

Frequency and specific sensitization to inhalant allergens within nuclear families of children with asthma and/or rhinitis

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Objective: The purpose of this study was to investigate the frequency of allergy in 85 families of pediatric patients with asthma and/or rhinitis.

Methods: Families enrolled were drawn according to a table of randomization, from those whose children were referred the outpatient clinic of the Pulmonology Department of Gaslini Institute (Genoa, Italy). In patients and in both their mothers and fathers, allergic sensitization to the three most common classes of inhalant allergens (house dust mites, pollens, and animal danders) was evaluated by skin prick test.

Results: As compared with their parents, children showed a similar prevalence of positive skin prick test (50.0% and 58.8%, respectively; $\chi^2 = 1.4$; $P > .1$), but a significantly higher frequency of specific sensitization to house dust mites, pollens, or pets ($P < .05$, each χ^2). These differences were at least partially related to the higher frequency of polysensitization (ie, sensitization to more than one class of allergens) in children than in their parents [$\chi^2 = 4.2$, odds ratio (OR) = 2.3, 95% confidence interval (CI_{95%}) = 1.0 to 5.1; $P < .05$]. In addition, both in children ($\chi^2 = 5.8$, OR = 11.3, CI_{95%} = 1.4 to 81.5; $P < .05$) and in their parents ($\chi^2 = 7.4$, OR = 4.8, CI_{95%} = 1.5 to 16.7; $P < .01$), allergy to pollens was less frequent in monosensitized than in polysensitized families, while the prevalence of sensitization to house dust mites was similar in monosensitized and in polysensitized families. The analysis of the role of parental sensitization in the development of allergy in the offspring demonstrated that the prevalence of allergic children: (1) seemed to be higher, without reaching statistical significance, in families with sensitized parents than in those with non-sensitized parents ($\chi^2 = 0.41$, $P > .1$) and (2) was higher in families with one or both polysensitized parents than in those with one or both monosensitized parents ($\chi^2 = 4.5$, OR = 4.0, CI_{95%} = 1.1 to 15.6; $P < .05$). In addition, within each family, the coincidence of sensitization to house dust mites was more frequent than that to pollens (60.0% and 36.0%, respectively; $\chi^2 = 7.6$, OR = 4.5, CI_{95%} = 1.5 to 14.3; $P < .01$), and it was not influenced by the number of parents sensitized to same allergen.

Conclusion: These data support the concept that, in addition to genetic predisposition, other factors (ie, environmental exposure) may influence the development of specific sensitization in children with respiratory symptoms. The different sensitization found in this study between children and their parents occurred in a generation span, so as it is more likely to be related to environmental changes than to genetic factors.

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INTRODUCTION

In childhood, sensitization to aeroallergens is a major cause of respiratory

disease such as hay fever and bronchial asthma.^{1–3} Since it is believed that al-

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lergy develops as the result of multiple interactions between the immune system and environmental agents, a variety of specific epidemiologic, immunologic, and clinical studies have been carried out to analyze the relative pathogenetic contribution of different genetic and non-genetic factors.^{4–11} Some reports have demonstrated that major risk factors for atopy could be parental atopy and early exposure to environmental allergens.^{4–7,10,12–15} The vast majority of these studies have evaluated parental atopy only through questionnaires, the accuracy of which depends on both the precision of the questions, and the standard of education of the parents and their willingness and conscientiousness in replying. Only few reports have used population-based data on specific immunologic response against inhalant allergens within family group.^{9,16} In addition, as far as we know, no study has been published evaluating monosensitization and polysensitization, respectively, in parents and their children. With this background we investigated by skin prick test the frequency of allergy in a group of 85 children with asthma and/or rhinitis and in their mothers and fathers. Plus, we evaluated the type of specific sensitization to airborne allergens and the prevalence of monosensitization and polysensitization.

MATERIALS AND METHODS

Children and their parents

We investigated the frequency of allergy in a group of children with asthma and/or rhinitis and in their parents. All the studied children lived in Genoa, a city located on the North-

western seacoast of Italy. Families enrolled in this study were drawn according to a table of randomization among those whose children were referred for the first time to our outpatient clinic of the Pulmonology Department of Gaslini Institute (Genoa, Italy) from October, 1994 to September, 1995, by their primary care physicians. Both parents were then asked to undergo skin prick tests. Oral informed consent was obtained from the parents.

Eighty-five children, 50 boys and 35 girls [male to female ratio 1.4], aged between 3 and 13 years (yr) (mean age = 5.1 yr), were included in this study. The mean age of the parents was 35 yr, range = 23 to 59. The patient evaluation included case history, physical examination, and skin prick test: 72.6% of the children suffered from asthma defined on the basis of clinical manifestations, according to the guidelines proposed by the Medical Section of the American Lung Association.¹⁷ The remaining children had rhinitis. None of the children or their parents was currently treated with antihistamines or systemic corticosteroids.

Skin Prick Test Procedure

Both in children and in their parents, sensitization to the three most common classes of aeroallergens was evaluated by skin prick test.¹⁸ The allergens tested 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, Graminae mix 10,000 UP/mL, Compositae 10,000 UP/mL, Betulaceae 10,000 UP/mL, Oleaceae 10,000 UP/mL), and (3) pet class (cat and dog skin scale allergen extracts 1:20), (Bayropharm, Milan, Italy). A histamine solution (10 mg/mL in distilled water) was used as positive control and the glycerol-buffer diluent of the allergen preparations as negative control. Each subject was skin tested in duplicate on the volar surface of the forearm using 1-mm prick-lancets (Dome/Hollister-Stier, Great Britain). The reactions were recorded within 15 minutes by evaluating the skin response rate to each allergen application in comparison to the wheal given by the negative control: a wheal diameter 4 mm larger than the negative control was considered as a positive reaction. Subjects sensitized to only one class of allergens (house dust mites or pollens or pets) were defined as monosensitized, while those sensitized to two or more classes of allergens were defined as polysensitized.

Statistical Analysis

Prevalence rates, odd ratios (OR), and confidence interval 95% (CI_{95%}) were calculated. Chi-square (χ^2) test was used to compare the rates between groups. *P* values $\leq .05$ and $\leq .01$ were respectively considered statistically significant and highly statistically significant.

RESULTS

Prevalence and Characteristics of Allergic Sensitization in Children and Their Parents

Sensitization to at least one of the nine allergens tested was found in 50 of the 85 children enrolled (58.8%), including 31 boys and 19 girls and in 85 of the 170 parents (50.0%), including 34 mothers (40.0%) and 51 fathers (60.0%). The slightly higher prevalence of sensitization observed in children as compared with their parents was not statistically significant ($\chi^2 = 1.43$; *P* > .1), (Table 1). When allergen-specific sensitizations in children and in their parents were compared, however, the children showed a significantly higher sensitization to house dust mites (51.8% and 34.1%, respectively; $\chi^2 = 5.63$, OR = 3.41, CI_{95%} = 1.20–10.15; *P* < .05), to pollens (32.9% and 17.0%, respectively; $\chi^2 = 5.31$, OR = 2.46, CI_{95%} = 1.13–5.37; *P* < .05), and to pets (25.9% and 3.5%, respectively; $\chi^2 = 23.94$, OR = 10.35, CI_{95%} = 3.50–32.07; *P* < .01) (Table 1). These findings were at least partially explained by the observation that sensitization to more than one class of allergens (polysensitization) was more frequent in children than in their parents (68.0% and 48.2%, respectively; $\chi^2 = 4.21$, OR = 2.28, CI_{95%} = 1.03–5.07; *P* < .05) (Table 2). In addition, in children, the prevalence of sensitization to pollens has been recorded less frequently in monosensitized than in the polysensitized group (6.3% and 79.1%, respectively) ($\chi^2 = 5.81$, OR = 11.3, CI_{95%} = 1.37–81.53; *P* < .05) while allergy to house dust mites in the monosensitized group was as frequent as in the polysensitized group (81.3% and 91.2%, respectively). Similarly, in parents, the frequency of sensitization to pollens was lower in monosensitized than in polysensitized individuals (25.0% and 58.5%, respectively) ($\chi^2 = 7.39$, OR = 4.80, CI_{95%} = 1.46–16.72; *P* < .01) while no difference in the percentage of adults monosensitized or polysensitized to house dust mites was observed (65.9% and 70.7%, respectively).

Table 1. Allergen-Sensitization of Children with Asthma and/or Rhinitis and of Their Parents

	Children	Parents	Chi-Square	ORs	95% CI	P value
All allergens						
Number	50	85	1.43	1.43	0.82–2.50	>.1
%	58.82	50.00				
House dust mites						
Number	44	58	5.63	3.41	1.20–10.15	<.05
%	51.76	34.12				
Pollens						
Number	28	29	5.31	2.46	1.13–5.37	<.05
%	32.94	17.06				
Pets						
Number	22	6	23.94	10.35	3.50–32.07	<.01
%	25.88	3.53				

Table 2. Distribution of Monosensitization and Polysensitization in Children and in Their Parents

	Children	Parents
Monosensitized individuals		
Number	16	44
%	32.00	51.76
Polysensitized individuals		
Number	34	41
%	68.00	48.24

Influence of Parental Allergy on Sensitization in Their Offspring

The prevalence of allergic children tended to be higher, without reaching statistical significance, in families with sensitized parents than in those with non-sensitized parents (65.0% and 50.0%, respectively; $\chi^2 = 0.41$; $P > 0.1$), (not shown). In addition, analyzing only the families with a positive history of allergy, it has been observed that the frequency of sensitized offspring was not different in families with unilateral parental allergy (ie, only one allergic parent) or bilateral parental allergy (ie, both allergic parents) (60.0% and 65.0%, respectively; $\chi^2 = 0.01$; $P > .1$), (not shown). Further, sensitization in children was significantly more frequent in families with at least one polysensitized parent (ie, only one or both parents) than in those with at least one monosensitized parent (77.8% and 46.4%, respective-

ly; $\chi^2 = 4.47$, OR = 4.04, CI_{95%} = 1.09–15.58; $P < .05$) (Table 3). The same difference was also observed when comparing the families with *only one* polysensitized parent and those with *only one* monosensitized parent (78.3% and 40.9%, respectively; $\chi^2 = 5.07$, OR = 5.20, CI_{95%} = 1.20–24.07; $P < .05$) (Table 3). The number of families with both monosensitized or with both polysensitized parents were too low to perform any statistical analysis.

Coincidence of Specific Allergic Sensitization in Children and Their Parents

Evaluating the characteristics of allergen-specific sensitization in children and in their parents, we observed that the coincidence of sensitization to house dust mites was significantly more frequent than that to pollens, ie, parents had a higher chance of having their children sensitized to the same specific allergen if they were sensitized to house dust mites than to pollens (60.0% and 36.0%, respectively; $\chi^2 = 7.56$, OR = 4.52, CI_{95%} = 1.47–14.30; $P < .01$). We then determined whether the number of reactive parents could influence the expression of the same allergen sensitization in the offspring, even though the number of families with bilateral sensitization was low. We found that the frequency of the children sensitized to same allergen was similar in families with one

or both parents sensitized to house dust mites (59.5% and 62.5%, respectively; $P > .1$), while it tended to be higher, but not significantly, in families with both parents sensitized to pollens as compared with families with only one parent with this specific sensitization (50.0% and 33.3%, respectively; $P > .1$) (Table 4).

DISCUSSION

During the last decades, attention has been paid to the observation that the incidence and the prevalence of atopic diseases, including asthma, are constantly increasing.^{19–24} Since many studies of the prediction of atopy have disclosed an increased risk for subjects with positive family histories,^{5,7} we investigated the frequency of allergy in a group of 85 families of children with asthma and/or rhinitis drawn, according to table of randomization, from those who attended the outpatient pulmonary clinic of the Gaslini Institute (GGI) in Genoa, a city located on the Northwestern seacoast of Italy. The GGI is a pediatric hospital to which the majority of the regional (Ligurian) inhabitants are referred. Even if not representative of a general population, the group of children evaluated in the pulmonary clinic reflects the Ligurian children who need medical assistance for respiratory symptoms. We found that (1) the frequency of allergy was slightly higher, but not significantly, in children as compared with their relatives, possibly due to the fact that most of the children were asthmatic; (2) specific sensitization to house dust mites, pollens or pets, and polysensitization was significantly more frequent in children than in their parents. In addition, evaluating the role of parental sensitization in the development of allergy in the offspring demonstrated that (1) the prevalence of allergic children seemed to be higher, without reaching statistical significance, in families with sensitized parents than in those with non-sensitized parents; (2) sensitization in children was significantly more frequent in polysensitized than in monosensitized families; and (3) the familial coincidence of sensi-

Table 3. Influence of Parental Monosensitization and Polysensitization in the Prevalence of Allergy in Their Offspring

Type of Families	Children			
	Allergic		Nonallergic	
	Number	%	Number	%
Monosensitized families with				
Only one AP* (N = 22)	9	40.91	13	59.09
Both APs (n = 6)	4	66.67	2	33.33
At least one AP (N = 28)	13	46.43	15	53.57
Polysensitized families with				
Only one AP (N = 23)	18	78.26	5	21.74
Both APs (N = 4)	3	75.00	1	25.00
At least one AP (N = 27)	21	77.78	6	22.22
Families with neither sensitized parents (N = 20)	10	50.00	10	50.00

* AP = allergic parent.

Table 4. Coincidence of Allergen-Specific Sensitization in Nuclear Families

Families with	Allergen-specific sensitization to					
	House dust mites		Pollens		Pets	
	Number	%	Number	%	Number	%
Only one AP* with the same specific sensitization as offspring	25	59.52	7	33.33	1	16.67
Both APs with the same specific sensitization as offspring	5	62.50	2	50.00	0	—
At least one AP with the same specific sensitization as offspring	30	60.00	9	36.00	1	16.67
Both APs without the same specific sensitization as offspring	14	40.00	19	31.67	21	26.58

* AP = allergic parent.

zation to house dust mites was significantly more frequent than that to pollens and it was not influenced by the number of sensitized parents, while the coincidence of sensitization to pollens tended to be more frequent, without reaching statistical significance, in families with both parents than in those with only one parent reactive to pollens.

The lower frequency of allergy and, particularly of polysensitization, in parents is an unexpected finding and conflicts with the concept that prolonged contact with allergens, which occurs naturally with age, is likely to enhance the degree of allergic sensitization. This hypothesis was at least partially supported by the recent demonstration that the ratio of monosensitized to polysensitized children is decreasing with the age of the subjects.²⁵ In addition, children were probably more likely to be polysensitized because they had respiratory symptoms.

On the other hand, it is possible that the progressive change in the environment in developed countries, which includes increasing air pollution, may be responsible for the high incidence of atopy in children.^{26,27} In Genoa, in the last decades, changes in the air pollution, due to increases in the vehicular traffic and in home heating, have been reported. Air pollutants are known to potentiate the effects of inhaled allergens by causing slight mucosal inflammation which facilitates the penetration of allergens.^{26,27}

A surprising result was obtained by analyzing allergen-specific sensitization in children and in their parents: in adults, the prevalence of sensitization to pets was much lower than in their children. This observation could be partially explained taking into account that, before the fifties, pets usually lived out of the domestic environment whereas, during the past 15 to 20 years, they have been more often kept inside the house.

The analysis of the role of parental sensitization in the development of allergy in the offspring, here reported, confirms data of a previous study by Poysa et al, which demonstrated that positive skin reactions were nearly as common in children with no family history of atopy as in children with positive family histories.²⁸ We found, however, that families with both reactive parents had a frequency of an allergic offspring that tended to be higher as compared with those with both non-sensitized parents. This observation is in agreement with previous studies which showed a significant increase in the risk of allergy in a "general population of children" if both parents were allergic.^{16,29-31}

The same studies also reported a proportional increase in the development of allergy in children related to the number of sensitized parents: the risk of allergic offspring was 50% if one parent was allergic and it was 66% if both parents were allergic.^{7,16} We could not confirm this correlation in

our study, possibly because of the relatively limited number of families investigated.

We observed that sensitization in children was significantly more frequent in polysensitized than in monosensitized families possibly related to inherited genetic factors (from the parents) or to exposure to multiple allergens present in the environment where all the members of a family live (parents and their children). Evaluating the familial coincidence of sensitization to the same allergen, we found that skin reactivity to house dust mites was statistically more frequent than that to pollens. This observation may be explained by different characteristics of environmental exposure to allergens or of genetic inheritance. In this context, house dust mites are a perennial and ubiquitous allergen and, as a consequence, predisposed individuals (ie, children and their parents), are more likely to become sensitized to this allergen than to seasonal allergens such as pollens.³²⁻³⁵ It is also possible that house dust mites may be a stronger "genetic marker," inherited and/or expressed with a higher frequency.^{3,4,36}

In conclusion, it is likely that sensitization to airborne allergens may develop in children as a result of interactions between the immune system and the environment. The different sensitization found in this study between children and their parents occurred within a generation span, so it is more

likely to be related to environmental changes than to genetic factors.

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