ICON: Food allergy

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Food allergies can result in life-threatening reactions and diminish quality of life. In the last several decades, the prevalence of food allergies has increased in several regions throughout the world. Although more than 170 foods have been identified as being potentially allergenic, a minority of these foods cause the majority of reactions, and common food allergens vary between geographic regions. Treatment of food allergy involves strict avoidance of the trigger food. Medications manage symptoms of disease, but currently, there is no cure for food allergy. In light of the increasing burden of allergic diseases, the American Academy of Allergy, Asthma & Immunology; European Academy of Allergy and Clinical Immunology; World Allergy Organization; and American College of Allergy, Asthma & Immunology have come together to increase the communication of information about allergies and asthma at a global level. Within the framework of this collaboration, termed the International Collaboration in Asthma, Allergy and Immunology, a series of consensus documents called International Consensus ON (ICON) are being developed to serve as an important resource and support physicians in managing different allergic diseases. An author group was formed to describe the natural history, prevalence, diagnosis, and treatment of food allergies in the context of the global community. (J Allergy Clin Immunol 2012;129:906-20.)

Key words: *Food allergy, global, consensus, diagnosis, treatment*

The International Collaboration in Asthma and Allergy initiated an international coalition among the American Academy of Allergy, Asthma & Immunology; European Academy of Allergy and Clinical Immunology; World Allergy Organization; and American College of Allergy, Asthma and Immunology on food allergy. An author group was formed and then divided into individual committees. Within the committee, teams of authors

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Abbreviations used
DBPCFC: Double-blind, placebo-controlled food challenge
NIAID: US National Institutes of Allergy and Infectious Diseases
PPV: Positive predictive value
sIgE: Food-specific IgE
SPT: Skin prick test

were created to generate content for specific sections of the article. Content was derived from literature searches, relevant published guidelines, and clinical experience. After a draft of the document was assembled, it was collectively reviewed and revised by the authors. Where evidence was lacking or conflicting, the information presented represents the consensus expert opinion of the group.

DEFINITION OF THE DISEASE AND EPIDEMIOLOGIC FEATURES

Food allergy

The term *food allergy* refers to an immune response directed toward food.[1] As defined in the 2010 US National Institutes of Allergy and Infectious Diseases (NIAID)–sponsored guidelines, food allergy is an "adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food."[2] This definition encompasses immune responses that are IgE mediated, non–IgE mediated, or a combination of both and is in agreement with other international guidelines.[3-5]

IgE-mediated reactions are characterized by an acute onset of symptoms generally within 2 hours after ingestion of or exposure to the trigger food. IgE-mediated reactions to foods typically involve the skin, gastrointestinal tract, and respiratory tract. Allergic sensitization occurs when food-specific IgE (sIgE) antibodies are produced by plasma cells that have differentiated from allergen-specific B lymphocytes. The sIgE antibodies bind to the surface of tissue mast cells and blood basophils, and on reexposure to the food, antigenic proteins in the food bind to and cross-link these cell surface–bound sIgE antibodies, which triggers the release of symptom-causing mediators, such as histamine and leukotrienes. Subjects can have allergic sensitization (production of sIgE) to food allergens without having clinical symptoms of an allergic reaction on exposure. Thus sensitization alone is not sufficient to define food allergy. An sIgE-mediated food allergy requires both the presence of sensitization and the development of specific signs and symptoms on exposure to that food.[2]

Non–IgE-mediated immunologic reactions (eg, cell mediated) include food protein–induced enterocolitis, proctocolitis, and enteropathy syndromes. These conditions primarily affect infants or young children who present with abdominal complaints, such as vomiting, abdominal cramps, diarrhea, and occasionally blood in the stool and failure to thrive or poor weight gain. Examples of food allergy comorbidities with mixed IgE- and non–IgE-mediated causes include eosinophilic esophagitis and atopic dermatitis.

Table I shows specific food-induced allergic conditions on the basis of pathophysiology. The table does not include symptoms or disorders that are not specific clinical syndromes associated with food allergy; thus infantile colic, constipation, and gastrointestinal reflux disease are not listed. Isolated chronic rhinitis and asthma are not commonly attributed to food allergy; however, occupational exposure can trigger asthma (eg, Baker's asthma from wheat) or contact dermatitis. Celiac disease (and dermatitis herpetiformis associated with celiac disease) is a cell-mediated response against an enzyme, tissue transglutaminase, that can be triggered by an immune response to a food protein, gluten. Because celiac disease is an autoimmune disorder with distinct symptoms and prognosis different than those of atopic disorders, it will not be discussed further in this document. There are numerous adverse responses to foods that do not involve an immune response and therefore are not considered the result of food allergies.[2] These include metabolic disorders, such as lactose and alcohol intolerance, responses to pharmacologically active food components (eg, caffeine), or illness in response to toxins from microbial contamination.[6] Certain psychological or neurological responses, such as food aversion or rhinorrhea caused by spicy foods, can also mimic food allergy but are not considered allergic disorders.

Food allergens

Food allergens, which are usually proteins but sometimes haptens, are recognized by allergen-specific immune cells and elicit specific immunologic reactions.[2] Most food allergens can cause reactions when ingested either in the raw form or after being cooked or even digested, but some allergens, such as those in fruits and vegetables, cause allergic reactions primarily if eaten raw. Food allergens can also cause reactions if the allergenic proteins are inhaled, although this should be differentiated from simply inhaling the fragrance of a food, which does not cause allergic reactions. Cross-reactivity can occur when a food allergen has structural or sequence similarity with a different food allergen or aeroallergen. The likelihood of having clinical allergic reactions to cross-reactive allergens is highly variable and depends on the type of food. For example, clinical cross-reactivity among legumes is generally uncommon (eg, most persons with peanut allergy tolerate beans and peas), whereas clinical cross-reactivity among different types of crustacean shellfish is common.

Although any food can trigger an allergic response and more than 170 foods have been reported to cause IgE-mediated reactions, a minority of foods cause the majority of allergic reactions, with most being attributed to the "major food allergens" peanut, tree nuts, egg, milk, fish, crustacean shellfish, wheat, and soy.[2] Celery, mustard, sesame, lupine, and molluscan shellfish have been identified as significant allergens in European countries, and in Japan buckwheat is also a common allergen.[7]

Protein-containing food additives and coloring agents, such as annatto, carmine, and gelatin, can induce allergic reactions. Chemical additives, such as artificial flavors (eg, tartrazine) and preservatives (eg, glutamates and sulfites), might cause adverse reactions, but an immune mechanism has not been identified, and such reactions are classified as intolerances.

Symptoms and severity

The likelihood of an allergic reaction is related to the level of sIgE. Symptoms of food allergy (Table II)[2] can occur within minutes to hours of ingesting the trigger food and can vary in severity from mild to life-threatening. Severity of allergic reactions varies based on the amount of food ingested, coingestion of other foods, and preparation of the food (cooked, raw, or processed).[2] Severity also can be influenced by the patient's age, as well as rapidity of absorption, which can be influenced by whether the food was eaten on an empty stomach or close to a time of exercise. The