

The epidemiology of food allergy

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In contrast to respiratory allergies, the epidemiology of food allergy has been little studied, and there is no strong evidence for an increasing incidence, either among infants and children or in adults. Neither are there any studies showing regional differences in prevalence. On the contrary, studies in Estonia, Iceland and Sweden indicate a similar prevalence during the first 2 years of life, both in verified food allergy and reported food intolerance. This is despite a low prevalence of respiratory allergies in the two former countries and a high prevalence in Sweden. The major problem with such epidemiological studies lies in the fact that there are no simple diagnostic criteria to verify the diagnosis. So far IgE determinations have been the only available diagnostic test, and their value is limited by poor sensitivity and the fact that at best they would only verify a small proportion of food intolerance, i.e. that caused by IgE-mediated reactions. A diagnosis of food allergy/intolerance must be based on a double-blind placebo-controlled food challenge, and not on the patient's or doctor's impression. More studies are required from different regions in order to identify similarities and differences in the patterns of food allergy. In particular, there is a need for properly conducted epidemiological studies in adults. Such studies should be interdisciplinary, as the cultural and social perceptions of food allergy and food intolerance would be expected to have a major impact on prevalence, perhaps even more than medical factors. *Curr Opin Allergy Clin Immunol* 1:225–227. © 2001 Lippincott Williams & Wilkins.

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Abbreviation

DBPCFC double-blind placebo-controlled food challenge

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Introduction

There is little doubt that the prevalence of respiratory allergies has increased considerably, particularly in industrialized countries with market economies over the past 40 years. There are also considerable geographical differences in prevalence, as conclusively shown by large international studies in children and adults employing a standardized methodology. Both the International Study of Asthma and Allergies in Children [1] and the European Respiratory Health Survey [2] have so far been limited to respiratory allergies, and similar studies have not been performed to define the prevalence of food allergies. There are several reasons for this. The criteria for the diagnosis are not clear. Clinical symptoms suggestive of food allergy may appear under many other circumstances than as a consequence of an allergic reaction. Also, the symptoms of a true food allergy may be difficult to recognize. Furthermore, food allergy is not easily verified, particularly in adults, as the only generally recognized diagnostic procedure, i.e. double-blind placebo-controlled food challenge (DBPCFC), is time consuming and potentially dangerous.

Over the past 2 years, some studies have addressed issues related to the epidemiology of food allergy. Although they are of interest from a clinical point of view, unfortunately none of them has provided any truly novel information regarding the incidence or prevalence of either food allergy or intolerance in a general population.

Definitions

The terms 'food allergy' and 'food intolerance' are often used loosely, and this fact is a major cause of confusion. According to the European Academy of Allergy and Clinical Immunology, 'food allergy' is defined as adverse reactions to foods caused by an immunological mechanism, whereas the term 'food intolerance' is used for non-immune-mediated reactions [3]. So far the only conclusively proved mechanism for food allergy is IgE mediated. These reactions are mostly seen in infants and young children, and are less common in adults. Other mechanisms, e.g. immune complexes, cell-mediated immune reactions are likely to be involved in some cases of food allergy but this has yet to be confirmed. These definitions are not always helpful in epidemiological surveys based on questionnaires. Furthermore, the term 'food intolerance' is subjective and is based on expectations and cultural perspectives. Diffuse symptoms from the gastrointestinal tract or other organs may thus be commonly ascribed to intolerance in one society, but not in another.

In the European Academy of Allergy and Clinical Immunology (EAACI) position paper [3] it was established that the diagnosis of food allergy/intolerance must be based on the observation of the patient's behaviour after exposure to the suspected food in a DBPCFC and cannot be based on the patient's or doctor's impression.

Epidemiological aspects

There are no simple questions by which food allergy would be identified with acceptable sensitivity and specificity in an epidemiological survey, and it would be expensive to verify a diagnosis by food challenges. The prevalence has been reported to vary considerably over Europe. These differences may not be real, however, as one would expect a lower prevalence in a society where much social activity takes place around the dinner table compared with a country in which eating is mainly perceived as essential to survival. It is thus possible that any regional differences are explained by cultural and social factors, rather than representing differences in the prevalence of disease.

In infants and young children under the age of 3 years, food allergy and any food intolerance often appear within an hour of ingestion, thus making the identification of an incriminated food item reasonably simple. In general, food hypersensitivity is a transient phenomenon in early childhood, but in many atopic individuals immediate-type food allergy is often the first evidence of a genetic predisposition towards the development of atopic disease, predicting later appearing allergic manifestations in the respiratory tract [4]. In such atopic children, food allergens (egg, nuts, peanuts and milk) dominate as sensitizing agents during the first 23 years of life. Differences in the disappearance rate depend on the particular allergen and on individual factors in the individual subject to the allergy. The likelihood of outgrowing a food allergy also depends on the allergen involved. Most children with cow's milk allergy thus tolerate at least small amounts of cow's milk before 3 years of age. Egg allergy usually subsides before 7 years of age, whereas allergy to fish, soy and nuts tends to remain for a considerably longer time.

Young children with food allergy seem to have a more than twofold higher chance of outgrowing their food allergy than school-aged children.

Food hypersensitivity is common in infancy and early childhood, but not later. The highest prevalence occurs between 1.5 and 3 years of age, when up to 25% of adverse reactions to food have been reported [5]. The prevalence of adverse reactions to food additives is much lower, and in one study was found to be present in 1% of school children. Furthermore, the positive oral provoca-

tion tests with preservatives and food colours were restricted to children with concomitant allergic manifestations to food allergens. However, only a minority of the reactions depend on immunological mechanisms, i.e. allergy. The prevalence is influenced by the family history and exposure to food allergens and factors acting as adjuvants for sensitization.

Although there are some population-based studies on the prevalence of food allergy in young children, more studies, preferably prospective studies are needed. Kristjansson and co-workers [6] studied the prevalence of adverse reactions to foods in 18-month-old infants in Sweden and Iceland. The study population was unselected in that all infants of the appropriate age were included who over a one-year period attended one of two primary healthcare centres in each country. The response rates were 79 and 90%, respectively, in Iceland and Sweden. The parents received a questionnaire that had been validated in a pilot study. The parents of children with reported adverse reactions were telephone interviewed, and infants with suspected allergy were offered a visit to a paediatric allergist and were subjected to skin-prick testing and in some cases DBPCFC. The prevalence of verified food allergy was 2% in both countries and of adverse reactions to a wide range of foods 28 and 27%, respectively. Therefore, only one in 15 infants with reported adverse reactions to food actually had a confirmed food allergy. The similar prevalence in the two countries is interesting in the light of the low prevalence of respiratory allergies among adults in Iceland compared with Scandinavia and the high prevalence of tobacco smoking at home (30% of the Icelandic families smoked at home, compared with 3% in Sweden).

In contrast to the increasing incidence and prevalence of respiratory allergies in children and young adults, there is no proof of an increased prevalence of food allergy during the past few decades. Indeed, the prevalence was similar over the first 2 years of life in a prospective study in Estonia [7], with a very low prevalence of respiratory allergy in Sweden. It is reasonable, however, to suspect that pollen-associated food allergies (e.g. against peaches and celery) may have increased as a consequence of the increasing incidence of hay fever.

It is more difficult to verify a food allergy in adults, as IgE-mediated reactions are much less common than in young children. Furthermore, the perceptions of food allergy would affect the outcome of a prevalence study more than in children. Any studies comparing different adult populations would therefore have to address social and cultural issues in addition to medical issues. Such interdisciplinary studies on food allergy and intolerance have not been performed.

Food allergy and eczema

It is well established in clinical practice that food allergy may cause childhood atopic dermatitis. The true prevalence is not known, because of the lack of properly conducted epidemiological studies that would allow an analysis of the prevalence in the general population. There are, however, hospital-based studies, in which children with atopic dermatitis with a suspected food allergy underwent blinded food challenges. In one recent German study [8], DBPCFC were performed in 107 children aged between 5 months and 12 years (median age 21 months, 83% under 4 years of age). They all had a suspected worsening of eczema or immediate-type clinical reactions. A total of 387 oral challenges were carried out, two-thirds of which were with a food and a third were with placebo. Positive reactions were obtained in 51% of the 259 challenges with food, whereas only one positive reaction was recorded after the 127 placebo challenges.

In that study, the clinical value of IgE determinations to four common food allergens was also assessed. Such analyses were of limited clinical value to identify beforehand those who had a positive reaction to the DBPCFC. The study confirmed several previous investigations showing that immediate-type food allergy is unlikely in children with a negative skin-prick test and no detectable circulating IgE antibodies to the food. The specificity was only 6–38%, however, for the four most commonly tested allergens, i.e. hen's egg, cow's milk, wheat and soy, indicating that circulating IgE antibodies to these foods are mostly not associated with allergic manifestations. Therefore, the positive and the negative predictive values of such tests are low, with the possible exception of reactions to soy. The study supported several previous studies in that IgE antibody determinations would not be very useful to determine the true prevalence of food allergy in a population, not even IgE-mediated food allergy.

Regional differences in food allergens

The most common food allergens globally include hen's egg, cow's milk, peanuts, and soy, followed by fish and

crustaceans. There may, however, exist other food allergens that could conceivably be important in certain areas. This was indicated by a study from Singapore [9], reporting the outcome of a population-based questionnaire survey of 6400 children. Among food allergens triggering systemic reactions, bird's nest was found to be the most common, i.e. it was more common than egg and crustacean seafood, which are commonly consumed. Edible bird's nest is a Chinese delicacy made from the saliva of a certain species of swiftlets. The IgE-mediated reactions are caused by a 66 000 M_r glycoprotein. It was also noted that peanuts caused no anaphylactic reactions. This is in striking contrast with the situation in Western countries. The reason for this is uncertain, as it is not likely to be explained by lack of exposure.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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