

Food Allergy

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Opinion statement

Although many emerging therapies demonstrate theoretical and practical promise, strict elimination of the allergenic food remains the only proven therapy for food hypersensitivity. Given such therapeutic limitations, accurate diagnosis and thorough patient education are critical for proper management. This is particularly important for individuals with anaphylactic potential, as food allergy is currently the single leading cause of anaphylaxis treated in hospital emergency departments [1,2].

Introduction

The potential allergenic components of foods are glycoproteins. More than 98% of ingested potentially antigenic food proteins are blocked by the gastrointestinal barrier. The minute quantities of immunologically recognizable protein that enter the circulation are met usually with tolerance; however, adverse reactions develop in some individuals. Although surveys in both children and adults show that approximately 25% of the population report a food allergy, the true prevalence is much less. Among infants and toddlers the prevalence approaches 8%; for adults, the true prevalence appears to be between 2% and 2.5% [3•]. Although any food can cause an allergic reaction, a few specific foods account for approximately 90% of reactions. In adults, these foods include peanut, tree nuts, fish, and shellfish. The most common allergenic foods in young children are milk, egg, fish, soy, peanut, and wheat [3•].

The diagnosis of food allergy often can be made by careful history alone. Classic symptoms of immunoglobulin E (IgE)-mediated disease occurring within minutes to a few hours of ingestion include itching or tingling of the lips, tongue, or throat. Sometimes these oral manifestations are self-limiting and are referred to as *oral allergy syndrome*, which often involves cross-reactions between foods (such as apples and melons) and certain pollens (such as birch and ragweed). More serious signs of food hypersensitivity may include swelling of the lips or tongue along with a sensation of throat tightness, hoarseness, or cough. The classic cutaneous manifestations are urticaria or angioedema. Gastrointestinal symptoms of nausea, abdominal cramping, vomiting, and diarrhea also can occur.

Pulmonary manifestations include chest tightness, wheezing, and even laryngeal edema. These more severe manifestations can involve progression to cardiovascular instability with hypotension and altered consciousness (systemic anaphylaxis). If the diagnosis is in question, skin-prick testing can be considered. Negative skin tests essentially rule out IgE-mediated disease. However, false positives are common. Thus, positive skin-prick tests require further evaluation with oral food challenge. The double-blind placebo controlled oral food challenge is considered the diagnostic gold standard.

After the diagnosis is established, strict elimination remains the only established therapeutic option. Detailed patient education regarding the prevalence of hidden food allergens is another key aspect of management. This is of critical importance to those with a prior history of anaphylaxis. Finally, patients thought to have anaphylactic potential should be provided self-injectable epinephrine and an antihistamine to carry in case of inadvertent allergen ingestion.

Non-IgE-mediated manifestations of food allergy are quite variable. Infants can present with symptoms ranging from eczema to projectile vomiting and hematochezia. In adults the nonspecific symptoms of bloating, abdominal cramping, or dyspepsia generally are unrelated to an immunologic process. Such symptoms more likely are related to food intolerance (abnormal physiologic response) or irritable bowel syndrome. Nevertheless, for a highly motivated patient an extensive elimination diet may prove helpful for diagnosis and management in a minority of

cases. If symptomatic improvement occurs, the foods thought least likely to provoke symptoms can be reintroduced sequentially.

Malabsorption syndromes such as celiac disease and allergic eosinophilic gastroenteritis are immunologically mediated. For celiac disease, a gluten-free diet

is the only effective treatment. Allergic eosinophilic gastroenteritis is a rare condition in which multiple immunologic mechanisms may play a role. A subset of patients may have multiple IgE food allergies. Treatment involves elimination of allergenic foods if present. Systemic steroids often are required.

Treatment

Diet and lifestyle

- Strict elimination of the allergenic food remains the only proven therapy for food hypersensitivity.
- Breast feeding children for at least 6 months (preferably for 1 year) has been shown to delay (but unfortunately not prevent) their chances of developing food allergy.
- Patients should learn to scrutinize food labels to recognize hidden food allergens. For example, egg protein may be contained in foods ranging from ice cream to mayonnaise. Common descriptions on food labels for substances containing milk protein include casein, caseinate, whey, or whey powder [4•].
- For children with a strong family history of allergy, avoidance of peanut for the first three years of life should be considered.
- Patients with a history of life-threatening anaphylaxis probably should avoid processed foods altogether.
- Patients should know that most severe reactions happen when eating away from home [5]. One of the most common reasons is contamination of a safe food. This can occur, for example, when the same serving or cooking utensils are used for several different food items in a restaurant setting.

Pharmacologic treatment

- Several medications including antihistamines, cromolyn, and oral corticosteroids have been used in an attempt to protect patients with food allergies. However, with the exception of oral corticosteroids for refractory cases of allergic eosinophilic gastroenteritis, no medication has proved acceptable [3•].
- Pharmacologic treatment generally is limited to treating symptoms after an inadvertent ingestion.
- Self-injectable epinephrine and antihistamines should be carried at all times by patients thought to be at high risk of anaphylaxis—those with a prior history of anaphylaxis, a prior reaction with respiratory features, and patients with asthma [7•].

Epinephrine for self-administration

Standard dosage EPIPEN Jr (Dey Labs, Napa, CA): For patients younger than 12, 0.15 mg (1:2000) intramuscularly with autoinjection device.
 EPIPEN (Dey Labs): For patients older than 12, 0.3 mg (1:1000) intramuscularly with autoinjection device.
 Ana-kit (Bayer Allergy, West Haven, CT) or Ana-guard (Bayer Allergy):
 Younger than 2 years: 0.05 to 0.1 mL (1:1000) intramuscularly.
 Between 2 and 6 years: 0.15 mL (1:1000) intramuscularly.
 Between 6 and 12 years: 0.2 mL (1:1000) intramuscularly.
 Adult: 0.3 mL (1:1000) subcutaneously or intramuscularly.

Contraindications	Cardiovascular disease, hypertension, hyperthyroidism, narrow angle glaucoma, and diabetes.
Main drug interactions	Pressor effects potentiated by monoamine oxidase inhibitors, tricyclics, furozolidone, antihistamines, levothyroxine, beta-blockers, and guanethidine. May be antagonized by nitrites, alpha-blockers, other vasodilators. Arrhythmias possible with digitalis, mercurial diuretics, quinidine.
Main side effects	Tachycardia, diaphoresis, tremor, dizziness, weakness, headache, and anxiety.
Special points	Most prefer EPIPEN and EPIPEN Jr because of ease of administration of the auto-injection system.
Cost/cost-effectiveness	Inexpensive, given limited use.

Antihistamines

Standard dosage	Per the instructions of the many over-the-counter preparations available.
Contraindications	Glaucoma, prostatism, cardiovascular disease.
Main drug interactions	Potentiates central nervous system depression with alcohol and other central nervous system depressants.
Main side effects	Drowsiness and anticholinergic effects.
Special points	Used to treat symptoms after inadvertent ingestion, not as a treatment to prevent symptoms.
Cost/cost-effectiveness	Over-the-counter preparations are inexpensive. Newer nonsedating prescription antihistamines are significantly more expensive.

Emerging therapies

- Preliminary data suggest that standard allergy shots may prove effective in patients with peanut allergy. However, reactions to the injections are frequent [8].
- Anti-IgE antibody therapy given as injections of recombinant humanized monoclonal antibody against human IgE has reached clinical trials [9,10]. The antibody binds to circulating IgE forming complexes that are then cleared from the body mainly via the reticuloendothelial system. After several months of therapy, circulating IgE levels decrease dramatically. Tissue mast cells also lose bound IgE and tend to lose their IgE receptors. Thus, patients should become nonreactive to IgE-mediated processes. Except for transient urticaria in a minority of patients (mainly after the first antibody infusion), no significant adverse effects have been noted. In order to maintain depressed IgE levels the injections appear to be required indefinitely [7•,9,10].
- Immunostimulatory DNA sequences (CpG motifs) given as injections are entering human trials. In animal studies these DNA sequences appear to suppress IgE-mediated reactions [11].
- An oral DNA vaccine containing the main peanut allergen protects against anaphylaxis in a mice model of peanut allergy [12].
- Finally, the prospect of combining anti-IgE antibody therapy with more traditional immunotherapy seems promising in our opinion. The protective effects of concurrent anti-IgE therapy may allow more aggressive, effective, and safer desensitization with allergen-specific immunotherapy. This strategy may also prove efficacious using the previously mentioned immunostimulatory DNA sequences.

References and Recommended Reading

Recently published papers of particular interest have been highlighted as:

- Of importance
- Of major importance

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