

Clinical Management of Food Allergy

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Date of Original Release: January 2015. Credit may be obtained for these courses until February 28, 2016.

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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

Target Audience: Physicians and researchers within the field of allergic disease.

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List of Design Committee Members: J. Andrew Bird, MD, Gideon Lack, MD, FRCPCH, and Tamara T. Perry, MD

Activity Objectives

1. To use tests for food allergy appropriately.
2. To instruct patients and families on recommendations for food allergen avoidance, including label reading, potential cross-contact, and eating away from home.
3. To recognize and appropriately treat a food-induced allergic reaction.
4. To provide appropriate guidance for a child with food allergy who is attending school.

Recognition of Commercial Support: This CME has not received external commercial support.

Disclosure of Significant Relationships with Relevant Commercial

Companies/Organizations: J. A. Bird has received research support from DBV Technologies, Allergen Research Corporation, and the Foundation of the American College of Asthma, Allergy and Immunology; and has received lecture fees from Nutricia North America. G. Lack has received research support from the Immune Tolerance Network/National Institute of Allergy and Infectious Diseases, Food Allergy Initiative, National Peanut Board, Food Allergy Anaphylaxis Network, the MRC Asthma UK Centre, Department of Health/National Institute for Health Research, and Food Allergy Research and Education; and has stock in DBV Technologies. T. T. Perry has received research support from the National Institutes of Health.

Food allergies are commonly seen by the practitioner, and managing these patients is often challenging. Recent epidemiologic studies report that as many as 1 in 13 children in the United States may have a food allergy, which makes this an important disease process to appropriately diagnose and manage for primary care physicians and specialists alike. Having a understanding of the basic immunologic processes that underlie varying presentations of food-induced allergic diseases will guide

the clinician in the initial workup. This review will cover the basic approach to understanding the immune response of an individual with food allergy after ingestion and will guide the clinician in applying appropriate testing modalities when needed by conducting food challenges if indicated and by educating the patient and his or her guardian to minimize the risk of accidental ingestion. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:1-11)

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No funding was received for this work.

Conflicts of interest: J. A. Bird has received research support from DBV Technologies, Allergen Research Corporation, and the Foundation of the American College of Asthma, Allergy and Immunology; and has received lecture fees from Nutricia North America. G. Lack has received research support from the Immune Tolerance

Network/National Institute of Allergy and Infectious Diseases, Food Allergy Initiative, National Peanut Board, Food Allergy and Anaphylaxis Network, the MRC Asthma UK Centre, Department of Health/National Institute for Health Research, and Food Allergy Research and Education; and has stock in DBV Technologies. T. T. Perry has received research support from the National Institutes of Health.

Received for publication April 7, 2014; revised June 9, 2014; accepted for publication June 11, 2014.

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<http://dx.doi.org/10.1016/j.jaip.2014.06.008>

Abbreviations used

AD- Atopic dermatitis
 DBPCFC- Double-blind, placebo-controlled food challenge
 FA- Food allergy
 FALCPA- Food Allergy Labeling and Consumer Protection Act
 FPIES- Food protein–induced enterocolitis syndrome
 OFC- Oral food challenge
 PA- Peanut allergy
 SPT- Skin prick test

Key words: Food allergy; Anaphylaxis; Skin prick test; Oral food challenge; Label reading; Travel; Cross-contact; Autoinjectable epinephrine

IgE-mediated food allergies (FA) may be life-threatening,¹ negatively impact the quality of life for affected individuals and their families,²⁻⁵ and require coordinated efforts among affected individuals and their caregivers to minimize the risk of accidental ingestion. The most recent epidemiologic studies show that approximately 1 in 13 US children has an FA,⁶ which makes FA an important disease process to be recognized, properly diagnosed, and effectively managed. This review primarily focuses on diagnosis and management of IgE-mediated FAs, with practical advice regarding avoidance and care of individuals with FA.

CLINICAL SPECTRUM

Specific food-induced allergic conditions

IgE-mediated FA occurs by cross linking of IgE on mast cells and basophils by allergenic proteins, which leads to the release of histamine and other mediators, and is the mechanism that underlies immediate hypersensitivity. Symptoms of IgE-mediated FA disease include urticaria, angioedema, vomiting, diarrhea, bronchospasm, and multisystem allergy that can result in anaphylaxis. A mild form of allergic disease, pollen–food syndrome, also referred to as oral allergy syndrome, occurs due to IgE cross-reactivity to PR10 proteins in fruits and nuts in patients with pollen allergies (Table I).^{7,8} These foods usually are tolerated in cooked or processed forms, and anaphylaxis is rarely seen in this condition. In more recent years, delayed food-induced anaphylaxis to meats has been described,⁹⁻¹¹ which appears to be mediated via IgE specific for an oligosaccharide in red meat, galactose-alpha-1,3-galactose, and sensitization is associated with Lone Star tick exposure. The reason for the appearance of delayed symptoms is unclear.

A summary of the spectrum of food-induced allergic disease is provided in Table II. There are a number of non-IgE-mediated FA diseases. Perhaps with the exception of celiac disease, there is little mechanistic understanding of the pathologic processes that underpin such diseases. Food protein–induced enterocolitis syndrome (FPIES) specifically presents with acute recurrent vomiting and diarrhea that starts between 2 and 8 hours of ingestion of food, most commonly milk or soy.¹² Although patients with FPIES are not at risk of anaphylaxis, they are at risk of developing shock and acidosis due to dehydration. Other non-IgE-mediated diseases of the gastrointestinal tract are typically characterized by eosinophilic inflammation of different segments of the gastrointestinal tract. Eosinophilic esophagitis may appear

at any age, and symptoms vary by age of presentation. Younger children may present with failure to thrive and frequent vomiting; whereas older children and adults may have symptoms including food impaction, dysphagia, and heartburn. tends to in older children and adults, with symptoms of food impaction, dysphagia, and heartburn. Eosinophilic proctocolitis presents with blood and mucous in the stools of young infants who are often exclusively breast fed but exposed to cow's milk or soy proteins in maternal milk.

Mixed IgE FA diseases can occur, for example, in eosinophilic esophagitis or atopic dermatitis (AD), in which FA can be demonstrated by elimination and reintroduction diets, but IgE to the food may only be present a portion of the time. Some people refer to these conditions as IgE-associated conditions because it is unclear whether the IgE (when detected) plays a pathologic role. It may be that IgE is acting through antigen-presenting cells and driving facilitated antigen presentation to T cells, which drive Th2 responses and recruitment of eosinophils to the affected tissue. Frequently, eosinophilic gastrointestinal diseases may occur together with AD and that, indeed, individuals can be affected by both IgE-mediated FA and mixed or non-IgE allergic conditions.

EPIDEMIOLOGY

There are both study limitations and methodologic problems that influence our estimation of the incidence and prevalence of FAs. The majority of studies that document the prevalence of egg allergy, milk allergy, and peanut allergy (PA) occur in Western countries, and, to our knowledge, there are no published studies that examined FA at a global level. There is very little knowledge about FA in the developing world, although it seems to be reported far less frequently. There are methodologic differences that explain different results that have been obtained in different surveys. Whereas double-blind, placebo-controlled food challenges (DBPCFC) are the criterion standard, these are performed in few studies.¹³ Other surveys use FA questionnaires (generally unvalidated), skin prick test (SPT) responses, or IgE sensitization as markers of FA. However, neither correlates with FA, and it is remarkable that, in countries such as Ghana, for example, where the prevalence of PA is much lower, IgE positivity to peanut is extremely high compared with Western countries. This appears to be due to cross-reactive low-affinity antibodies to carbohydrate determinants.¹⁴

In the United States, FAs are thought to occur in approximately 6% to 8% of infants and preschool children. Egg and milk allergies are the most common FAs in most countries and cultures. However, a meta-analysis of 51 articles from different countries showed that the self-reported prevalence of allergy varied from 0.2% to 7% for egg and from 1.2% to 17% for milk.¹⁵ Allergy determined by challenges was estimated to be much lower, which ranged from 0% to 1.7% for egg, and 0% to 3% for milk. The prevalence and rise of PA has been greatest in Western countries. PA is much less common in certain countries, for example, Israel, where sesame seed allergy is more common.¹⁶ Mustard allergy is more commonly reported in France,¹⁷ whereas buckwheat and wheat allergies are most commonly reported in Japan. Generally, the most common allergens in childhood include egg, milk, peanut, tree nuts, wheat, soy, fish, shellfish, and sesame. Fish and shellfish allergies do occur in childhood but are more prevalent in adolescents and adults. If pollen–food syndrome is included, in which IgE to pollens such as birch cross

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