

Sensitization to airborne allergens in children with respiratory symptoms

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Background: Allergy is one of the most common causes of respiratory symptoms in childhood and youth.

Objective: Evaluate the presence and the type of allergic sensitization in a paediatric population with respiratory symptoms.

Methods. We studied 564 consecutive children, 5 months to 17 years of age, with a male to female ratio (M/F) = 1.4, referred to our outpatient clinic in a 12-month period retrospectively. Patients were arbitrarily divided into four groups (grs) according to their age: gr1 = 5 months to 4 years old (181 patients), gr2 = 4 to 7 years (201 patients), gr3 = 7 to 10 years (96 patients), and gr4 = 10 to 17 years (86 patients). Sensitization to house dust mites, pollens, animal dander, and molds was determined by skin prick testing.

Results: Sensitization to at least one class of allergen occurred in 304 of the 564 patients (53.9%, M/F ratio = 2.0); the percentage of allergic patients increased with age as follows: 29.8% (54 patients) of the patients in gr1, 55.2% (111 patients) in gr2, 68.8% (66 patients) in gr3 and 84.9% (73 patients) in gr4 ($\chi^2 = 84.1$, $P < .01$). In the entire allergic population and in gr1 to gr3, the most common positive allergic reaction was to house dust mites ($P < .01$, χ^2 test each comparison). In contrast, gr4 patients showed a nearly equal percentage of sensitization to pollens and to house dust mites (79.5% and 78.1% respectively) ($\chi^2 = 0.0$, $P > .1$). Sensitization to only one class of allergen occurred in 51.3% of the allergic patients and the percentage of these monosensitized patients tended to decrease from gr1 to gr4 ($\chi^2 = 15.2$, $P < .01$). In the monosensitized group, sensitization to house dust mites was the most frequent in gr1 to gr3 (age < 10 years) as in the whole sample. In gr4, the frequency of sensitization to house dust mites was similar to that of sensitization to pollens. On the contrary, within the patient group sensitized to two or more allergens (polysensitized patients), sensitization to house dust mites was as frequent as sensitization to pollens already in gr2 as compared with monosensitized patients.

Conclusions: In children with respiratory symptoms, the percentage of allergic individuals was high and increased with the age of the patients. This phenomenon was associated with an age-related enhancement in the ratio of polysensitized to monosensitized patients and with an age-related increase in the frequency of sensitization to seasonal allergens (ie, pollens).

Ann Allergy Asthma Immunol 1996;76:239–244.

INTRODUCTION

The incidence and prevalence of the atopic diseases, including asthma, have increased in recent decades.^{1–6} They

have been associated with different factors, including progressive movement from breast-feeding to formula-feeding of infants^{7–9} and enhanced outdoor and indoor air pollution.^{10–27} The degree and type of sensitization may be related not only to genetic factors but also to the intensity (concentration of allergens in the air) and duration of exposure.²⁸ In fact, the pathogenetic determinants leading to clinical manifestations of atopy are both genetic predisposition and environmental fac-

tors.^{29,30} It is likely that subjects genetically prone to sensitization require prolonged exposure to allergen for development of symptoms of respiratory allergy. Increases in the percentage of allergic subjects with age should be expected, in agreement with data previously reported.^{31–36} Although some factors facilitating the development of allergy have been identified,^{29,30,37–39} the development of allergic sensitization in children and factors that may influence sensitization to one or more different types of allergens are still unknown.

The aim of the present study was to evaluate retrospectively prevalence and characteristics of allergic sensitization to the four most common classes of airborne allergens in a population of children with respiratory symptoms in Liguria (an Italian region located in the Northwestern sea coast).

MATERIALS AND METHODS

Patients

We retrospectively analyzed the records of children who attended as outpatients the Pulmonology Department of the Giannina Gaslini Institute (Genoa, Italy) for respiratory symptoms (asthma and/or rhinitis), in the period January–December 1992; these patients were referred to our department by their primary care physicians. Five hundred sixty-four consecutive patients, 331 males and 233 females [male to female ratio (M/F ratio) 1.4], aged between 5 months (mo) and 17 years (yr) were included in this study. The patient evaluation included case history, physical examination, and skin prick test; the diagnosis of asthma, defined by clinical manifestations according to the guidelines proposed by the Medical Section of the American Lung Association,⁴⁰ was established in

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Supported by Grant "Ricerca Finalizzata Farmacogenetica n° 93.14.01F", from Ministero della Sanità, Roma.

Received for publication March 14, 1995.

Accepted for publication in revised form June 28, 1995.

362 patients (64.2%). At the time of the visit, no patient was currently treated with antihistamines or systemic corticosteroids. According to their age, the patients were arbitrarily divided into four groups: group 1 (gr1 = 181 patients; 5 mo to 4 yr old), group 2 (gr2 = 201 patients; 4 to 7 yr), group 3 (gr3 = 96 patients; 7 to 10 yr), and group 4 (gr4 = 86 patients; 10 to 17 yr).

Skin Prick Test

Sensitization to the four most common classes of airborne allergens was determined by skin prick testing. The panel included (1) house dust mites (*Dermatophagoides pteronyssinus* 5,000 PNU/mL and *Dermatophagoides farinae* 5,000 PNU/mL), (2) pollens (*Parietaria officinalis* 1,000 UP/mL, mix of Graminae 10,000 UP/mL, Compositae 10,000 UP/mL, Betulaceae 10,000 UP/mL, Oleaceae 10,000 UP/mL), (3) pet danders (cat and dog skin scale allergen extracts 1:20), and (4) molds (mix of *Aspergillus* 10,000 PNU/mL, *Cladosporium* 10,000 PNU/mL, *Alternaria tenuis* 10,000 PNU/mL), (Bayropharm, Milan-Italy). A histamine solution (10 mg/mL) was used as positive control and the glycerol-buffer diluent of the allergen preparations as negative control.⁴¹ Each child was skin tested on the volar surface of the forearm. One millimeter prick-lancets (Dome/Hollister-Stier, Great Britain) were used for pricking. The needle was introduced through the drop of the tested solution at a 45° angle with the skin. The reactions were recorded after 15 minutes by evaluating the skin response rate to allergens, in comparison to the response to the negative control: a wheal diameter 3 mm larger than the

wheal diameter of the negative control was considered as a positive reaction. All the children tested had positive control (histamine) wheals larger than 3 mm. Children sensitized to only one class of allergen (house dust mites or pollens or pets or molds) were defined as monosensitized, while subjects sensitized to two or more classes of allergens were defined as polysensitized.

Statistical Analysis

Prevalence rates were calculated; chi-square (χ^2) or McNemar's (paired χ^2) tests were used to compare the rates between groups. *P* values $\leq .05$ or $\leq .01$ were respectively considered statistically significant and highly statistically significant.

RESULTS

Prevalence and Characteristics of Allergic Sensitization in the Entire Population Studied

Sensitization to at least one of the 12 tested allergens was found in 304 of the 564 individuals (53.9%), including 202 males and 102 females, (mean M/F ratio 2.0). Among the 304 allergic children, 257 subjects (84.5%) were sensitized to at least one of the two house dust mites (ie, *Dermatophagoides pteronyssinus* and/or *Dermatophagoides farinae*), 168 subjects (55.3%) to at least one of the pollens, 62 subjects (20.4%) to pet dander and 16 subjects (5.3%) to molds. Among the 168 pollen-sensitized individuals, 104 (34.2%) were sensitized to *Parietaria*, 96 (31.6%) to Graminae, 53 (17.4%) to Oleaceae, 29 (9.5%) to Betulaceae, 19 (6.3%) to Compositae. Among the 62 pet-sensitized subjects, 54 (17.8%) were sensitized to cat and

17 (5.6%) to dog dander. Among the 16 mold-sensitized patients, 14 (4.6%) were sensitized to *Alternaria*, 6 (2.0%) to *Cladosporium*, 5 (1.6%) to *Aspergillus* (data not shown). There were 156 (51.3%) monosensitized children, 103 males and 53 females, mean M/F ratio 1.9 whereas 148 children (48.7%), 99 males and 49 females, mean M/F ratio 2.0, were sensitized to two or more classes of allergens (Table 1). In the entire monosensitized population, allergy to house dust mites was the most prevalent sensitization [119 patients (76.3%)], followed by pollens [32 patients (20.5%)], pets [4 patients (2.6%)], and molds [1 patient (0.6%)] (Table 1). In the polysensitized population, the frequency of sensitization to house dust mites was not significantly different from the frequency of sensitization to pollens [138 patients (93.2%) and 136 patients (91.9%) respectively]. In this group, only 58 subjects (39.2%) were pet-sensitized and 15 (10.1%) were mold-sensitized (Table 1).

Differences in Allergic Sensitization Among Age Groups

The percentage of sensitized subjects tended to increase with age, being respectively 54 (29.8%) in gr1, 111 (55.2%) in gr2, 66 (68.8%) in gr3, 73 (84.9%) in gr4 ($\chi^2 = 84.1$, $P < .01$) (Fig 1A). The frequency of sensitization to house dust mites was similar in the three youngest age groups (gr1 to gr3) ($\chi^2 = 1.7$, $P > .1$) (Fig 2A, 2B, 2C). The frequency of patients sensitized to pollens was similar in gr1 and gr2 ($\chi^2 = 0.02$, $P > .1$) (Fig 2A, 2B) but increased in gr3 and gr4 ($\chi^2 = 25.1$, $P < .01$) (Fig 2C, 2D). The sensitization to house dust mites was more

Table 1. Distribution of Monosensitization and Polysensitization to Various Classes of Allergens in the Entire Sample Population

	All Allergens		House Dust Mites		Pollens		Pets		Molds	
	No	%	No	%	No	%	No	%	No	%
Monosensitized patients	156	51.3	119	76.3	32	20.5	4	2.6	1	0.6
Polysensitized patients	148	48.7	138	93.2	136	91.9	58	39.2	15	10.1
Monosensitized patients + Polysensitized patients	304		257		168		62		16	

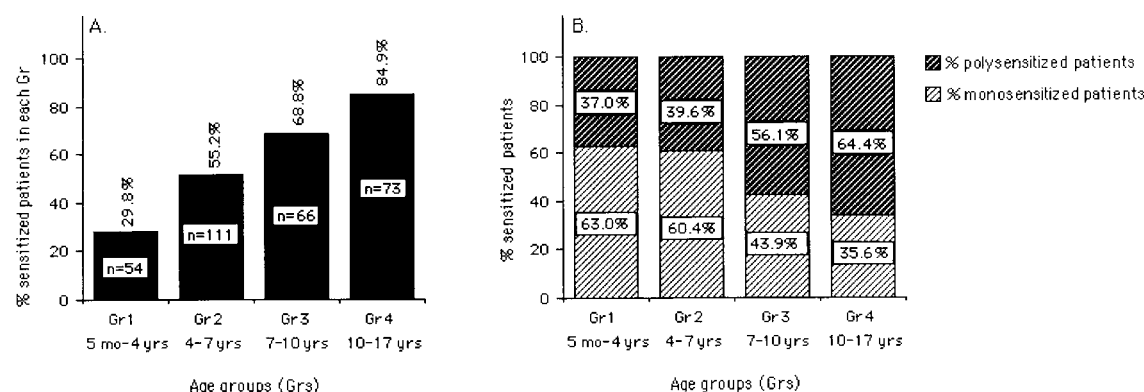


Figure 1. Distribution of allergic sensitization determined by skin prick testing: (A) the percentage of allergic individuals and (B) the percentage of monosensitization or polysensitized children in each age group. On the abscissa, the 4 age groups of patients arbitrarily divided are shown: group 1 (gr1 = 5 months to 4 years old), group 2 (gr2 = 4 to 7 years), group 3 (gr3 = 7 to 10 years), group 4 (gr4 = 10 to 17 years); on the ordinate, the percentages of allergic patients in each age group are indicated. The numbers within each bar in panel (A) and (B) correspond respectively to the numbers of sensitized patients (A) and to the percentages of monosensitized or polysensitized patients (B).

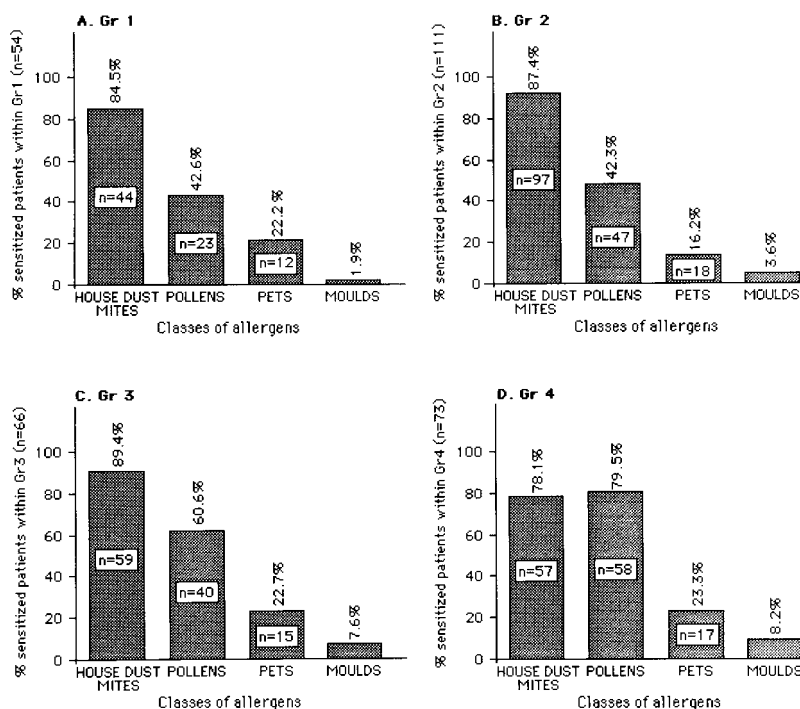


Figure 2. Distribution of the sensitization to each class of allergen (house dust mites, pollens, pets, molds) in each age group: (A) group 1 (gr1 = 5 months to 4 years old); (B) group 2 (gr2 = 4 to 7 years); (C) group 3 (gr3 = 7 to 10 years); (D) group 4 (gr4 = 10 to 17 years). On the abscissa, the different classes of allergens (house dust mites, pollens, pets or molds) are shown; on the ordinate, the percentages of allergen-sensitized patients within each age group are indicated. The numbers within each bar correspond to the numbers of patients sensitized to each allergen.

frequent than the sensitization to pollens in gr1, gr2, and gr3 (respectively in gr1: $\chi^2 = 10.3$, $P < .01$; in gr2: $\chi^2 = 33.3$, $P < .01$ and in gr3: $\chi^2 = 11.2$,

$P < .01$) (Fig 2A, 2B, 2C) but not in gr4 (gr4: $\chi^2 = 0.0$, $P > .1$) (Fig 2D). No tendency was found in the prevalence of the pet-sensitization among

the four age groups ($\chi^2 = 1.9$, $P > .1$) (Fig 2A, 2B, 2C, 2D), whereas a progressive increase with the age in the frequency of the subjects sensitized to molds was observed, even through statistical significance was not achieved ($\chi^2 = 3.9$, $P > .1$) (Fig 2A, 2B, 2C, 2D).

The percentage of patients sensitized to only one class of allergen tended to decrease with the age of the subjects: they were 34 (63.0%) in gr1, 67 (60.4%) in gr2; 29 (43.9%) in gr3, and 26 (35.6%) in gr4. An opposite tendency was observed in polysensitized individuals, who were 20 (37.0%) in gr1, 44 (39.6%) in gr2; 37 (56.1%) in gr3; 47 (64.4%) in gr4 ($\chi^2 = 15.2$, $P < .01$) (Fig 1B). Within the monosensitized group, as in the entire population studied, sensitizations to house dust mites and pollens were the most frequent. Sensitization to house dust mites was shown to be the highest frequency in gr1 to gr3. In gr4 subjects, the sensitization to house dust mites was similar to sensitization to pollens (53.8% and 46.2% respectively) (Table 2).

In contrast, within the polysensitized group, the frequency of subjects sensitized to house dust mites was higher than the frequency of subjects sensitized to pollens in gr1, whereas it was similar in gr2 and gr3. In the oldest age group (gr4), the frequency of

Table 2. Distribution of Monosensitization and Polysensitization to Various Classes of Allergens in Each Age Group*

	Gr1 (5 mo–4 yr)				Gr2 (4–7 yr)				Gr3 (7–10 yr)				Gr4 (10–17 yr)			
	MS		PS		MS		PS		MS		PS		MS		PS	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
House dust mites	24	70.6	20	100.0	58	86.6	39	88.6	23	79.3	36	97.3	14	53.8	43	91.5
Pollens	9	26.5	14	70.0	7	10.4	40	90.9	4	13.8	36	97.3	12	46.2	46	97.9
Pets	1	2.9	11	55.0	1	1.5	17	38.6	2	6.9	13	35.1	0	0.0	17	36.2
Molds	0	0.0	1	5.0	1	1.5	3	6.8	0	0.0	5	13.5	0	0.0	6	12.8
All allergens	34	63.0	20	37.0	67	60.4	44	39.6	29	43.9	37	56.1	26	35.6	47	64.4

* Gr = age group; MS = monosensitized patients; and PS = polysensitized patients.

children polysensitized to pollens tended to be higher than that of patients polysensitized to house dust mites. Sensitizations to pets or to molds were always lower than sensitizations to house dust mites or to pollens in each age group (Table 2).

DISCUSSION

The main findings of the present study performed on children with respiratory symptoms are (a) more than 50% of the patients was sensitized to at least one of the four classes of allergens tested (b) the frequency of allergic individuals increased with the age of subjects (c) sensitization to house dust mites was the most frequent in children younger than 10 yr whereas it was similar to sensitization to pollens in children older than 10 yr. Dividing the patients into monosensitized or polysensitized individuals, we also found that (a) the percentage of monosensitized children tended to decrease with the age of the subjects; (b) in monosensitized individuals, as in the entire patient sample, sensitization to house dust mites was the most frequent in children younger than 10 yr and (c) in polysensitized children older than 4 yr, the frequency of sensitization to house dust mites was as frequent as sensitization to pollens.

The group of individuals studied included children with respiratory symptoms, evaluated as outpatients in the Pulmonology Department of the Gianina Gaslini Institute (GGI) in Genoa, a city located on the Northwestern sea coast of Italy. The GGI is a pediatric hospital that provides care for the majority of the regional (Ligurian) inhab-

itants. The group of children evaluated, even if not representative of a general population, reflects the Ligurian children that need medical assistance for respiratory symptoms.

This may explain the higher frequency (>50%) of patients sensitized to airborne allergens as compared with data reported in randomized samples of populations. Indeed, studies on school children aged between 6 and 19 yr have disclosed an allergic frequency ranging from 25% to 34%.^{37,38,42}

Evaluation of the frequency of skin reactivity to the various classes of allergens (house dust mites, pollens, pets, and molds) demonstrated that allergy to house dust mites was the most frequent, followed by sensitization to pollens, pets, and molds. The prevalence of positive reactions to house dust mites in our sample population was much higher than previously reported,^{37,38,43,44} possibly reflecting regional factors. In addition, the percentages of patients sensitized to only one or to more classes of allergens were similar. Interestingly, a higher relative prevalence of sensitization to house dust mites was seen in the monosensitized group as compared with the polysensitized group.

Different hypotheses may explain these results. Subjects with a high "sensitization threshold" (monosensitized patients?) will probably develop allergy more frequently to a perennial and ubiquitous allergen like house dust mites, rather than to seasonal allergens. On the contrary, subjects with a low "sensitization threshold" (polysensitized patients?) could develop sensitization also to allergens present at low

concentrations and in short periods of the year. This hypothesis is partially supported by the demonstration that the immune responses of patients allergic to only one allergen seems to differ from that of the subjects allergic to multiple allergens.^{45–47}

We also noticed that in our population the percentage of allergic individuals tended to increase with the age of patients. Although we did not perform a longitudinal analysis, this finding is in agreement with studies that disclosed allergy tends to vary with the age of the subjects.^{32–36} According to the data of Barbee et al who reported longitudinal follow-up data on a large subset of a community, peak prevalence of allergy (53.5%) occurred at 25 to 34 yr; and a steady decline occurred after the age of 35 yr, accelerating after 55 yr.³² Age-related change in atopic predisposition is consistent with age-related change in serum total IgE.³¹

Our analysis of the distribution of allergic sensitization at different ages demonstrates that, during childhood, indoor allergens such as house dust mites impose a higher risk of sensitization than outdoor allergens. On the contrary, sensitization to outdoor allergens like pollens, constantly low in the younger groups, increased in subjects older than 7 yr of age, becoming similar to that to house dust mites, moving from childhood to adulthood. A possible explanation for these results may be higher exposure to indoor allergens, than to outdoor allergens in young children. In this context, Mariani et al recovered in the sera of subjects aged 1 yr IgG1 subclass antibodies against subclass antibodies against *Dermato-*

phagoides pteronyssinus suggesting that house dust mites are able to stimulate the immune system early in life.⁴⁸

Our results are also consistent with the studies by Niemeijer and deMonchy²⁸ who observed that the percentage of adult asthmatic subjects (newly referred to specialists in asthma centers) sensitized to pollens was as prevalent as that of patients sensitized to house dust mites. The analysis of monosensitization and polysensitization showed that the prevalence of sensitization to only one class of allergen decreased with age and, conversely, polysensitization increased.

Even if little is known about factors that influence the development of monosensitization or polysensitization, it could be hypothesized that exposure to new allergens is likely to occur with age and that some of the subjects, initially sensitized to only one class of allergen, may become subsequently sensitized to more allergens. The vast majority of monosensitized patients, up to 10 yr of age, were sensitized to house dust mites whereas only a small percentage of them were sensitized to pollens, pets, or molds. On the contrary, in the polysensitized group, the percentages of subjects sensitized to the house dust mites and to pollens were similar by 4 yr of age. It could be hypothesized that monosensitized individuals need a much stronger exposure to allergens, such as the ubiquitous and perennial house dust mites, to become sensitized. It is also possible that among the monosensitized subjects two subpopulations could exist (a) a group of young patients tending, with age, to become sensitized to other allergens (and becoming polysensitized) and (b) a group of patients not tending to develop further sensitizations. On the basis of these results, it would be very interesting to perform a longitudinal study to further investigate age-related changes in skin reactivity to each class of allergen and in monosensitization and polysensitization.

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