

Prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and food hypersensitivity among teenagers

Brett Pereira, MD,^{a,*} Carina Venter, BSc,^{a,*} Jane Grundy, RN,^a C. Bernie Clayton, RM,^a
S. Hasan Arshad, MD,^a and Taraneh Dean, PhD^{a,b} *Isle of Wight and Portsmouth,*
United Kingdom

Background: There is a paucity of information on food hypersensitivity (FHS) among teenagers.

Objectives: We sought to investigate the sensitization rates, perception of FHS, food avoidance, and FHS assessed by means of food challenges among teenagers.

Methods: This cohort study recruited 757 eleven-year-olds and 775 fifteen-year-olds in the United Kingdom. Sensitization rates, reported rates of FHS, and rates of food avoidance were measured. The prevalence of FHS was established by using food challenges.

Results: The prevalence of reported FHS among the 11- and 15-year-old cohorts was 11.6% (90/775) and 12.4% (94/757), respectively. One hundred twenty-two (15.7%) and 142 (18.7%) of the 11- and 15-year-olds reported they were avoiding some food. The rates of sensitization to the food allergens were 5.1% (36/699) and 4.9% (32/649) for the 11- and 15-year-olds, respectively. FHS was confirmed in 8 (1.0%) 11-year-old children and 8 (1.0%) 15-year-old children by means of open food challenge and in 1 (0.1%) 11-year-old and 4 (0.5%) 15-year-olds by means of double-blind, placebo-controlled food challenge. The prevalence of FHS, as confirmed by using open food challenges and positive skin prick test responses plus a history of adverse reactions, was 18 (2.3%) of 775 in the 11-year-old cohort and 17 (2.3%) of 757 in the 15-year-old cohort.

Conclusions: The rate of reported FHS was significantly more than sensitization to the predetermined allergens (odds ratio, 2.17; 95% CI, 1.47-3.18; $P < .001$ in the 11-year-olds; odds ratio, 2.73; 95% CI, 1.81-4.13; $P < .001$ in the 15-year-olds). By means of objective assessment, 2.3% of both 11- and 15-year-old children had FHS, with the majority showing immediate reactions. (*J Allergy Clin Immunol* 2005;116:884-92.)

Key words: Food hypersensitivity, teenagers, food challenges, skin prick testing

An increasing prevalence of asthma, allergic rhinitis, and atopic dermatitis has been registered in Europe.¹ There are, however, a very limited number of studies that have investigated the prevalence of food hypersensitivity (FHS) and its trends. A recent proposal² regarding the nomenclature used in asthma and allergy advised that an adverse reaction to food should be called FHS. When immunologic mechanisms have been demonstrated, the appropriate term is "food allergy," and if the role of IgE is highlighted, the term should be "IgE-mediated food allergy." All other reactions, previously referred to as "food intolerance" should be referred to as nonallergic FHS. Severe, generalized allergic reactions to food are classified as anaphylaxis. The prevalence of FHS in the community and its changes over time are very dependent on public awareness, diagnostic approaches, and the eating habits of that community.¹ Our experience suggests that an increasing number of individuals are being referred from primary care to specialist allergy clinics with a possible diagnosis of FHS. It is not clear, however, whether this represents a real increase, an increase in awareness, or an improvement in diagnosis.³ Many of these referrals are teenagers, who often avoid certain foods because of a self-perception of food allergy. In a growing child and adolescent, this type of food avoidance can have serious nutritional and psychological implications. The few studies that have investigated perception of FHS have reported large discrepancies between perceived and proved FHS.⁴⁻⁶

When a child is referred to an allergy clinic with a possible diagnosis of food allergy, skin prick tests (SPTs) are often carried out as part of the diagnostic repertoire.^{7,8} A positive SPT response to a food indicates sensitization to that food, and any positive SPT response reflects the atopic state of that individual (ie, genetic predisposition for allergies).

Skin prick testing to food allergens has a high negative predictive value, and an individual with a negative SPT response to a food allergen is highly unlikely to have an immediate type I allergy to that food. Some individuals have positive SPT responses to food allergens but are

From ^aThe David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Newport, Isle of Wight, and ^bthe Portsmouth Institute of Medicine Health and Social Care, University of Portsmouth, Portsmouth.

*Drs Pereira and Venter contributed equally to this work.

Supported by the Food Standards Agency, United Kingdom (grant no. T07023). All researchers conducting this work are independent of the Food Standards Agency.

Received for publication February 4, 2005; revised May 25, 2005; accepted for publication May 26, 2005.

Available online September 3, 2005.

Reprint requests: Taraneh Dean, PhD, School of Health Sciences and Social Work, University of Portsmouth, St George's Building, 141 High St, Portsmouth, PO1 2HY, United Kingdom. E-mail: tara.dean@port.ac.uk.

0091-6749/\$30.00

© 2005 American Academy of Allergy, Asthma and Immunology

doi:10.1016/j.jaci.2005.05.047

Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge
FHS: Food hypersensitivity
HDM: House dust mite
OFC: Open food challenge
OR: Odds ratio
SPT: Skin prick test

asymptomatic. Whether these sensitized individuals will have symptoms at a later stage is not clear.⁹

Most severe allergic reactions and deaths caused by FHS appear to be in the teenage population.^{10,11} Hence it is of paramount importance that we have robust, population-based epidemiologic data regarding food problems and sensitization in this age group on which any recommendations can be based. Although there are some data on FHS in infancy and early childhood, in contrast to respiratory allergies, there is a paucity of data in the teenage population regarding adverse reactions to foods, its perception, and the rate of sensitization to key food allergens. Food challenges, specifically double-blind, placebo-controlled food challenges (DBPCFCs), have long been accepted as the standard for objectively diagnosing FHS, although even DBPCFCs have their limitations.^{12,13} Therefore the aim of this study was to establish the prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and objectively assessed FHS among all 11- and 15-year-old children living on the Isle of Wight.

METHODS

The study was carried out between September 2002 and September 2003. The target populations for the study were all 11- and 15-year-olds (with birth dates between 1991-1992 and 1987-1988, respectively) who were resident on the Isle of Wight at the time of the study. Ethical approval for the study was obtained from the Isle of Wight, Portsmouth, and South East Hampshire Local Research Ethics Committee (Ref: 09/01). The target population was approached through the schools after discussions with the Isle of Wight Education Authority and all head teachers. All schools consented to participate in the study. The schools comprised 8 high schools (5 state and 3 independent schools), 19 middle schools (16 state and 3 independent schools), and 2 schools for pupils with special needs. To ensure confidentiality and data protection, the schools posted the study information, consent form, a self-administered questionnaire, and a prepaid envelope to the parents-guardians of all eligible pupils. They were asked to send their questionnaires and consent forms directly to the allergy center. After approximately 2 weeks, reminders were sent to the nonresponders.

The reported prevalence of adverse reactions to food and rates of foods avoided were established by using a questionnaire that was completed by the parent and child. If they stated that they had a current adverse reaction to any food, they were asked to describe the symptoms that they experienced.

All the children consenting to participate were offered SPTs to a predefined panel of food allergens (milk, egg, wheat, fish, peanut,

and sesame) and aeroallergens (house dust mite [HDM], cat, and grass pollen). In addition, they were offered skin tests to other allergens reported to be a problem. Sensitization to fresh fruits or vegetables was tested by using prick-to-prick testing.

SPTs were conducted with commercial extracts of standard food allergens and aeroallergens (Soluprick SQ allergens-ALK Allergologisk Laboratorium A/S, Horsholm, Denmark). Two experienced allergy nurses performed the SPTs. The wheal response was measured after transfer to paper from the skin with translucent tape. Measurement was undertaken in standard fashion, measuring the largest wheal diameter and the diameter orthogonal to it. The mean wheal diameter was calculated. Results were expressed as positive if the mean diameter was 3 mm or more in the presence of a negative control and a positive histamine reaction after 15 minutes.

Children who were sensitized to various allergens were offered appropriate advice. The results were communicated to the parents, who were given an opportunity to discuss concerns if they wished.

Two members of the research team screened information from the questionnaires, and those who reported an adverse reaction to a food were contacted, and a more detailed history was taken to ascertain which foods were implicated in producing the symptoms. The following children were invited for food challenges: (1) those with a positive SPT response who had never previously knowingly eaten a large amount of the food, and (2) those who indicated a previous adverse reaction to foods (regardless of their SPT data).

Before the food challenges, children were advised to avoid the offending food or ingredient. Children were advised to avoid the offending food for at least 4 weeks before the challenge and for 2 days before the challenge in the case of food additives.¹² Challenges were performed according to an algorithm adhering to the history in terms of dose and timing, where available. All food for challenges was freshly prepared for each individual child, taking into consideration the range of food each child would prefer as a vehicle.

Challenge protocols were developed on the basis of current available literature. Because there are no agreed-upon international protocols, the draft protocols were circulated to experts in the United Kingdom, Europe, and the United States. A consensus was reached, and protocols were established for the diagnosis of immediate (1-day challenge, [Appendix 1](#)) and delayed (1-week challenge, [Appendix 2](#)) symptoms.¹⁴⁻¹⁷ One-day challenge protocols were based on the consumption of a total of 8 to 10 g of dried food,¹⁸ unless the history clearly indicated differently. The required amount of food was calculated to provide 10 g of dried product (eg, 100 mL of semiskimmed milk = 89.8 g of water and thus contains 10.1 g of dried product).¹⁹ At the end of a negative challenge, the child was expected to consume a normal portion of the food. If the child refused the food at this stage, the parents were asked to give a normal portion of this food to the child at home on the same day.²⁰ One-week challenges were based on normal daily consumption for the specific age group, unless the history clearly indicated differently. A normal portion was defined as an amount indicated by the history or as a normal portion for that age group calculated by using the National Diet and Nutritional Survey.²¹

All children eligible for challenge underwent open food challenges (OFCs), and only those with a positive reaction were invited to participate in a DBPCFC. To ensure adequate blinding the study team, parents and children tested foods used for the DBPCFCs. Those with a history of immediate symptoms had food challenges performed in a pediatric day unit. Challenges were performed at home if the history indicated delayed symptoms and the SPT response was negative. For the DBPCFC, those children with severe reactions or a history of anaphylaxis were excluded. Parents reported reactions during home challenges on a symptom diary.

TABLE I. Major foods-ingredients reported to cause problems in the 2 cohorts

Food	No. reporting an adverse event	
	11-year-olds	15-year-olds
Milk and dairy	22	26
Additives	26	14
Egg	12	23
Peanut	14	19
Tree nuts	9	17
Wheat	10	9
Fish	7	14
Shellfish	2	5

A variety of other food and food ingredients were reported to cause problems in both groups, including tomatoes, meat, fruits and fruit juices, fizzy drinks, spicy food, flavored squashes, coconut, rice, green things, Horlicks (GlaxoSmith-Kline, Middlesex, United Kingdom), mushroom, prawn-flavored crisps, tinned fruit, vinegar, yeast, and Marmite (CPC International Inc, Surrey, United Kingdom).

All data obtained were double entered onto SPSS (v10.0; SPSS Inc, Chicago, Ill) by 2 separate operators, compared, and verified before analysis.

RESULTS

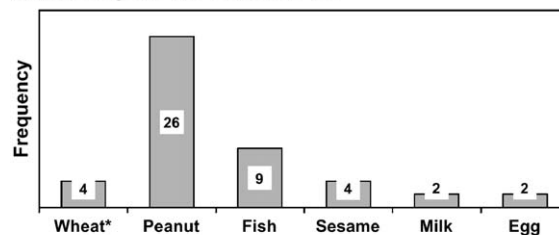
The target eligible population comprised 1636 eleven-year-olds and 1508 fifteen-year-olds. The final response rate was 47.4% for the 11-year-olds and 50.2% for the 15-year-olds. There was no difference in response between the respondents and nonrespondents in terms of sex, age, or area of residence. The response pattern did not differ between the state and independent-sector pupils. A sample of nonresponders ($n = 100$) was contacted, and lack of interest was quoted by 82 of them as the main reason for nonparticipation. Data were available on 775 (male = 388) 11-year-olds and 757 (male = 379) 15-year-olds.

Reported rates of FHS

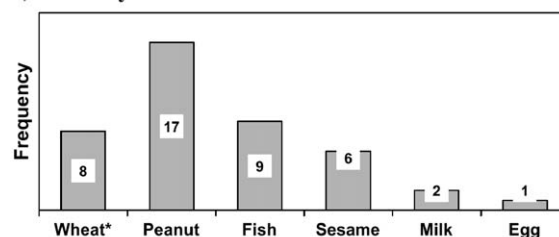
Parents of 90 eleven- and 94 fifteen-year-old children reported that their child had a current problem with a food, with 33 and 27 children, respectively, reporting problems with more than one food or food ingredient. Hence the prevalence of reported FHS among these cohorts was 11.6% (90/775) and 12.4% (94/757). The difference between the 2 cohorts was not statistically significant (odds ratio [OR], 0.93; 95% CI, 0.68-1.26; $P = .68$). Only 64 of 90 eleven-year-olds and 76 of 94 fifteen-year-olds who reported a current problem were avoiding one or more foods, and these did not necessarily include the food to which they reported an adverse reaction.

Wide ranges of foods or food ingredients were implicated in reported adverse reactions in both cohorts (Table I). The problems associated with consuming these foods as reported by the parents included asthma, wheeze, cough, rash, angioedema, headache, nausea, abdominal pain, dislike, hyperactivity, and other behav-

a) Eleven-year-old cohort $n=699$



b) Fifteen-year-old cohort $n=649$



*Not including grass cross-reactors

FIG 1. Frequency of sensitization to the predefined food panel.

ioral problems, with behavioral (hyperactivity and dislike) and gastrointestinal (abdominal pain, nausea, vomiting, and diarrhea) issues being the most common.

Rates of food avoidance

A total of 122 (15.7%) 11-year-olds and 142 (18.7%) 15-year-olds were avoiding some food or food ingredients. The difference between the 2 cohorts was not statistically significant (OR, 0.81; 95% CI, 0.62-1.06; $P = .13$). The avoiders included 64 of the 90 children reporting adverse reactions to foods in the 11-year-old cohort and 76 of the 94 children in the 15-year-old cohort. The numbers of children avoiding different foods for the 2 cohorts (11- and 15-year-olds) were 27 and 44 avoiding fish, 38 and 40 avoiding peanuts, 26 and 37 avoiding egg, 21 and 28 avoiding milk or dairy products, 37 and 27 avoiding tree nuts, 3 and 10 avoiding sesame, and 5 and 7 avoiding wheat, respectively. Sixty and 58 children of the respective cohorts were avoiding more than one food. The specific reason for this avoidance was not given in most cases, and we assumed this to be due to the perceived problems with the particular food or food ingredient.

Prevalence of sensitization

Six hundred ninety-nine and 649 eleven- and fifteen-year-old children consented to undergo skin testing, and among these, the rate of sensitization to any allergen tested was 26% and 28.2%, respectively.

The rate of sensitization to any of the predefined food allergens was 13.7% (96/699) and 13.4% (87/649), respectively. However, large numbers in each cohort were sensitized to both grass and wheat. Cross-reactivity between grass and wheat allergen is well established in subjects with grass pollen allergy.²² If subjects with

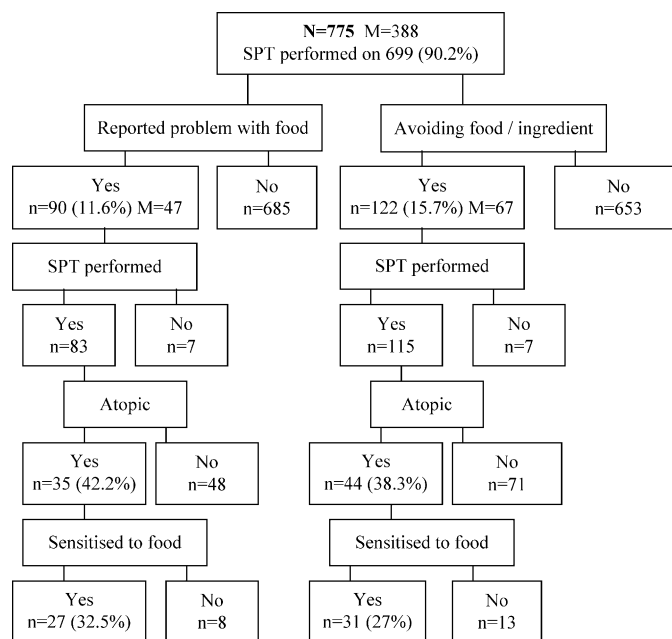


FIG 2. Eleven-year-old cohort.

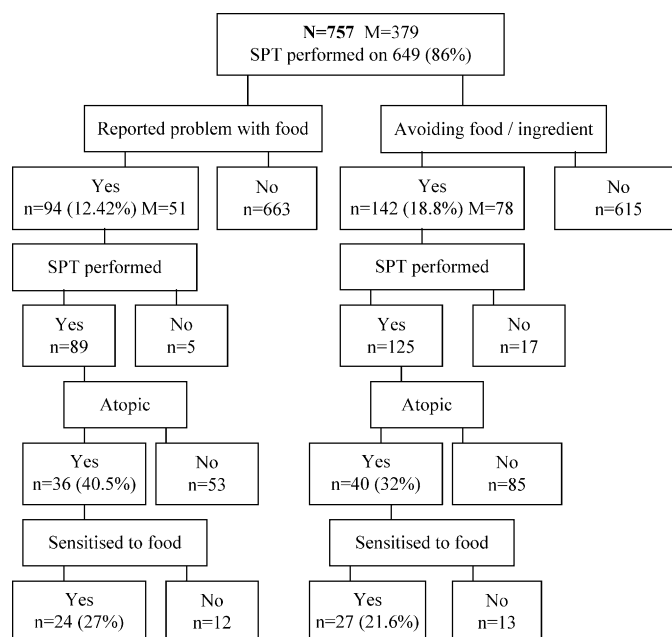


FIG 3. Fifteen-year-old cohort.

a history of grass pollen allergy who were sensitized to both grass and wheat (while asymptomatic to wheat) are removed, the true rates of sensitization to any of the predefined food allergens will be 5.1% (36/699) and 4.9% (32/649) for the 11- and 15-year-old cohorts, respectively. The individual rate of food sensitization to the predefined panel of allergens is shown in Fig 1.

Figs 2 and 3 demonstrate the rates of sensitization among those who reported a problem with a food or avoided one or more foods-ingredients.

A total of 178 (22.9%) 11-year-olds and 175 (26.9%) 15-year-olds were sensitized to one or more of the aeroallergens tested (HDM, grass, and cat). Individually, the rates of aeroallergen sensitization in the 11-year-old

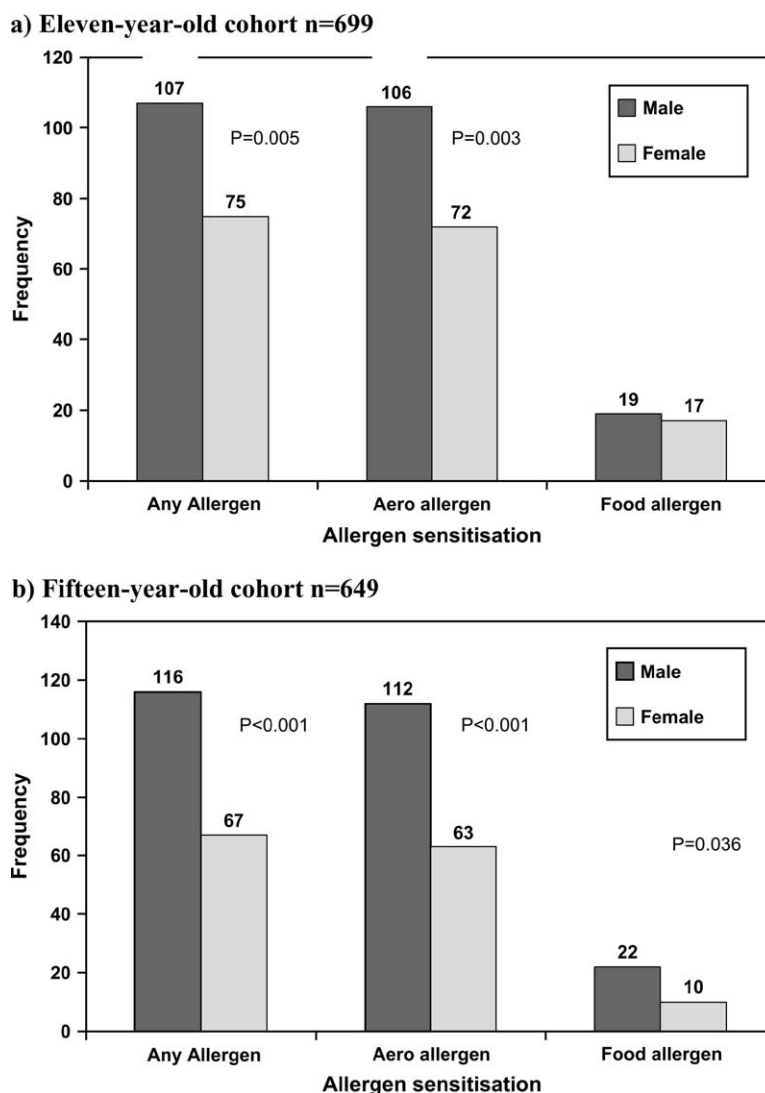


FIG 4. Male and female sensitization rates in 11- and 15-year-old children.

(15-year-old) children were as follows HDM, 116 (116); cat, 58 (55); and grass, 120 (101). In addition to this, 6 children in each cohort were tested to other aeroallergens on request, and 3 eleven-year-olds (1 each to tree pollen, tree mix, and silver birch) and 2 fifteen-year-olds (1 to dog and 1 to tree mix) were found to have positive responses.

Atopic children were significantly more likely to report a problem with any food in both the 11-year-old cohort (OR, 2.33; 95% CI, 1.41-3.83; $P = .001$) and the 15-year-old cohort (OR, 1.9; 95% CI, 1.17-3.11; $P = .009$), although they were more likely to be avoiding some food in the 11-year-old cohort (OR, 2.0; 95% CI, 1.29-3.12; $P = .002$) and not so in the 15-year-old cohort (OR, 1.25; 95% CI, 0.81-1.95; $P = .347$). We observed significant differences between the rates of sensitization in boys and girls, with boys having significantly higher rates of

sensitization to aeroallergens in both cohorts but not to foods in the 11-year-old cohort (Fig 4).

Food challenges

Of the 90 eleven-year-olds and 94 fifteen-year-olds who reported a problem with a food or foods, 60 eleven-year-old and 58 fifteen-year-old children were excluded from food challenges for a variety of reasons summarized in Table II.

Thirty and 36 eleven- and fifteen-year-olds were eligible for food challenges and were invited for challenge. In the 15-year-old cohort, 2 children did not improve on the elimination diet, which resulted in 34 children eligible for food challenges. A number of children in each cohort who were eligible for a food challenge did not undergo a challenge for various reasons:

physician's diagnosis of FHS ($n = 12$ [6 eleven- and 6 fifteen-year-olds]), positive SPT responses to a food that they previously reacted to and to which they did not wish to undergo a challenge ($n = 3$ [1 eleven- and 2 fifteen-year-olds]), and declined food challenge ($n = 14$ [2 eleven- and 12 fifteen-year-olds]). Hence 21 eleven- and 14 fifteen-year-olds underwent a total of 25 and 17 OFCs, respectively, because some children underwent challenges to more than one food.

Twenty-one 11-year-olds underwent open challenges to 10 different foods-ingredients (peanut, almond, soya, sesame, fish, cheese, kiwi, tomato, milk, and additives), and 8 (38%) children had a positive challenge result (7 one-day and 2 one-week challenges, with 1 child undergoing 2 challenges).

Fourteen 15-year-old children underwent open challenges to 11 foods-ingredients (milk, wheat, melon, chocolate, soya, hazel nut, raisin, kiwi, sesame, additives, and shellfish), and 8 (53%) had positive challenge results (5 one-day and 3 one-week challenges).

All children who had a positive OFC result were invited to undergo DBPCFCs. Only 2 (2/8) children in the 11-year-old cohort and 7 (7/8) in the 15-year-old cohort underwent DBPCFCs, with parental refusal being the main reason for not undergoing DBPCFCs in the 11-year-old cohort and difficulty performing DBPCFCs for oral allergy syndrome in the 15-year-old cohort.

Of the 2 eleven-year-olds who underwent DBPCFCs (both 1-week challenges), one child had a positive challenge result to milk and experienced nasal congestion.

Four of 7 of the 15-year-old children had a positive DBPCFC result (2 one-day [milk and shrimp] and 2 one-week [milk and wheat] challenges).

Estimation of FHS

With OFC as the primary end point, the prevalence of FHS was 8 (1.0%) of 775 in the 11-year-old cohort and 8 (1.0%) of 757 in the 15-year-old cohort. It was noted that a number of children did not undergo food challenges, and many of these had convincing histories with a positive SPT response. Hence it would be justifiable to base the prevalence of FHS on a range of outcomes. Among the 11-year-olds, the prevalence of FHS on the basis of a combination of positive OFC result ($n = 8$), a clear history of previous reactions in the presence of a positive SPT response ($n = 1$), or a physician's diagnosis ($n = 9$) was 18 (2.3%) of 775 (95% CI, 1.3-3.6). For the 15-year-olds, the prevalence of FHS based on a combination of a positive OFC ($n = 8$), a clear history of previous reactions in the presence of a positive SPT or raised specific IgE ($n = 3$), or a physician's diagnosis ($n = 6$) was 17 (2.3%) of 775 (95% CI, 1.3-3.6).

With DBPCFC as the end point, the prevalence of FHS on the basis of those who underwent these challenges was 1 (0.1%) of 775 in the 11-year-old cohort and 4 (0.5%) of 757 in the 15-year-old cohort.

Among the 11-year-olds, when the diagnosis of FHS was based on a combination of a positive DBPCFC result

TABLE II. Reasons for excluding some children from food challenges

Reason	11-year-olds ($n = 60$)	15-year-olds ($n = 58$)
Had problems with a fizzy drink as an infant. This fizzy drink is not available any more.	1	0
Dislikes a particular food, such as crabsticks, rice, a glass of milk, or baked beans, but eats it without any reaction.	8	17
Vomited after episodes of overeating only.	2	0
Inconsistent history (eg, eats cheese but cannot eat cauliflower cheese, eats cod fish cakes but cannot eat cod) or reported a problem with hyperactivity to additives.	40	31
High-fiber diet a problem but not wheat.	1	1
Had reaction to food once but has eaten it since then without a problem.	3	2
Afraid of eating peanuts, dislikes peanuts.	3	5
Parents reported problems during infancy, but food is well tolerated at this stage.	2	2

($n = 1$), a clear history of previous reactions in the presence of a positive SPT response ($n = 1$), or a physician's diagnosis ($n = 9$), the prevalence of FHS was 11 (1.4%) of 775.

For the 15-year-olds, the prevalence of a diagnosis of FHS on the basis of a combination of a positive DBPCFC result ($n = 4$), a clear history of previous reactions in the presence of a positive SPT response ($n = 3$), or a physician's diagnosis ($n = 9$) was 16 (2.1%) of 757.

DISCUSSION

This study is the first population-based study establishing reported food problems and sensitization among 11- and 15-year-old children.

A total of 11.6% and 12.4% eleven- and fifteen-year-olds, respectively, reported a problem with a food or food ingredient. The rate of sensitization to the predefined panel of food allergens was 5.1% and 4.9% for the 11- and 15-year-olds, respectively.

The prevalence of FHS on the basis of a combination of a positive OFC result, a clear history of previous reactions in the presence of a positive SPT response, or a physician's diagnosis was 2.3% for both the 11- and 15-year-olds. With the same criteria and DBPCFC, the rate of FHS was 1.4% and 2.1%, respectively.

The response rates for this study were 47.4% and 50.2% for the 11- and 15-year-old cohorts, respectively. It is possible that this could have led to a selection bias, with mainly atopic individuals or those who are more aware of allergy-related problems (eg, with an allergic family member) being more likely to respond. Although we cannot rule this out completely, we endeavored to address this by sampling a group of nonresponders. The rate of reported problems was similar in this group, and they did not vary in terms of other related factors. In addition to this, if selection bias was significant, one would have anticipated a high rate of reported adverse reactions and sensitization among the respondents, which was not the case in this study. The rates of atopy in the 2 cohorts were 26.0% and 28.2%, which are in line with previously reported rates of atopy in the general population and children of similar age.^{23,24} When exploring reasons for nonparticipation with a sample of nonresponders, lack of interest or fear of needles were the main reasons given.

The majority of studies attempting to address the population rates of sensitization to foods have been conducted with adult populations. A population-based study in the Netherlands demonstrated that the prevalence of self-reported adverse reactions to foods among school-children (aged, 5-15 years) was 7.2%, with food additives and chocolate being the most common foods avoided. In this study 7% of school-aged children avoided certain foods or ingredients because of self-reported FHSs.²⁵ Unfortunately, they did not perform SPTs or food challenges on their cohort, and we cannot draw objective comparisons with our 2 populations.

A total of 15.7% and 18.7% of our 11- and 15-year-old cohorts, respectively, reported that they were avoiding some food from their diet. A proportion of parents attributed various behavioral problems in their children to consumption of food additives, colorings, and other ingredients. The likelihood of FHS with these was only investigated if objective symptoms suggestive of immediate allergy were reported rather than behavioral problems. Adler et al²⁶ reported that 56% of atopic asthmatic children had reported some symptoms with foods, with behavioral disturbance being the most common. In that study the most common foods implicated were food additives (31%), egg (27%), milk (26%), chocolate (23%), and orange (15%).

Twenty of our children in the 15-year-old cohort reported gastrointestinal problems with various foods. A total of 26 children were reported to have a problem with milk and dairy products, and 28 were avoiding these foods. Similarly, in the 11-year-old cohort, 15 reported gastrointestinal problems with various foods, 22 reported a problem with milk, and 21 were avoiding milk and dairy products. In a study of 1000 new patients attending a district hospital gastroenterology clinic, patients subsequently given diagnoses of a functional disorder were more likely than those with organic disease to report food allergies (OR, 4.1; 95% CI, 2.7-6.2) or foods that worsened their abdominal symptoms (OR, 3.0; 95% CI,

2.3-4.1).²⁷ Kokkonen et al,²⁸ in Finland, have found some evidence to corroborate the claim that cow's milk protein-sensitive enteropathy at school age is an identifiable clinical entity. There is a possibility that some of the children in our study might have such an entity, which could explain their symptoms.

In a study of cases of fatal anaphylaxis, Pumphrey¹¹ demonstrated that all fatal food-related anaphylaxis caused difficulty breathing and in 86% of cases led to respiratory arrest, whereas shock was more common in iatrogenic or venom-related anaphylaxis. It would be important to know whether these patients with food-related anaphylaxis were also sensitized to aeroallergens and whether the aeroallergen sensitization was relevant to the episode of anaphylaxis. In our study 12.3% of 15-year-olds were sensitized to both food allergens and aeroallergens, and of the 94 children who reported a problem with a food or food ingredient, one third was sensitized to an aeroallergen. In the 11-year-old cohort, 13.5% were sensitized to both food allergens and aeroallergens, with 33 of 90 who reported food-related problems sensitized to an aeroallergen. Atopic children in the 15-year-old cohort were almost twice as likely to report a food-related problem as nonatopic children (OR, 1.9; 95% CI, 1.1-3.1; $P = .009$). This was also true for the 11-year-old cohort (OR, 2.3; 95% CI, 1.4-3.8).

In our study there appeared to be a large proportion of cross-reactivity between wheat and grass on skin prick testing (72/80 fifteen-year-olds and 76/80 eleven-year-olds who were sensitized to wheat were also sensitized to grass and were tolerating wheat and wheat-containing products in their diets). In Baltimore, of 145 children with FHS to cereal grains, grass, and wheat, only 21% had symptomatic reactivity on food challenge.²² These findings are reflected in our study, with only a small proportion of those sensitized to wheat reporting clinical reactivity to wheat.

A similar proportion of male and female subjects reported food problems and food avoidance in both cohorts, but although rates of atopy were significantly higher in male subjects in both cohorts, sensitization to food allergens in the 11-year-old cohort was not significantly different (OR, 1.1; 95% CI, 0.6-2.2; $P = .8$) but was significant in the 15-year-old cohort (OR, 2.3; 95% CI, 1.1-5.0; $P = .03$). Sex differences in atopy and asthma have been previously reported, and this might simply reflect this pattern.²⁹

It has previously been demonstrated that patients with grass pollen allergy-induced respiratory disease report adverse food reactions more frequently than patients allergic to HDM³⁰ and that IgE to food allergens are highly prevalent in patients allergic to pollens with and without symptoms of food allergy.³¹ We did not have data regarding manifestations of respiratory disease but could demonstrate that grass pollen-sensitized children were more likely to report a food-related problem in both cohorts. Among 15-year-olds, grass sensitization was associated with a 3-fold increase in food problems reported (OR, 2.9; 95% CI, 1.7-5.1), and among 11-year-

olds, there was a more modest likelihood (OR, 1.7; 95% CI, 0.9-3.5).

With OFCs, the prevalence of FHS was 1% in both 11- and 15-year-old children. A number of children declined food challenges (33% and 58% in the 11- and 15-year-old cohorts, respectively); however, 23 children had already received diagnoses of FHS previously or had a positive SPT response plus a clear recent history. Of these, 6 children had SPT sizes greater than the predictive cutoff points suggested in various publications.^{8,32} The prevalence of FHS on the basis of a combination of a positive OFC result, a clear history of previous reactions in the presence of a positive SPT response, or a physician's diagnosis was 2.3% for both the 11- and 15-year-old children. With the same criteria and DBPCFC, the rate of FHS was 1.4% and 2.1%, respectively.

There are no population-based studies in these age groups with which to compare our data, but our figures are lower than in adult populations (2.4%)³³ and slightly higher than those in a previous study in adults and children (1.4% to 1.8%).⁶ This could perhaps be explained by the fact that we included all foods in our study, whereas the study by Young et al⁶ only looked at 8 major food allergens. In addition, food challenges were not carried out in children in that study.

We confirmed FHS in only 19% (18/90) and 18% (17/94) of the 11- and 15-year-olds who reported a food problem, despite the fact that we had mimicked the history in terms of dose needed and duration of exposure. This compares with 35% in a study performed by Bock¹² in infants (0-3 years) and 10% in the population-based study by Zuberbier et al.³⁴

Among the 11-year-olds, the foods most commonly implicated in FHS were peanuts, tree nuts, egg, milk, shell fish, gluten (coeliac disease), green beans, cheese, kiwi, tomato, and additives.

Among the 15-year-olds, the foods implicated were peanut, tree nuts, gluten, wheat, shellfish, egg, milk, and additives. This is in line with other publications³⁵⁻³⁷ suggesting that peanut, tree nut, and shellfish allergy are often reported in older children and young adults.

Six (0.8%) of 757 fifteen-year-old children and 8 (1%) of 775 eleven-year-old children had peanut allergy in this study, which is similar to rates (1.5%) in a group of 3- to 4-year-olds in the same geographic region.³⁸

Unanswered questions and areas for future research

Are all atopic children more likely to report food problems? Increased awareness of asthma as a public health problem has been shown to reflect increases in asthma prevalence, asthma-related visits to hospital emergency departments, and asthma-related mortality.³⁹ It is not known whether a similar increased awareness of FHS and increased reporting in the medical literature and popular media could contribute to the reported food-related problems.

Conclusion

Reported food problems are common in 11- and 15-year-old children, but the rate of sensitization to food allergens is low. Reported food problems, food avoidance, and food sensitization were not statistically different between the 2 cohorts, although significant differences between sexes with respect to atopy were seen. By means of objective assessment, 2.3% of both 11- and 15-year-old children had FHS, with the majority showing immediate reactions.

We acknowledge the cooperation of the children and parents who participated in this study. We also thank Kerstin Voigt and Sharon Matthews for their considerable assistance with many aspects of this study. Finally, we thank our contributors: Nasir Siddique for clinical review and advice to children, Monica Fenn for assisting with the skin prick testing procedure, Bernie Higgins for statistical support, Gillian Glasbey for managing and coordinating the study, and Linda Terry and Lisa Matthews for entering the data.

REFERENCES

1. Oslo KA, Göteborg NA, Bachert C, Bergmann K, Bergmann R, Bonini S, et al. Allergic Diseases as a public health problem in Europe. In: European Allergy White Paper. Belgium: The UCB Institute of Allergy; 1997.
2. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol* 2004;113:832-6.
3. Mösges R. The increasing prevalence of allergy: a challenge for the physician. *Clin Exp Allergy Rev* 2002;2:13-7.
4. Altman DR, Chiamonte LT. Public perception of food allergy. *J Allergy Clin Immunol* 1996;97:1247-51.
5. Woods RK, Stoney RM, Raven J, Walters EH, Abramson M, Thien FC. Reported adverse food reactions overestimate true food allergy in the community. *Eur J Clin Nutr* 2002;56:31-6.
6. Young E, Stoneham MD, Petrukevitch A, Barton J, Rona R. A population study of food intolerance. *Lancet* 1994;343:1127-30.
7. Hansen TK, Host A, Bindslev-Jensen C. An evaluation of the diagnostic value of different skin tests with egg in clinically egg allergic children having atopic dermatitis. *Paediatr Allergy Immunol* 2004;15:428-34.
8. Eigenmann PA, Sampson HA. Interpreting skin prick tests in the evaluation of food allergy in children. *Paediatr Allergy Immunol* 1998;9:186-91.
9. Tariq SM, Stevens M, Matthews S, Ridout S, Twiselton R, Hide DW. Cohort study of peanut and tree nut sensitisation by age of 4 years. *BMJ* 1996;313:514-7.
10. Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 2001;107:191-3.
11. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy* 2000;30:1144-50.
12. Bock SA. Prospective appraisal of complaints of adverse reactions to foods in children during the first 3 years of life. *Pediatrics* 1987;79:683-8.
13. Niggemann B, Beyer K. Diagnostic pitfalls in food allergy in children. *Allergy* 2005;60:104-7.
14. Majamaa H, Moisiö P, Holm K, Kautiainen H, Turjanmaa K. Cow's milk allergy: diagnostic accuracy of skin prick and patch tests and specific IgE. *Allergy* 1999;54:346-51.
15. Majamaa H, Moisiö P, Holm K, Turjanmaa K. Wheat allergy: diagnostic accuracy of skin prick and patch tests and specific IgE. *Allergy* 1999;54:851-6.
16. Baehler P, Chad Z, Gurbindo C, Bonin AP, Bouthillier L, Seidman EG. Distinct patterns of cow's milk allergy in infancy defined by prolonged, two-stage double-blind, placebo-controlled food challenges. *Clin Exp Allergy* 1996;26:254-61.

17. Isolauri E, Turjanmaa K. Combined skin prick and patch testing enhances identification of food allergy in infants with atopic dermatitis. *J Allergy Clin Immunol* 1996;97:9-15.
18. Sampson HA. Use of food-challenge tests in children. *Lancet* 2001;358:1832-3.
19. Holland B, Welsh A, Unwin I, Buss DH, Paul AA, Southgate AT, McCance and Widdowson's: the composition of foods. London: The Royal Society of the Chemistry and Ministry of Agriculture, Fisheries and Food; 2000.
20. Sampson HA. Adverse reactions to food. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, Busse WW, editors. *Allergy: principles and practice*. St Louis: Mosby; 1998. p. 1162-82.
21. Gregory JR, Lowe S, Bates CJ, Prentice A, Jackson LV, Smithers G, et al. National Diet and Nutrition Survey: young people aged 4 to 18 years. Vol. 1: report of the diet and nutrition survey. London: Ministry of Agriculture Fisheries and Food; 2000.
22. Jones SM, Magnolfi CF, Cooke SK, Samson HA. Immunologic cross-reactivity among cereal grains and grasses in children with food hypersensitivity. *J Allergy Clin Immunol* 1995;96:341-51.
23. Barraclough R, Devereux G, Hendrick DJ, Stenton SC. Apparent but not real increase in asthma prevalence during the 1990s. *Eur Respir J* 2002;20:826-33.
24. Kurukulaaratchy RJ, Fenn M, Matthews S, Arshad SH. Characterisation of atopic and non-atopic wheeze in 10-year-old children. *Thorax* 2004;59:563-8.
25. Crespo JF, Pascual C, Burks AW, Helm RM, Esteban MM. Frequency of food allergy in a pediatric population from Spain. *Pediatr Allergy Immunol* 1995;6:39-43.
26. Adler BR, Assadullahi T, Warner JA, Warner JO. Evaluation of a multiple food specific IgE antibody test compared to parental perception, allergy skin tests and RAST. *Clin Exp Allergy* 1991;21:683-8.
27. Bhat K, Harper A, Gorard DA. Perceived food and drug allergies in functional and organic gastrointestinal disorders. *Aliment Pharmacol Ther* 2002;16:969-73.
28. Kokkonen J, Haapalahti M, Laurila K, Karttunen TJ, Maki M. Cow's milk protein-sensitive enteropathy at school age. *J Paediatr* 2001;139:797-803.
29. PausJenssen ES, Cockcroft DW. Sex Differences in asthma, atopy, and airway hyperresponsiveness in a university population. *Ann Allergy Asthma Immunol* 2003;91:34-7.
30. Boccafogli A, Vincentini L, Camerani A, Cogliati P, D'Ambrosi A, Scolozzi R. Adverse food reactions in patients with grass pollen allergic respiratory disease. *Ann Allergy* 1994;73:301-8.
31. Bircher AJ, Van Melle G, Haller E, Curty B, Frei PC. IgE to food allergens are highly prevalent in patients allergic to pollens, with and without symptoms of food allergy. *Clin Exp Allergy* 1994;24:367-74.
32. Hill DJ, Hosking CS, Reyes-Benito LV. Reducing the need for food allergen challenges in young children: a comparison of in vitro with in vivo tests. *Clin Exp Allergy* 2001;31:1031-5.
33. Jansen JJ, Kardinaal AF, Huijbers G, Vlieg-Boerstra BJ, Martens BP, Ockhuizen T. Prevalence of food allergy and intolerance in the adult Dutch population. *J Allergy Clin Immunol* 1994;93:446-56.
34. Zuberbier T, Edenharter G, Worm M, Ehlers I, Reimann S, Hantke T, et al. Prevalence of adverse reactions to food in Germany—a population study. *Allergy* 2004;59:338-45.
35. Mattila L, Kilpelainen M, Terho EO, Koskenvuo M, Helenius H, Kalimo K. Food hypersensitivity among Finnish university students: association with atopic diseases. *Clin Exp Allergy* 2003;33:600-6.
36. Sicherer SH, Furlong TJ, Munoz-Furlong A, Burks AW, Sampson HA. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. *J Allergy Clin Immunol* 2001;108:128-32.
37. Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of seafood allergy in the United States determined by a random telephone survey. *J Allergy Clin Immunol* 2004;114:159-65.
38. Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts. *J Allergy Clin Immunol* 2002;110:784-9.
39. Self-reported asthma in adults and proxy-reported asthma in children—Washington, 1997-1998. *MMWR Morb Mortal Wkly Rep* 1999;48:918-20.

APPENDIX 1

Rub the lower mucosa of the lip with cooked egg.
If no reaction, proceed to:

1 g of egg to be eaten
15-minute observation

↓

2 g of egg to be eaten
15-minute observation

↓

5 g of egg to be eaten
15-minute observation

↓

10 g of egg to be eaten
15-minute observation

↓

22 g of egg to be eaten
2-hour observation

↓

1 egg to be eaten (for children <1 year = 1 medium egg, children >1 year = 1 large egg, children >12 years = 1 extra large egg)
2-hour observation.

APPENDIX 2

For the 7-day challenge, you are expected to provide the following amounts of wheat-containing foods to your child:

Age of child	
6 mo to 2 y	2-3 portions
2-3 y	4 portions
6 y	4-5 portions
11 and 15 y	4-6 portions

You could give half portions of a larger variety of wheat-containing foods as well. To provide 3 portions to a 1-year-old child, you could give 6 × half portions.

The following foods are all equal to 1 wheat portion:

1 slice of bread,
3 tablespoons of cereal (not rice cereals or corn cereals),
1 Weetabix (Weetabix Ltd, Northamptonshire, United Kingdom) or Shredded Wheat (Cereal Partners, Malley, Switzerland),
1 biscuit,
1 slice of cake, or
1 tablespoon of pasta.

Apart from the foods on the above list, it is important to remain on the wheat-free diet, as discussed with the dietitian. Because your child has been avoiding wheat for the past few weeks or months, we would advise you to trial just 1 to 2 wheat portions on day 1 if your child has not had an initial challenge at the hospital. Could you please complete the food diary provided to you?