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Food-induced Anaphylaxis and Oral Allergy Syndrome

Priyamvada Tatachar, MBBS,* Smita Kumar, MD†

Author Disclosure
Drs Tatachar and Kumar did not disclose any financial relationships relevant to this article.

Objectives After completing this article, readers should be able to:

1. Recognize symptoms of food-induced allergy in general and oral allergy syndrome and anaphylaxis in particular.
2. Know when to refer those who have these problems to an allergist.
3. Discuss how to educate parents about food allergy.

Case Report
A 16-year-old boy presents to the allergy clinic with complaints of perioral itching and tingling after handling apples at his father’s fruit stall. He had experienced such symptoms on previous occasions, but this time he has developed mild lip swelling and tongue itching, as well. He has a history of seasonal allergic rhinitis that is controlled by nasal steroid spray. His father is concerned that the reaction might be due to pesticides. A skin prick test with fresh apples gives a positive response that confirms the clinical diagnosis of oral allergy syndrome (OAS).

Definition and Prevalence
Food allergies are an increasingly common problem faced by pediatricians. Food allergy is defined as an immune-mediated adverse reaction to foods causing symptoms affecting the skin, gastrointestinal (GI) tract, or respiratory system. The reactions can be immune globulin E (IgE)-mediated and non-IgE-mediated processes.

Currently, food allergies affect 2% of the general population and 6% to 8% of children. They are most prevalent in the first few postnatal years. Although many children outgrow their food allergies by adulthood, most allergies to peanuts, tree nuts, and seafood are not outgrown. About 35% of children who have moderate-to-severe atopic dermatitis have IgE-mediated food allergies, and about 6% of children who have asthma have food-induced wheezing. The most common food allergens in the pediatric population include cow milk, eggs, peanuts, tree nuts, soy, and wheat; peanuts, tree nuts, fish, and shellfish are implicated most commonly in adults.

Pathophysiology
The human GI tract presents many barriers to ingested immunogenic food proteins. Mucosal-associated secretory IgA, gut-associated lymphoid tissue, gastric acidity, and pancreatic proteases are the primary defense mechanisms. Immaturity of all these mechanisms renders infants susceptible to developing food allergies. In adults, 2% of the ingested food allergens are absorbed and transported throughout the body in an immunologically intact form but do not cause symptoms because of the development of oral tolerance. Oral tolerance is believed to be due to T-cell anergy or induction of regulatory T cells.

Antigen-presenting cells (especially intestinal epithelial cells), dendritic cells residing within the lamina propria, Peyer patches, and the regulatory T cells play important roles in the development of tolerance. Five regulatory T cells have been identified. These cells are potent sources of transforming growth factor-beta, which is generated in response to low-dose antigen. Properties of the antigen, dose, and frequency of exposure influence the induction of tolerance. Deletion of effector T cells is seen in high-dose tolerance, whereas low-dose tolerance is mediated by activation of regulatory T cells with suppressor function.

*Resident, Department of Pediatrics.
†Clinical Assistant Professor of Pediatrics, Division of Allergy and Immunology, Kings County Hospital Center and SUNY Downstate Medical Center, Brooklyn, NY.
When immune tolerance fails, sensitization to ingested food occurs, leading to generation of allergic IgE antibodies that facilitate immediate-type reactions such as food-induced anaphylaxis, urticaria, angioedema, bronchospasm, and GI symptoms such as diarrhea and vomiting. In other cases, allergic sensitization affects T lymphocytes primarily without generating an IgE antibody. These situations represent the non-IgE-mediated reactions, such as food-induced proctocolitis syndrome. Many disorders, including atopic dermatitis and eosinophilic gastroenteritis, have mixed mechanisms, with both IgE- and T cell-mediated responses.

Food allergies have been grouped conventionally as class I or class II, depending on the properties of the inciting proteins. Sensitization to food allergens occurs via the GI tract in class I allergy. These proteins are water-soluble and resistant to heat, acid, and proteases. The proteins implicated commonly in this class are milk, egg, seafood, wheat, soy, peanut, and tree nuts. Proteins responsible for class II allergy are plant-derived, heat-labile, and difficult to isolate. These allergens include profilins, pathogenesis-related proteins (PrP), lipid transfer proteins, peroxidases, and protease inhibitors common to many plants. Sensitization is via the respiratory tract.

Clinical Features of Food Allergy
IgE-mediated food allergy starts within minutes to 1 hour (rarely more than 2 h) after contact with the allergen. Cutaneous reactions include flushing, urticaria, angioedema, rash, and pruritus. Among the respiratory symptoms are sneezing, rhinorrhea, chest tightness, cough, hoarseness, wheezing, and difficulty breathing. GI symptoms include nausea, vomiting, diarrhea, and abdominal pain.

Food-induced anaphylaxis represents the most severe form of IgE-mediated food allergy and is defined clinically as a food-allergic reaction involving two or more organ systems. Symptoms include coughing, wheezing, chest tightness, sense of impending doom, and cutaneous reactions within minutes of contact with an allergen. Anaphylaxis may be life-threatening, and the major risk factors for severe illness are a history of peanut allergy, asthma of any severity, and delay in epinephrine administration. In about 25% of cases, there is a biphasic course, with initial onset of symptoms followed by improvement and subsequent recurrence 1 to 2 hours later, which is the late-phase reaction. Therefore, an observation period of at least 4 hours following an allergic reaction is recommended. Table 1 summarizes the characteristics of food-induced anaphylaxis.

Non-IgE-mediated disorders include food-induced pulmonary hemosiderosis (Heiner syndrome) and celiac disease/dermatitis herpetiformis. Mixed reactions comprising both IgE and non-IgE mechanisms are involved in atopic dermatitis and allergic eosinophilic gastroenteritis/esophagitis.

Oral Allergy Syndrome
OAS is an IgE-mediated allergic manifestation affecting the oropharynx, also known as pollen-food allergy syndrome. Most patients experience mild symptoms such as tingling around the mouth after eating or handling fresh fruits or vegetables (Table 2).

OAS affects approximately 50% of adults who have allergic rhinitis to inhalant pollens and is the most common adult food allergy. The symptoms are believed to be due to cross-reactivity between proteins present in pollens and those expressed by fruits and vegetables designated as PrP.

The different fruits and vegetables that are implicated in OAS are grouped as those cross-reacting with the birch family (apples, plums, peaches, nectarines, cherries, and almonds), with the ragweed family (melons, bananas, and tomatoes), with the grass family (melons and kiwi fruit), and with the mugwort family (celery, spices, and carrots).

Symptoms
Most patients who have OAS and allergic rhinitis develop tingling and itching of the lips, palate, and tongue on contact with the offending fruit or vegetable. Some patients experience abdominal discomfort, nausea, and vomiting. No symptoms are reported when the offending agent is consumed in cooked or processed forms.

Table 1. Characteristics of Food-induced Anaphylaxis

1. An estimated 30,000 emergency department visits and 200 deaths per year in the United States are due to food anaphylaxis.
2. IgE-mediated massive release of mediators affects two or more target organs.
3. Symptoms include flushing, pruritus, generalized urticaria, angioedema, vomiting, cramping, abdominal pain, cough, wheezing, chest tightness, hypotension, shock, and collapse.
4. Recurrence can occur within 2 to 4 hours and rarely may persist for a few days.
5. Risk factors are asthma, peanut/tree nut allergy, and delayed or no treatment with epinephrine.
Some patients who demonstrate IgE antibodies to fruits and vegetables also are allergic to natural rubber latex (latex-fruit cross-reactivity), wherein latex cross-reacts with avocado, banana, chestnut, fig, and kiwi.

Although the symptoms of OAS are mild, a small subset of affected patients experience systemic symptoms. The risk factors for progression to anaphylaxis are unclear but may be related to the heat-stable and protease-resistant lipid transfer proteins and storage proteins found in specific fruits and vegetables.

**Pathogenesis**

PrP comprise a large number of class II allergenic proteins found in various vegetables and fruits. These proteins are induced when pathogens or certain environmental stresses, such as drought or heat, stress the plant. PrP account for most of the cross-reactivity and symptoms of OAS. Profilin is an actin-binding protein that was identified initially in birch pollen and now is recognized as an allergenic protein in a number of fruits and vegetables. Profilins are responsible for the celery-mugwort-spice syndrome and are responsible for OAS to apple, pear, carrot, celery, and potato in patients who are allergic to birch pollen.

**Diagnosis of Food Allergy**

By far the most important element in diagnosing food allergy is the history. The following information should be obtained when interviewing the patient and family:

- Foods responsible for the reaction, quantity of the suspected food ingested, and the length of time between the ingestion and onset of symptoms
- Any history of similar symptoms when such food was ingested previously
- Other associated factors such as a history of symptoms with exercise after ingestion of certain foods
- Personal history of asthma, eczema, or allergic rhinitis

It is useful for patients to keep food diaries because important clues may become available from record keeping.

**Skin Prick Tests**

For IgE-mediated disorders, skin prick tests are used to screen patients for specific foods. A wheal of at least 3 mm or greater than that of the negative control is considered to be positive, indicating that the patient has symptomatic reactivity to the specific food (positive predictive value <50%). However, negative test results can confirm the absence of IgE-mediated reactions (negative predictive value >95%). For children younger than 2 years of age, skin prick tests to milk, egg, or peanuts that have wheal diameters of at least 8 mm are almost 95% predictive of clinical reactivity.

**Radioallergosorbtent Tests**

Radioallergosorbtent testing assays are used to identify food-specific IgE antibodies. Food-specific IgE concen-
Concentrations exceeding diagnostic values indicate that the patient is more than 95% likely to have an allergic reaction if he or she ingests the specific food. Undetectable concentrations (\(<0.35\) KIU/L) indicate that the child is unlikely to have that food allergy.

**Oral Food Challenge and Double-blind, Placebo-controlled Food Challenge**

An oral food challenge test is the most accurate method of diagnosing food allergy. The test can be open (both patient and test administrator know the food being administered) or a double-blind, placebo-controlled food challenge (DBPCFC).

DBPCFC is considered the gold standard for diagnosing food allergies. Small increments of lyophilized powder containing the offending food are given orally to the patient along with a placebo. This procedure usually is conducted in a controlled setting such as a hospital or intensive care unit. The test is stopped at the first sign of an allergic reaction.

**Therapy for Food Allergy: General Principles**

The following steps can be helpful in managing food allergy:

- Educate parents to recognize early symptoms and initiate avoidance and treatment
- Educate parents to carry self-injectable epinephrine at all times for children who have experienced systemic reactions
- Antihistamines relieve some symptoms of OAS and IgE-mediated skin reactions
- The American Academy of Pediatrics recommends that infants at high risk for atopy be breastfed exclusively and that introduction of solid foods be delayed until 6 months of age. Introduction of dairy products should be delayed until 1 year of age; eggs until 2 years of age; and peanuts, nuts, and fish until 3 years of age. Lactating mothers should avoid peanuts, other nuts, and high-risk allergens in their diets.

**Management of Generalized Anaphylaxis**

The airway, breathing, and circulation should be evaluated promptly. Airway patency, oxygen saturation, and the presence of stridor or wheezing should be assessed and 100% supplemental oxygen administered. Endotracheal intubation may be necessary if respiratory signs and symptoms worsen progressively. Volume status should be assessed and intravenous saline boluses administered if the patient exhibits hypotension.

Specific therapy involves administration of epinephrine 0.01 mL/kg of a 1:1,000 solution (maximum of 0.5 mg) intramuscularly, subcutaneously, intravenously, or via endotracheal tube. Some clinicians recommend adding a histamine blocker (diphenhydramine) and a histamine2 blocker (ranitidine), although antihistamines are believed to be more effective for cutaneous symptoms than for cardiovascular or respiratory dysfunction. Bronchospasm should be treated with nebulized beta-2 agonists. Steroids administered either orally or parenterally may blunt the late-phase response of an allergic reaction. Patients should be observed in the emergency department for 6 to 8 hours for possible late-phase reactions after an anaphylactic attack.

**Management of OAS**

OAS should be managed with the following procedures:
- Obtain a detailed history with specific questions relating to exposure to raw fruits or vegetables prior to the development of symptoms.
- Perform skin prick tests with the offending fruit or vegetable (fresh, raw fruits) to diagnose OAS. Oral food challenges are undertaken in controlled settings, and diagnosis is confirmed if symptoms occur with raw foods and are absent when the same food is consumed after cooking or processing. For patients who have allergic rhinitis, skin testing to inhalant pollens or measurement of serum IgE concentrations to specific pollens can be performed.
- Educate parents and patients about the allergies and avoidance of inciting agents to prevent symptoms.
- Modify the food (washing and peeling, cooking, microwaving and baking) to alter the immunogenic properties of the antigens and make the food more tolerable.
- In the event of an allergic reaction, stop food consumption and administer antihistamines to control the reactions.
- Instruct the patient who has OAS and a history of systemic signs and symptoms to carry self-injectable epinephrine at all times.
- According to the latest research, immunotherapy against pollen allergens has shown benefits in the treatment of OAS.

**Summary**

- Food allergy can produce reactions ranging from itching of the mouth to anaphylactic shock.
- Allergic reactions to food can be IgE-mediated, nonIgE-mediated, or mixed.
- Food-induced anaphylaxis can be life-threatening and
requires immediate therapy and sustained observation because a late-phase reaction can occur 1 to 2 hours after the first episode.

- OAS is characterized by perioral and oropharyngeal symptoms after contact with fresh fruits or vegetables that usually are mild but can be generalized or severe. Many patients who have OAS also have allergic rhinitis.
- Referral to an allergist is indicated to undertake testing and better delineate foods to be avoided to minimize allergic reactions and prevent unnecessary limitation of foods.
- Allergists can provide immunotherapy.
- Education of parents is critical for children who have food allergy.

**Suggested Reading**


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