

Specific IgE antibodies to aeroallergens and food among Israelis

Yulia Kornizky, MD*; Marcel Topilsky, MD*; Elizabeth Fireman, PhD†; Shaye Kivity, BSc†; and Shmuel Kivity, MD†

Background: There are no data about specific IgE antibodies to food and aeroallergens in the Israeli population.

Objective: We sought to determine the relationship between selected demographic parameters and rate of sensitivity to various allergens throughout all ages.

Methods: Analysis was carried out on 776 positive specific IgE from 655 patients (347 to food, 429 to aeroallergens, and 121 to both). The studied parameters were age and gender.

Results: Age-related analysis showed the highest positivity to food (eggs, legumes, and milk) and the lowest to pollens during infancy. High sensitivity to house mites prevailed at all ages. Sensitivity to pollens and epidermals increased with age while sensitivity to eggs, legumes, and milk decreased. Above the age of 30 years, the rate of sensitivity to all tested aeroallergens and food was similar and close to the average value. Our data showed a significant cross-sensitivity between various foods and aeroallergens and also confirmed cross-sensitivity results reported earlier.

Conclusions: (1) Age is a dominant factor affecting type I hypersensitivity. House mite is the most common allergen throughout life. (2) The age distribution and nature of sensitivity to allergens in Israel has some similarities to Spain but differ from other countries. (3) Cross-sensitivity between food and aeroallergens was found.

Ann Allergy Asthma Immunol 1999;83:149–152.

INTRODUCTION

Allergic diseases affect at least 15% of the population and are the cause of chronic illness.¹ The investigation of allergy patients includes skin tests and challenge procedures [eg, food and aeroallergens tests] as well as various specialized laboratory investigations [eg, total IgE, radioallergosorbent tests (RAST)].¹ Skin tests have for many years been widely used in the diagnosis of allergic diseases. Prick skin tests are highly reproducible and frequently utilized to screen patients with suspected IgE-mediated allergies. Positive skin tests indicate the possibility that

the patient has symptomatic reactivity to the specific food or aeroallergens, whereas negative skin tests confirm the absence of IgE-mediated reactions.

RAST and similar in vitro assays (including enzyme-linked immunosorbent assays) for identifying specific IgE antibodies are also frequently used to screen for IgE-mediated food allergies. Although generally considered slightly less sensitive than skin tests, one study comparing Phadebas RAST with double-blind, placebo-controlled oral food challenges (DBPCFC) found prick skin tests and RAST to have similar sensitivity and specificity when a Phadebas score of 3 or greater was considered positive. Utilizing Phadebas scores of 2+ or greater slightly improved the sensitivity, but reduced the specificity of the test. In general, in vitro measurement of serum, food-specific IgE performed in high-quality laboratories, provides information similar to prick skin tests.²

There are no data about specific IgE antibodies to food and aeroallergens in the Israeli population. An earlier study conducted in the municipal hospital of Tel Aviv established total IgE values in Israelis with different allergic diseases and in healthy controls.³ Most publications on the profile of type I hypersensitivity are based on skin tests alone. In addition, data on infants are not available since skin tests are difficult to obtain in this age group. This work is the first attempt to utilize RAST in order to establish and classify the allergic profile of atopic individuals in Israel, a country of various climates zones and specific dietary habits.

The RAST results accumulated over the last 6 years in the same hospital are presented in the following report, and the age and sex effect on these results is analyzed.

MATERIALS AND METHODS

A total of 1,250 RAST were done at the Allergy Laboratory of Tel Aviv Sourasky Medical Center over a 6-year period. Among those, 776 of the tests performed on 655 patients (some of them had more than one test) were reported as being positive (ie, 2+ or higher). All the patients were referred due to a clinical suspicion of respiratory or food allergy including allergic rhinitis, asthma, and/or food hypersensitivity. All patients gave their written consent to be included in the study. The characteristics of patients are listed in Table 1.

We used the ALA STAT microplate allergen-specific IgE, a kinetic enzyme immunometric assay system designed for the measurement of allergen-specific IgE in serum. ALA STAT is unique in its use of allergens in a liquid format. The allergens are covalently

* Departments of Internal Medicine "H" and † Allergy and Pulmonary Disease, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

Received for publication August 1, 1998.

Accepted for publication in revised form December 19, 1998.

Table 1. Characteristics of Patients

Age (yr)	Male	Female	Total
0 to 2	49	26	75
3 to 5	49	21	70
6 to 20	110	72	182
21 to 30	40	79	119
Above 30	95	114	209
Total	343	312	655

bound to a soluble polymer/copolymer matrix, which in turn is labeled with a ligand—the same ligand user for coating the reaction wells. The use of an amino acid copolymer amplifies the amount of allergen that the matrix can support.

The system is not subject to interference from high total IgE levels and other nonspecific binding problems which affect solid-phase systems. Ligand-labeled allergen complexes (or a panel of allergen complexes) and a patient sample are pipetted into ligand-coated wells and then incubated for one hour. During this time, any endogenous IgE specific for the test allergen (or for one or more of the allergens in the panel) binds to it. The allergen/IgE

complex linked to the microplate wells are reacted with horseradish peroxidase-labeled monoclonal anti-IgE during a third 1-hour incubation, after which excess enzyme label is washed away.

A chromogenic indicator (3,3', 5,5'-tetramethylbenzidine) in a buffered hydrogen peroxide solution, which is reactive with the enzyme label, is then added. The rate of color development measured in millioptical density units per minute (mOD/min) are directly related to allergen-specific IgE concentration.

The foods and aeroallergens evaluated in our study are listed in Table 2. Only those allergens having considerable statistical significance were included in the final analysis.

The results were analyzed by the Chi-square test and a *P* value <.05 indicated statistical significance.

RESULTS

Table 1 plots the change in ratio associated with gender and age: an approx-

imately equal number of male (343) and female (312) patients was tested. Among the patients under 5 years old, the ratio between males and females was approximately two to one. With increasing age, the number of female patients rose (the female-male ratio was 2:1 between 21 and 30 years). A number of female patients after 30 years (114) was slightly higher than a number of males (95).

As shown in Table 3, sensitivity to food was found in 347 of subjects examined, sensitivity to aeroallergens was found in 429 subjects, and 121 subjects had sensitivity to both food and aeroallergens. These data were statistically analyzed, and the frequency of IgE sensitivity for each age group appears in the same Table.

Sensitivity to food was very high in the <2 years age group. From 3 to 5 years of age, the relatively high levels persisted, after which they decreased to a level considered average for patients from 6 to 20 years. The lowest sensitivity to food was noted in the age group from 21 to 30 years, after which it rose again to average.

In <2-year age group, sensitivity to aeroallergens showed the lowest level. Then, from age 3 to 5, it increased to average and continued to increase for the 6 to 20-year age group, in which it reached its highest level. From 21 to 30 years of age, sensitivity to aeroallergens remained relatively high, and then returned to average in the >30-year age group. In essence, sensitivity to both food and aeroallergens was at the average levels in patients over 30 years of age.

The main food groups which were statistically significant in causing allergic reactions included fruits, vegetables, legumes, milk, meat, and eggs. Aeroallergens that were statistically significant in causing allergic reactions included pollens, epidermal allergens (cats and dogs), and *Dermatophagoides pteronissius*.

Table 4 displays the sensitivity to each allergen group according to age group. In general, sensitivity to pollens and *Dermatophagoides* is dominant in the aeroallergens while sensitivity to

Table 2. Allergens Included in the Assay

Food Allergens		Aeroallergens	
Group	Allergens	Group	Allergens
Vegetables	Tomatoes	Pollens	Pecan
	Carrots		White oak
	Lettuce		Olives
	Green peas		Cypress
Fruits	Oranges		Common ragweed
	Apples		Mugwort sagebrush
	Mangoes		English plantain
	Peaches		Russian thistle
Legumes	Kiwi		Common cocklebur
	Soya		Rough pigweed
	Almonds		Nettle
	Peanuts		Pellitory
	Pecans		Bermuda
	Sesame		Orchard grass
Ungrouped	Eggs		Perennial rye grass
	Milk		Timothy grass
	Meat	Epidermal	Cats
	Codfish		Dogs
	Wheat flour	Mold	<i>Penicillium notatum</i>
	Rice		<i>Cladosporium</i>
	Tuna		herbarium
	Strawberries		<i>Aspergillus fumigatus</i>
	Corn	Ungrouped	<i>Alternaria tenuis</i>
			<i>Dermatophagoides</i>
			<i>Pteronyssinus</i>

Table 3. Frequency of IgE Sensitivity

Group No. 7	Age	Sensitivity to Food	Sensitivity to Inhalants
1	0 to 2	Highest (58)	Lowest (31)
2	3 to 5	High (42)	Average (44)
3	6 to 20	Average (95)	Highest (140)
4	21 to 30	Lowest (41)	High (83)
5	Above 30	Average (111)	Average (131)
Totals		347	429

legumes and fruits is dominant in food. The statistical interpretation is also shown in the same table The <2 years of age group showed the highest sensitivity to legumes, eggs, and dermatophagoides; high sensitivity to milk; average sensitivity to fruits, vegetables, and meat; low sensitivity to epidermis; and the lowest sensitivity to pollens. The 3 to 5-year age group showed the highest sensitivity to eggs and dermatophagoides, high sensitivity to legumes and milk, low sensitivity to pollens, and average to fruits, vegetables, epidermis, and meat.

The age group 6 to 20 years old showed high sensitivity to pollens, epidermis and dermatophagoides, average sensitivity to fruits, vegetables, legumes, eggs, milk, and meat.

The age group 21 to 30 years old showed the highest sensitivity to pollens; high sensitivity to Dermatophagoides; the lowest to legumes; and average sensitivity to fruits, vegetables, epidermis, eggs, milk, and meat. Patients older than 30 showed no significant difference in sensitivity among the different allergens.

Levels of sensitivity to fruits, vegetables, and meat were equally frequent throughout all the age groups.

Associations between allergy to aeroallergens and to food allergens were studied in 121 patients who showed a positive RAST to both food

and aeroallergens. The correlations found between different allergens appear Table 5. Significant correlation was found between milk and meat ($P = .0087$), between milk and eggs ($P = .0002$), and between eggs and legumes ($P = .029$). A positive RAST to sesame closely correlated with a positive test to fruits ($P = .0075$), tomatoes to grasses ($P = .009$), peanuts to mold, ($P = .016$), soya to vegetables ($P = .0092$), pollens to vegetables ($P = .025$), and epidermis to fruits ($P = .029$). For the full details of correlation found between different allergens, please refer to Table 5.

DISCUSSION

Previous studies have suggested that high concentrations of food-specific IgE antibody are predictive of food-induced allergy.⁴⁻⁷ In the same studies, crossreactive IgE antibodies were found to be responsible for allergic reactions in patients allergic to pollen and ingestion of food. Monoclonal antibodies specific for the major mugwort pollen allergen, Art v1, crossreacted with proteins of comparable molecular weight in fruit and vegetables.

Few studies have addressed the relationship between sensitization and the development of atopic disease over the years. IgE antibodies in children are usually associated with current, future, or previous atopic disease.

Table 5. Significant Relationships Found Between Allergens

No.	Dependency	P
1	Milk vs Meat	.0087
2	Milk vs Eggs	.0002
3	Eggs vs Legumes	.009
4	Sesame vs Fruits	.0075
5	Tomato vs Grass	.009
6	Peanut vs Mold	.016
7	Soya vs Vegetables	.0092
8	Pollens vs Vegetables	.025
9	Epidermal vs Fruits	.029

Condition for significant relationship → $P < .05$.

In the present study, the results of RAST to food and aeroallergens from 655 Israeli patients with allergic symptoms and a positive response to at least one of the tested allergens were analyzed. Although this group of patients was not randomly selected, it is most likely a true representation of what occurs among youngsters because most of the children under 5 years of age were tested in vitro. Our results confirmed that infants younger than 2 years are sensitive to different kinds of foodstuff, including eggs and milk. In our study, infants were also sensitive to legumes and meat; a finding that can be explained by the early introduction of these foods into Israeli infants' diet. For older age groups, the prevalence of the allergic reactions to food becomes lower, but it increases to aeroallergens, reaching the highest level in the age group of 6 to 20 years.

One of the prominent findings of this study is that the prevalence of a positive RAST to pollens is lowest in infants, and that it constantly increases with age, reaching its highest value at ages 6 to 20 years, after which it slightly decreases but remains rela-

Table 4. Frequency of IgE Sensitivity to Major Food/Inhalant Categories

Age	Fruits	Vegetables	Legumes	Pollens	Epidermal	Eggs	Milk	Meat	Dermatophagoiges
0 to 2	Average (17)	Average (9)	Highest (24)	Lowest (11)	Low (10)	Highest (40)	High (19)	Average (9)	High (16)
3 to 5	Average (17)	Average (8)	High (20)	Low (20)	Average (14)	Highest (16)	High (15)	Average (11)	Highest (27)
6 to 20	Average (43)	Average (33)	Average (48)	High (78)	High (41)	Average (15)	Average (17)	Average (13)	High (76)
21 to 30	Average (15)	Average (16)	Lowest (15)	Highest (58)	Average (21)	Average (10)	Average (8)	Average (6)	High (54)
Above 30	Average (45)	Average (38)	Average (54)	Average (87)	Average (36)	Average (27)	Average (28)	Average (18)	Average (46)
Total	137	104	161	254	122	108	87	57	219

tively high in the age group of 21 to 30 years. Sensitivity to epidermal allergens is also low in infants (probably because parents tend to keep pets away from infants) and increases with age, especially in the age group of 6 to 20 years when contacts with pets become more intensive.

Dermatophagoides pteronyssinus is recognized as being the most common single allergen⁹ and one of the main aeroallergens in Israel as well. Sixteen of our patients were already sensitive by the age of 2 years as were 27 who were younger than 5 years. Sensitivity to this allergen was high as early as in infancy, highest in ages 3 to 5 years, and remained high until 30 years of age. Our findings for the 0 to 5-year-old patients from our region were not reported previously and we think it is essential to spread them among the primary care physician as well the specialist.

It is known that patients who are allergic to pollens may be hypersensitive to a variety of raw fruits, vegetables, and/or nuts.^{10,11} Cross-sensitivity to tomato/grass and tomato/pollens was recently suggested as well.¹² We, too, found a correlation between sensitivity to different foodstuffs: as expected, there was a strong correlation of sensitivity to milk and eggs, mostly in infants. In addition, we showed a similar correlation of sensitivity between milk and meat, eggs and legumes, sesame and fruits, tomatoes and grass, peanuts and mold, and soya and vegetables. An interesting correlation of sensitivity between pollens and vegetables and epidermal allergens to fruits was also detected. Epidemiologic studies in other regions of the world have noted geographic differences in allergy to food or inhalants in Scandinavia, sensitivity to different kinds of fish is very prevalent,¹³ while in Israel, allergy to fish is marginal to such an extent that these kinds of foodstuffs were not included in the final results due to their statistical insignificance. A Spanish review¹⁴ showed prominent sensitivity to fruits reaching 46.8% (which is similar to our results),

seafood (14.9%), and vegetables (12.8%) but infrequent sensitivity to cow milk and eggs. The highest sensitivity noted was to timothy grass, *Dermatophagoides*, and olive.¹⁵ In Japan,¹⁶ 16% of patients were found to be sensitive to wheat; 14% to shrimp; and 12% to crab meat, rice, and egg white. As for aeroallergens in Japan, the positive rates to inhalant allergens were as follows: *Dermatophagoides farinae* 65%, house dust 58%, cat epithelium 17%, and Japanese cedar 9%. It is interesting to speculate that the similarity of results obtained in the present study in showing high-level sensitivity to pollens and *Dermatophagoides* in Israel might be explained by a similar climate zone as that of Spain.

We presented our data regarding specific IgE findings in a selective group of an allergic Israeli population. These data showed that type I hypersensitivity to food and aeroallergens has some differences than other countries, and age is a dominant factor effecting sensitivity. We believe these data will contribute to the further understanding of causes and of the increased prevalence of allergic diseases in our region as well as in other countries.

REFERENCES

1. Good allergy practice-standards of care for providers and purchasers of allergy services within the national Health Service. Royal College of Physicians and Royal College of Pathologists. *Clin Exp Allergy* 1995;25:586-95.
2. Sampson HA. Adverse reactions to foods. *Clin Science* 1988;66:1661-80.
3. Hetman S, Kivity S, Greif J, et al. IgE values in the allergic and healthy Israeli population. *Ann Allergy* 1988;61:123-27.
4. James JM, Sampson HA. Immunologic changes associated with The development of tolerance in children with cow milk allergy. *J Pediatr* 1990;117:561-67.
5. Bernhisel-Broadbent J, Dintzis HM, Dintzis RZ, Sampson HA. Allergenicity and antigenicity of chicken egg ovomucoid (Gal d III) compared with ovalbumin (Gal d I) in children with egg allergy and in mice. *J Allergy Clin Immunol* 1994;93:1047-59.
6. Novembre E, de Martino M, Vierucci A. Foods and respiratory allergy. *J Allergy Clin Immunol* 1988;81:1059-65.
7. Bock SA. Respiratory reactions induced by food challenges in children with pulmonary disease. *Pediatr Allergy Immunol* 1984;74:26-33.
8. Sigurs N, Hatteving G, Kjellman B, et al. Appearance of atopic disease in relation to serum IgE antibodies in children followed up from birth for 4 to 15 years. *J Allergy Clin Immunol* 1994;94:757-63.
9. Matricardi PM, Nisini R, Biselli R, D'Amelio R. Evaluation of the overall degree of sensitization to airborne allergens by a single serologic test: implications for epidemiologic studies of allergy. *J Allergy Clin Immunol* 1993;1:68-79.
10. Van Ree R, Aalberse RC. Pollen-vegetable food crossreactivity. *J Clin Immunoassay* 1993;16:124-30.
11. De Martino M, Novembre E, Cozza G, et al. Sensitivity to tomato and peanut allergens in children monosensitized to grass pollen. *Allergy* 43:206-213. 1988.
12. F. de Blay, Pauli G, Bessot JC. Cross-Reactions Between Respiratory and Food Allergens *Allergy Proc.* 1991;12:313-317.
13. Hansen TK, Bindslev-Jensen C, Skov PS, Poulsen LK. Codfish allergy in adults: IgE cross-reactivity among fish species. *Ann Allergy Asthma Immunol.* 1997;78(2):187-94.
14. Joral A, Villas F, Garmendia J, Villareal O. Adverse reactions to food in adults. *J Investig Allergol Clin Immunol.* 1995;5(1):47-9.
15. Soriano JB, Tobias A, Kogevinas M, et al. Atopy and nonspecific bronchial responsiveness. A population-based assessment. *Am J Respir Crit Care Med.* 1996;154(6 Pt 1):1636-40.
16. Kosugi T, Saitoh S et al: Evaluation of the sensitized condition of patients with allergic diseases in Okinawa using the MAST allergy system. *Arerugi.* 1992;41(7):766-71.

Requests for reprints should be addresses to:
Shmuel Kivity, MD
Department of Allergy & Pulmonary Disease
Tel Aviv Sourasky Medical Center
6 Weizman St
Tel Aviv 64239
Israel