

ORIGINAL COMMUNICATION

Reported adverse food reactions overestimate true food allergy in the community

RK Woods¹*, RM Stoney², J Raven³, EH Walters³, M Abramson¹ and FCK Thien⁴

¹Department of Epidemiology and Preventive Medicine, Central and Eastern Clinical School, Monash University and the Alfred Hospital, Australia; ²Department of Nutrition and Dietetics, Alfred Hospital, Australia; ³Department of Respiratory Medicine, Central and Eastern Clinical School, Monash University and the Alfred Hospital, Australia; and ⁴Department of Allergy, Asthma and Clinical Immunology, Central and Eastern Clinical School, Monash University and the Alfred Hospital, Australia

Objective: To determine the extent to which perceived adverse food reactions were associated with IgE mediated food allergy, as defined by skin prick testing (SPT).

Design: A cohort epidemiological study. Participants underwent SPT to five common food allergens (cow's milk, peanut mix, egg white, shrimp and whole grain wheat mix) and were asked whether they had ever suffered any food 'illness/trouble', and if so to list such food(s). A positive SPT was defined as wheal diameter of ≥ 3 mm. Cohen's kappa (κ) was used to assess the agreement between SPT and self-reported reactions to food(s) which contained the allergen of interest.

Setting: Randomly selected adults who took part in the follow-up of the European Community Respiratory Health Survey (ECRHS) in 1998.

Subjects: The subjects were 457 adults aged 26–50 y.

Results: Fifty-eight (13%) adults were sensitised to at least one food allergen whilst 99 adults (22%) reported illness to food(s) nearly always. However, only seven subjects who reported illness to a food also had a positive SPT to the same food. The prevalence of adverse food reactions associated with IgE mediated allergy in the adult general population would be less than 1.5% (7/457). The agreement between SPT and self-reported illness to food(s) was poor for cow's milk ($\kappa=0$) and wheat ($\kappa=0$), slight for shrimp ($\kappa=0.16$) and egg white ($\kappa=0.09$) and fair for peanut mix ($\kappa=0.37$).

Conclusions: There was little agreement between self-reported perceived illness to food(s) known to contain the food allergen of interest, and positive SPT, suggesting that most reactions are not due to IgE mediated food allergy.

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*Correspondence: RK Woods, Department of Epidemiology and Preventive Medicine, Central and Eastern Clinical School, Commercial Rd, Prahran VIC 3181, Australia.

E-mail: Rosalie.Woods@med.monash.edu.au

Guarantor: RK Woods.

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Introduction

Perceived adverse food reactions are common in many developed countries. Community based studies have previously been conducted to determine the prevalence of reported food allergy and intolerance in the UK, Holland, USA, Sweden and Australia (Young *et al*, 1994; Jansen *et al*, 1994; Altman & Chiarmonte, 1996; Bjornsson *et al*, 1996; Woods *et al*, 1998a). These studies have reported food intolerance levels of 20, 12, 16, 25 and 17% respectively.

Whilst the true prevalence of food allergy in adults is unknown, it is generally thought to be uncommon, and estimates suggest a community prevalence ranging from 1 to 2% (Metcalf *et al*, 1997; Anderson, 1991). Double-blind placebo-controlled food challenges are the 'gold standard'

for the diagnosis of adverse food reactions to foods and food additives (Metcalf & Sampson, 1990). Previous studies indicate that less than half of those who perceive food intolerance have it confirmed by double-blind placebo-controlled challenge (Sampson, 1988a).

The reasons for the obviously large gap between perceived adverse food reactions and the true prevalence of food allergy remains unclear. Several researchers have found evidence that many subjects with perceived adverse food reactions have various psychiatric disorders (Knibb *et al*, 1999; Pearson, 1988; Howard & Wessely, 1993). However others have found no such association (Peveler *et al*, 1996). Other possible causes or contributing factors are yet to be identified.

It is important that the correct diagnosis of food allergy is made, as the current treatment is elimination of the food(s) and beverage(s) concerned (Bousquet *et al*, 1997). If false positive diagnoses are made then people will be unnecessarily restricting their dietary intake and therefore be at risk of developing nutritional deficiencies. It has been previously documented in children that unnecessarily restrictive diets can result in nutritional deficiencies and may in extreme cases be fatal (Bierman *et al*, 1978; David *et al*, 1984; Robertson *et al*, 1988; Labib *et al*, 1989).

Only two community-based studies have gathered data on both perceived adverse food reactions and objective measures of true adverse food reactions (Young *et al*, 1994; Bjornsson *et al*, 1996). However, neither of these studies was able to demonstrate the proportion of those with both perceived adverse food reactions and IgE mediated food allergy. Therefore, the aim of the current study was to determine to what extent perceived adverse food reactions were associated with IgE mediated food allergy. For this study, IgE mediated food allergy was defined as a positive wheal to skin prick testing (SPT) with the relevant food extract.

Method

Subjects

A community sample of young adults aged 20–44 y was recruited in 1992/1993 to undertake one-arm of the European Community Respiratory Health Survey (ECRHS) in Melbourne, Australia. Seven hundred and fifty seven participants attended the laboratory for that particular study. The full methodology of this study has been published elsewhere (Burney *et al*, 1994; Abramson *et al*, 1996), but briefly, 4500 adults aged between 20 and 44 y were randomly selected from the electoral rolls from three federal electorates in the inner south-eastern area of Melbourne, the capital city of Victoria. These subjects were invited to complete a brief postal questionnaire (phase I of the study). A response rate of 72% ($n = 3200$) was achieved from this phase of the study. A random sub-sample of 1642 subjects was identified as eligible for follow-up in the second phase of the study. A second symptomatic sub-sample was identified comprising

433 respondents who had reported in the first phase being woken by shortness of breath, having had an attack of asthma during the last 12 months or taking medication for asthma. Thus a total of 2075 young adults were invited to our laboratory for testing between November 1992 and March 1994. A total of 757 (553 from random sub-sample and 204 from the symptomatic sub-sample) attended our laboratory at that time.

The ECRHS was repeated in 1998 with 463 participants (336 from the random sub-sample, 127 from the symptomatic sub-sample) attending the laboratory in Melbourne. The participants were administered the full ECRHS respiratory questionnaire and SPT were performed. The results of this analysis pertain to the 457 subjects for whom complete data sets are available.

The Standing Committee on Ethics in Research on Humans at Monash University and The Alfred Hospital Ethics Committee approved this project. Written informed consent was obtained from all participants.

Dietary questions

There were four questions relating to diet in the ECRHS questionnaire. The first three questions gathered information on the amount of convenience-type food and drinks that participants consumed and between-meal snack patterns, but these responses will not be considered further in this analysis. The fourth question asked whether respondents had ever suffered from any 'illness/trouble' from food ingestion and whether this response occurred 'nearly always' after eating the same food. The offending food(s) and associated symptoms were then listed in order to distinguish between symptoms of indigestion/food poisoning and food allergy or intolerance.

Skin prick testing

SPT for seven aeroallergens and five food allergens was performed on the volar surface of the forearm with standardised allergen extracts (Bayer Corporation, Sydney, Australia). The allergen panel consisted of *Dermatophagoides pteronyssinus*, Cat, Ragweed, Rye grass, *Cladosporium*, *Alternaria*, *Aspergillus*, cow's milk, peanut mix, shrimp, egg white, whole grain wheat mix, positive (histamine) and negative controls. Wheals were measured after 15 min. A positive SPT result was defined as a wheal diameter ≥ 3 mm. Due to ethical concerns, subjects who had reported previous anaphylactic-type responses to any of the food allergens did not have SPT to that allergen performed ($n = 6$). However, they have been included as SPT positive in the analysis.

Definitions

For this analysis, *atopy* was defined as a positive skin reaction (≥ 3 mm wheal diameter) to any allergen, in the context of a positive histamine control and a negative reaction to the

negative control, on SPT (Haahtela, 1993; Backman, 1994). *Food allergy* was defined as an immunological (IgE) reaction which occurred most commonly to food proteins whilst *food intolerance* referred to an abnormal physiological response to an ingested food or food component via non-immunological mechanisms (Dietitians Association of Australia, 1996). *Adverse food reaction* was the sum of food intolerance and food allergy.

Statistical analysis

Data from the questionnaires and SPTs were entered and verified into an AccessTM database. Range and logic tests were performed to confirm the validity of the data. Analyses were conducted using the Statistical Package for the Social Sciences (SPSS) computer package (Norusis, 1993). Cohen's kappa (κ) was used to assess the agreement beyond chance between SPT and self-reported reactions to food(s) which contain the allergen of interest. A $\kappa < 0$ indicated poor agreement; < 0.2 = slight agreement; $0.2-0.4$ = fair agreement; $0.4-0.6$ = moderate agreement; $0.6-0.8$ = substantial agreement and $0.8-1.0$ = almost perfect agreement (Landis & Koch, 1977).

Results

Subject characteristics

Four hundred and fifty seven adults (48% male) with a mean age of 39.2 y (s.d. = 6.3 y) participated in this study. A fifth of the study participants were current smokers, whilst half reported having ever smoked. Forty-two per cent of subjects reported having experienced a wheeze in the past 12 months and 19% have current asthma. Two thirds of the study group were atopic, on SPT, to at least one allergen. The participants

Table 1 Relationship between positive skin prick tests to common food allergens and reported illness to food(s) known to contain the allergen of interest ($n = 457$)

Allergen	Positive SPT n (%) of population)	Reported food illness n (%) of population)	Positive SPT and reported food illness n (% of population)	κ^* (P)
Cow's milk	3 (0.7%)	22 (4.8%)	0	—
Peanut mix	26 (5.7%)	5 (1.1%)	2 (0.4%)	0.37 (0.10)
Shrimp	17 (3.7%)	15 (3.3%)	4 (0.9%)	0.16 (0.27)
Egg white	8 (1.8%)	6 (1.3%)	1 (0.2%)	0.09 (0.64)
Whole grain wheat mix	10 (2.2%)	6 (1.3%)	0	—
Total	64 (14.4%) ^a	54 (11.8%) ^b	7 (1.5%)	

*Cohen's kappa (κ) was used to assess the agreement beyond chance between SPT and self-reported reactions to food(s) which contain the allergen of interest. A $\kappa < 0$ indicates poor agreement; < 0.2 = slight agreement and $0.2-0.4$ = fair agreement.

^aOf the 64 subjects with a positive SPT, 58 were sensitised to one allergen and six subjects were sensitised to two allergens.

^bOf the 54 subjects reporting illness to food nearly always for the five allergens of interest, 49 reported illness to one food and five subjects reported illness to two foods.

were slightly overweight as a group, with a mean body mass index (BMI) of 26.4 kg/m² (s.d. = 4.8 kg/m²).

Prevalence of sensitisation to skin prick tests

Fifty-eight (13%) adults were sensitised to at least one food allergen extract (Table 1). Almost all of these subjects ($n = 54$) were also sensitised to one or more of the common aero-allergens (data not shown). Six subjects (1.3%) had a positive SPT to two food allergen extracts (one to peanut mix and shrimp, two to peanut mix and egg and three to peanut mix and whole grain wheat mix). No one had a positive SPT to more than two food allergen extracts. Six subjects did not undergo SPT to one of the food allergens due to reported previous anaphylactic-type reactions to that particular allergen (two to peanut mix, three to shrimp and one to egg). None of these six subjects were sensitised to any of the other food allergens that we tested for.

Prevalence of reported illness to food

Ninety-nine (22%) adults reported illness to food nearly always and 31 different types of food were reported (Table 2). When this was limited to the five food allergens of interest (cow's milk, peanut mix, shrimp, whole grain

Table 2 Foods reported as nearly always causing illness ($n = 99$)

Food	% of responses
Dairy products	12.3
Fruits (fresh/frozen/canned)	11.0
Seafood	9.7
Monosodium glutamate	6.5
Alcohol	4.5
Herbs/spices	4.5
Dried fruits	3.9
Fats/oils	3.9
Eggs	3.9
Nuts	3.2
Chocolate	3.2
Restaurant meals/take-away	3.2
Vegetables	2.6
Red meat	2.6
Preservatives	2.6
Fruit juice	1.9
Gluten	1.9
Wheat products	1.9
Sauces	1.9
High fat foods	1.9
Soft drinks/cordials, other	1.9
Other	1.9
Yeast	1.3
Artificial colours	1.3
Poultry	1.3
Pickled vegetables	0.6
Sweet biscuits/cakes	0.6
Tea/coffee	0.6
High sugar foods	0.6
Acidic foods	0.6
Spicy food	0.6
Miscellaneous mixed dishes	0.6

wheat mix and egg) only 49 adults (11%) reported illness to food nearly always (Table 1). Five of these adults reported illness to more than one of the allergens of interest.

Prevalence of positive skin prick test and reported illness to food

Only 26% ($n=15$) of those who were sensitised to at least one food allergen ($n=58$) also reported illness following ingestion of food nearly always. Twelve different types of foods or additives were cited as precipitating the problem. The most commonly reported foods were dairy foods ($n=5$), seafood ($n=5$) and monosodium glutamate ($n=3$).

Prevalence of 'true food allergy' (positive skin prick test and reported illness to the same food)

Only seven adults reported illness to a food and also had a positive SPT to the same food (Table 1). Six of these seven people were the subjects that did not have SPT performed to one of the food allergens of interest due to reported previous anaphylactic-type reactions to that particular allergen (two to peanut, three to shrimp and one to egg). No one who had a positive SPT to cow's milk reported experiencing illness from ingested dairy products. Similarly, no one was found to have both a positive SPT and food illness to wheat. Only two people who had positive SPT to peanut mix reported experiencing illness following the ingestion of peanuts. For shrimp and egg white, the number of people reporting both clinical symptoms and a positive SPT were four and one respectively. The agreement (κ) between SPT and self-reported reactions to food(s) which contained the allergen of interest was poor for cow's milk and whole grain wheat mix, slight for shrimp and egg white and fair for peanut mix (Table 1). None of these values were significantly better than chance alone. For all allergens, except cow's milk, a large number of adults had positive SPT results but did not report any clinical symptoms of food allergy. Therefore using these results, the prevalence of reported adverse food reactions with an IgE mediated immunological mechanism in the general adult population would be 1.5% (7/457).

Discussion

This study has found that 22% of young adults perceive that they have adverse food reactions whilst 13% had positive SPTs to five common food allergens. However, when combined (ie those with a positive SPT and who reported a perceived adverse reaction to that food) only 1.5% of adults were likely to have a 'true food allergy'. In this study, the majority of subjects had a positive SPT to only one food allergen.

These results must be interpreted with caution, as a positive SPT merely indicates sensitization. However, corre-

lation with a positive clinical history strongly suggests that the reported food reaction is a true food allergy due to an immunological IgE mediated mechanism. Our results are also consistent with the relative frequencies of adults who are known to have true food allergy (ie peanut and shrimp allergy are the most common allergens in adults) (Anderson, 1994). Nevertheless, to determine the prevalence of true food allergy in the community, double-blind, placebo-controlled food challenge (DBPCFC) studies need to be performed on all of those individuals who were likely to have a 'true food allergy' from this study. Unfortunately, we did not have the resources to conduct DBPCFC studies on these subjects. If those with 'true food allergy' cannot be confirmed by DBPCFC, these individuals would then be able to reintroduce the perceived 'food allergen' into their diet and thus free them from the extra burden associated with carrying the diagnosis of having a food allergy.

Furthermore, the generalisability of the participants to the community should also be considered. We have previously found that the randomly selected sub-sample who attended the laboratory were more likely to be older, male and symptomatic compared to those who were interviewed by telephone and reported a wheeze or an attack of asthma in the past 12 months (Dharmage *et al*, 1997). However, this is unlikely to affect the relationship between reported food reactions and skin test results and therefore we consider that these results can be considered to be representative of young adults in the Melbourne community.

The prevalence of adverse food reactions and food allergy as reported in this study is consistent with that found in previous studies. Young *et al* (1994), found that approximately 20% of a two-stage UK community studied perceived that they had adverse food reactions, however when these subjects underwent DBPCFC to eight common foods only 1.4–1.8% were confirmed to have a true adverse food reaction. The differentiation between food intolerance and food allergy was not determined in that study. Similarly, Bjornsson *et al* (1996), found that 25% of a random community sample of 1397 subjects in Sweden reported symptoms of adverse food reactions, whilst only 6% had specific IgE antibodies to one of the five food allergens that were tested. In a non-random sample analysis, the Swedish study did find a significant correlation between the number of subjects with food-specific IgE antibodies to egg and fish (but not peanut, soy, milk or wheat) and reported adverse food reaction to that food. The Swedish sample was enriched with subjects who reported any of the following: using asthma medication, episodes of acute asthma or wakening because of shortness of breath. The Swedish study also found that sensitisation to food allergens was more common in atopic subjects, those reporting current asthma and those with bronchial hyper-responsiveness. They concluded that the prevalence of specific IgE antibodies to one of the five food allergens that were tested was likely to be an overestimate of true IgE mediated food allergy.

The agreement between the perception of adverse food reactions and positive SPT to common food allergens in adults was poor for cow's milk and whole grain wheat mix, slight for peanut mix and egg white and fair for shrimp. However, these results do need to be interpreted cautiously due to the small numbers of subjects involved.

For all food allergens, except cow's milk, a large number of adults had positive SPT results but did not report any clinical symptoms of allergy.

These results confirm that there is indeed a wide gap between perceived adverse food reactions and those with probable IgE mediated food allergy. We did not collect any data that would explain why these adults perceived that they have an adverse food reaction. Knibb *et al* (1999) who conducted a community study on some 955 subjects in England, concluded that perceived food intolerance is associated with psychological distress in women and neurotic symptoms in both men and women. However, the response rate for this study was low, at only 55%. Conversely, another English community based study conducted by Peveler *et al* (1996) did not find any significant association between psychological impairment and perceived food intolerances. This study also concluded that the reported associations between perceived food intolerances and psychiatric disorder in allergy clinic patients was likely to be due to referral bias. An editorial on this issue concluded that psychological factors were relevant but their exact role was yet to be established (Howard *et al* 1993). Other possible causes or contributing factors remain to be identified. Future research studies need to explicitly explore this issue in detail.

The opposite was true for cow's milk, with many adults reporting clinical symptoms following cow's milk ingestion but without positive objective measurements. It is possible that some of this discrepancy may be due to subjects reporting lactose intolerance, rather than IgE mediated food allergy. However, it is unlikely that lactose intolerance accounts for all of this difference, as the prevalence of lactose intolerance in the Australian adult population is estimated to be 4–20% (Cobiac, 1994). This result suggests that adults continue to perceive that cow's milk allergy is common despite the lack of scientific support for this perception (Haas *et al*, 1991; Pinnock *et al*, 1990; Woods *et al*, 1998b; Simpson *et al*, 1980).

Those subjects with a positive SPT to a food allergen and reported adverse reaction to ingestion of that food in this study, are still likely to overestimate the true prevalence of IgE mediated food allergy. It is known that only approximately 50% of those with positive SPT reaction to food allergens are deemed to have food allergy when they undergo the gold standard for food allergy testing—DBPCFC (Metcalfe & Sampson, 1990; Sampson, 1988a). We also know that SPT has a poor positive predictive value (many false positives), but a good negative predictive value (Sampson, 1988a). In addition to this, six of the seven subjects who we have classified as having 'true food allergy' did not in fact have SPT performed to one of the food allergens due to reporting having experienced an anaphy-

lactic-type reaction previously to that food allergen. This would indicate that the true prevalence of food allergy in adults is likely to be less than 1.5% of the general population.

Several studies have shown that in both adults and children a limited number of foods cause most allergic reactions (Sampson, 1988b). According to Sampson six foods (egg, peanut, milk, shellfish, soy and wheat) account for nearly 90% of positive reactions by blinded food challenge. Foods frequently implicated such as various fruits and chocolate, have not been found to elicit positive responses by blinded challenge. Hence, although there may be some subjects with true IgE mediated allergy to a food not tested in the panel, the number is likely to be small. It is therefore unlikely that our results significantly underestimate the prevalence of food allergy in young adults.

In conclusion, this study found that there was little agreement between the perception of adverse food reactions and positive SPTs to common food allergens in adults. This suggests that most perceived reactions are not due to IgE mediated food allergy. Further research is required to determine the true prevalence of IgE mediated food allergy using DBPCFCs. As our results suggest that the number of people modifying their diet is many times higher than the number who need to due to possible food allergy, public education is required to ensure that adults are not unnecessarily restricting their dietary intake.

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