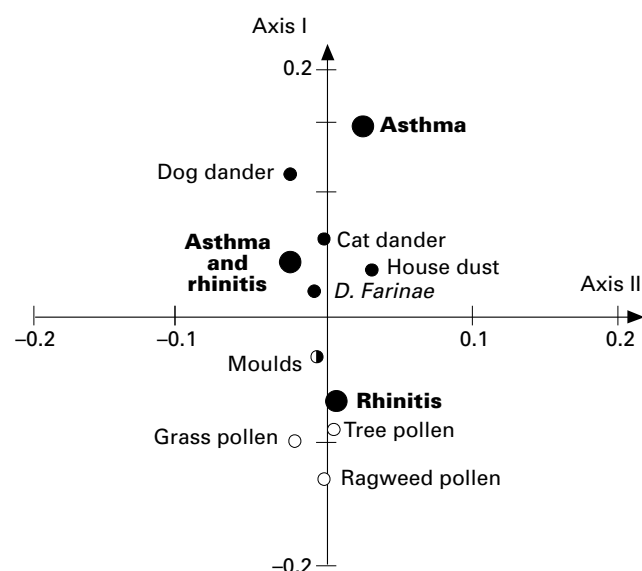


Fig. 2. Associations among diagnoses of asthma, rhinitis, and both, according to the type of allergen. These reflect the potential contribution that sensitization to the different allergens makes to the clinical expression of allergy.

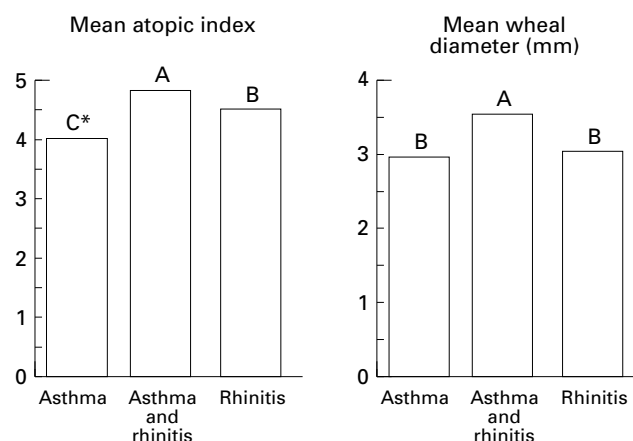


Fig. 3. Mean atopic index (4.0 ± 2.0 , 4.8 ± 2.0 , 4.4 ± 2.0) and mean wheal diameter (2.9 ± 1.8 mm, 3.5 ± 1.9 mm, 3.0 ± 1.7 mm) compared among subjects with diagnosis of asthma, asthma and rhinitis, or rhinitis. *Tukey's test: groups with different letters are significantly different ($P < 0.05$).

exclusively asthma (4.0 ± 2.0) or rhinitis (4.4 ± 2.0 , $P < 0.0001$; Figure 3), but it remained in the same proportions among the three groups when house dust was excluded from the analysis (asthma: 3.1 ± 1.8 , asthma and rhinitis: 3.9 ± 1.8 and rhinitis: 3.6 ± 1.9 , $P < 0.0001$).

The mean wheal diameter was significantly greater in the group with asthma and rhinitis (3.5 ± 1.9 mm) than in the groups with either asthma (2.9 ± 1.8 mm) or rhinitis (3.0 ± 1.7 mm, $P < 0.0001$); these latter two groups showed no statistically significant difference; when house dust was excluded, the changes were minimal.

Prevalence and degree of sensitization according to age category

The age distribution of subjects was: category 0–5 years, 2.5%; 6–15 yr, 27.0%; 16–25 yr, 21.6%; 26–45 yr, 34.1%; 46–65 yr, 12.6%; and over 66 yr, 2.2%. The prevalence of sensitization to common allergens increased with age from category 0–5 yr to category 16–25 yr, and then decreased progressively. The maximal prevalence was in age category 16–25 yr, with 91.5% of subjects being sensitized to at least one common allergen; it then decreased to 44.4% in the age category over 66 yr. It was in age category 16–25 yr that we observed the highest percentage of subjects sensitized to both indoor and outdoor allergens; in this same age category we also noted the lowest percentage of subjects sensitized exclusively to either indoor or outdoor allergens.

The relative proportion of allergens to which subjects were sensitized remained the same in all age categories, with indoor allergens being the most frequent (house dust,

Table 3. Percentage of subjects sensitized to each allergen according to age

Allergen	Age category (yr)					
	I 0–5	II 6–15	III 16–25	IV 26–45	V 46–65	VI ≥ 66
House dust	(1) 40.0	(1) 68.1	(1) 80.1	(1) 70.5	(1) 46.8	(1) 42.1
Cat hair-epithelium	(2) 37.7	(2) 64.2	(2) 74.9	(2) 63.3	(2) 36.1	(3) 31.9
Dog hair-dander	(3) 30.6	(3) 47.0	(3) 62.1	(3) 54.7	(3) 34.2	(4) 27.1
<i>D. Farinae</i>	(4) 20.0	(4) 46.7	(4) 54.2	(7) 41.0	(4) 30.6	(2) 32.7
Grass pollen	(6) 12.9	(5) 39.8	(5) 53.9	(4) 45.2	(6) 24.5	(6) 21.5
Tree pollen	(4) 20.0	(6) 31.9	(6) 50.4	(5) 42.9	(7) 22.6	(7) 16.8
Ragweed pollen	(8) 7.1	(7) 29.4	(7) 46.5	(6) 41.0	(5) 24.9	(5) 23.4
Moulds (<i>Alternaria</i>)	(7) 10.6	(8) 19.9	(8) 26.7	(8) 21.3	(8) 11.4	(8) 9.4

*Rank order of allergens from 1 to 8 by category of age, according to the percentage of subjects sensitized (from 1 = highest to 8 = lowest % of subjects sensitized).

cat hair-epithelium, dog hair-dander and house dust mite) (Table 3). The mean atopic index and mean wheal diameter are shown in Table 4.

Discussion

We should first point out that this study was not a survey of a representative sample of the whole population of the Quebec metropolitan area, but rather an evaluation of a specific population presenting with symptoms of respiratory allergy and referred to one of two asthma and allergy tertiary centers. Therefore, our conclusions should be restricted to this particular population, although these observations provide us with useful information on the type of sensitization observed and the clinical expression of the allergic status.

Furthermore, we realize that many atopic subjects have no respiratory symptoms, but the present evaluation is

restricted to those who have symptoms of either asthma and/or rhinitis and not to the overall atopic population, where we looked at the comparative prevalence and degree of sensitization to relevant indoor/outdoor allergens.

We found that the majority of the subjects we studied, with asthma and/or with rhinitis, were sensitized to indoor aeroallergens. Sensitization to this last category of allergens seemed to contribute to both allergic rhinitis and asthma, while exclusive sensitization to pollens was found most commonly in subjects with rhinitis. Prevalence of atopy and atopic indices peaked at 16–25 yr, regardless of the type of allergen, and thereafter decreased progressively with age.

Allergy plays an important role in the development of asthma and rhinitis. Increased exposure to indoor allergens has been suggested as a potential explanation for the recently described increase in the prevalence of allergic diseases [1,2]. However, while the duration of exposure, intensity, allergenic particle size and type of allergen to

Table 4. Mean atopic index and mean wheal diameter according to age

Age (yr)	Mean atopic index	Tukey's**	Mean wheal diameter (mm)	Tukey's**
0–5	2.9 ± 1.6 (2.4 ± 1.3*)	C	2.0 ± 1.2 (1.9 ± 1.1)	D**
6–15	4.4 ± 1.9 (3.6 ± 1.7)	B	2.9 ± 1.5 (2.7 ± 1.4)	C
16–25	4.9 ± 2.0 (4.1 ± 1.8)	A	3.6 ± 1.8 (3.5 ± 1.8)	A
26–45	4.5 ± 2.0 (3.8 ± 1.8)	B	3.3 ± 1.9 (3.2 ± 1.9)	B
46–65	3.7 ± 2.1 (3.0 ± 1.8)	C	2.5 ± 1.7 (2.4 ± 1.7)	D
≥ 66	3.0 ± 1.7 (2.5 ± 1.5)	C	2.1 ± 1.4 (2.0 ± 1.4)	D

* In brackets, data when house dust is not included.

** Tukey's test: groups with different letters are significantly different ($P < 0.05$). Statistics were similar when house dust was excluded from the analysis.

which the subject is sensitized can influence the development of some types of allergic manifestation, it is still unclear why some subjects develop only a rhinitis while others develop asthma.

Rhinitis is closely associated with asthma, and subjects with allergic rhinitis, when compared with non-rhinitic subjects, have an increased airway responsiveness [22]. The nose is usually considered a protective barrier against inhalants, contributing to the reduction of allergen load to the airways. It is possible that the upper airway inflammatory reaction *per se* influences the development of bronchial inflammation and hyperresponsiveness, for example by the release of inflammatory mediators.

The type of allergen may influence the type of allergic manifestation, which may be related to its size or other properties. For example, pollen particles are somewhat larger than those of house dust or animal origin and are more easily trapped in the nose, inducing a local allergic response. We cannot, however, exclude the possibility that intensity and duration of exposure may also explain the observed differences in clinical expression of these types of allergy. In cold climates, pollen exposure is more limited than exposure to indoor allergens. Geographical distribution of allergens can also influence allergic manifestations.

Our observations are in keeping with those of Gergen and Turkeltaub [23], who showed that the prevalence of asthma and rhinitis increased with the increasing number of positive allergen skin tests. Asthma was associated with sensitization to allergens such as house dust and *Alternaria*; allergic rhinitis without asthma was associated with ragweed, ryegrass and housedust. Burrows *et al.* also showed that in allergy skin tests performed on 13-year-old New Zealand children, the size of the response to house dust mite, cat, dog and *Aspergillus* species was significantly related to the bronchial responsiveness index [24].

Regarding the relationship between atopy and age, an increased prevalence of sensitization to common allergens with age up until adulthood has been described, and this is in keeping with our findings [25,26]. There seems, however, to be a decreased effect of atopy on airway responsiveness with increasing age [27].

According to the previous publications by Sears *et al.*, atopy and current asthma were significantly more common among boys in early life than in girls [28,29]. In fact, the increase in asthma prevalence was explained by the higher incidence of atopy; these gender differences disappeared when controlled for atopic status. A roughly equivalent prevalence of asthma and atopy was found in both genders at adulthood [30–32]. In our study, in subjects <18 years old, atopic indices were similar in both genders, while in those >18 years old, they were slightly higher in males.

Different measures have been suggested to reduce the indoor antigen load and prevent outdoor antigen exposure

[33,34]. The efficacy of allergen load reduction at home has led to significant improvement in allergic asthmatic children [35]. Furthermore, some recent studies report that the fact that sensitization developed, rather than the subsequent level of exposure of sensitized subjects, is more closely related to asthma [32]; this suggests that to prevent sensitization to indoor allergens, one should begin avoidance of exposure to those allergens early.

Finally, one cannot rule out the effects of the use of different batches of allergens with time on the outcome but the standardization of the skin test material should have kept these effects to a minimum.

In conclusion, this study shows that the clinical expression of allergy is different according to the type of allergen to which subjects are sensitized, with sensitization to pollens being more closely related to rhinitis, while sensitization to indoor allergens seems a major determinant of allergic asthma. Our findings highlight the role of indoor allergen sensitization in the development of asthma and rhinitis. Early preventive measures, particularly for indoor allergens, could be the best way to reduce the prevalence and severity of allergic asthma.

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