



CLINICAL PERSPECTIVES

Food allergy in adolescents and adultsJ. Yun¹ and C. H. Katelaris^{1,2}¹Campbelltown Hospital, Campbelltown, and ²School of Medicine, University of Western Sydney, Sydney, New South Wales, Australia**Key words**

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Abstract

There has been an increase in the prevalence of food allergy in the last few decades. Adult food allergy may represent persistence of reactions that commenced in infancy and early childhood or it may be initiated in adulthood through new sensitizations. Persistence of peanut allergy is an example of the former situation. Approximately 20% of children will develop tolerance to peanuts, so there will be an increasing number of individuals reaching adulthood where this problem will need ongoing management. In addition to peanut, tree nuts, fruits, vegetables and seafood are implicated as common causes of food allergy in adulthood. Sensitization may occur directly to a food allergen or indirectly through cross-reactivity with an aeroallergen. Adults may present with a spectrum of clinical manifestations from oral allergy syndrome to fatal anaphylaxis. The management of food allergy consists of appropriate education regarding avoidance of implicated foods, modifying potential risk factors for anaphylaxis, such as asthma and prompt recognition and treatment of acute reactions.

Introduction

In the past few decades, there has been a definite increase in the prevalence of food allergy (FA) in infancy and childhood. As these children reach adulthood, a proportion of them will have persistence of their FA so adult physicians will increasingly be called upon to manage these problems. FA encompasses a spectrum of disorders, with symptoms that may be cutaneous, gastrointestinal, respiratory or generalized. Food-related disorders also differ in their pathophysiology with a variety of immunological mechanisms proposed. IgE-mediated food reactions are the most completely understood and best studied of these will be the subject of this review.

Up to 25% of adults believe that they or their children suffer from FA; however, the actual prevalence is much lower: approximately 5–8% of children and 1–2% of adults suffer from objective FA.^{1,2} This is demonstrated by the detection of food-specific IgE accompanied by a convincing history of type I hypersensitivity-mediated

symptoms after suspected food ingestion or by eliciting characteristic symptoms after controlled oral challenge.

Adult FA may represent persistence of reactions that commenced in infancy or in early childhood. Infants and children have a greater predisposition to develop FA, many of which may be transient. Immunologic tolerance to certain foods may develop over time, with some foods more likely than others to be tolerated in later years. Alternatively, FA may be initiated in adulthood through new sensitizations. Allergies to fruits and vegetables are more common in adulthood. They are rarely life-threatening and often result from cross-sensitization with certain inhalant allergens. On the other hand, nuts and seafoods may cause severe allergic reactions. Symptoms of FA in adults may encompass those seen in early childhood, although a relationship with atopic dermatitis is far less frequent and oral allergy syndrome (OAS) is a much more common manifestation.

Persistence of FA starting in infancy

Some allergies to common foods in adults are due to persistence from early childhood. Cow's milk allergy persisting into adulthood is an uncommon phenomenon.

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In a Danish study, 97% of cow's milk-allergic children were able to tolerate cow's milk by the mid-teen years.³ However, cow's milk allergy in this study was associated with an increased risk of developing other FAs and other atopic disorders, such as asthma and allergic rhinitis. Persistence of egg allergy into adulthood is more common, yet more than 80% of the paediatric population with egg allergy will eventually become tolerant.⁴ The persistence of soy allergy is similar to that seen with egg allergy.

Peanut allergy receives a great deal of attention and the noted increase in its occurrence has been accompanied by much emotion and media attention, as a substantial portion of anaphylactic deaths from FA are due to peanuts. Previously, it was considered that children rarely outgrow peanut allergy, but a recent study by Skolnick *et al.* showed that approximately 20% of peanut allergic patients will become tolerant by late childhood.⁵ The likelihood of outgrowing peanut allergy was higher if the skin prick test was negative or if the peanut-specific IgE level was absent or lower than the initial estimation. Persistence of childhood acquired peanut allergy accounts for the majority of peanut allergy in adulthood. However, peanut allergy may be acquired for the first time in adult life, although the frequency of this is unknown.

FA commencing in adulthood

Peanut, tree nuts, fruits, vegetables and seafood are implicated as common causes of FA in adulthood. Sensitization may occur directly to the food allergens or indirectly through cross-reactivity with aeroallergens. Food allergens may also sensitize through inhalation in certain occupational settings, and in this case, symptoms are primarily respiratory in nature.

Clinically, adult onset FA may present with local oropharyngeal symptoms, such as oral itching or angioedema (OAS), isolated gastrointestinal symptoms or systemic symptoms. In adults, FA rarely contributes to atopic dermatitis and, contrary to some beliefs, is rarely a cause of chronic urticaria.

Oral allergy syndrome

OAS refers to a cluster of characteristic symptoms that usually begin within minutes of ingestion. Patients describe itching of the mouth, tongue and throat and this may be accompanied by lip swelling. In some, the oral symptoms may be followed by gastrointestinal symptoms, such as vomiting, cramping and diarrhoea. The reactions may not progress past these early symptoms. However, patients can develop generalized urticaria, rhinoconjunctivitis, asthma symptoms and even anaphy-

laxis. In a review of several studies, nearly 10% had associated systemic symptoms. OAS is present in up to 70% of subjects with pollen allergy.⁶

To understand the nature of plant-derived FA, the phenomenon of cross-reactivity where an antibody to a specific antigen recognizes different antigens because of their structural similarity in epitopes needs to be outlined.

The majority of plant food allergens can be grouped into four protein families known as the prolamin, cupin, profilin and Bet v1 superfamilies. Similarly, all known pollen allergens can also be grouped into a few major pollen allergen families, of which two are the same as the plant food allergens, namely profilins and Bet v1 superfamily. Bet v1 is the major allergen in Birch pollen, a major aeroallergen in Europe and many other cold climate regions. Bet v1 food allergens are found in a number of plant food families – Rosaceae (apple, stone fruit), Apiaceae (celery and carrot), Fabaceae (peanut, soy, lentil and pea).⁷ There is a marked homology between these proteins. Therefore, an individual primarily sensitized through inhalation of Birch pollen may demonstrate cross-reactivity to a variety of plant foods as listed. In many, this is a non-clinically relevant sensitization where food avoidance is unnecessary. However, some do develop clinical symptoms, most commonly with manifestations of OAS. Other known associations between certain pollen and foods include mugwort, celery and spice and ragweed and melon. Latex-allergic individuals may develop allergies to a variety of foods, such as avocado, banana, kiwi fruit, potato and peach. Strong homology between storage proteins in these plants is responsible for this phenomenon.

It is also possible for an individual to become sensitized to these fruits and vegetables directly and not as a result of cross-reactivity. For example, while apple allergy may occur through cross-reactivity because of the mechanism outlined above, it may also occur through ingestion of apple, resulting in direct sensitization to protein Mal d 3, a lipid transfer protein (LTP). Mal d 3 is not associated with cross-reactivity with pollen Bet v 1 and these patients do not have pollen allergy.⁸ However, because of cross-reactivity of Mal d 3 with other LTPs, a substantial number of these patients are also allergic to other fruits. It is likely that structural resistance of LTPs to degradation and digestion may play an important role in this route of sensitization and in their capacity to be allergens.

Allergen cross-reactivity is found outside the plant kingdom. Castillo *et al.* quoted in Crespo and Rodriguez found that 82% patients with prawn allergy were sensitized to house dust mite on skin testing.⁹ Tropomyosin is the protein involved in this particular cross-reactivity. Isolated adult onset egg allergy has been reported, but this is more likely to be preceded by bird allergy although

they are both rare. The latter is manifested as OAS and these patients have specific IgE to livitin, a protein found in both egg yolk and bird dander.

Food-dependent exercise-induced anaphylaxis

Food-dependent exercise-induced anaphylaxis is a condition where exercising soon after food ingestion causes anaphylaxis. While a number of foods may be responsible, it is most commonly associated with wheat. The mechanism by which a particular food acts as a cofactor is largely unknown.

Adult onset allergy to common foods

Adult onset allergy to common foods also occurs, although these are more commonly seen as a continuation of FA from childhood. Rarely, adult onset milk allergy and egg allergy can be observed. Stoger *et al.* quoted in Crespo and Rodriguez found that in adult onset milk allergy, respiratory and skin symptoms were most commonly experienced while gastrointestinal and cardiovascular symptoms were less likely to occur than in childhood.⁹ In contrast to milk allergy in early childhood, adult onset is usually associated with long-lived sensitivity.

Seafood allergy is a common long-lived allergy and is rarely outgrown. Cross-reactivity among various fish species is common, although allergy to single species of fish exists because of species-specific allergens. Among crustaceans, allergy to prawn is the most common, and cross-reactivity with other crustaceans, such as crab and lobster, is frequently seen. Other seafood allergy may involve molluscs, which include squid, octopus, mussel, oyster and scallop. Anaphylaxis to seafood is not uncommon and careful investigation and food challenges are usually required in order to identify 'safe' seafood. In addition, food avoidance can be complicated by clinically significant cross-reactivity between related seafood subgroups and by cross-contamination of different types of seafood in the food processing.

Allergy to legumes is rarely reported in adults with the exception of peanut. More recently, lupin allergy has been described in 30% of peanut allergic adults in one study.¹⁰ Inhalation of lupine flour and soybean dust has provoked occupational asthma in adults. Similarly, grains and grain products are most commonly linked to IgE-mediated occupational asthma.

Fatal food anaphylaxis in adulthood

The rate of fatal food anaphylaxis is very low overall and is a rare event in pre-school children, despite the fact that the majority of food allergies occur in this age group.

According to pooled data from the American Academy of Allergy, Asthma and Immunology (AAAAI) registry of anaphylactic deaths in the USA, 89% of 63 reported anaphylactic deaths occurred in adolescents and adults, with approximately 50% occurring in teenagers.^{11,12} The majority, but not all, of deaths in subjects over 10 years of age were caused by peanut or tree nuts, with peanut being the culprit in approximately two-thirds of the cases. In New South Wales, the annual risk of a teenager dying from anaphylaxis to peanut or tree nut is estimated to be 1 in 10 000 to 1 in 100 000.¹³

Risk factors for fatal food anaphylaxis

Ultimately, food anaphylaxis resulting in death is an unpredictable event. There is a number of identified risk factors.

Delay in use of adrenaline

In the AAAAI registry of anaphylactic deaths quoted above, most of the patients either did not have an EpiPen (CSL Biotherapies Pty Ltd, Parkville, VIC, Australia) at the time of the fatal reaction or did not administer it until significant time had elapsed.

Risk taking behaviours especially in adolescents

A study by Sampson *et al.* showed that approximately 20% of adolescent patients do not always carry their EpiPen and knowingly eat foods that may contain allergens.¹⁴

Coexisting asthma

The presence of severe asthma increases the risk of severe life-threatening bronchospasm by sevenfold.¹⁵ Most food-allergic adolescents and adults who died of anaphylaxis were known to have asthma, highlighting the importance of asthma as a comorbidity.

Severity of prior reactions

While it is logical to assume that those who have had previous severe reactions are at greater risk of death, the severity of prior reactions has not been shown to be a predictor for severe anaphylaxis. In the study of fatal anaphylaxis by Pumphrey and Gowland, a significant proportion of prior FA reactions experienced by individuals were mild.¹⁶

Evaluation and management of FA in adults

The diagnosis of FA involves a stepwise approach, including medical history taking, demonstration of

specific IgE and, where necessary, confirmation by oral food challenge. This is particularly important in adults where immunological cross-reactivity between foods and pollen may be present. The management of the food-allergic patient at present consists of education regarding food avoidance, early recognition of a reaction and first-aid principles in the management of an acute allergic reaction. This includes prompt use of intramuscular adrenaline. Referring patients to suitably trained clinicians for evaluation and interpretation of skin prick tests or specific IgE to allergens is advisable to avoid inappropriate investigations, misinterpretation of tests, incorrect diagnosis or unnecessary food avoidance, particularly in those where FA is not straightforward. This is particularly important as there are widespread uses of unreliable and inappropriate tests in the community. Provision of an EpiPen in those who are at risk of anaphylaxis with careful instruction on how and when to use it can be life-saving. As asthma is a strong risk factor for fatal anaphylaxis, its aggressive treatment may potentially reduce the risk of death.

At the present time, immunotherapy is not available for FA management. Several immunotherapeutic approaches are under investigation and are most advanced in the area of peanut allergy. In the future, these strategies offer the hope of reducing or even eliminating the risk of food-allergic reactions.

Conclusion

FA in adolescents and adults may be due to either persistence of childhood allergy or acquired sensitization in adulthood. Sensitization later in life may be due to either cross-reactivity with aeroallergens or by direct sensitization. Currently available management strategies are avoidance of implicated food(s), modifying potential risk factors and appropriate management of acute reactions, including early use of EpiPen when appropriate.

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