

Prevalence and severity of food allergy – need for control

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Medical expenses and work absence due to allergic diseases cost the member states of the EU an estimated 29 billion ECU per annum (1). Allergic asthma accounts for the majority of these direct and indirect costs. It is not known what might be the added costs to families of having a member affected by food allergy. Similarly, the costs to industry of risk-assessment procedures, changes of manufacturing and labelling practices, and the recall of products actually or potentially contaminated with allergens are unknown. These costs are likely to be considerable: for example, in the USA, a grade 1 recall (due to contamination with a food recognized as causing anaphylaxis) can cost \$3 million (S. Taylor, personal communication).

All affected parties – families, physicians, manufacturers, and regulatory authorities – need better information regarding food allergens and the risk of exposure of sensitized individuals to these foods on which to base activities of daily family life (such as food shopping), medical advice to both individuals and populations, and good manufacturing practice.

It is clearly in the remit of allergists and food safety technologists to evaluate logically the published evidence regarding foods that are commonly or occasionally allergenic and to produce a list of foods whose presence must be declared, irrespective of dose or concentration (Table 1). Such an approach is being coordinated by the ILSI Europe Task Force on Food Allergy and Intolerance. It must be noted that situations do exist in which allergic reactions to foods are inconsistent over time or are exacerbated by other factors, such as prescribed medication (2),

coincident consumption of alcohol with the implicated meal (3), and, particularly, exercise-induced, food-related anaphylaxis (4, 5).

Prevalence and severity

Basic information regarding prevalence and severity is available for some food allergens, but not for many others. Decisions about the regulation, of other foods are more difficult when significant, even life-threatening allergic reactions to the food have been reported but for which data regarding prevalence of allergy to that food are lacking (Table 2).

The prevalence of allergy to individual foods clearly varies with the dietary practices of different populations, even within Europe and allowing for reporting bias. Case series show that reaction to ingestion of fruits with associated birch-pollen allergy is a common problem in Scandinavia (6), though, anecdotally, unusual in the UK. Fish allergy is apparently common in Spain and Portugal (7). Seafood and milk caused most episodes of food-related anaphylaxis in children reported recently from Italy (8), whereas, in the UK and the USA, the overwhelmingly common causes of food-related anaphylaxis in children and adults are peanut and tree nuts (3, 9, 10, 11). Allowing for these international differences, a list of “usual suspects” is an achievable proposition. Such a list must be based on the best available evidence of allergenicity – currently either a positive double-blind, placebo-controlled food challenge (DBPCFC) or an unequivocal report of a reaction with the typical features of an IgE-mediated severe

Table 1. Ingredient foods (and derivatives) that should be declared, irrespective of quantity

Cow's milk
Hen's egg
Peanut
Soya
Wheat
Fish
Crustacea
Tree nuts (including almond and cashew)
Seeds (sesame, cottonseed)

allergic or anaphylactic reaction (12). DBPCFC studies in children and adults have repeatedly shown that a relatively short list of eight foods (and derivatives) accounts for 90% of genuine IgE-mediated allergic reactions (12, 13). There can be little doubt that this group of foods should be declared on a label, considering that very low doses of allergenic protein can elicit allergic reactions. A dose response has been demonstrated for peanut, with 100 µg causing minor symptoms, and 5 mg causing a severe systemic reaction (14). Higher doses of between 50 and 100 mg have elicited reactions in DBPCFC of subjects reporting cottonseed (15) and soya allergies (16).

Estimates of prevalence of allergy or intolerance to foods

Two European studies have estimated the prevalence of food allergy and intolerance in the general population. Niestijl Jansen et al. (17) studied a random sample of 1500 Caucasian Dutch adults, using a questionnaire in a door-to-door survey. A total of 198 (13%) stated they had food allergy or intolerance. Ninety agreed to participate further, and 36/90 were excluded on the basis of nondefinable symptoms. History and skin prick testing found 54/90 people as possibly having food allergy or intolerance. Seventeen dropped out. Of the remaining 37 subjects, only 12 were confirmed by open or blind challenge to have food allergy or intolerance. Only one was a typical allergic reaction (immediate throat itch after kiwi fruit). Therefore, the minimum prevalence of food allergy or intolerance in the adult Dutch population was 12/1483 or 0.8%. The minimum rate of food allergy was 1/1483 or 0.06%. The authors comment that if rates are assumed to be equal in participants, nonparticipants, and dropouts, the prevalence of food allergy or intolerance is 2.4%, with intolerance being more common than allergy by at least one order of

Table 2. Other foods known to cause significant allergic reactions

Kiwi
Molluscs
Prunoideae (peach, prune, apricot)
Cereals (excluding wheat but including buckwheat)
Rice
Celery
Mustard

magnitude. The rate of proven allergy or intolerance (0.8%) is approximately 10 times lower than the perceived rate (13%).

Young et al. (18) reported that 2152/10 522 (19%) of UK subjects reported adverse reactions to foods. A wide variety of foods and food components was implicated, such as caffeine, meat, alcohol, and additives as well as more "typical" allergenic foods. A total of 1799 subjects were offered interviews. However, only 93 subjects completed the protocol of DBPCFC. Of them, 18/93 (19.4%) were positive on challenge, giving an estimated minimum prevalence of food intolerance and allergy of 1.4%. Including 47 subjects with allergies considered too severe to include in the challenges and assuming a 50% reaction rate in this latter group, the prevalence would have increased to 1.9%. Therefore, the estimated minimum prevalence (1.4%) was 10 times lower than the perceived prevalence of 19%. These population-based data do not reflect the fact that most allergies to foods are most prevalent in children, particularly preschool infants (19). Prevalence data for individual foods are really reliable only for the most commonly allergenic foods and are largely based on carefully studied birth cohorts.

Cow's milk allergy

Cow's milk allergy has been shown by several groups to affect up to 2.8% of children in the first years of life (20). Høst & Halken's study (20) of 1749 unselected infants showed that the parents of 117 infants (6.7%) reported symptoms on exposure to cow's milk. Only 39/117 (2.2% of the total cohort) had symptoms that were reproduced on formal challenge. These figures are similar to those produced in studies in the UK by Hide & Guyer (21) and in The Netherlands (22). Typical IgE-mediated reactions soon after exposure to milk proteins are common, but life-threatening anaphylaxis is unusual (20). Gastrointestinal and late-phase IgE-mediated cutaneous reactions such as exacerbation of atopic dermatitis are also common. Milk allergy is common in preschool infants but

wanes with the passage of time. By the third birthday, 34/39 milk-allergic children in the Danish study had become tolerant of cow's milk (20).

Therefore, cow's milk and its derivatives clearly constitute a risk to a substantial number of children, particularly infants. Though the risk of serious reaction is relatively low (5–8%), the absolute numbers of at-risk children are clearly substantial. Longitudinal data suggest that persistence of milk allergy beyond the age of 5–6 years is predicted by severe disease and other atopic manifestations (23). Therefore, older affected children may have a greater risk of anaphylaxis. Milk should be a declared ingredient.

Egg allergy

Hen's egg is a commonly allergenic food in the first 3–4 years of life. In a recent report of the German Multicenter Allergy Study (MAS), 1314 children were followed from birth to 3 years. Egg allergy was the most prevalent allergy at 12 months (8–9%) and at 24 months (158 children, 12%) (24). In the control group of Zeiger & Heller's study (25) of food allergen avoidance in high-risk children, 29/185 children (15%) had demonstrated a positive SPT to egg by the age of 24 months. Egg-specific IgE >2 kU/ml at 12 months of age is a marker for future sensitization to aeroallergens (24). Anaphylaxis due to egg has been reported (10), and egg has been implicated in several series of patients with food-sensitive atopic dermatitis (13, 26).

Peanut and tree nuts

A cohort study of 1456 UK children found that 15/981 (1.5%) tested at 4 years had a positive SPT to peanut or tree nut, with 13/15 being peanut allergic. Only 6/13 (0.6%) had suffered a clinical reaction to peanut. The other seven peanut-SPT-positive children did not undergo DBPCFC. The minimum prevalence of peanut allergy in preschool UK children is, therefore, 0.6% (27). This cohort study was supported by a recent telephone survey in the USA, which found that 164/12 032 (1.36%) individuals, adults and children, reported allergy to peanut and/or tree nuts (28). Peanut allergy is established early in life and is characterized by a high frequency of accidental exposure (29, 30), and a predominance of severe reactions (30). Peanut causes 25–30% of anaphylactic reactions in the community in the UK (excluding medication-related and perioperative anaphylaxis in hospitals (9)). Peanut allergy is relatively common, and peanut use is widespread in catering and cooking. The prevalence of peanut allergy, the apparent frequency of coincident tree nut allergy (or cross-

reactivity), the typically severe nature of peanut-induced allergic reactions, and the many uses of peanut all suggest that peanut should always be a listed ingredient, irrespective of dose.

Tree nut allergy has been studied less intensively than peanut, with few double-blind studies. Case series or reports of single subjects allergic to pistachio, Brazil nut, hazelnut, walnut, almond, and pecan suggest that tree nut allergy causes symptoms as severe (occasionally fatal) as peanut allergy in individuals sensitized to that nut (3, 11, 28, 31–33). Taxonomically, cashew and almond are not tree nuts but fruit seeds, but they are commonly considered alongside tree nuts. Tree nuts should be labelled ingredients, irrespective of dose or concentration.

Fish and shellfish

Fish and shellfish allergies are unusual in young children but are well recognized in adults, possibly reflecting dietary practice (fear of inhalation of bones by young children) (34, 35). Anaphylactic reactions to fish and crustacean shellfish are well described (3, 33). DBPCFC have shown reproducible reactions (34). The severity of fish and shellfish allergies suggest they should be listed ingredients.

Soya

Soya or soya products such as lecithin are common ingredients of prepared foods. Soya has been shown to cause anaphylactic reactions (35) and is a significant factor in food-related atopic dermatitis (13, 26). Soya sensitization is commonly found in food-allergic individuals, but clinically significant soya allergy is rare (36, 37). In one study, only 8/131 (6.1%) of soya SPT-positive children were clinically reactive on food challenge (16).

Wheat

Of 34 children with atopic dermatitis, 33 had positive SPT to wheat and 14/33 had a positive oral challenge with wheat (38). Of 83 positive DBPCFCs in 64 children with atopic dermatitis, five were due to wheat (13). Wheat appears to be particularly associated with exercise-induced food-related anaphylaxis in adults (12/19 patients with exercise-related allergic symptoms in a French study (5) (due to the practice of pasta "loading" before extreme exertion such as long-distance running?).

Seeds

Reactions to seeds such as sesame (39, 40), cottonseed (15), and mustard (41) have been described; sesame, in particular, appears to be associated with severe reactions (40, 41).

Summary

Food allergy is an increasingly recognized manifestation of atopy. Patient and public awareness of food allergy is also increasing. Justifiable demands are being made for better medical guidance of the practice of food labelling for industry and catering businesses. Such advice must bear in mind the relative frequency and severity of allergies to certain foods. Some commonly allergenic foods (milk, egg, soya, wheat) are staple components of the diets of populations, used widely in prepared foods. The frequency of the allergies to these foods and their widespread uses means they and their derivatives must be declared on food labels. Less commonly used foods such as fish, shellfish, peanut, and tree nuts demand declaration due to the severity of reactions induced in the admittedly more rare, but increasingly common, sufferers of these allergies. Reactions to more unusual foods are increasingly being identified, and the "minimum" list is likely to be extended in the future.

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