

Short communication

Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel

Objective: To determine the prevalence, importance, and the order of frequency of IgE-mediated food allergens among infants and young children in Israel.

Study design and patients: In a cross-sectional study, the prevalence of IgE-mediated food allergy was investigated in 9070 infants and young children (0–2 years) who were followed-up at 23 Family Health Centers (FHCs) in central Israel. Patients with suspected IgE-mediated food allergic reactions, were recruited for further evaluation (detailed questionnaire and skin-prick test (SPT)).

Results: We identified 150 out of 9070 (1.7%) patients with suspected IgE-mediated food allergy. Among them, 102/150 (67%) [59 males, 43 females; mean age 10.3 months] completed a detailed questionnaire and underwent SPT. Evaluation revealed 131 positive SPTs in 78/102 (76.5%) patients. Twenty-seven positive SPTs in 18 patients were considered clinically irrelevant based on previous consumption of the relevant foods without clinical symptoms. Thus, there were 104 relevant positive SPTs in 78 patients. The overall prevalence of clinically relevant IgE-mediated food allergic reactions among these patients is estimated to be 1.2% (104/9070). The most common food allergens were egg, cow's milk, and sesame. Anaphylaxis was the presenting symptom in 14/78 (18%) including six sesame-induced cases. A history of other atopic diseases was reported in 27 (35%) patients. In addition, 22 (28%) had a history of atopy in first-degree family members.

Conclusions: We found sesame to be a major cause of IgE-mediated food allergy in Israel. In fact, it is second only to cow's milk as a cause of anaphylaxis. We recommend that testing for food allergens be tailored to each community based on local experience and should include sesame in appropriate populations.

I. Dalal,^{1,2} I. Binson,² R. Reifen,³
Z. Amitai,⁴ T. Shohat,⁴ S. Rahmani,⁴
A. Levine,² A. Ballin,² E. Somekh,^{1,2}

¹Pediatric Allergy and Clinical Immunology Unit,

²Department of Pediatrics, E. Wolfson Medical Center,

³School of Nutritional Sciences, Hebrew University,

⁴Tel Aviv Health District, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Key words: anaphylaxis, children, food allergy, IgE-mediated, infants, Israel, sesame.

Dr Ilan Dalal, MD
Department of Pediatrics
E. Wolfson Medical Center
Holon 58100
Israel

Accepted for publication 19 October 2001

The true prevalence of food hypersensitivity in the general population is uncertain. Although up to one third of American households believe that someone in their family has had a 'food allergy', the true prevalence is probably much lower, estimated to be 2–8% in infants and young children and 1–2% in the adult population (1–4). Studies from the Netherlands, the United Kingdom, and France, have reported prevalences of 0.8–2.4%, 1.4–1.8%, and 3.2%, respectively (5–7). A survey in Japan, however, has estimated that 12.6% of children have an immediate-type food allergic reactions (8). These widely variable prevalences of food allergy probably reflect differences in the diagnostic criteria and study design.

While in principle any food may cause an allergic reaction, in practice the majority of reported food allergic reactions in the paediatric population are accounted for by cow's milk, egg, peanut, tree nuts, soy, wheat and fish. Most of these allergies, especially to egg, cow's

milk, soy, and wheat, usually disappear by the age of 3 years, while those associated with peanuts, tree nuts, fish and seafood, are usually sustained for life (2–4).

The order of importance of specific allergens varies in different countries, reflecting a possible interaction of genetic factors, cultural and dietary habits, and exposure to new allergenic products early in life. For example, peanut allergy is very common in the UK (9), France (10), Switzerland (11), and North America (12, 13), but very rare in Italy (14), and Singapore (15).

In Israel, during a pilot study, we had observed that peanut allergy is less common than in North America and Europe, while on the contrary, sesame allergy is more prevalent. We conducted a cross-sectional study in order to determine the prevalence, importance, and order of frequency of IgE-mediated food allergic reactions among infants and young children (0–2 years) in Israel.

Material and methods

Selection of patients

This cross-sectional study was conducted among infants and young children (0–2 years) who were followed-up in 23 FHCs in central Israel. These government-operated centers provide universal preventive health services to infants and children up to 5 years of age. It is estimated that 95% of all children visit these centers. Approximately 9070 patients (birth to 1 years – 4630, 1–2 years – 4440) were followed-up on a regular basis at the time of the study at these FHCs and consisted the base for our study population. All infants and children, suspected of having IgE-mediated food allergic reactions (within 2 h after exposure to the suspected food), were recruited for further evaluation. Possible clinical manifestations included cutaneous symptoms [urticaria, angioedema, exacerbation of atopic eczema/dermatitis syndrome (AEDS)], gastrointestinal symptoms (vomiting, diarrhoea), respiratory symptoms (cough, wheezing, rhinitis) and anaphylaxis as defined by the EAACI task force (16). These patients were identified by the following methods:

1. Information obtained from the patients' medical records at the FHCs, and from the FHCs' staff, including nurses and dietitians
2. Announcements through the local newspaper and monthly publication of the FHCs
3. Brochures that were distributed to all families who visited the FHCs.

All parents of patients with a suggestive history of IgE-mediated food allergy were asked to fill out a questionnaire, including the children's history of food allergy (description of the symptoms, type and quantity of food required to evoke a reaction, whether the food is raw or cooked, the time elapsed between ingestion and the onset of symptoms, the age of onset, and the number of episodes of allergic reactions), and personal and family history of atopic diseases. A single attending physician in the paediatric out-patient clinic (I.B.) interviewed the parents. Patients with suspected IgE-mediated reactions were called for SPT at the Pediatric Allergy/Immunology Unit at the E. Wolfson Medical Center. We did not use oral challenge because the strict clinical criteria together with positive SPT were diagnostic.

The study was examined and approved by the Ethics Committee of the E. Wolfson Medical Center, and informed consent was obtained from all the patients' caregivers.

Spt

Commercial extracts (Center Laboratories, Port Washington, NY, USA) of the most common allergens: cow's milk, egg, wheat, peanut,

soy, fish, and any other food suspected by history, were used. For sesame testing, both commercial (Bencard, Mississauga, Ontario) sesame extract and brown sesame seed freshly crushed and diluted in physiologic saline (1 : 10 w/v), were utilized. Positive (histamine 1 mg/ml) and negative (50% glycerosaline) controls were applied by the same technique. SPTs were interpreted as positive when the wheal diameter was ≥ 3 mm. As previously reported, SPT can be performed and interpreted without any difficulties even in infants (17).

Results

We identified 150 out of 9070 (1.7%) patients with suspected IgE-mediated food allergic reactions. Among them, 128 (85.3%) completed the questionnaire, of whom 26 (20.5%) refused further investigations and prick testing. Thus, a total of 102 patients were enrolled in this study, including 59 males and 43 females with a mean age of 10.3 months at diagnosis (range 1–24 months). Screening of these patients revealed 131 positive SPTs in 78 (76.5%) of them. In this group, we identified 18 patients for which some of their positive SPTs ($n=27$) were considered clinically irrelevant, based on previous consumption of the relevant foods without any clinical manifestations. Nine of these patients (50%) had a history of AEDS, a condition, which is associated with a high number of clinically irrelevant positive SPTs (18, 19).

Altogether, we identified 104 relevant positive SPTs in 78 patients. In this group, the most common food allergens were egg, cow's milk and sesame (Table 1). Mean ages of patients allergic to these three major foods were as follows: cow's milk, 5.6 months (range 1–15); egg, 9.9 months (range 4–19); sesame, 10.5 months (range 6–21). The allergic reactions, reported by the 78 patients to the three major food allergens, are listed in Table 2. Anaphylaxis was the presenting symptom in 14/78 (18%), including six sesame-induced cases. Of note, that in three cases of sesame allergy the SPT was negative with the commercial extract, but was positive with the brown, native sesame extract. This observation

Table 1. Prevalence of IgE-mediated food allergic reactions in 102 infants and young children

Food	Diagnosis by history <i>n</i> =9070 (%)	Diagnosis by history and SPT <i>n</i> =9070 (%)
Egg	67 (0.74)	42 (0.50)
Cow's milk	37 (0.40)	28 (0.30)
Sesame	18 (0.20)	16 (0.18)
Peanut	6 (0.06)	4 (0.04)
Soy	3 (0.03)	3 (0.03)
Tree nuts	3 (0.03)	2 (0.02)
Strawberry	3 (0.03)	2 (0.02)
Beef	2 (0.02)	2 (0.02)
Fish	2 (0.02)	1 (0.01)
Chicken	1 (0.01)	1 (0.01)
Tomato	1 (0.01)	1 (0.01)
Garlic	1 (0.01)	1 (0.01)
Chocolate	1 (0.01)	1 (0.01)
Total	145 (1.70)	104 (1.20)

Table 2. Clinical symptoms of IgE-mediated reactions to three major food allergens in 78 patients

Symptoms	Egg	Cow's milk	Sesame
Urticaria	28	11	4
Urticaria and angiodema	9	3	4
Anaphylaxis	1	7	6
Gastrointestinal	1	6	1
Urticaria and AEDS exacerbation	3	1	1

AEDS, atopic eczema/dermatitis syndrome.

has been reported previously (20). Forty-eight of the 78 patients (61.5%) were allergic to one food, 21 (27%) to two foods, and nine (11.5%) to three or more foods. A history of other atopic diseases was reported in 27 of the 78 patients (35%) (AEDS (15), asthma (16), allergic rhinitis (4)), and a history of atopy in first-degree family members was reported in 22 (28%) patients.

Discussion

In this cross-sectional study, we further establish the concept that food allergy is also a matter of geography. Some foods, such as cow's milk and egg, appear to be universal allergens in infants and young children, while the prevalence of others, such as peanut and sesame differ significantly.

The overall prevalence of IgE-mediated food allergy among our patients was in the range of 1.2–1.7%. This figure was calculated by using the number of 9070 patients, who were followed-up at FHCs, as the denominator. On the other hand, we did not attempt to calculate the prevalence of positive SPTs in the general paediatric population, because we only tested patients with suspected IgE-mediated food allergic reactions. It is clear that we have underestimated the prevalence of all food allergic reactions, as we focused on IgE-mediated reactions only.

We found sesame to be a major cause of IgE-mediated food allergic reactions in our population. In fact, it is second only to cow's milk as a cause of anaphylaxis and third as an overall cause of IgE-mediated food allergy. A dominant contribution to these findings could be the

early exposure to sesame in Israel. It is a common practice among FHCs' nurses and dietitians to recommend adding Tehini or Halva (sesame seed-based dip and sweets) to the diet of children in the first year of life as a good source of calories and bio-available iron. Common foods containing sesame seeds are Middle Eastern foods, a variety of bakery products, dips, salad dressings, vegetarian dishes and 'health foods'. Until recently, there were only a few reports (mainly case reports) regarding sesame allergy including some cases of IgE-mediated, non-IgE-mediated, occupational hypersensitivity, and anaphylaxis (21–31). Some of the reports drew attention to the risk of allergic reactions to sesame oil because traces of sesame proteins persist in the oil. The use of sesame oil is not limited to cooking only, but it is also used in cosmetics and pharmaceutical products (20, 23, 27). The use of sesame seeds/oil-containing products has spread to North America and Europe in recent decades, owing to the introduction of new trends such as vegetarianism, 'health foods', and exposure to 'exotic' foods. This may cause a significant increase in the frequency of recognized sesame allergic patients, as has been recently reported in Australia (32). The protein(s) carrying the allergenic determinants of sesame have not been fully determined. However, Kolopp-Sarda et al. pointed to the possible involvement of a 25-kDa protein in IgE-mediated reaction to sesame (28).

Peanut, a major food allergen in Europe and North America, was found to be a rare allergen in Israel. This difference is probably owing to early introduction and heavy consumption (12), different cooking methods (33), and probably other, yet, unidentified factors, of peanut-containing products (in the form of peanut butter) in the regular diet. Our findings suggest that sesame is the equivalent 'peanut butter' of the Middle East. Other reports have supported the concept that the prevalence of allergic reactions to individual foods clearly varies with the dietary habits of different communities. Fish allergy is common in Spain and Portugal (34, 35). Seafood has been reported as a major cause of food-induced anaphylaxis in Italy (14), and mustard was found to be a major allergen in France (10). In Singapore, the most common food allergen is bird's

Table 3. Food allergens among children in different countries*

Australia	France	Israel	Italy**	Japan	Singapore**	Spain
Egg	Egg	Egg	Fish	Egg	Bird's nest	Egg
Milk	Peanut	Milk	Milk	Milk	Seafood	Fish
Peanut	Milk	Sesame	Nuts	Seafood	Egg	Milk
Nuts	Mustard	Peanut	Egg	Wheat	Milk	Peach
Sesame	Cod	Soy	Fruit	Snacks	Chinese herbs	Nuts
Wheat	Hazelnut	Nuts	Cereals	Beans		Lentil
Soy	Kiwi	Strawberry	Vegetables	Chicken		Peanut
Fish	Wheat	Beef	Goat milk	Vegetables,		Chick pea
		Chicken, Tomato		Nuts		

*Food allergens are written in order of frequency.

nests (15). Table 3 summarizes comparative data regarding food allergens in children from different countries, highlighting the different patterns of sensitization (8, 10, 14, 15, 32, 34).

In summary, we found sesame to be a major cause of IgE-mediated food allergic reactions in Israel. Moreover, it is second only to cow's milk as a cause

of anaphylaxis. Currently, the panel of foods recommended for use in screening tests corresponds mainly to children living in westernized countries. Different feeding habits, together with other factors, may lead to different patterns of sensitization, thereby, requiring re-evaluation of this list in different countries.

References

1. SLOAN AE, POWERS ME. A perspective on popular perceptions of adverse reactions to foods. *J Allergy Clin Immunol* 1986;**78**:127–133.
2. BURKS AW, SAMPSON HA. Food allergies in children. *Curr Probl Pediatr* 1993; **23**:230–252.
3. SAMPSON HA. Food allergy. Part 1: Immunopathogenesis and clinical disorders. *J Allergy Clin Immunol* 1999; **103**:717–728.
4. BOCK SA. Prospective appraisal of complaints of adverse reaction to foods in children during the first 3 years of life. *Pediatrics* 1987;**79**:683–688.
5. JANSSEN JJ, KARDINAAL AF, HUIJBERS G, Vlieg-Boerstra BJ, MARTENS BP, OCKHUISEN T. Prevalence of food allergy and intolerance in the adult Dutch population. *J Allergy Clin Immunol* 1994;**93**:446–456.
6. YOUNG E, STONEHAM MD, PETRUCKEVITCH A, BARTON J, RONA R. A population study of food intolerance. *Lancet* 1994;**343**:1127–1130.
7. KANNY G, MONERET-VAUTRIN DA, FLABBE J, BEAUDOUIN E, MORISSET M, THEVENIN F. Population study of food allergy in France. *J Allergy Clin Immunol* 2001;**108**:133–140.
8. IKURA Y, IMAI Y, IMAI A et al. Frequency of immediate-type food allergy in children in Japan. *Int Arch Allergy Immunol* 1999;**118**:251–252.
9. EMMETT SE, ANGUS FJ, FRY JS, LEE PN. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members. *Allergy* 1999;**54**:380–385.
10. RANCE F, KANNY G, DUTAU G, MONERET-VAUTRIN DA. Food hypersensitivity in children: Clinical aspects and distribution of allergens. *Pediatr Allergy Immunol* 1999;**10**: 33–38.
11. PHILIPPE A. Eigenmann and Anne-Marie Calza. Diagnosis of IgE-mediated food allergy among Swiss children with atopic dermatitis. *Pediatr Allergy Immunol* 2000;**11**:95–100.
12. HOURIHANE JO'B. Peanut allergy – current status and future challenges. *Clin Exp Allergy* 1997;**27**:1240–1246.
13. SICHERER SH, MUNOZ-FURLONG A, BURKS AW, SAMPSON HA. Prevalence of peanut and tree nut allergy in the United States of America. *J Allergy Clin Immunol* 1999;**103**:559–562.
14. NOVEMBRE E, CIANFERONI A, BERNARDINI R et al. Anaphylaxis in children: clinical and allergologic features. *Pediatrics* 1998;**101**:1–8.
15. GOH DLM, LAU YN, CHEW FT, SHEK LPC, LEE BW. Pattern of food-induced anaphylaxis in children of an Asian community. *Allergy* 1999;**54**:78–92.
16. JOHANSSON SG, HOURIHANE JO, BOUSQUET J et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI task force. *Allergy* 2001;**56**:813–824.
17. MENARDO JL, BOUSQUET J, RODIERE M, ASTRUC J, MICHEL FB. Skin test reactivity in infancy. *J Allergy Clin Immunol* 1985;**75**:646–651.
18. SAMPSON HA, MACCASKILL CC. Food hypersensitivity and atopic dermatitis: evaluation of 113 patients. *J Pediatr* 1985;**105**:669–675.
19. BURKS AW, MALLORY SB, WILLIAMS LW, SHIRRELL MA. Atopic dermatitis: clinical relevance in food hypersensitivity. *J Pediatr* 1998;**113**:447–456.
20. KANNY G, DE HAUTECLOCQUE C, MONERET-VAUTRIN DA. Sesame seed and sesame seed oil contain masked allergens of growing importance. *Allergy* 1996;**51**:952–957.
21. RUBINSTEIN L. Sensitivity to sesame seed and sesame oil. *NY State J Med* 1950; **50**:343–344.
22. MALISH D, GLOVSKY MM, HOFFMAN DR, GHEKIERE L, HAWKINS JM. Anaphylaxis after sesame seed ingestion. *J Allergy Clin Immunol* 1981;**67**:35–38.
23. CHIU JT, HAYDIK IB. Sesame seed oil anaphylaxis. *J Allergy Clin Immunol* 1991;**88**:414–415.
24. KAGI MK, WUTHRICH B. Falafel burger anaphylaxis due to sesame seed allergy. *Ann Allergy* 1993;**71**:127–129.
25. EBERLEIN-KONIG B, RUEFF F, PRZYBILLA B. Generalized urticaria caused by sesame seeds with negative prick test results and without demonstrable specific IgE antibodies. *J Allergy Clin Immunol* 1995;**96**:560–561.
26. ALDAY E, CURIEL G, LOPEZ-GIL MJ, CARRENO D, MONEO I. Occupational hypersensitivity in sesame seeds. *Allergy* 1996;**51**:69–70.
27. BIRNBAUM J, PORRI F, CASTELIAN M, VERVOLET D. Sesame seed and oil anaphylaxis. *J Allergy Clin Immunol* 1997;**99**:287.
28. KOLOPP-SARDA MN, MONERET-VAUTRIN DA, GOBERT B et al. Specific humoral immune responses in 12 cases of food sensitization to sesame seed. *Clin Exp Allergy* 1997;**27**:1285–1291.
29. ASERO R, MISTRELLO G, RONCAROLO D, ANTONIOTTI PL, FALAGIANI P. A case of sesame-induced anaphylaxis. *Allergy* 1999;**54**:526–527.
30. PAJNO GB, PASSALACQUA G, MAGAZZU G, BARBERIO G, VITA D, CANONICA GW. Anaphylaxis to sesame. *Allergy* 2000; **55**:199–201.
31. LEVY Y, DANON YL. Allergy to sesame seed in infants. *Allergy* 2001;**56**: 193–194.
32. HILL DJ, HOSKING CS, HEINE RG. Clinical spectrum of food allergy in children in Australia and South-East Asia: identification and targets for treatment. *Ann Med* 1999;**31**:272–281.
33. BEYER K, MORROW E, LI XM et al. Effects of cooking methods on peanut allergenicity. *J Allergy Clin Immunol* 2001;**107**:1077–1081.
34. CRESPO JF, PASCUAL C, BURKS AW, HELM RM, ESTEBAN MM. Frequency of food allergy in pediatric population from Spain. *Pediatr Allergy Immunol* 1995;**6**:39–43.
35. OEHLING A, FERNANDEZ M, CORDOVA H, SENZ MC. Skin manifestation and immunological parameters in childhood food allergy. *J Invest Allergol Clin Immunol* 1997;**7**:155–159.