

# Asthma and food allergy

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### Purpose of review

Food allergy associated clinical and social burdens have increased substantially in prevalence in the past decade. Coexisting asthma is a significant problem as food reactions tend to be more severe when they involve the lung. Food allergy also increases asthma morbidity in adults and children.

### Recent findings

Especially in early infancy, food allergy can be related to the development of future asthma. For diagnosis, cut-off values are very important for both specific IgE levels and skin-prick test when interpreting food allergy. For the treatment, oral immunotherapy is showing promise for refractory patients with IgE-mediated food allergies.

### Summary

Food allergies can be classified as IgE-mediated or non-IgE-mediated. Besides foods, some additives and preservatives can also trigger asthma in certain people. Asthma may develop in about 5% of individuals who suffer from food allergy and current asthma may be triggered by foods among 6–8% of children and 2% of adults. Because of the difficulty of confirming diagnosis of food allergy, novel approaches are currently being investigated and new therapy modalities are being sought. For total asthma control and for better quality of life, steps should be taken to avoid foods in cases of food allergy.

### Keywords

asthma, diagnosis, food allergy, treatment

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## Introduction

Food allergy is defined as an adverse immunological response to food that is reproducible under blinded conditions. As a result of changing environmental conditions, westernized life style, air pollution, and the consumption of lots of additives and preservatives with foods, food allergy and asthma are increasing worldwide. Mullins [1] showed that food allergy increased 12-fold for children aged 0–5 years over the 12 years from 1995 to 2006 in Australia. There was marked heterogeneity about the rate of food allergy between studies regardless of type of assessment or food item considered. Self-reported prevalence of food allergy varied from 1.2 to 17% for milk, 0.2 to 7% for egg, 0 to 2% for peanuts and fish, 0 to 10% for shellfish, and 3 to 35% for any food [2]. In general, food allergy affects about 6–8% of children and 3–4% of adults [3,4].

## Mechanisms of food allergy

Food-allergic disorders can be broadly divided into IgE-mediated or non-IgE-mediated reactions. A person who is genetically predisposed to atopy produces specific IgE antibodies to certain proteins. In IgE-mediated food allergy, food allergens bind with these food-specific IgE antibodies residing on mast cells and basophils, to activate

the cells to release potent mediators like histamine. In non-IgE-mediated food-allergic disorders, activation and recruitment of lymphocytes and eosinophils are cardinal features of the diseases and symptoms are typically of late onset [5]. Allergic reactions to food may occur anywhere in the body, but usually in the digestive system, the skin, and occasionally in the nose and lungs. Skin symptoms such as eczema and hives and symptoms of the digestive tract such as stomach cramps, vomiting and diarrhea are more common in food allergy than asthma. In most cases, foods cause reactions in allergy-prone individuals if they are swallowed. In certain people, food may cause reactions such as asthma if inhaled. Flour can cause asthma in bakers who are allergic to this substance. Inhalation of aerosolized food particles such as fish and shellfish during cooking may cause respiratory symptoms in selected food-allergic individuals [6].

## Diagnosis of food allergy

The diagnosis of a food allergy includes skin or in-vitro testing as an initial study when the history suggests food allergy. While negative testing generally rules out a food allergy, positive testing should be followed by a food-challenge procedure for a definitive diagnosis. Controlled oral food challenges are considered to be the gold

standard in the diagnosis of food-related symptoms, especially if performed in a double-blind, placebo-controlled food challenges manner [7]. The CAP-radio-allergosorbent test (RAST) fluoroenzyme immunoassay (FEIA) system is an improved in-vitro measure that in some cases may decrease the need for food challenges. However, cut-off values are very important for interpreting food allergy such as in peanut allergy; peanut specific-IgE level of 0.37 kU/l was 98% sensitive but 33% specific. A level of 10 kU/l was 100% specific. Similarly, skin-prick test specificity was 67% at 8 mm and 100% at 15 mm [8]. The diagnosis of food allergy is easy when the adverse reaction occurs soon after ingestion of an uncommonly used food item but more difficult if the reaction occurs several hours or days later, or if commonly used food is involved. The final mainstay of diagnosis is the demonstration of the relief of symptoms on removal of a given food item and recurrence of symptoms on its re-introduction (eliminate–challenge testing).

### **The epidemiological link between asthma and food allergy**

Food allergy and asthma are both atopic diseases so therefore they may coexist, but asthma alone as a manifestation of a food allergy is rare and atypical. In general, inhaled allergens such as house dust mites, cat fur and pollen are more likely to trigger asthma than foodstuffs. Food and respiratory allergy are also closely associated because sensitization to pollen proteins can result in food-allergic reactions to fruits and vegetables with homologous proteins (pollen food syndrome) [9].

The most common foods responsible for allergic reactions are eggs, cow's milk, peanuts, soya, fish and shellfish in children and peanuts, tree nuts, shellfish and fish in adults. Individuals can also be affected by substances that are used as food additives and preservatives. In one of our studies [10], which covered 125 asthmatic patients, we found that the incidence of food allergy was 7.2%. Berns *et al.* [11] found that the prevalences of fish, peanut, tree-nut, shellfish and seed allergies were 3, 3, 3, 13, and 1% in adult asthmatics. There is a perception among patients attending asthma clinics in both Europe and Australia; over two-thirds believed that food induced their asthma [12]. This rate is very high as patients considered that ice cream, cold water and carbonated drinks are bad for their asthma. However, the underlying mechanism responsible for generating bronchospasm with those foods is more likely to be cold or acid than an allergic reaction.

### **Food allergy as a risk factor for future asthma**

Birth cohort studies with a long period of follow-up showed that some special food allergies can be a predictor

of asthma later in life. For example, the presence of egg protein allergy is considered to be a risk factor for the future development of asthma, particularly for children [13<sup>•</sup>]. Host *et al.* [14] found that children sensitized to cow's milk proteins and also having atopic eczema are at higher risk for asthma. Similarly Rhodes *et al.* [15] found that skin sensitivity to hen's egg, cow's milk or both in the first 5 years of life was predictive of asthma.

Those with probable IgE peanut and shrimp allergy were significantly more likely to have current asthma and doctor-diagnosed asthma. Wheeze and history of eczema were also associated with peanut allergy, whereas nasal allergies were associated with shrimp allergy [16].

### **Food-induced asthma**

Food-induced asthma is generally an IgE-mediated illness that may result from ingestion of a causative food or from the inhalation of vapors released during cooking. Food-triggered asthma occurs among 6–8% of children and 2% of adults with asthma [17]. Patients with food allergy and asthma were generally younger and had a medical history of atopic dermatitis [17]. Rarely, food additives such as sulfating agents can cause respiratory reactions. This reaction occurs primarily in patients with underlying asthma, particularly in patients with more severe asthma.

### **Coexistence of asthma and food allergy**

Food allergy has been implicated as a risk factor for life-threatening asthma and asthma also seems to be a risk factor for life-threatening food allergy. Patients with underlying asthma are more likely to experience fatal or near-fatal food reactions [13<sup>•</sup>]. Compared with non-asthmatic children, asthmatic children have a 14-fold higher risk of developing a severe allergic reaction to food [18]. Patients with allergies to more than one food had statistically increased asthma hospitalizations, emergency department visits, and use of oral steroids [19]. Specifically, allergy to fish was associated with a greater risk of health resource utilization and increased frequency of oral steroid use. Simpson *et al.* [20] reported that peanut and milk allergies were both associated with a statistically increased number of hospitalizations and milk allergy was associated with increased use of systemic steroids in pediatric asthmatics. It has been reported that half of adults with brittle asthma report coexistent food allergies, and avoidance of food allergens may also lead to improvement in asthma control. As a result of this, food allergy should be considered in patients in whom asthma is poorly controlled despite persistent use of appropriate asthma medications.

## Food-dependent exercise-induced anaphylaxis

Food-dependent exercise-induced anaphylaxis is a rare disease and it is classified into physical allergy and/or a subtype of food allergy induced by physical exercise. The pathophysiology and epidemiology of food-dependent exercise-induced anaphylaxis are not well known. Symptoms are typically generalized urticaria and severe allergic reactions such as shock or hypotension. Whereas various food items are responsible for the development of food-dependent exercise-induced anaphylaxis, wheat is reported to be the allergen with the highest frequency in Japan [21]. The  $\alpha$ -amylase inhibitor was confirmed to be the most important wheat allergen in food allergy and to play a role in wheat-dependent exercise-induced anaphylaxis [22].

## New treatment methods for food allergy and asthma

The most effective approach to treating food-allergy-related asthma is to avoid the offending food(s) in the first place. This involves extensive education and care about reading ingredient statements on food labels, which is now easier following new labeling legislation. However, identifying the offending food may not be easy or it may not be possible to completely avoid it. Fortunately new therapy modalities are being explored to be used with or without allergen avoidance. Humanized monoclonal anti-IgE antibodies are one of these new therapies. Leung *et al.* [23] examined the role of monthly subcutaneous injections of anti-IgE (TNX-901) on patients with peanut allergy in a double-blind placebo-controlled study. With the therapy, threshold sensitivity to peanut increased to a protection level in 76% of patients. On the other hand, use of another monoclonal antibody against IgE (omalizumab) was discontinued for peanut allergy as a result of safety concerns after severe reactions occurred during initial oral challenges [24].

Oral immunotherapy is showing promise on patients with IgE-mediated food allergies. Patriarca *et al.* [25<sup>••</sup>] demonstrated oral desensitization by sublingual therapy with the most common food allergens caused a significant decrease in specific IgE and a significant increase in specific IgG<sub>4</sub> in all treated patients with a success rate of 85.7%. Alonso *et al.* [26] observed that birch-pollen-specific immunotherapy decreased allergy to foods containing birch-pollen-homologous allergens in 16 adult patients suffering from vegetable food allergy (hazelnut, walnut, lettuce, peach and cherry) after immunotherapy.

Human interleukin-5 is the major cytokine for the growth and differentiation, recruitment and survival of eosinophils. Preliminary studies with anti-interleukin-5 mepoli-

zumab seem to be promising, especially in eosinophilic esophagitis [27<sup>••</sup>].

## Conclusion

Birth cohort studies with a long period of follow-up showed that some special food allergies can be a predictor of asthma later in life. Food allergy has been implicated as a risk factor for life-threatening asthma and asthma also seems to be a risk factor for life-threatening food allergy. The presence of food allergy is associated with increases in asthma morbidity in both adults and children, so food allergy should be considered in patients in whom asthma is poorly controlled despite persistent use of appropriate asthma medications.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 86).

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