

Approach to Patients with Symptoms of Food Allergy

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ABSTRACT

“Allergy” is a term often used by patients to describe symptoms that arise after eating. The term “adverse reaction to food” is preferred unless the event has an immunologic basis. True food allergy, primarily mediated by immunoglobulin (Ig)E antibodies to food proteins, is present in 3% to 4% of US adults. Symptoms range from mild mouth itching (“oral allergy syndrome”) to anaphylaxis. The diagnosis is established by history and appropriately performed skin testing or in vitro assays for specific IgE antibodies to the suspected food. Because food-allergic reactions can be fatal, it is important to identify and avoid the causative food. Food-allergic reactions are treated by prompt use of intramuscular epinephrine. Patients may be referred to an allergy/immunology specialist when the diagnosis is uncertain or if avoidance measures are not successful. Investigational therapies may ultimately be preventative or curative.

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Patients commonly present with symptoms of food allergy. An *adverse reaction to food* may be a better term (Table 1). Allergy describes the subset of adverse reactions to foods that have an immunologic basis. Food allergy affects 3% to 4% of adults.¹ Food intolerances are far more common (with the exception of lactase/other disaccharidase deficiencies) and often originate from as yet unknown factors.

Immunologic reactions to foods typically are IgE mediated but can involve cellular mechanisms, for example, celiac disease.¹ A number of foods have been identified as provoking allergic reactions, but relatively few are responsible for the majority of serious reactions: crustaceans (shrimp, crab, and lobster), fish, tree nuts (eg, pecan, walnuts), peanut, milk, and egg. In adults, shellfish, nuts, and peanuts are the most frequent culprits; milk and egg allergy are uncommon.^{2,3}

Anaphylaxis can occur on ingestion of foods contaminated with non-food allergens to which the individual is sensitized (eg, house dust or storage mites in flour) or cross-reactive allergens (eg, peanut-allergic patients eating lupine, flour products).

Food allergy may have a role in eosinophilic gastrointestinal disorders. The diagnosis is established by biopsies of the esophagus, stomach, or intestine. Evaluation of these patients may identify foods that should be avoided.⁴

PATHOPHYSIOLOGY

IgE-mediated food allergy results from a breakdown in intestinal immunologic tolerance to foods.^{1,2} Most food-allergic individuals have a family history of allergy and manifest other allergic conditions (allergic rhinitis, asthma). Children may have food allergies that persist into adulthood, whereas some with isolated milk or egg allergies lose sensitivity over time.^{1,2}

The food-allergic reactions occur when an allergen (often a protein or glycoprotein) is recognized by T-helper 2 lymphocytes that induce the formation of IgE antibodies produced by B cells and plasma cells. Circulating IgE binds to mast cells and basophils through the FcεR1 (high-affinity) IgE receptor. Reexposure to the allergen triggers histamine release and generation of other mediators that cause an immediate allergic response. Subsequent recruitment of eosinophils and basophils into tissues can produce a late-phase allergic response 4 to 6 hours after the initial exposure.¹

Biochemical mediator release leads to pruritus, urticaria and angioedema, gastrointestinal symptoms (vomiting, diar-

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Table 1 Some Conditions in Which Adverse Food Reactions Might Be Involved

IgE mediated	OAS (pollen-food), urticaria/angioedema, anaphylaxis, eosinophilic gastrointestinal disorders, EIA (specific, nonspecific food dependent)
Cellular mediated	Celiac disease, eosinophilic gastrointestinal disorders
Intolerances	Lactase/disaccharidase deficiency, nonspecific symptoms (gastrointestinal symptoms from a variety of foods)
Pharmacologic effects	Caffeine, alcohol (headaches)

EIA = exercise-induced anaphylaxis.

rhea), rhinitis, asthma, and, in the case of anaphylaxis, hypotension, cardiac arrhythmias, and laryngeal edema. Food-allergic reactions can range from a mild mouth and throat itching (“oral allergy syndrome” [OAS]) to anaphylaxis.¹⁻³

The OAS (ie, pollen-food syndrome) results from sensitization to plant pollen, for example, birch tree or ragweed, that immunologically cross-reacts with specific foods.² Proteins in the pollens cause seasonal allergic rhinitis and oral symptoms when the individual ingests related raw fruits and vegetables. In birch-pollen allergies, raw apples, carrots, cherries, and hazelnuts, among others, may produce these symptoms.^{2,3} The cross-reactive protein is a heat-labile member of the profilin protein family; patients with OAS can safely ingest cooked forms of the foods except hazelnut. In ragweed allergies, oral symptoms occur with eating melons, bananas, or cucumbers. Other syndromes have been described (Table 2). In rare instances, systemic anaphylaxis from the cross-reactive food allergen can occur.

A variant of food allergy is food-dependent, exercise-induced anaphylaxis (EIA).² Although EIA may occur independently of food, 2 types of food-dependent exercise anaphylaxis have been described: nonspecific and specific food related. In the first instance, the ingestion of *any* food in proximity to exercise provokes the symptoms. In the second, ingestion of a food to which the person has IgE sensitivity (eg, wheat, celery, and other foods) combined with exercise precipitates the reaction. In both instances, exercise alone or ingestion of food (nonspecific or to a food to which the patient has IgE antibodies) without exercise is tolerated.

Table 2 Examples of Oral Allergy Syndrome (Pollen-Food)

Pollen Sensitizer	Some Commonly Associated Foods
Birch (Betula)	Raw apple, raw carrot, raw cherry, hazelnuts (filberts)
Ragweed (Ambrosia)	Watermelon, cantaloupe, musk melon, cucumber, banana
Mugwort (Artemisia)	Celery, anise

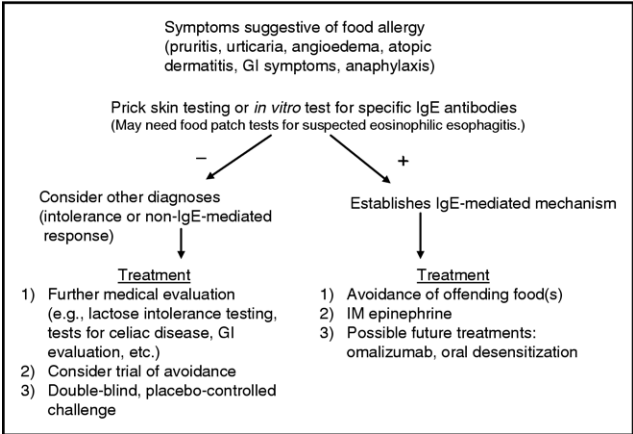


Figure Approach to diagnosis and treatment of food allergy in adults. Ig = Immunoglobulin; GI = gastrointestinal; IM = intramuscular.

Less commonly, cellular immune mechanisms are involved in adverse food reactions, for example, gluten-sensitive enteropathy (celiac disease).^{1,2} Patients with celiac disease may present with a variety of gastrointestinal symptoms and iron-deficiency anemia. They often have circulating IgA and IgG antibodies to tissue transglutaminase. If the diagnosis of celiac disease is suspected and serologic tests are not supportive, small-intestine biopsy may be necessary.^{1,2}

There is no convincing evidence that food allergies play a role in chronic diseases such as rheumatoid arthritis, fibromyalgia, or systemic lupus erythematosus.

DIAGNOSIS

The diagnosis of food allergy requires skillful history taking. Characteristics include onset of symptoms, within minutes, almost always within 2 hours of ingestion; reproducibility of the response with repeat ingestion; and provocation with minute amounts of the food. A “food diary” (a record of all ingestants with each reaction) is useful when the responsible food is initially unclear. The diagnosis is confirmed by either prick skin testing or demonstration of specific IgE antibody to the food by in vitro methods (eg, ImmunoCap, Pharmacia, Uppsala, Sweden).¹⁻³ Tests for food-specific IgG or IgG4 are not informative. Allergists will often ask the patient to bring in the suspected food for testing. Fresh foods (eg, raw apple or carrot) often are used for skin testing in cases of OAS because some unstable proteins may not be present in commercially available skin tests or in vitro reagents. Intradermal testing with food allergens is not recommended (frequent false-positive test results and risk of anaphylaxis). A plasma tryptase (a mast-cell constituent) level drawn within 3 to 4 hours of a suspected food-induced anaphylactic event can be helpful. Sometimes a double-blind, placebo-controlled oral food challenge may be necessary when the diagnosis cannot be established with certainty (Figure).¹⁻³

Table 3 Key Points

Most adverse food reactions in adults are due to intolerances versus immunologic (IgE or cellular-mediated) mechanisms. Food allergenic reactions can lead to serious, life-threatening events.

Diagnosis of food allergy is established by careful history and confirmed by prick-skin or in vitro testing for specific IgE antibodies.

Treatment consists of:

Avoidance

Prompt use of intramuscular epinephrine for reactions

Useful resources:

Food Allergy and Anaphylaxis Network:

<http://www.foodallergy.org/>

American Academy of Allergy, Asthma and Immunology:

<http://www.aaaai.org>

American College of Allergy, Asthma and Immunology:

<http://www.acaai.org>

Intramuscular epinephrine administration:

<http://www.epipen.com> and <http://www.twinject.com>

Ig = immunoglobulin.

Challenges should only be performed by experienced physicians with the capability to treat an anaphylaxis.

In eosinophilic gastrointestinal disorders (especially eosinophilic esophagitis), patch testing may be necessary to identify the offending food(s). In cases of suspected lactose intolerance, hydrogen breath tests can be performed.^{2,3}

Food additives have been reported to cause adverse reactions, ranging from the “monosodium glutamate syndrome” (numbness, chest tightness, flushing), sulfiting-agent-induced asthma, and anaphylaxis from organically derived food colorants (carmine, annatto). Diagnosis of additive reactions often requires a double-blind, placebo-controlled challenge because IgE might not play a role. Skin testing or in vitro tests may be positive to the proteins of organically derived dyes.⁴

TREATMENT

The treatment of food allergy is avoidance of the offending food.¹⁻³ Accidental exposure, especially when eating outside of the home, is not uncommon. When an individual experiences a food-allergic reaction, immediate self-administration of intramuscular epinephrine is imperative.⁵ Fatalities often arise when patients or physicians wait to determine the severity of the reaction and delay treatment.⁶ Minor symptoms (mild, generalized pruritus or urticaria) that initially appear responsive to antihistamines can precede severe anaphylaxis. The use of epinephrine, however, does not preclude the use of antihistamines, and they should be given. Corticosteroids can be administered, but they should not replace epinephrine for acute events.⁵ Individuals who experience OAS (scratchy throat, mouth itching) may benefit from antihistamines alone, but if respiratory

distress, urticaria, or other systemic symptoms occur, epinephrine should be given. Food-allergic patients should be educated about and provided with self-administered intramuscular epinephrine devices (EpiPen, Dey Pharmaceutical Company, Napa, Calif).¹⁻⁵ In more than one third of cases of anaphylaxis, a second dose of epinephrine might be required.⁷ Therefore, 2 doses of epinephrine should be provided to those who have had severe reactions (2-Pak, EpiPen, Dey Pharmaceuticals, or Twinject, Verus Pharmaceuticals, San Diego, Calif [see referenced websites for detailed administration]).

Nonspecific food-dependent EIA is managed by exercising in a fasting state or avoiding the food that contains the allergen (specific) for 4 to 6 hours before exercise.^{2,3}

Individuals who severely limit their diet should be evaluated by a specialist.⁴ A nutritionist can help individuals sensitive to widely distributed food allergens (eg, soy, wheat, milk, egg). In food-related eosinophilic gastrointestinal disorder, strict avoidance of the offending food or foods may reduce the need for corticosteroids or repeated esophageal dilations.

Subcutaneous immunotherapy is contraindicated because of risks of anaphylaxis. New modalities hold promise, for example, probiotics may prevent food allergies and oral “desensitization” and anti-IgE (omalizumab) can prevent or reduce reaction severity.¹⁻³

CONCLUSIONS

IgE-mediated food-allergic reactions are unusual in adults, but their recognition and treatment are important to avoid fatalities. Diagnosis of food allergy requires a careful history, physical examination, and confirmation by detecting food-specific IgE via in vitro assays or prick-skin testing. Avoiding the food is the treatment of choice. Food-allergic reactions need prompt treatment with intramuscular epinephrine because delays can be fatal. “Antihistamines treat hives, epinephrine saves lives!” (Table 3).

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