

Symptoms of respiratory allergies are worse in subjects with coexisting food sensitization

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Summary

Food sensitization was evaluated in 78 subjects with respiratory allergies, both by skin tests with commercial and fresh allergens, and by specific IgE determination. On the basis of the presence or absence of the latter the population was divided into two groups. The group with food-specific IgE showed more severe features of respiratory allergy, including a greater number of positive skin tests and specific IgE determinations, more class 3 and 4 reactions, and more symptoms. The hypothesis that early food sensitization can predispose to severe inhalant allergy is discussed.

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Introduction

In recent years different groups have reported various associations between respiratory and food allergies. These associations range from the long known fresh fruit/tree pollen syndrome [1,2], to the possible crossreactions between grass pollens, and tomato and peanut antigens [3]. Moreover, anecdotal reports of single cases like the recent observation of a major reaction to camomile tea in a boy with mugwort allergy [4] are not infrequent.

Food sensitivity in patients with respiratory allergies may be demonstrated with the usual clinical and laboratory methods, and imply different grades of symptoms when the patient is exposed to the offending food.

Evidence that coexisting food sensitization affects the clinical picture of respiratory allergies is presented in this paper.

Materials and methods

Measurement of food-specific IgE was carried out on serum samples obtained from 78 subjects with respiratory allergies, independently from the presence of symptoms of food intolerance. The group comprised 38 males and 40 females with a mean age of 25.9 ± 1.5 yr, living in the same geographical area.

The test was carried out using the multiple allergosor-

bent chemiluminescent assay (CLA, Hollister Stier, Mountain View, U.S.A.) [6], using panel II for inhalants and panel V for foods according to manufacturer's instructions.

In the subjects entering the study a previous diagnosis of allergic respiratory disease had previously been obtained on the basis of positive skin tests and CLA results, together with typical symptoms and a positive history. None of them had previously been seen by other allergologists, nor had they received specific desensitization.

Skin tests were carried out by an epicutaneous (prick) method on the forearm, using 1 mm prick lancets (Hollister Stier Inc.). The panel comprised 15 allergens responsible for almost all respiratory allergies in Northern Italy, a positive (histamine dihydrochloride 1 mg/ml) and a negative (allergen diluting solution) control. Results were recorded after 15 min and graded from 0 to + + + + comparing the weals to that of histamine, as previously suggested [7]. Reactions of the same size as the histamine weal (+ + +) and greater (+ + + +) were considered positive. All medication was stopped before the tests for the periods recently suggested [8].

Prick tests for foods have also been carried out in all the subjects in this study, using a commercially available collection (Hollister Stier Inc.), using the technique described above.

Finally, allergy to carrot, garlic, onion, orange, pea, tomato, potato, celery and apple was also evaluated with a prick by prick method, using fresh foods [9]. Food-specific IgE were detected in 40 subjects who are referred

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Table 1. Main clinical features of the two groups

	Group A	Group B	P-value
Age (yr)	27.2 ± 2	25.1 ± 2.4	n.s.
Duration of symptoms (yr)	6.9 ± 1.1	9.4 ± 1.2	n.s.
Positive family history	22	19	n.s.
Clinical score	2 ± 0.1	2.4 ± 0.1	0.01
Smokers	7	8	n.s.
Males/females	14/22	24/14	0.02

Age range is 8–65 yr for group A and 2–59 yr for group B. P-value refers to two-tailed Student's *t*-test.

to as group B. The remaining 38 subjects, with no food-specific IgE, formed the control group (group A).

In group B, fresh fruit caused major symptoms in one subject and mouth mucosal itching in 12. Clinical history included the following:

1. concomitant diseases: patients with any other diseases were excluded from the study;
2. smoking habits;
3. family history: this was considered positive when allergy had been demonstrated in at least one of these relatives: mother, father, brother, sister, son, daughter;
4. duration of disease: time in years from the onset of the first symptom;
5. clinical score: each of the following symptoms received a score of one when present: conjunctivitis, rhinitis, asthma, recurrent bronchitis, urticaria, eczema. The two latter symptoms were not included when calculating the respiratory score.

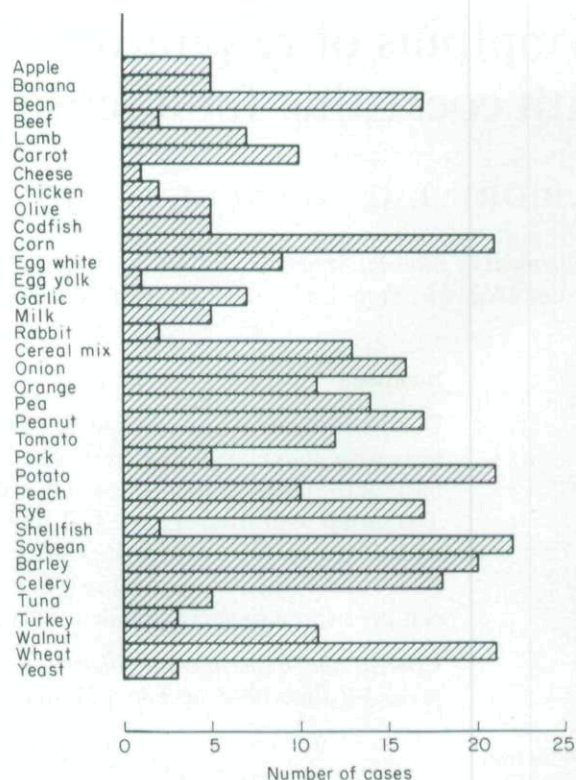
For statistical analysis, two-tailed Student's *t*-tests and chi-square tests were used when appropriate.

Results

As mentioned above, the presence of food-specific IgE was used to divide a population of 78 subjects with respiratory allergies into two groups.

Table 1 shows the main clinical features of the two groups. As can be seen, no differences were observed in age, duration of symptoms, smoking habits and familiarity. Conversely, this sorting generated great disparities in the clinical score and the male/female ratio.

The pattern of positive food reactions in group B is shown in Fig. 1. These results obtained with CLA were compared with those of prick tests and prick by prick tests (when performed). Concordance for the single allergens ranged from 31 to 69% for the first, and from 13 to 63% for the second. In both cases, orange had the weakest and potato the highest concordance. In spite of the low correlation, assignment of subjects to the two groups did

**Fig. 1.** Results of food allergen specific IgE determination in group B.

not change if performed on the basis of prick or prick by prick testing.

The two groups presented many differences in the pattern of sensitization to aero-allergens, as evaluated both by CLA and skin testing. The results of CLA showed significantly higher scores in group B for seasonal allergens, with the exception of trees, while perennial allergens tended to give lower scores (Table 2). Generally comparable results were obtained with prick tests; in addition they gave greater differences for mites, which became statistically significant (Table 3). Moreover, subjects of group B had a significantly increased number both of total and of class 4-positive reactions to aero-allergens when evaluated either by skin testing or CLA (Table 4).

Finally, when the month of birth of the patient was considered, a comparable distribution all over the year was found in the two groups (Fig. 2).

Discussion

Many factors have been shown to affect the onset and, possibly, the clinical manifestations of respiratory allergies. Examples are the geographical area where the subject lives [10], the period of birth [11], early antigen contacts [12,13], and adjuvant factors (14–16). Finally, the fact that many infants with food allergies will then develop inhalant allergies has long been known [17].

Table 2. CLA results for aero-allergens in the two groups

	Group A	Group B	P-value
Three trees mix*	1.2 ± 0.3	1.8 ± 0.2	n.s.
Acacia	0.1 ± 0.1	0.8 ± 0.2	< 0.001
Ash	0.0 ± 0.0	0.6 ± 0.2	0.002
Beech	0.1 ± 0.1	1.0 ± 0.2	< 0.001
Olive	0.2 ± 0.1	1.1 ± 0.2	< 0.001
Oak	0.2 ± 0.1	0.9 ± 0.2	0.002
London plane	0.0 ± 0.0	0.9 ± 0.2	< 0.001
Four grass mix†	1.3 ± 0.3	2.9 ± 0.2	< 0.001
Bermuda	0.4 ± 0.1	1.9 ± 0.3	< 0.001
Reed	0.3 ± 0.1	1.4 ± 0.3	< 0.001
Cultivated rye	0.9 ± 0.2	2.4 ± 0.3	< 0.001
Corn pollen	0.2 ± 0.1	1.7 ± 0.3	< 0.001
Oat pollen	1.4 ± 0.3	2.7 ± 0.3	< 0.001
Rape	0.0 ± 0.0	1.1 ± 0.2	< 0.001
Wheat pollen	1.4 ± 0.2	2.7 ± 0.2	< 0.001
Ragweed mix	0.1 ± 0.1	1.0 ± 0.2	< 0.001
Lambs quarter‡	0.0 ± 0.0	0.9 ± 0.2	< 0.001
Plantain	0.8 ± 0.2	2.3 ± 0.3	< 0.001
Mugwort	0.3 ± 0.1	0.9 ± 0.2	0.008
Nettle	0.2 ± 0.1	1.9 ± 0.2	< 0.001
Pellitory	0.4 ± 0.2	1.0 ± 0.2	0.028
Dandelion	0.3 ± 0.1	1.0 ± 0.2	0.008
Cat dander	0.4 ± 0.2	1.0 ± 0.2	0.034
Dog dander	0.3 ± 0.1	0.8 ± 0.2	0.042
Mite (<i>D. farinae</i>)	1.5 ± 0.3	1.1 ± 0.2	n.s.
Mite (<i>D. pteronyssinus</i>)	1.5 ± 0.3	1.0 ± 0.2	n.s.

Values represent means ± s.e.m. of positivity class.

P-value was obtained by two-tailed Student's *t*-test.

* Birch, hazel, alder.

† Timothy, cocksfoot, meadow grass, rye grass.

‡ *Chenopodium album*.

In the present work we have shown that the phenotypic manifestations of respiratory allergies are worse in subjects with food-specific IgE. This could be explained simply by the fact that food sensitization which is known frequently to be associated with certain inhalant allergies [1-3], could occur more frequently in subjects in which respiratory symptoms are worse.

However, many factors stand against this hypothesis. First, after sorting on the basis of food IgE positive or negative reactions, no difference was noticed in the two groups for the factors reported to influence the development of respiratory allergies, i.e. month of birth [11], geographical distribution [10] and familial predisposition [18]. Furthermore, age and smoking habits, which are known to affect IgE levels were comparable in the two groups. Only sex differences were significant with less women in group B, and this is in agreement with previous reports of lower IgE levels in females [22,23].

Table 3. Results of prick tests for aero-allergens in the two groups

	Group A	Group B	P-value
Timothy	0.9 ± 0.2	2.2 ± 0.3	< 0.001
Cocksfoot	1.5 ± 0.3	2.5 ± 0.4	0.026
Bermuda	1.0 ± 0.2	2.2 ± 0.3	0.006
Pellitory	0.3 ± 0.2	1.2 ± 0.3	0.012
Plantain	0.4 ± 0.2	1.2 ± 0.3	0.008
Mugwort	0.4 ± 0.2	1.2 ± 0.3	0.02
Olive	0.6 ± 0.2	1.1 ± 1.6	n.s.
Birch	1.3 ± 0.3	2.2 ± 0.3	n.s.
Hazel	1.2 ± 0.3	2.1 ± 0.3	n.s.
Alder	1.1 ± 0.3	1.5 ± 0.3	n.s.
Dog	0.3 ± 0.1	0.2 ± 0.1	n.s.
Cat	0.3 ± 0.1	0.8 ± 0.3	n.s.
Mite (<i>D. pteronyssinus</i>)	1.2 ± 0.2	0.3 ± 0.1	0.002
Mite (<i>D. farinae</i>)	1.3 ± 0.3	0.5 ± 0.2	0.016
<i>Alternaria</i>	0.1 ± 0.1	0.2 ± 0.1	n.s.

Values represent mean ± s.e.m. of weal grade. P-value was calculated as in Table 2.

Table 4. Positive reactions and class 4 reactions for aero-allergens in the two groups by CLA and prick testing

	Group A	Group B	P-value
Positive reactions (prick)	6.4 ± 0.7	9.0 ± 0.8	0.02
Positive reactions (CLA)	6.0 ± 0.8	15.9 ± 1.3	< 0.001
Class 4 reactions (prick)	1.3 ± 0.3	2.4 ± 0.4	0.018
Class 4 reactions (CLA)	1.5 ± 0.3	4.0 ± 0.6	< 0.001

Values represent mean ± s.e.m.

P-value was calculated as in Table 2.

Secondly, it should be considered that asthma, one of the worst symptoms in respiratory allergies, nearly always appears to be associated with IgE reactions [24], and that patients sensitized to foods may have more frequent contact with allergens responsible for IgE-mediated reactions.

Finally, it is well demonstrated that food allergies usually occur in early childhood, while inhalant allergies take place later [25].

We therefore propose that in our group B subjects, the early presence of food-specific IgE, even if asymptomatic, could be partially responsible for later aero-allergen sensitization and worsening of symptoms as observed by others in follow-up studies [26]. This could partially be explained by the presence of crossreacting antigens [2], as suggested by the concomitance of high CLA scores for grasses and cultivated cereals in our group B subjects.

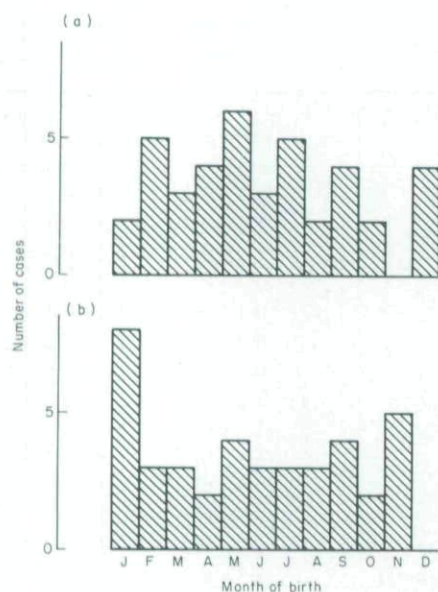


Fig. 2. Month of birth distribution in the two groups. (a) Group B, (b) group A.

Further work is in progress to evaluate the impact of early food allergy on respiratory function and its prognostic importance in subjects with inhalant allergies. At present we suggest that food sensitization should always be determined in patients with respiratory allergies when they (1) are males, (2) show major symptoms, and (3) have many, and/or (4) have high score reactions when tested with extracts of aero-allergens. This can be done either by prick testing or specific IgE measurement. However, since the concordance of the two methods is not 100%, both should be used whenever possible.

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