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Prevalence of food allergy: an overview

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At present the only cure for food allergy is to avoid eating the food responsible for the allergy. Thus, food allergy or food hypersensitivity is a disease that is not only of concern to the individual who is affected but also to those involved directly and indirectly in supplying and preparing food for the food-allergic individual, and its impact on society should be evaluated on this basis. It is generally assumed that questionnaire-based studies vastly overestimate the prevalence of food hypersensitivity. The reported perceived prevalence of food hypersensitivity varies from 3.24% to 34.9%, which may be explained partly by the difference in reporting lifetime prevalence compared with point prevalence. However, of more importance is the apparent inverse correlation between response rate and prevalence (the higher the response rate, the lower the perceived prevalence). The three most-recent prevalence studies on food hypersensitivity (one on perceived food hypersensitivity and two on confirmed food hypersensitivity) all report estimates for prevalence of approximately 3%, but their criteria for including subjects as being positive are not identical, although they do overlap. Furthermore, because of differences in methodology there is no definitive information to indicate whether the prevalence of food allergy is increasing. However, the high prevalence of pollen-related food allergy in younger adults in the population suggests that the increase in pollen allergy is also being accompanied by an increase in pollen-related food allergy.

Prevalence: Food allergy: Food hypersensitivity

Currently, food allergy can only be cured by avoiding the food responsible. Consequently, food hypersensitivity, including food allergy, is a problem for both the individual and all those involved in supplying and preparing food for the individual with food allergy, including family and friends, caterers, restaurants and the food industry. Thus, the impact on society should be evaluated on this basis.

The European Academy of Allergy and Clinical Immunology has proposed a revised nomenclature for allergic and related reactions (Johansson *et al.* 2001). According to this proposal adverse reactions to food should be termed food hypersensitivity. The term food allergy should be used when immunological mechanisms have been demonstrated, and includes both IgE- and non-IgE-mediated reactions. All other reactions, which have sometimes been referred to as 'food intolerance', should be termed non-allergic food hypersensitivity (Fig. 1).

Symptoms of IgE-mediated food allergy include: oral allergy syndrome, with itching and swelling of the oral mucosa; gastrointestinal symptoms, such as vomiting and diarrhoea; symptoms associated with the skin, i.e. urticaria and atopic dermatitis, and the eyes and respiratory system, such as conjunctivitis, rhinitis, asthma; generalised symptoms, i.e. anaphylaxis (Bruijnzeel-Koomen *et al.* 1995). However, non-IgE-mediated food allergies and non-allergic food hypersensitivity may have symptoms that resemble IgE-mediated food allergy (Fuglsang *et al.* 1993; Bengtsson *et al.* 1996; Feighery, 2005), e.g. sulphite may induce non-allergic asthma (Taylor *et al.* 1997). There is no simple diagnostic test for food hypersensitivity, allergic or non-allergic. The gold standard for diagnosing IgE-mediated food allergy is the double-blind placebo-controlled food challenge (DBPCFC), which is very expensive and time-consuming and depends on a high extent of

Abbreviation: DBPCFC, double-blind placebo-controlled food challenge.
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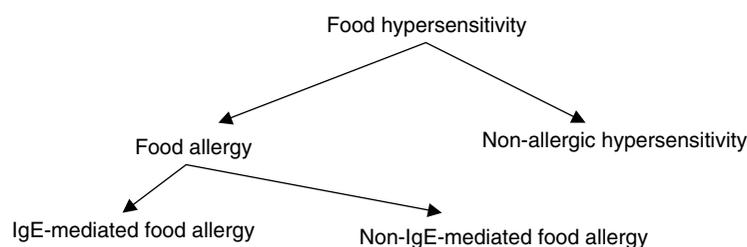


Fig. 1. Nomenclature proposed by the European Academy of Allergology and Clinical Immunology (Johansson *et al.* 2001).

compliance (Bruijnzeel-Koomen *et al.* 1995). The diagnostic difficulties are a major challenge when studying the prevalence of food hypersensitivity.

Madsen (1997) has estimated the prevalence of food hypersensitivity in Europe to be approximately 5% by combining information from the available literature on food allergy and food intolerance. This estimate does not include oral itching as the only symptom or lactose intolerance. Subsequently, there have been a number of population-based studies that have given more insight into the 'true' prevalence of food hypersensitivity.

Prevalence studies

The general population cannot be expected to differentiate IgE-mediated food allergy, non-IgE-mediated food allergy, allergic food hypersensitivity and non-allergic food hypersensitivity. Thus, questionnaires must rely on the common perception of food hypersensitivity, including food allergy, in a population. However, it is generally assumed that questionnaire-based studies vastly overestimate the prevalence of food hypersensitivity, as compared with studies in which questionnaires have been followed by a food challenge or IgE measurement.

In a study in The Netherlands (Jansen *et al.* 1994) 12.4% of the 1483 subjects reported that they had experienced food allergy or intolerance, which was subsequently confirmed by DBPCFC in 0.8% of the 1483 subjects. If it is assumed that the prevalence is the same for participants and non-participants, the estimated prevalence of food allergy or intolerance in the Dutch population is 2.4%. The initial information was obtained by door-to-door interview of a representative sample of subjects in Utrecht, and the response rate was 86%. The question on food allergy was: 'do you have allergic or intolerance reactions after eating or drinking specific foods, or are there any foods you don't use any more because they give you trouble'.

The population study conducted in the UK by Young *et al.* (1994) also reports a marked difference between the perceived prevalence and the confirmed prevalence. Of the subjects interviewed 20.4% reported adverse reactions to food, and food allergy or intolerance was confirmed by DBPCFC in 1.4–1.8% of the subjects. As only eight foods were used for the food challenge and they accounted for approximately 50% of the reported reactions, the true prevalence estimate could be 3–4%. The questions asked were about perceived connection between food ingested

and itching, eczema, urticaria, angio-oedema, asthma, rhinitis, intestinal symptoms, joint symptoms, behavioural or mood changes and headaches. Of the subjects surveyed 61% responded.

In Sweden 1397 randomly-selected subjects from the European Community Respiratory Health Survey (age 20–44 years) were asked a total of seventy-one questions (Björnsson *et al.* 1996). The questions on food allergy were: 'have you ever had an illness or trouble caused by eating a particular food or foods'; 'what type of food was this'; 'did this illness include: a rash or itchy skin; diarrhoea or vomiting; runny or stuffy nose; severe headache; breathlessness; other symptoms.' Subjects responding positively to one or more of these questions were considered to have food intolerance. Of the 25% that reported symptoms of food intolerance, 6% had elevated IgE in response to egg white, peanuts (*Arachis hypogea*), soyabean, milk, fish or wheat. However, testing for IgE is not sufficient to diagnose food allergy and cannot detect non-IgE-mediated food allergy or non-allergic food hypersensitivity. In the age-group studied the inclusion of pollen-related foods in the IgE analyses would have been expected to have produced a different result. Although the study group is described as being randomly selected, there may have been a selection bias because the study population comprised the subjects who were willing to participate in both skin-prick testing and blood sampling.

Despite being geographically close to Sweden, Denmark reveals quite a different result. In the Danish Health Interview Survey 6000 adult Danes were asked a series of questions on health problems by a professional interviewer, including a question about various factors that had elicited allergies during the previous year (Table 1; Keiding, 1997). Combining the responses relating to food colours or preservatives and foods and beverages (1994 survey) gives an overall 1-year prevalence of food hypersensitivity of 6.8% (L Keiding, personal communication); the corresponding value for the 25–44 years age-group is 6.9%.

These four studies were all performed in the period 1989–94. In 1997 Kanny *et al.* (2001) conducted a large population-based questionnaire survey in France, which comprised 44 000 subjects aged <61 years and had a response rate of 75.6%. The intention was to establish the prevalence of IgE-mediated food allergy. Two questionnaires were used. In the first questionnaire three questions concerning reactions to food were intentionally placed in seventh, eighth and ninth position. The phase-2 questionnaire, which was sent to subjects who had an adverse food reaction according to the first questionnaire,

Table 1. Results obtained in the category 'yes, I am allergic or have hypersensitivities*' in response to the question: 'are you allergic or have hypersensitivity to some of the following items'; data from Danish Institute of Clinical Epidemiology's survey on health problems in the adult Danish population (age > 16 years; Keiding, 1997)

Item	Results (%)	
	1987	1994
Pollen	5.3	9.2
Animals (dog, cat, horse, etc.)	2.5	4.5
House dust mites	2.3	3.8
Mould	0.5	1.1
Food colours or preservatives†	0.7	1.4
Certain foods†	2.0	3.3
Certain drugs or medicine	1.7	2.9
Certain chemicals or metals	4.2	4.8
Certain beverages†	1.1	1.9
Cosmetics or skin care products	1.8	5.0
Other items	5.3	3.4

*Other possible categories of response were: 'no, I am not allergic or have hypersensitivity, but do not know to what' and 'don't know'.

†Food items.

asked about specific symptoms, i.e. anaphylactic shock, urticaria, angioedema, atopic dermatitis, asthma, rhinitis, diarrhoea, vomiting, abdominal pain, migraine and other symptoms. Single answers such as abdominal pain or headache were not taken into consideration if these symptoms were not associated with other signs of food allergy. The prevalence of present food allergy (point prevalence) was estimated to be 3.24%. The most frequent allergens were found to be (%): fruits from Rosaceae (i.e. apple, cherry, peach etc.) 14; all types of vegetables 9; milk 8; crustaceans 8; shellfish 7; fruits that cross-react with latex (i.e. avocado (*Persea americana*), kiwi fruit (*Actinidia chinensis* Planch.), banana (*Musa × paradisiaca* L.), chestnut (*Castanea vesca*) 5; egg 4; tree nuts (which include cashew (*Anacardium occidentale* L.), almond (*Amygdalus communis* L.), hazelnut (*Corylus avellana*), pecan (*Carya illinoensis* (Wangenh.) K. Koch), walnut (*Juglans regia*), Brazil nut (*Bertolletia excelsa*), pistachio nut (*Pistacia vera*) and macedonia nut and Queensland nut (*Macedonia temifolia*) 3; peanuts 1.

Osterballe *et al.* (2004) have studied the prevalence of food hypersensitivity to the most common allergenic foods in an unselected population of children and adults in Odense, Denmark using a cohort born in the period from 1998 to 1999. The children and their relatives (parents and siblings) entered the study when the probands were 3 years of age; for clarity only the results for the 3-year-old children (*n* 486) and their parents (*n* 936, median age 33.7 years) are discussed. Food hypersensitivity to the most common allergenic foods was examined using a questionnaire, skin-prick test, histamine release and specific IgE. Subjects with suspected food hypersensitivity (reported in

the questionnaire or positive results in one of the tests) who had no clear-cut negative history underwent an open challenge or a DBPCFC.

The investigators subdivided food hypersensitivity into primary food hypersensitivity, defined as independent of pollen sensitisation, and secondary food hypersensitivity, defined as reactions to fruits, vegetables or nuts in pollen-sensitised individuals. The confirmed prevalence of primary food hypersensitivity was found to be 2.3% in the 3-year-old children, of whom 0.6% reacted to cow's milk, 1.6% to hen's eggs and 0.2% to peanut, and 3.2% in the adults, for whom fruits or vegetables (2.7%) and peanut (0.4%) were found to be the most prevalent foods eliciting a reaction. In addition, 7.6% of the adults were found to have secondary food hypersensitivity. Thus, the overall prevalence of IgE-mediated food allergy for the younger section of the adult population is 10.8%, with the majority showing oral allergy syndrome (Osterballe *et al.* 2005).

In an attempt to include non-allergic food hypersensitivity in the study the eleven 3-year-old children and six parents who had reported suspecting reactions to food additives were challenged with the confectionery item implicated, which contained carmine (E120), tumeric (E100) and copper chlorophyll (Osterballe *et al.* 2005). None of the children and one of the adults was found to have a positive challenge. It was surprising that all seventeen subjects implicated a food with the same three additives. However, these additives may not have been the best choice for the detection of food-additive hypersensitivity (Fuglsang *et al.* 1993).

The aim of the study conducted by Zuberbier *et al.* (2004) was to identify the prevalence of all kinds of adverse reactions to food. A random sample of 13 300 residents of Berlin were contacted and asked to answer questions about their perceived connection between food ingestion and itching, eczema, urticaria, angioedema, rhinitis, asthma, intestinal symptoms, headache and other symptoms. The response rate was 31% and the self-reported lifetime prevalence of any reaction to food was found to be 34.9%. The responders were contacted by phone and 814 of these were invited to participate in a personal investigation. They underwent a skin-prick test and blood was taken to determine specific IgE. The subjects who were still considered to have food hypersensitivity following the investigation of their personal history, the blood test and the skin-prick test underwent food challenge tests. Of the 216 DBPCFC performed a clearly positive reaction was found in 116 individuals. The overall prevalence of food hypersensitivity in all age-groups in the population of Berlin was calculated to be 3.6%, 2.5% being IgE-mediated and 1.1% being non-IgE mediated. For the IgE-mediated reactions the highest frequency (4.3%) was found in the age-group 20–39 years and the most common foods eliciting IgE-mediated reactions were found to be pollen-related fruit and vegetables (frequency; %): nuts, fruits with pips and fruits with stones 77.6; vegetables 54.4; other fruits 32.4; other foods 22.1; flour 14.9; milk 4.5; egg 2.9. For the non-IgE-mediated reactions the foods were found to be (frequency; %): nuts, fruits with pips and fruits with stones 40; other fruits

Table 2. Reported perceived prevalence of food hypersensitivity

Reference	Response rate (%)	Lifetime prevalence (%)	Point prevalence (%)	1-Year prevalence (%)
Zuberbier <i>et al.</i> (2004)	31	34.9		
Young <i>et al.</i> (1994)	61	20.4		
Kanny <i>et al.</i> (2001)	76		3.24	
Keiding (1997)	78			6.8
Jansen <i>et al.</i> (1994)	86	12.4		

20.5; vegetables 20.5; food additives 18.2; ethanol 18.2; milk 15.9.

Food commonly involved in IgE-mediated food allergy

The results of the epidemiological studies reflect the foods that most frequently elicit food allergy in the whole population.

In general, the most common food allergens in children worldwide are milk and eggs (Hill *et al.* 1997; Dalal *et al.* 2002; Osterballe *et al.* 2004), but local eating habits may also explain important food allergies. Sesame allergy is frequent in Israel, probably because of the early introduction of tahini (Dalal *et al.* 2002), and in Sweden an epidemic of coeliac disease has been related to the early introduction of gluten-containing cereals (Ivarsson *et al.* 2000).

The foods that most often cause allergy in adults are fruits and vegetables, and the primary sensitisation mainly comes from pollen. Thus, sensitisation does not reflect eating habits but rather the flora, and it is also possible that pollution acts as an adjuvant in sensitisation.

The InformAll database on allergenic foods (InformAll EU Project, 2005) describes the current knowledge on food allergens. The criterion for inclusion of a food in the database is that evidence of an IgE-mediated allergy after ingestion of the food has been published in the refereed literature, and the importance of each food as an allergen is indicated by the numbers of papers and patients listed for the food. The first version of the database includes entries for sixty-two plant foods, and a second release that will include allergenic foods of animal origin (such as milk, eggs and fish) is due in the near future (Jenkins *et al.* 2005).

EuroPrevall

Recently, the European Commission has instigated a collaborative project on food allergy under the EU Framework 6 Programme (EuroPrevall, 2005) to characterise the patterns and prevalence of food allergies across Europe in children and adults at ten centres and in infants at five centres. Both questionnaires and DBPCFC will be used in what will be one of the biggest studies to date, which aims to estimate the prevalence of IgE-mediated food allergies and provide information on their development in the first years of life.

Discussion

Table 2 shows that the reported perceived prevalence of food hypersensitivity varies by a factor 10, which may be explained partly by the difference in reporting lifetime prevalence compared with point prevalence. However, of more importance is the apparent inverse correlation between response rate and prevalence (the higher the response rate, the lower the prevalence).

Kanny *et al.* (2001) emphasise that the questions on reactions to food are intentionally placed as the seven, eight and ninth questions and that specific symptoms are listed in the second questionnaire. Björnsson *et al.* (1996) also have questions on food reactions as a part of a larger questionnaire and Zuberbier *et al.* (2004) specify symptoms, but both groups of investigators have high estimates of perceived prevalence. Thus, the main reason for the low perceived prevalence estimate reported by Kanny *et al.* (2001) could be the high number of responders. However, as the intention of this study was to study IgE-mediated food allergy, single answers such as headache or abdominal pain were not taken into consideration if these symptoms were not associated with other signs of food allergy, and it is not specified whether oral itching as the only symptom is also excluded. The relatively low overall prevalence suggests that these investigators have excluded oral itching as only symptom, at least when the results are compared with those of Osterballe *et al.* (2004), who have found that the prevalence of (IgE-mediated) food hypersensitivity including oral itching is 10.8% for young adults (median age 33.7 years). The results of the Zuberbier *et al.* (2004) study suggest that this age-group (20–39 years) has the highest frequency (4.3%) of IgE-mediated reactions, although it is not clear what consideration was given to oral itching.

All three groups of investigators (Kanny *et al.* 2001; Osterballe *et al.* 2004; Zuberbier *et al.* 2004) agree that the food items that most frequently elicit food hypersensitivity are pollen-related fruits and vegetables. When the subjects in the Osterballe *et al.* (2004) study are divided into those who have a primary food allergy without pollen allergy and those who have a food allergy secondary to pollen sensitisation, fruits and vegetables are the foods that most frequently elicit a reaction in the non-pollen-sensitised adults. Furthermore, Zuberbier *et al.* (2004) report that fruit and vegetables are the foods that most frequently elicit non-IgE mediated reactions. However, it is possible that the results reflect the specificity of the diagnostic tests

rather than true non-IgE-mediated or non-pollen-related fruit and vegetable allergy.

Kanny *et al.* (2001) estimate a point prevalence for (perceived) IgE-mediated food allergy of 3.24% in the French population, while Zuberbier *et al.* (2004) estimate a prevalence of confirmed food hypersensitivity in the population of Berlin to be 3.6% and Osterballe *et al.* (2004) estimate that the prevalence of confirmed food allergy in a cohort of 3-year-old Danish children is 2.3% and that of their parents is 3.2%, when excluding food allergy secondary to pollen allergy. Thus, the three most recent prevalence studies on food hypersensitivity, including food allergy, all estimate prevalence to be approximately 3%, but their criteria for including subjects as being positive are not identical, although they do overlap. It will be interesting to follow the results of the EuroPrevall study and find out whether it will reveal geographical differences in the prevalence of IgE-mediated food allergy.

The methodological differences in the current prevalence studies make it difficult to establish whether the prevalence of food allergy is increasing. However, the high prevalence of pollen-related food allergy in the younger section of the adult population (Osterballe *et al.* 2004; Zuberbier *et al.* 2004) suggests that the increase in pollen allergy is also accompanied by an increase in pollen-related food allergy. Most of these reactions are oral itching and not life threatening, but they nevertheless have an impact on the choice of food. If a growing section of the population avoids eating fresh fruit and vegetables because of adverse reactions it may have nutritional implications.

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