



## Approach to Diagnosis and Management of Food Allergies in the Primary Care Setting

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**F**ood allergy is associated with a substantial burden of disease for both patients and families, not only due to the morbidity and potential mortality from anaphylaxis, but also from psychosocial and financial implications of food allergen avoidance.

### What is food allergy?

Food allergy is an adverse reaction to a food that is mediated by the immune system, specifically by IgE antibodies. The immune response is food specific and occurs reproducibly with ingestion. This is in contrast to other adverse food reactions

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Importantly, food allergy testing is fraught with pitfalls, so it is critical that children be tested for food allergies only when appropriate. A “positive” test result only indicates sensitization and is not always associated with a true clinical allergy. Sensitization means that the immune system has generated IgE antibodies against the antigen, which can be detected by blood or skin prick testing. In particular, positive serum specific IgE is commonly observed in children with atopic dermatitis or other atopic conditions with no clinical history to suggest food allergy.

that are not immune mediated, such as intolerance (e.g., lactose intolerance) or other ill effects (e.g., reflux).

In general, self-reported food allergy will overestimate its actual prevalence, as nonimmune-mediated adverse food reactions are often mistaken for allergy. In the U.S., rates of convincing clinical food allergy are estimated to be 7.6%.<sup>1</sup>

### Non-IgE-mediated adverse reactions to food

When evaluating symptoms associated with ingestion of a particular food, it is important to keep non-IgE-mediated diagnoses in the differential diagnosis, including food protein-induced enterocolitis syndrome (FPIES); food protein-induced allergic proctocolitis (FPIAP); oral allergy syndrome (also known as pollen-food allergy syndrome); eosinophilic esophagitis (EoE); and irritant contact dermatitis. The chart on pages 5-6 has additional information on the pathogenesis, onset, clinical manifestations, management, and prognosis of each of these diagnoses.

### Food allergy testing

The gold standard test for diagnosis of food allergy is an ingestion challenge. If a patient can tolerate ingestion of a given food, they are by definition not allergic. Food allergy testing by skin prick or serum specific IgE assays are complementary modalities to detect food sensitization in patients with clinical suspicion of food allergy. Food allergy testing should be considered confirmatory of the clinical history, rather than a screening test.

In the absence of a convincing clinical history of signs or symptoms of anaphylaxis (see chart) within minutes to two hours of ingestion of a specific food, food allergy testing has a very high false positive rate (sensitization without clinical allergy) and has the potential for harm. False results may compel patients to unnecessarily avoid a wide array of foods, possibly compromising nutrition and quality of life. In addition, in young children, unnecessary avoidance of common food allergens can increase the risk of developing an IgE-mediated food allergy, particularly in those with atopic dermatitis. For these reasons, the American Academy of Pediatrics



and the American Academy of Allergy, Asthma, and Immunology strongly recommend against screening for a variety of food allergens with food panels (serum specific IgE to a wide array of foods).

### Food allergies and eczema

Atopic dermatitis, or eczema, is a chronic skin condition that typically has a waxing and waning course. In the past, it was thought that environmental or food allergens may be involved in the pathogenesis of the disease. However, we now know that allergy to foods or environmental allergens is not the underlying cause of eczema and does not direct medical management. Young children with eczema have an approximately 35% risk of developing IgE-mediated food allergies<sup>1</sup>, compared to 7.6% for the general population. Nonetheless, food allergy testing for patients with eczema should only be performed if there is a history of signs or symptoms of anaphylaxis associated with ingestion of a particular food.

There are two notable exceptions for which food allergy testing is performed in a patient *without* a clinical history of allergic reaction<sup>2,3</sup>:

1. Infants with *severe* atopic dermatitis in early infancy that is *poorly controlled* despite optimized management should be referred to an allergist/immunologist for screening for peanut allergy prior to early introduction of peanut at home. Infants with severe, refractory eczema are frequently sensitized to peanut prior to any known ingestion. Screening for food allergens other than peanut is not recommended.
2. Infants with a clinical history and positive diagnostic testing for egg allergy should be screened for peanut allergy prior to early introduction at home. Again, routine screening for egg allergy without a convincing clinical history of a reaction to eggs is not recommended.

Outside of these two very limited groups, food allergy testing is not recommended as a screening measure to determine risk of food allergy. If a patient in either of those two exception groups is already ingesting and tolerating peanut, testing is not indicated.



### When to refer for food allergy?

For patients with a clinical history of signs or symptoms of anaphylaxis with ingestion of a specific food, referral to an allergy/immunology specialist is recommended. When comparing skin prick versus serum specific IgE testing to foods, skin prick testing is more sensitive, has a high negative predictive value, and may be the preferred test. There is no minimum age for skin prick testing. While awaiting an allergy/immunology appointment, at which clinically relevant specific food allergy testing may be performed, prescribe epinephrine auto-injector pens and counsel the patient to strictly avoid the suspected food allergen. Additional food allergy educational resources can be found at [www.foodallergy.org](http://www.foodallergy.org).

### Early introduction to peanut

We recommend that common food allergens be introduced early in infancy to potentially prevent IgE-mediated food allergy. The most convincing data for this comes from the Learning Early About Peanut (LEAP) trial<sup>3,4</sup>, which showed that early introduction of peanut significantly decreased incidence of peanut allergy in high-risk infants. Other studies have suggested similar benefit with milk, egg, and tree nuts<sup>5,6</sup>. Once introduced, the goal is to ingest each food frequently, approximately two to three times per week if possible, in order to maintain tolerance, or prevent development of food allergy.

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### Knowledge check

1. A 3-year-old boy presents with concern for food allergies. He has never experienced symptoms of anaphylaxis, but has an older brother with peanut allergy, and his mother would like him to be screened to see if he is allergic to any foods. What is your recommendation?

- a) Skin prick and/or serum IgE testing to peanut
- b) Serum IgE testing to the most common food allergens due to family history
- c) No further testing

*Answer C:* The boy does not have a history consistent with anaphylaxis after ingestion of any food, so testing would not be indicated. Performing this testing inappropriately may result in false positive results.

2. An 11-month-old girl presents with concern for food allergies. On two separate occasions, she developed generalized hives, lip swelling, and wheezing 30 minutes after ingestion of peanut butter. The second episode required emergency room evaluation where she received IM epinephrine. Her parents were counseled to avoid peanuts and are now seeking additional food allergy screening to determine if she is at risk for future reactions. What is your recommendation?

- a) Skin prick and/or serum IgE testing to peanut
- b) Skin prick and/or serum IgE testing to the most common food allergens
- c) No further testing

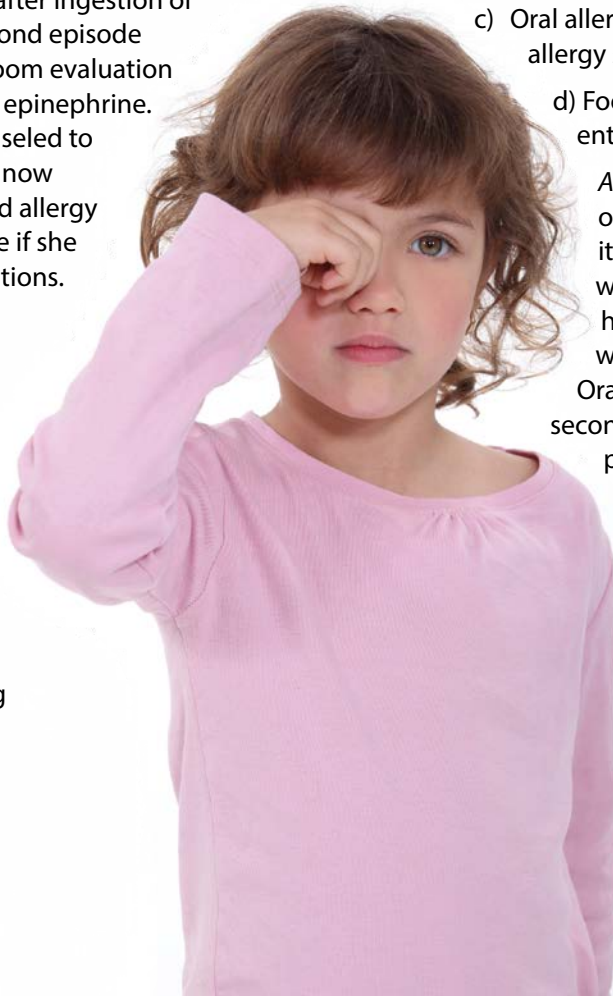
*Answer A:* The girl has a history consistent with anaphylaxis shortly after ingestion of peanut. Referral to an allergy/immunology specialist for skin prick and/or serum specific IgE testing to peanut is indicated. However, screening for allergies to other foods for which there is no clinical history consistent with anaphylaxis is not recommended.

3. A 9-year-old girl presents with concerns for food allergy. She has a history of nasal congestion, rhinorrhea, and itchy eyes during the spring and fall seasons. For the past six months she complains of oral itching, tingling, and slight swelling of the lower lip with ingestion of raw banana, but continues to ingest banana on a regular basis. She does tolerate banana bread. She denies rash, trouble breathing, tongue swelling, or GI symptoms associated with ingestion. Which of the following is the most likely diagnosis?

- a) IgE-mediated allergy to banana
- b) Irritant dermatitis
- c) Oral allergy syndrome/pollen-food allergy syndrome
- d) Food protein-induced enterocolitis syndrome

*Answer C:* The patient has symptoms of oral allergy syndrome, namely oral itching, tingling, and slight lip swelling with ingestion of banana, along with a history suspicious for allergic rhinitis with sensitization to seasonal pollens. Oral allergy syndrome is thought to be secondary to cross-sensitization between pollens and food allergens. This most commonly occurs with raw fruits and vegetables. This condition typically presents in older childhood and is not described in infancy.

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# FOOD ALLERGY CHART

	Food Allergy	Food Protein-Induced Enterocolitis Syndrome	Food Protein-Induced Allergic Proctocolitis	Oral Allergy Syndrome (Pollen-Food Allergy Syndrome)	Eosinophilic Esophagitis	Irritant Contact Dermatitis
<b>Pathogenesis</b>	IgE-mediated (anaphylaxis).	Non-IgE-mediated (likely T cell-mediated hypersensitivity).	Non-IgE-mediated.	IgE-mediated. Older children and adults with sensitization to specific pollens that cross-react with specific foods.	Unclear-immune mediated. Chronic inflammatory disorder characterized by eosinophilic inflammation of the esophagus.	Non-IgE-mediated. Keratinocytes (skin cells) release proinflammatory cytokines in response to a chemical irritant.
<b>Age of Onset</b>	Infancy through adulthood (infancy and early childhood most common).	Infancy through early childhood.	1 week to ~3 months of age.	Older childhood through adulthood.	Infancy through adulthood.	Any age.
<b>Clinical Manifestations</b>	≥ 1 of the following signs/symptoms of anaphylaxis: urticaria, angioedema, flushing, stridor, shortness of breath, cough, wheezing, abdominal pain, vomiting, diarrhea, syncope, dizziness, hypotension, irritability, sudden behavioral changes.	Acute: Vomiting, decreased activity level, pallor; if severe: dehydration, hypotension, leukocytosis, thrombocytosis, metabolic acidosis, and methemoglobinemia.  Chronic: Occurs with daily ingestion of food, can see intermittent emesis, chronic diarrhea, poor weight gain, or failure to thrive (FTT).	Visible specks or streaks of blood mixed with mucous in the stool.  Must have lack of the following: vomiting, diarrhea, and poor growth.	Pruritus, tingling, mild erythema, and subtle angioedema of the lips and oropharynx; sometimes accompanied by a sensation of mild throat swelling.	Infancy: Feeding dysfunction (reflux, vomiting, pain, or FTT).  Early childhood through adulthood: Dysphagia, pain, food impaction and +/- symptomatic with ingestion of specific foods.	Macular erythema (or blotchy, red appearance of skin).  Can be associated with pruritus and swelling.

# FOOD ALLERGY CHART

	Food Allergy	Food Protein-Induced Enterocolitis Syndrome	Food Protein-Induced Allergic Proctocolitis	Oral Allergy Syndrome (Pollen-Food Allergy Syndrome)	Eosinophilic Esophagitis	Irritant Contact Dermatitis
<b>Most Common Food Triggers</b>	Peanut (2.2%), cow's milk (1.9%), shellfish (1.3%), tree nut (1.2%), egg (0.9%), fish (0.6%), soy (0.5%), wheat (0.5%), and sesame (0.2%).	Rice, oats, barley, wheat, vegetables, fruit, cow's milk, soy, eggs, fish, shellfish, meat (i.e., chicken, turkey, lamb).	Cow's milk (76%), egg (16%), soy (6%), and corn (2%).	Raw fruits and vegetables; rarely soy, peanut, hazelnut.	Most common IgE-mediated food allergens, cow's milk is the most common trigger.	Acidic foods most common: berries, pineapple, orange, tomato, sauces (e.g., marinara, ketchup, ranch dressing, etc.).
<b>Medical Management</b>	Epinephrine Auto-injector Pens (IM- 1:1000 dilution): <ul style="list-style-type: none"> <li>0.01 mg/kg IM for infants &lt; 15 kg.</li> <li>0.15 mg IM for patients 15-30 kg.</li> <li>0.30 mg IM for patients ≥30 kg.</li> </ul> <ul style="list-style-type: none"> <li>Strict avoidance of suspected food trigger(s).</li> <li>Must seek immediate medical attention.</li> </ul>	<ul style="list-style-type: none"> <li>IV fluids.</li> <li>IV methylprednisolone.</li> <li>Use IV ondansetron.</li> <li>If not tolerating oral hydration, seek medical attention immediately.</li> </ul>	Avoidance of triggering food.	<p>May avoid triggering foods.</p> <p>Cook the foods (fruits and vegetables) that cause symptoms.</p>	<ul style="list-style-type: none"> <li>Elimination diet.</li> <li>Protein pump inhibitors.</li> <li>Oral corticosteroids.</li> </ul> <p>For food impaction, seek immediate medical attention.</p>	Benign, spontaneously resolves. Can apply topical barrier (e.g., petroleum jelly) to lips and face to avoid contact as possible.
<b>Prognosis</b>	Percent outgrown in childhood: Egg (~79%), milk (~79%), wheat (~65%), soy (~69%), peanut (~20%), tree nuts (~10%), sesame (~10-20%), fish (~10%), and shellfish (~10%).	Typically resolves in early or older childhood. <ul style="list-style-type: none"> <li>May consider challenge visit for reintroduction 18-24 months after last reaction.</li> </ul>	Resolution during infancy – 50% outgrown by 6 months of age, 90% by 9 months of age, ~100% by 12 months of age.	Persistent. Low risk of systemic reaction.	Persistent.	Resolves in early childhood.





4. A 6-month-old infant presents for evaluation after presenting to the emergency room with vomiting and dehydration that started three hours after ingesting rice cereal at home. There is no rash, swelling, or shortness of breath. The infant appears pale and lethargic. The child is treated with IV fluids, ondansetron, and systemic corticosteroids and monitored for several hours with improvement and is discharged home. Which of the following is the most likely diagnosis?
- a) IgE-mediated allergy to rice
  - b) Food protein-induced enterocolitis syndrome
  - c) Food protein-induced allergic proctocolitis
  - d) Food poisoning

**Answer B:** The child presents with signs and symptoms of FPIES with onset of vomiting and dehydration 30 minutes to four hours after ingesting rice cereal. Cow's milk, soy, rice, oats, and certain fruits and vegetables are common triggers of FPIES (see chart). Treatment is supportive with fluid resuscitation, ondansetron, and systemic corticosteroids. FPIES may resolve after 18-24 months of strict avoidance of the offending food. Referral to an allergy/immunology specialist is warranted for further evaluation and consideration for an oral ingestion challenge after 18-24 months have passed.

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### Additional Resources

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