Goals & Objectives:
• Know the common presenting signs of and foods associated with food allergies in children.
• Know how to distinguish anaphylaxis from oral-allergy syndrome.
• Demonstrate proper administration of an EpiPen.
• Know the indications for food allergy testing and how it is performed.

Pre-Meeting Preparation:
Please read the following enclosures:
• “Clinical Management of Food Allergy” (Pediatric Clinics of North America, 2015)
• “Preventing Peanut Allergy Through Early Consumption: Ready for Prime Time?” (NEJM, 2015)

Conference Agenda:
• Group Exercise: Practice giving epinephrine using an EpiPen Tester
• Review Food Allergies Quiz
• Complete Food Allergies Discussion Questions & Cases

Post-Conference: Board Review Q&A

Extra-Credit:
• The Learning Early About Peanut Allergy Study: The Benefits of Early Peanut Introduction, and a New Horizon in Fighting the Food Allergy Epidemic, (Pediatric Clinics of North America, 2015)
• Diagnosis of Food Allergy (Pediatric Clinics of North America, 2015)
• AAP Section on Allergy & Immunology—provider & parent resources
• Resources for Patients/Parents:
  o www.acaai.org – American College of Allergy, Asthma & Immunology
  o www.healthychildren.org – articles about allergies under “Health Issues”
  o www.foodallergy.org/ - The Food Allergy & Anaphylaxis Network
  o www.kidswithfoodallergies.org/ - largest online support community

© Developed by LT Kari Wagner. Updated 2016 by LT Karen Ganacias
Reviewed by LCDR Taylor Banks & MAJ Jennifer Hepps
Clinical Management of Food Allergy

Benjamin L. Wright, MDa,b, Madeline Walkner, BSc, Brian P. Vickery, MDa, Ruchi S. Gupta, MD, MPHd,*

INTRODUCTION

Food allergy affects approximately 8% of children in the United States.1 Of those children with food allergies, 38.7% have experienced a severe reaction.1 At present there are no proactive treatments available for food allergy; consequently, the mainstay of therapy is education and avoidance.2 Often pediatricians are the first physicians encountered by patients with food allergies; therefore, it is critical that pediatricians are trained in the principles of proper diagnosis, management, and referral. This article reviews the 5 main steps of food allergy management in a primary care clinic: (1) clinical history and physical examination, (2) appropriate use of diagnostic testing, (3) medication, (4) counseling/education for patients and families, and (5) referral to an allergist.

KEY POINTS

- There are no proactive treatments currently available for food allergy.
- Severe life-threatening reactions typically only occur following oral ingestion.
- Identifying the potential food trigger is critical, and diagnostic testing along with clinical history is needed for diagnosis, with a food challenge being confirmative.
- Providers should teach recognition and treatment of allergic reactions and provide an emergency action plan.
- Children with food allergies should be seen annually to assess for interval ingestions, provide education, and monitor for tolerance.

INTRODUCTION

Food allergy affects approximately 8% of children in the United States.1 Of those children with food allergies, 38.7% have experienced a severe reaction.1 At present there are no proactive treatments available for food allergy; consequently, the mainstay of therapy is education and avoidance.2 Often pediatricians are the first physicians encountered by patients with food allergies; therefore, it is critical that pediatricians are trained in the principles of proper diagnosis, management, and referral. This article reviews the 5 main steps of food allergy management in a primary care clinic: (1) clinical history and physical examination, (2) appropriate use of diagnostic testing, (3) medication, (4) counseling/education for patients and families, and (5) referral to an allergist.
CLINICAL HISTORY

A pertinent clinical history is the single most important tool a physician should use in the diagnosis of pediatric food allergy. Many patients may report symptoms related to food ingestion, but key historical elements can distinguish food allergies from other food-related disorders. All allergic disorders have their roots in inappropriate immune responses, from immunoglobulin E (IgE)-mediated immediate hypersensitivity (eg, anaphylaxis) to non–IgE-mediated conditions.

Differential Diagnosis

The differential diagnosis of food allergy is broad, and encompasses immune-mediated and non–immune-mediated processes. Table 1 details the differential diagnosis of adverse reactions to foods.3

Allergy Versus Intolerance

Food allergies are often mistakenly defined as any adverse reaction owing to ingestion of specific foods or types of food. A true food allergy is an immunologic reaction leading to effector cell (ie, mast cell, basophil, T cell) activation, which results in a

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Differential diagnosis of adverse food reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td><strong>Disorder</strong></td>
</tr>
<tr>
<td>Immune mediated</td>
<td>Celiac disease</td>
</tr>
<tr>
<td></td>
<td>Eosinophilic gastrointestinal disorders</td>
</tr>
<tr>
<td></td>
<td>Food protein-induced enterocolitis syndromes</td>
</tr>
<tr>
<td></td>
<td>IgE-mediated food allergy</td>
</tr>
<tr>
<td></td>
<td>Milk protein allergy</td>
</tr>
<tr>
<td></td>
<td>Pollen-food allergy syndrome</td>
</tr>
<tr>
<td>Non–immune mediated</td>
<td>Auriculotemporal (Frey) syndrome</td>
</tr>
<tr>
<td></td>
<td>Chemical effects</td>
</tr>
<tr>
<td></td>
<td>Food intolerance/aversion</td>
</tr>
<tr>
<td></td>
<td>Metabolic disorders</td>
</tr>
<tr>
<td></td>
<td>Pharmacologic reactions</td>
</tr>
<tr>
<td></td>
<td>Toxic reactions</td>
</tr>
</tbody>
</table>
stereotypic clinical presentation (see later discussion). Many patients and some clinicians may attribute disorders such as celiac disease or irritable bowel syndrome to food allergies. Although some of these disorders certainly have immunologic underpinnings, they can largely be distinguished from hypersensitivity reactions based on key findings in the clinical history such as timing, reproducibility, and symptom complex. For example, a teenage patient who newly develops abdominal pain and diarrhea alone 6 hours after drinking a glass of milk is more likely to have lactose intolerance than an IgE-mediated milk allergy. Adverse reactions such as these should be labeled as intolerances and managed appropriately. Described here are salient clinical features that will assist in distinguishing IgE-mediated food allergies from other adverse reactions to foods.

**Suspected Triggers**

Although children can be allergic to any food, the 8 most common pediatric food allergens are peanut, cow’s milk, shellfish, tree nuts, egg, fin fish, wheat, and soy. Often families may be unsure of the exact food that precipitates a reaction. Common food allergens are usually explicitly stated on food labels. However, in cases where a trigger is not obvious, clinicians must assess the potential for cross-contamination, which commonly occurs in bakeries, buffets, ethnic restaurants, and ice cream parlors, among other locations.

The pathogenesis of IgE-mediated food allergies requires antigen exposure for sensitization to occur. Of note, most childhood food allergies are detected when the child is first introduced to the food. Recent evidence suggests that cutaneous exposure in the context of barrier disruption (ie, atopic dermatitis), presumably early in life, may lead to food sensitization. This aspect has important implications for food allergy prevention, as recent literature suggests that early oral exposures may be important for inducing tolerance. In a landmark study, Du Toit and colleagues demonstrated that children 4 to 11 months of age randomized to early oral exposure to peanut versus avoidance had an 86% reduction in the incidence of peanut allergy by 5 years of age. Previous guidelines to avoid potentially allergenic foods during the first few years of life are no longer recommended, and may actually lead to food sensitization.

**Type of Reaction**

IgE-mediated reactions are distinguished by rapid onset (usually within 2 hours of ingestion) and typically resolve within 24 hours. Characteristic symptoms may include any of the following alone or in combination: hives, swelling/angioedema, vomiting, respiratory compromise, and anaphylaxis. Less common symptoms may include eczematous rash (late onset), rhinorrhea, diarrhea, or abdominal pain. Clinicians should note which medications (antihistamines, epinephrine) were administered and the type of medical care that was given. Additional factors such as alcohol ingestion, exercise, concurrent fever, and use of nonsteroidal anti-inflammatory drugs may serve to augment food-induced reactions and should be noted in the patient’s clinical history.

Although most patients will have rapid symptoms that resolve relatively quickly, a significant minority will have biphasic reactions, defined as a recurrence of symptoms within 72 hours of an initial reaction. An even smaller number of patients may develop refractory or persistent anaphylaxis requiring volume resuscitation and inotropic support.

**Current Diet**

In addition to classifying food-induced reactions, it is also important to determine which foods a child is currently avoiding. For example, if a patient suspects a distant
episode of hives was due to a peanut allergy, the clinician should ask about ingestion of peanut-containing foods since the time of reaction. In cases where the food was previously tolerated and is currently incorporated into the diet, no further testing is warranted. It is noteworthy that some children with food allergies to milk or egg proteins are able to tolerate these foods in extensively heated forms because the IgE molecules in these individuals are likely specific for conformational epitopes, which are denatured during the heating process. As a result, some children may be able to tolerate egg in a muffin but not in an omelet. These children should continue to ingest the allergen in its baked form, as it may signal and hasten the development of oral tolerance. By contrast, IgE to peanuts, tree nuts, and shellfish (among others) are specific for linear epitopes, which are not denatured with heating, and these allergies tend to persist.

Physical Examination

Physical examination of the patient should focus on the signs of an allergic reaction in addition to other atopic disorders commonly associated with food allergies. For example, many patients have comorbid atopic dermatitis. Others may have a history of asthma, which coupled with food allergy increases the risk of mortality from childhood asthma and anaphylaxis. Photographs of acute reactions, if available, may also be helpful. The physical examination may prove useful in distinguishing other conditions with specific findings. It is also important to assess growth parameters in children with food allergy, as this is an established risk factor for growth impairment. Children at special risk include those allergic to milk and/or multiple foods. Consultation with an experienced nutritionist may be considered for all children with food allergy, especially those with poor growth. Speech and feeding therapists may also be called upon to evaluate food-allergic children who may demonstrate dysfunctional feeding behavior.

Immunoglobulin E Mediated Versus Non–Immunoglobulin E Mediated

Although IgE-mediated food allergies are the most common, additional immune-mediated food sensitivities known as eosinophilic gastrointestinal disorders have become increasingly prevalent. Eosinophilic esophagitis (EoE), a disorder characterized by eosinophilic infiltration of the esophageal lining, has emerged as a closely related disease state. In contrast to the rapid symptoms of IgE-mediated food reactions, EoE is defined by a more insidious course resulting in failure to thrive, vomiting, reflux, and food aversion. Constant inflammation of the esophagus may eventually lead to dysphagia, stricture formation, and food impaction in adolescents and adults. Eosinophilic gastrointestinal disorders, however, are not confined to the esophagus and may also involve other segments of the gastrointestinal tract.

DIAGnostic TESTING

Several tools are currently used to assist in the diagnosis of food allergy. Table 2 lists available tools and the settings in which they may be utilized.

Pediatric Clinic

Specific Immunoglobulin E (ImmunoCAP)

Allergen-specific IgE (sIgE) testing measures the presence of allergic antibody to a particular antigen. This blood test can be performed at any age and is not limited by concurrent antihistamine use. As in many other clinical situations, the detection of an antibody by a highly sensitive but nonspecific immunoassay does not necessarily
The presence of sIgE simply denotes allergic sensitization to a particular food protein. Many individuals, especially children with atopic dermatitis, may be sensitized but not clinically allergic. Although sIgE is not routinely recommended for the diagnosis of food allergies, a pediatrician may consider targeted sIgE testing to likely triggers. It is important that this testing be based on a supportive clinical history after ingestion (eg, a high pretest probability of clinical food allergy) and not be ordered indiscriminately. Bird and colleagues recently demonstrated that bulk testing to multiple food antigens with food allergy panels leads to unnecessary cost and dietary restriction. Therefore, if a child tolerates a particular food in his or her diet regularly without clear evidence of allergic disease, sIgE testing should not be ordered. sIgE testing should also not generally be used to screen patients for food allergies before the first ingestion. The application of serologic IgE testing in the diagnosis and management of food allergy patients by primary care physicians has been recently reviewed elsewhere.

Traditionally sIgE has been assessed for an entire food molecule composed of multiple component proteins. Recently, component-resolved diagnostics (CRD) have become available, potentially increasing the sensitivity and specificity of IgE measurements, although this is still being studied. Although CRD for milk, egg, peanut, tree nuts, fish, and shellfish are commercially available, their use is not routinely recommended in food allergy diagnostic guidelines, and many such tests are not covered by insurance carriers. Most of the data supporting CRD come from English and European studies of component IgE testing in peanut-allergic patients, a topic that has been recently reviewed elsewhere.

### Allergy Clinic

#### Skin-prick testing

In addition to sIgE, skin-prick testing (SPT) may be useful in confirming clinical food allergy. SPT is an in vivo assessment of mast cell activation whereby a small amount of allergen is placed in the epidermis. Sensitized patients usually develop a wheal and flare reaction at the site of antigen placement within minutes. Skin reactions are then compared with positive and negative controls, as recent antihistamine use or dermatoigraphism may result in false-negative or false-positive results, respectively. This approach is a safe, rapid, and relatively inexpensive way to assess for food sensitization. In general, SPT has an excellent negative predictive value (NPV; ~95%) but a poor positive predictive value (PPV; ~50%).

For those patients who successfully avoid culprit foods and for whom the persistence of food allergy remains uncertain, serial sIgE and SPT may be used to determine whether an oral food challenge is warranted to definitively establish ongoing allergy or tolerance. Table 3 gives general recommendations for the frequency of laboratory tests.

<table>
<thead>
<tr>
<th>Table 2: Food allergy diagnostic testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>sIgE</td>
</tr>
<tr>
<td>Full protein</td>
</tr>
<tr>
<td>Component&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Skin-prick test</td>
</tr>
<tr>
<td>Oral food challenge</td>
</tr>
</tbody>
</table>

<sup>a</sup> The utility of component testing in diagnosing food allergy is still under investigation.
monitoring and SPT in children with food allergies. Interpretation of SPT and sIgE must be performed in the appropriate clinical context. Regardless of test values, patients with a recent history of anaphylaxis within the past year should not undergo oral food challenge. Conversely, children who have incorporated a food into their diet without symptoms do not require further testing.

**Oral food challenge**

The double-blinded placebo-controlled food challenge is the gold standard for the diagnosis of food allergy or confirming its persistence.\(^\text{10}\) Because of its labor-intensive and time-intensive nature, open food challenges with commercially available food products are usually used in clinical practice. Before performing an oral food challenge (OFC), the patient should understand the risks associated with the procedure and also display an interest in eating the food afterward if he or she passes the challenge. Well-accepted protocols for OFCs have been published\(^\text{34}\) but, in general, gradually increasing amounts of a food allergen are administered over successive intervals under close clinical observation. Once a designated quantity is safely consumed, a patient is allowed to incorporate the food into the diet.

**Interpretation of test results**

Challenge thresholds for interpretation of sIgE and SPT have been established.\(^\text{3,35}\) Table 4 provides the decision points used by many allergists in deciding whether to perform an OFC. These recommendations provide 95% PPV and 50% NPV for reactions to OFCs. A challenge is usually not recommended when sIgE and SPT are greater than 95% PPV. Conversely, a challenge may be considered when the sIgE and SPT are less than 50% NPV. Positive and negative predictive thresholds do not

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Test</th>
<th>≤5 y Old</th>
<th>&gt;5 y Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk, egg, wheat, soy, peanut</td>
<td>sIgE, SPT</td>
<td>Every 12–18 mo</td>
<td>Every 2–3 y</td>
</tr>
<tr>
<td>Tree nuts, fish, shellfish</td>
<td>sIgE, SPT</td>
<td>Every 2–4 y</td>
<td>Every 2–4 y</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Food</th>
<th>&gt;95% Positive</th>
<th>~50% Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SPT</td>
<td>sIgE</td>
</tr>
<tr>
<td>Egg white</td>
<td>≥7</td>
<td>≥7</td>
</tr>
<tr>
<td></td>
<td>≥2 if age &lt;2 y</td>
<td></td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>≥8</td>
<td>≥15</td>
</tr>
<tr>
<td></td>
<td>≥5 if age &lt;1 y</td>
<td></td>
</tr>
<tr>
<td>Peanut</td>
<td>≥8</td>
<td>≥14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish</td>
<td>—</td>
<td>≥20</td>
</tr>
</tbody>
</table>

exist for many food allergens, and those listed cannot be extrapolated to antigens such as wheat and soy. These foods typically have much higher sIgE reaction thresholds. It should be noted that most predictive cutoffs were developed using the ImmunoCAP system in children with a high pretest probability of food allergy presenting to a tertiary care allergy subspecialty clinic; therefore, values generated using other testing platforms cannot be reliably compared with these thresholds. In addition, population-based estimates have shown that these cutoffs may be much higher if testing is performed indiscriminately or in the general population, whereby the tests may detect sensitization more readily than clinical allergy.

**MEDICATIONS**

*Prescription of Epinephrine*

As a provider it is important to identify those patients most likely to develop fatal or near-fatal anaphylaxis and to prescribe injectable epinephrine. Box 1 presents clinical scenarios known to represent increased risk, although it is well established that allergic reactions to food are inherently unpredictable, making risk stratification difficult. Therefore, epinephrine prescription may be considered in any patient with IgE-mediated food allergy, as the severity of subsequent reactions cannot be predicted. Additional factors to consider, in addition to those listed in Box 1, include the age of the patient (adolescents and young adults at higher risk for fatality) and the distance from the patient’s home to an appropriate medical facility.

First-line treatment of anaphylaxis is always epinephrine. Second-line medications such as albuterol or antihistamines may also be prescribed for treatment of mild symptoms or adjunctive therapy, but unlike epinephrine they have no direct effect on the mast cells or basophils themselves. Prompt treatment with epinephrine is encouraged, as this may slow or halt progression of severe anaphylaxis. Furthermore, most fatalities from food-induced anaphylaxis are associated with delayed administration of epinephrine; however, despite this knowledge there is a persistent and well-established underutilization of epinephrine in the treatment of anaphylaxis. When an epinephrine autoinjector is prescribed, families should be taught how and when to administer it. Written anaphylaxis action plans are encouraged, listing medications and their doses, and detailing emergency follow-up procedures including activation of emergency medical services.

---

**Box 1**

**Guidelines for prescription of an epinephrine autoinjector**

Prescribe epinephrine if a child has any one of the following:

- History of anaphylaxis
- Prior history of systemic allergic reaction
- History of food allergy and asthma
- Known food allergy to peanut, tree nuts, fish, and crustacean shellfish (ie, allergens known to be associated with more fatal and near-fatal allergic reactions)

Consider epinephrine prescription in any child with a history of IgE-mediated food allergy.

Other Medications: Antihistamines, Albuterol, and Steroids

Antihistamines such as diphenhydramine and cetirizine are commonly given for mild food-induced reactions. Although these medications may be useful in relieving symptoms, such as itch, they do not halt the progression of an allergic reaction, and are best considered an adjunctive therapy. Albuterol should be used as adjunctive therapy for respiratory symptoms, especially in patients with a history of bronchospasm or asthma. Asthmatic individuals experiencing lower respiratory symptoms such as cough or wheeze during an allergic reaction to food should always receive epinephrine. Corticosteroids have a delayed onset of effect, making them unhelpful in immediate management. Although commonly used in this context, there is little evidence supporting their effectiveness.

COUNSELING AND EDUCATION

Despite their best efforts, most patients with food allergies will be exposed to culprit foods. Therefore it is incumbent on health care providers to prepare families to recognize and treat anaphylaxis. Food-induced reactions may be subtle, and it is useful to teach patients that anaphylaxis may present anywhere on a spectrum of symptoms ranging from a few hives and throat clearing to respiratory failure and cardiac arrest. Because anaphylaxis may progress rapidly, early detection and action is a critical step in successful management. Patients and families should be encouraged to inject epinephrine at the first sign of anaphylaxis, even if relatively mild. More educational and counseling food allergy resources for providers and caregivers can be found at http://www.ruchigupta.com/i-will-thrive-video/.

Epinephrine Use

Patients, or their caregivers, should immediately inject epinephrine for any obvious signs of a potentially severe systemic reaction, including: cardiovascular collapse (lethargy, pallor, behavioral changes); respiratory distress (wheezing, coughing, increased work of breathing); or laryngeal edema (drooling, difficulty swallowing, throat tightness). It is important to convey to affected individuals and caregivers that anaphylaxis may not present with such potentially life-threatening symptoms at the onset. Operationally, a generalized allergic reaction involving symptoms affecting more than 1 organ system can be identified as anaphylaxis. For example, a child experiencing urticaria and vomiting after a likely or confirmed allergen exposure can be considered as having anaphylaxis, and such a child should receive epinephrine even if symptoms are not considered to be immediately life-threatening. More specific indications can be individualized based on the patient’s medical history.

Use of an epinephrine autoinjector first requires removal of the safety lock. Once removed, the epinephrine should be injected into the lateral thigh. Clothing need not be removed, as the needle of the autoinjector should pass through without difficulty.

<table>
<thead>
<tr>
<th>Brand</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaclick (generic)</td>
<td>0.15 mg (for children 15–30 kg), 0.3 mg (for children ≥30 kg)</td>
</tr>
<tr>
<td>Auvi-Q</td>
<td>0.15 mg (for children 15–30 kg), 0.3 mg (for children ≥30 kg)</td>
</tr>
<tr>
<td>EpiPen</td>
<td>0.15 mg (for children 15–30 kg), 0.3 mg (for children ≥30 kg)</td>
</tr>
</tbody>
</table>

Ensure that the child has 2 autoinjectors accessible at all times.
The autoinjector should be held in place for at least 10 seconds to ensure complete dose delivery. One removed from the thigh, a protective sheath will cover the needle. If symptoms do not resolve within 5 to 15 minutes, patients experiencing anaphylaxis should be given a second dose. The patient should be placed in the recumbent position with the lower extremities elevated. Patients and families should be instructed to call the emergency services once epinephrine has been administered. Trainer devices from several manufacturers are available for demonstration and testing of proficiency.

**Emergency Action Plan**

Once a provider is comfortable with a patient’s and caregiver’s competency using the device, its indications for use should be discussed. Formulating an emergency action plan may facilitate this. Personalized action plan forms are available in English and Spanish through the American Academy of Allergy, Asthma and Immunology (www.aaaai.org) and Food Allergy Research and Education (www.foodallergy.org) Web sites. These forms list patients’ food triggers and provide guidelines for treatment.

**Avoidance**

Strict avoidance of allergens is the only sure way to prevent food-induced reactions. Relatively small amounts of food can trigger acute reactions in highly sensitized individuals. However, reactions may vary considerably depending on the patient and the allergen, resulting in misdiagnosis or a false sense of security if small amounts of food can be ingested without symptoms. One must be aware that the severity of a food-induced reaction does not predict the severity of future reactions; therefore, a child with a peanut allergy who only develops hives after an initial ingestion might develop life-threatening anaphylaxis following subsequent exposure.

Although patients may be exposed to food antigens through a variety of routes (cutaneous, respiratory, oral), typically only oral ingestion causes severe reactions. Investigators have examined the potential for food-induced reactions through casual contact. In 2003, Simonte and colleagues performed a randomized, double-blind, placebo-controlled trial of 30 children with significant peanut allergy. Subjects underwent cutaneous and inhalation challenge with peanut, and none experienced a systemic or respiratory reaction. Mild cutaneous symptoms were noted in a minority of patients. A notable exception is that in children with asthma and food allergy, bronchial challenge with aerosolized food allergens can provoke respiratory symptoms, particularly in those with allergy to fish or crustacea. For symptoms to occur, protein antigens must be vigorously aerosolized during food preparation (eg, cooking seafood in a rolling boil) and come in direct contact with the respiratory mucosa. An important distinction is that the smell of foods produced by volatile organic compounds does not cause clinical reactions.

**Food Labeling**

To properly adhere to recommended elimination diets, patients and families should be instructed to pay careful attention to ingredient lists and food labels. The Food Allergen Labeling and Consumer Protection Act (FALCPA) of 2004 was passed in an effort to make food labels more accurate and understandable for consumers with food allergies. This legislation requires manufactures to label in plain English foods containing any of the 8 major food allergens (peanut, milk, crustacean shellfish, tree nuts, egg, fin fish, wheat, and soy). Major implications of this law are listed in **Box 2**.

In addition to those foods listed containing allergens, patients should also be counseled to avoid products that are processed in a facility where other food allergens are
processed, causing cross-contamination. It should be noted that use of the phrases “may contain,” “may contain traces of,” and “manufactured in a facility that also processes” are voluntary; therefore, families must be aware of the potential for cross-contamination. A recent study in Canada found that 17% of accidental exposures resulted from unintentional cross-contamination during manufacturing or packaging, with no precautionary statement being provided. Unfortunately, widespread and inconsistent use of these phrases has also resulted in a devaluation of this warning; consequently, up to 40% of individuals ignore “may contain” statements and consume foods with potential food allergens. Helpful patient information to assist with food allergen avoidance is available through the Food Allergy Research and Education Network (www.foodallergy.org) and the Consortium of Food Allergy Research (www.cofargroup.org).

**Different Environments**

Although most food-induced reactions occur in the home, many families find that eating out at a restaurant or a friend’s home can be difficult. At home, ingredient lists can be screened and meals carefully prepared to prevent cross-contamination, but eating away from home may pose unique challenges. Studies suggest that 40% to 100% of fatalities from food-induced reactions are due to food prepared or catered outside the home. Although risks can be mitigated with advance planning, it is important to identify high-risk situations. Ice cream parlors, ethnic restaurants, bakeries (peanut, egg, milk, and tree nuts), and buffets (all foods) are common places where cross-contamination or occult exposure may occur. Such environments seem to pose a special risk to adolescents and young adults, who may be relatively inexperienced in self-management and have been shown to willfully engage in risk-taking behavior pertaining to food allergen exposure.
REFERRAL TO AN ALLERGIST

If a food allergy is suspected or diagnosed, the patient should be referred to an allergist. As mentioned previously, allergists can provide additional diagnostic testing (ie, SPT, OFC) and are equipped to manage anaphylaxis in the clinic. In addition to assisting with diagnosis, allergists can monitor and assess for the development of tolerance and can help manage the comorbid conditions commonly encountered in food-allergic children, such as atopic dermatitis and asthma.

Monitoring for Tolerance

An OFC, performed in the allergist’s office, is the gold-standard test to determine whether tolerance has occurred. Serial measurements indicating a decline in the patient’s allergen-specific IgE level often provide useful predictive power that a patient is outgrowing a food allergy, and that a challenge is indicated. IgE-based online calculators developed by the Consortium of Food Allergy Research are available for public use to generate individualized probabilities for outgrowing milk and egg allergies. Often the patient’s interval history can provide important clues; for example, a child may accidentally be exposed to a trigger food without developing symptoms. If a significant quantity of the food has been tolerated several times without ill effect, the food allergy has likely resolved. Acquisition of tolerance is more likely to occur in younger children, who are allergic to foods such as wheat, soy, milk, or egg. By contrast, allergies to nuts including peanut, fish, and shellfish are much less commonly outgrown.

Tolerance of Extensively Heated Allergens

As mentioned previously, some children with milk or egg allergy may be able to tolerate these allergens in their baked forms. Researchers hypothesize that this is due to sensitization to conformational epitopes that are unable to cross-link surface IgE molecules when extensively heated. Some data suggest that tolerance to baked milk or egg may be an early intermediate step in the development of immunologic tolerance to the food antigen, and that consumption of baked allergens may actually hasten the resolution of clinical allergy. OFCs with products containing baked milk or egg are routinely performed in the allergist’s office.

Routine Follow-Up

A specialist in allergy and immunology should see patients with food allergies at least annually. Periodic visits allow for the following:

- Assessment of interval progress including a history of accidental ingestions
- Renewal of epinephrine prescription
- Renewal and revision of emergency action plans
- Additional education regarding avoidance and recognition/treatment of anaphylaxis, and transition to self-management for teenagers
- Assessment of nutritional status
- Monitoring of coexisting conditions, such as asthma or atopic dermatitis
- Monitoring for development of tolerance to food antigens

Allergen-specific immunotherapy as a proactive treatment strategy for food allergy is currently being developed in phase II/III clinical trials. Its use is not recommended outside of research settings at present, but allergists may be able to routinely provide this life-changing clinical treatment in coming years (Appendices 1 and 2).
SUMMARY

Successful diagnosis and management of food allergies is complex, and demands collaboration from both pediatricians and board-certified allergists, in addition to skilled nurses, nutritionists, and occasionally other team members such as psychologists and feeding therapists. It is hoped that these 5 steps for primary care providers will provide a more straightforward approach: (1) clinical history and physical examination, (2) diagnostic testing, (3) medication, (4) counseling/education for patients and families, and (5) referral to an allergist. Although some clinical trials of interventional food allergy treatments have generated promising preliminary data, the standard of care continues to focus on prescribing the proper elimination diet, education, and training in the recognition and management of accidental allergic reactions.

REFERENCES

Preventing Peanut Allergy through Early Consumption — Ready for Prime Time?

Rebecca S. Gruchalla, M.D., Ph.D., and Hugh A. Sampson, M.D.


Kids can't take peanut butter to school. Some airlines no longer serve peanuts because of fear of anaphylaxis among passengers. These developments are just the tip of the iceberg as the prevalence of peanut allergy among children continues to increase worldwide, especially in westernized countries. In the United States alone, the prevalence has more than quadrupled in the past 13 years, growing from 0.4% in 1997 to 1.4% in 2008 to more than 2% in 2010. Peanut allergy has become the leading cause of anaphylaxis and death related to food allergy in the United States.

In 2000, largely in response to outcomes reported in infant feeding trials conducted in Europe and the United States, the American Academy of Pediatrics (AAP) recommended that parents refrain from feeding peanuts to infants at risk for the development of atopic disease until the children reached 3 years of age. However, since the number of cases of peanut allergy continued to rise, many investigators and clinicians began questioning this advice. In 2008, after reviewing the published literature, the AAP retracted its recommendation, stating that there was insufficient evidence to call for early food avoidance. Shortly thereafter, Du Toit et al. noted that the prevalence of peanut allergy among Jewish children in London who were not given peanut-based products in the first year of life was 10 times as high as that among Jewish children in Israel who had consumed peanut-based products before their first birthday. In addition, subsequent studies that evaluated the early introduction of other allergenic foods, including egg and cow's milk, showed that earlier introduction of egg and milk into an infant's diet was associated with a decrease in the development of allergy.

But since these studies were observational, we needed data from controlled trials to provide reliable clinical guidance regarding the best time to introduce allergenic foods (e.g., milk, egg, peanuts, and tree nuts) to infants at high risk for the development of allergies (i.e., those from atopic families). Du Toit et al. now address this question in the Journal in their landmark study, Learning Early about Peanut Allergy (LEAP). The investigators hypothesized that early introduction of peanut-based products (before 11 months of age) would lead to the prevention of peanut allergy in high-risk infants. More than 500 infants at high risk for peanut allergy were randomly assigned to receive peanut products (consumption group) or to avoid them (avoidance group). Approximately 10% of children, in whom a wheal measuring more than 4 mm developed after they received a peanut-specific skin-prick test, were excluded from the study because of concerns that they would have severe reactions. At 5 years of age, the children were given a peanut challenge to determine the prevalence of peanut allergy. The results are striking — overall, the prevalence of peanut allergy in the peanut-avoidance group was 17.2% as compared with 3.2% in the consumption group.

The trial was designed to examine two groups — children who had negative results on the peanut skin-prick test at enrollment (nonsensitized) and those who had "mild" sensitization at enrollment (wheals with mean diameters of 1 to 4 mm in response to the test). In these two groups the results on the prevalence of peanut allergy were equally striking. Among the children who initially had a negative result on the skin-prick test, the prevalence of peanut allergy was 13.7% in the avoidance group and 1.9% in the consumption group, and among those who had mild sensitization the prevalence was 35.3% in the avoidance group versus 10.6% in the consumption group. Thus, early consumption was effective not only in high-risk infants who showed no indication of peanut sensitivity at study entry (primary prevention) but also in infants who had slight peanut sensitivity (secondary prevention).

Du Toit et al. carefully defined their high-risk population, which included children with severe eczema, egg allergy, or both. Moreover, they determined whether these infants were sensitized to peanut at study entry and then challenged those in the peanut-consumption group to ensure that these children were unresponsive before sending them home to consume peanut-based products on a regular basis.
Given the results of this prospective, randomized trial, which clearly indicates that the early introduction of peanut dramatically decreases the risk of development of peanut allergy (approximately 70 to 80%), should the guidelines be changed? Should we recommend introducing peanuts to all infants before they reach 11 months of age? Unfortunately, the answer is not that simple, and many questions remain unanswered: Do infants need to ingest 2 g of peanut protein (approximately eight peanuts) three times a week on a regular basis for 5 years, or will it suffice to consume lesser amounts on a more intermittent basis for a shorter period of time? If regular peanut consumption is discontinued for a prolonged period, will tolerance persist? Can the findings of the LEAP study be applied to other foods, such as milk, eggs, and tree nuts?

These questions must be addressed, but we believe that because the results of this trial are so compelling, and the problem of the increasing prevalence of peanut allergy so alarming, new guidelines should be forthcoming very soon. In the meantime, we suggest that any infant between 4 months and 8 months of age believed to be at risk for peanut allergy should undergo skin-prick testing for peanut. If the test results are negative, the child should be started on a diet that includes 2 g of peanut protein three times a week for at least 3 years, and if the results are positive but show mild sensitivity (i.e., the wheal measures 4 mm or less), the child should undergo a food challenge in which peanut is administered and the child's response observed by a physician who has experience performing a food challenge. Children who are nonreactive should then be started on the peanut-containing diet. Although other studies are urgently needed to address the many questions that remain, especially with respect to other foods, the LEAP study makes it clear that we can do something now to reverse the increasing prevalence of peanut allergy.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

This article was published on February 23, 2015, at NEJM.org.

From the Departments of Internal Medicine and Pediatrics and Division of Allergy and Immunology, University of Texas Southwestern Medical Center, Dallas (R.S.G.); and Department of Pediatrics, Division of Allergy–Immunology, and Jaffe Food Allergy Institute at the Icahn School of Medicine at Mount Sinai, New York (H.A.S.).

References

   CrossRef | Web of Science | Medline

   CrossRef | Web of Science | Medline

   Full Text | Web of Science | Medline

   CrossRef | Web of Science | Medline

   CrossRef | Web of Science | Medline
ACROSS:
1. The gold standard test (abbreviation) for diagnosing a food allergy.
5. Anaphylaxis is characterized by the involvement of 2 or more of the following systems: the skin, GI tract and ___ system.
8. Up to ___ percent of children have food allergies.
10. The most common food allergy in adults.

DOWN:
2. Food allergies to tree nuts, seafood and ___ are unlikely to be outgrown.
3. Risk for a severe allergic reaction to food include a delay in administering this medication.
4. In children this condition may present with vomiting, reflux symptoms or feeding disorders.
6. This age group is at the most risk to have a fatal food allergic reaction.
7. Anaphylaxis is an ___-mediated reaction.
9. The most important element in diagnosing a food allergy.
Case 1:
Bobby is a 2 year old boy who presents to the clinic with parental concern for food allergy. His mother reports that on two occasions in the past he has developed an itchy, raised rash over his face, chest and abdomen, lip swelling, and hoarseness after eating eggs. The last episode was yesterday. He ate roughly 1 cup of scrambled eggs and 40 minutes later developed symptoms. He did not have any vomiting, diarrhea, or labored breathing. Bobby's mother gave him a dose of diphenhydramine and his symptoms resolved after 1-2 hours. He eats baked goods containing eggs without developing similar reactions.

What additional history will you obtain?
- What other foods was he eating prior to the reactions?
- Past medical history, especially history of eczema, asthma or allergic rhinitis. Remember that asthma is a risk factor for more severe food allergy reactions.
- Family history of atopic disease
- Current medications and drug allergies

Bobby’s mother reports that the only other foods he ate with the eggs were toast, butter, and orange juice. He has had all of these alone recently and tolerated them well. He had eczema as an infant, but only required frequent applications of Aquaphor. He was breastfed for 9 months and then switched to a cow’s milk formula. Eggs were introduced first at 18 months of age. His mother had asthma as a child and one of Bobby's older sisters has allergic rhinitis. He is not currently taking any medications and does not have any medication allergies.

Are you concerned Bobby has an egg allergy? How will you further evaluate him?
- His history of respiratory symptoms (hoarseness), lip swelling, and hives as well as the timing of symptom onset is concerning for an egg allergy.
- Options for further evaluation include:
  - **Immunocap, Egg-specific IgE**: The detection of an antibody by a highly sensitive, but nonspecific immunoassay does not necessarily equate to a particular food protein allergy. Some individuals, especially children with atopic dermatitis, may be sensitized but no clinical allergy. *SO, in general, food allergy panels should be avoided as there is a high false positive rate and positive results do not always correlate with clinical symptoms.* Can also see false negative results. A clinical history consistent with food allergy is the best indicator.
  - May refer to **Allergy & Immunology** where options for further evaluation may include skin testing or the gold standard, oral food challenge.
You discuss your concerns with Bobby’s mother and put in a prescription for an Epipen Jr. When and how should she administer the Epipen Jr? What can she expect after she injects the medication?

- **Epinephrine** should be given if there is suspected egg intake and any clinical symptoms of anaphylaxis. *It is important to give epinephrine early!* In general, epinephrine can be given if the child has one of the following: history of anaphylaxis, prior history of systemic allergic reaction, history of food allergy and asthma, known food allergy to peanut, tree nut, fish, and crustacean shellfish (allergens known to be associated with fatal and near-fatal allergic reactions), or a child with a history of IgE-mediated food allergy.

- **Side effects** from epinephrine include tachycardia, flushing, anxiety, nausea, or vomiting.

- Can give an **antihistamine** as needed for cutaneous symptoms, some people recommend also giving an **H2 blocker**. **Albuterol** can be given as needed for wheezing; however, this has no direct effect on mast cells and basophils themselves and is second-line treatment.

- After administering epinephrine he should be taken to the **ER** for further support and monitoring. He could have a **late phase reaction 6-10 hours later**, so observation for a minimum of 4-8 hours following an episode of anaphylaxis is warranted.

As you’re wrapping up Bobby’s clinic visit you notice that he has not gotten his influenza vaccine this year. **Given your concerns for a food allergy to eggs, can Bobby get the influenza vaccine today?** Bobby's mother also asks if he will always be allergic to eggs?

- He may not be able to get the influenza vaccine today, but an **allergy to eggs is not a contraindication to give the influenza vaccine**. You can refer him to the Allergy & Immunology clinic to safely administer the vaccine.

- Allergies to egg, wheat, soy and milk are the most common allergies that improve by adulthood. Allergies to peanuts, tree nuts, shellfish and fish are most likely to persist.

Case 2:

You are seeing Isabella, a 4 month old previously healthy infant who presents for a routine well visit. Parental concern today is whether she can start eating complementary foods. Family history includes asthma in her mother and an older sibling with a severe food allergy to peanuts and eggs. On your exam, she has good muscle strength/tone and is able to hold her head upright.

*Isabella’s mother asks what foods she should avoid to prevent Isabella from developing a food allergy. Mom is also planning returning to work and intends to stop breast feeding and wants to know what formula to switch to?*

- Complementary foods including potential allergens should not be restricted after 4-6m of age.

- Should encourage Isabella's mother to **continue breast-feeding** and pumping breast milk once she returns to work. If continuing breast feeding is not feasible, given that her sister has a history of food allergies, would recommend switching to a **hydrolyzed formula**.
Consider the results of the LEAP trial: 640 high-risk infants between 4-11 months of age were assigned randomly either to avoid peanut entirely or to regularly include at least 6g of peanut protein per week in their diets. Regimens were continued until 5 yrs of age. Found an overall 81% reduction of peanut allergy in children who began early, continuous consumption of peanut compared to those who avoided peanut.

Case 3:
Lionel is a 10 year old boy with a history of allergic rhinitis who presents for a routine physical. His only concern today is that he gets tingling around his mouth after eating apples. He denies any other associated symptoms. The tingling self-resolves over 1 hour.

What additional questions will you ask?
- Timing of his symptoms, similar symptoms with other foods?
- Current medications, history of drug allergies?

Lionel reports that the tingling occurs within 30 minutes of eating apples. He reports he is a meat and potatoes guy and he does not like any other fruits. Besides allergic rhinitis he has been healthy. He currently takes Fexofenadine daily as needed, when his allergic rhinitis symptoms flare. He does not have any known medication allergies.

What is the most likely cause of his symptoms. How will you evaluate him further and how will you treat him? What other foods may cause him to experience similar symptoms?
- History is consistent with oral allergy syndrome to apples due to a cross-reaction with birch
- Evaluation may include:
  - Measurement of serum IgE to birch pollens
  - Allergy Immunology Referral for further testing which may include:
    - Skin testing with raw apple or birch pollens
    - Oral food challenge
- Treatment:
  - Avoidance of apples and other fruits that cross-react with birch
  - Cooking, microwaving or baking apples prior to consuming, which may make them more tolerable.
  - Antihistamines as needed for symptoms
  - If he should develop systemic symptoms in the future, may recommend that he carry an Epipen at all times.
  - May be a candidate for immunotherapy against pollen allergens
- Other foods that cross-react with birch antigens = plums, peaches, nectarines, cherries, almonds, kiwi, celery, almond, hazelnut, watermelon.
Food Allergies Board Review

1. The parents of a 10-year-old boy who has a peanut and tree nut food allergy ask your advice on the treatment of food allergy reactions at school. They describe a scenario that occurred last year when their son started itching diffusely and having difficulty breathing during lunchtime after inadvertently eating some of his friend’s chocolate candy bar that contained peanuts. At his current school, the child is allowed to carry his own self-injectable epinephrine. His current weight is 90 lb (41 kg).

Of the following, the BEST advice for the child, if a similar situation occurs, is to
A. have the school call emergency services, who should evaluate and administer epi if needed
B. have the school nurse observe the child for 10 to 15 minutes while calling his parents
C. immediately administer 0.15 mg of self-injectable epinephrine
D. immediately administer 0.30 mg of self-injectable epinephrine
E. take an oral antihistamine immediately

The boy described in the vignette experienced an anaphylactic reaction, a potentially life-threatening event. In children, the most commonly identified causes for anaphylaxis are food, insects, drugs, latex, and vaccines. Food allergy is the most common cause of anaphylaxis in the home or school setting and accounts for an estimated 50% of all pediatric cases annually.

Some 85% to 90% of allergic reactions to food in children are due to milk, egg, soy, wheat, peanuts, tree nuts, fish, and shellfish. Peanuts and tree nuts account for most cases of fatal anaphylaxis from foods in the United States.

Recently, a panel of experts published a set of clinical criteria for diagnosing anaphylaxis. The skin and respiratory system are the most commonly affected systems in cases of food allergy-induced anaphylaxis, as described for the boy in the vignette. Fatal anaphylaxis almost always is due to airway edema and subsequent respiratory failure.

For a person experiencing anaphylaxis, epinephrine should be administered immediately and without delay. Observation of the child while calling his parents wastes precious time in this situation. In the school setting, self-injectable intramuscular epinephrine is used. Other methods of delivery, used primarily in the hospital setting, include intravenous, intraosseous, and via an endotracheal tube. Current epinephrine injectors are available in two strengths: 0.15 mg and 0.30 mg. The child in the vignette, who weighs more than 30 kg, should be given the 0.30-mg dose, preferably in the lateral thigh. Antihistamines may decrease pruritus or flushing, but their effect has a slow onset, and they are not recommended as the initial treatment for anaphylaxis. Because some children may require additional doses of epinephrine and observation, emergency services should be called, but waiting for them to arrive to make a decision regarding the initial dose of epinephrine is not recommended.

Caregivers of children who have experienced food-induced anaphylaxis should have epinephrine readily available, understand the indications for its use, have a written action plan, and understand the proper technique for use of self-injectable epinephrine devices.
2. You have been asked by a local school to provide recommendations about the use of self-injectable epinephrine for anaphylaxis. The school supervisor is concerned about the increased incidence of peanut and tree nut food allergy. School officials have requested that each child who has a diagnosis of "food allergy" have two self-injectable epinephrine devices at the school nurse’s office.

Of the following, the BEST response regarding anaphylaxis is that
A. a patient should not receive a second dose of epinephrine unless a clinician is present
B. epi reaches higher peak plasma concentrations if injected into the thigh rather than arm
C. families should keep one epi autoinjector in the car in case a reaction occurs after school
D. skin manifestations (eg, flushing, itching, urticaria) are rare in severe anaphylaxis
E. subcutaneous injection of epinephrine is preferable to intramuscular injection

The prevalence of food allergies has continued to increase over the past 3 to 4 decades. Specifically, many children, parents, and school officials have been faced with the need to know about and understand how to recognize and appropriately treat food anaphylaxis in the school. Education and counseling of school officials and health-care clinicians is paramount to reduce morbidity and mortality from food anaphylaxis.

The most common antigenic triggers of anaphylaxis are foods, drugs, insect venom, radiocontrast media, and latex. After exposure to an antigenic trigger, symptoms generally develop within 5 to 30 minutes, although symptoms can occur up to several hours after the exposure. Severe allergic reactions usually occur after binding of specific immunoglobulin (Ig) E to the high-affinity IgE receptor, with subsequent cross-linking of receptors and mediator release (eg, histamine, tryptase) from mast cells and basophils.

Cutaneous manifestations such as urticaria, flushing, pruritus, and angioedema are the most common symptoms in anaphylaxis, occurring in 80% to 90% of episodes. Respiratory symptoms such as dyspnea, wheezing, shortness of breath, and cough are the next most frequent symptoms. Cardiovascular symptoms include cardiovascular collapse, tachycardia or relative bradycardia, and arrhythmias. Among the gastrointestinal manifestations are nausea, vomiting, diarrhea, abdominal pain, and cramping. Finally, many patients complain of either a metallic taste or "a sense of impending doom."

Appropriate treatment of anaphylaxis consists of early administration of epinephrine. Because anaphylaxis can occur in the absence of a health-care professional such as at school home, or a birthday party, children at risk always should have self-injectable epinephrine nearby.

Although parents or other adults may be reluctant to inject a child with epinephrine, this agent, not an antihistamine, is the drug of choice for anaphylaxis. In the past, outpatient administration of epinephrine was subcutaneous, but research has demonstrated that intramuscular injection, specifically in the thigh, is the preferred route and location due to higher and faster peak plasma concentration. If epinephrine is administered, parents or school personnel should follow an emergency action plan. This should involve calling emergency services to evaluate the child and transport him or her to the emergency department for further evaluation. The effects of a single dose of epinephrine typically last for 5 to 15 minutes; up to 20% of individuals experiencing anaphylaxis may require a second epinephrine dose. When symptoms persist, a second (or third) dose should be administered, even if the parent or school professional still is awaiting the ambulance. Although epinephrine always is the drug of choice in anaphylaxis, glucagon may be required in refractory cases for patients using beta blockers.

Self-injectable epinephrine should be available for all locations (ie, the patient usually carries one to two injectors), but leaving the device in the car is not recommended because extreme temperature changes can
decrease the efficacy. Recommended storage temperatures are 20° to 25°C at home and 15 to 30°C during trips outside the home, school, or workplace. Approximately 5% to 20% of patients who suffer initial anaphylactic events can experience a "late-phase" response 4 to 24 hours later in which symptoms such as flushing, pruritus, or airway obstruction recur. Such later symptoms result from the recruitment of inflammatory cells after the initial hypersensitivity response.

3. A 12-month-old girl presents with a 3-month history of a pruritic rash that involves her cheeks, neck, anterior trunk, and antecubital and popliteal areas. The rash improves after use of an over-the-counter topical steroid cream but still is present most days, and the infant often wakes up at night scratching. On physical examination, you observe a raised erythematous rash that has areas of lichenification.

Of the following, the MOST helpful intervention is to
A. eliminate fruit and acidic juices from the diet
B. eliminate milk, eggs, soy, and wheat from the diet
C. perform aeroallergen allergy testing
D. perform food allergy testing
E. recommend a skin biopsy

*PREP2009 Answer:* Some 30% to 40% of infants who have moderate-to-severe atopic dermatitis (AD), such as described for the infant in the vignette, may have an underlying immunoglobulin (Ig) E-mediated food allergy exacerbating the AD. For some infants, food ingestion may result in immediate worsening of AD severity, although most infants do not demonstrate this immediate reaction. Many foods have been implicated in AD, but 5 (milk, eggs, soy, wheat, and peanut) account for 90% of the causative allergens. Both allergy skin testing and measurement of serum IgE concentrations to these foods can help to identify and eliminate likely triggers. Either a negative IgE blood test (<0.35 kU/L) or a negative skin test for a specific food provides a high negative predictive value. On the other hand, the positive predictive value for a skin or blood test may be only 50%.

Although the most commonly implicated foods often are eliminated from the diet, such an approach does not improve symptoms in most (60% to 70%) children because they do not have IgE-mediated AD. The unnecessary elimination of multiple foods can have an adverse effect on nutrition, and food avoidance should be guided by the dietary history, eczema severity, and skin or blood testing.

Frequently, children experience perioral rashes after drinking fruit juice. Such rashes typically are nonpruritic, limited to the area of contact, and resolve within a few hours. The mechanism of such rashes is unknown, but children generally outgrow such reactions by age 4 years. In cases involving more widespread cutaneous symptoms, such as described in the vignette, elimination of fruit or acidic juices is unnecessary.

Parents often request testing for environmental allergies. House dust mites have been implicated in some cases of AD, although they are less likely a cause for moderate-to-severe atopic dermatitis than food allergies. Climate changes such as cold, dry air or hot, humid weather can worsen AD, but specific seasonal allergens such as oak tree or ragweed are not associated with eczema in infants.

A skin biopsy can provide insight into the pathophysiology of chronic rashes or lesions. Generally, skin biopsies neither are advised nor provide insight into the causes of typical AD manifestations in infants, but atypical presentations or lack of expected improvement with appropriate therapy should prompt consideration of a dermatology referral.
4. A mother brings in her 11-month-old son after he broke out in "hives" today during breakfast. The infant had stayed home from child care with a low-grade fever, and the mother had let him eat eggs for the first time. Immediately after breakfast, the mother noted a diffuse erythematous, pruritic rash covering the boy’s trunk and extremities. She is concerned that her son may have an egg allergy.

**Of the following, the BEST statement regarding Ig-E-mediated egg food allergy is that**

A. cooking the egg eliminates its allergic potential  
B. egg is the most common food allergy in the first postnatal year  
C. egg white is more allergenic than egg yolk  
D. most children do not outgrow their egg allergy  
E. the measles-mumps-rubella vaccine is contraindicated in children who have egg allergy

Immunoglobulin (Ig) E-mediated egg allergy is one of the more common childhood food allergies, affecting approximately 1% to 2% of children. As described in the vignette, cutaneous features are common, including atopic dermatitis, urticaria, and pruritus. Once the diagnosis of egg allergy is determined, patients generally are advised to avoid all egg food products with the hope that most children will outgrow their egg allergy within 3 to 5 years.

The primary allergenic egg protein is ovomucoid, a protein predominantly in the egg white. Approximately 50% of children may be able to tolerate small amounts of egg protein that has been heated extensively (eg, baked goods). Prolonged heating at high temperatures can denature proteins from a conformational form to a linear form. Some children who are allergic to eggs do not recognize the linear protein form as an allergen and, therefore, do not experience a reaction. Of note, the brief cooking used to make scrambled eggs will not denature heat-stable proteins.

The relationship between egg allergy and vaccination is a common question. The measles-mumps-rubella vaccine is safe for children who have egg allergy and should be administered without special precautions. The trivalent influenza and live attenuated influenza vaccines contain small amounts of egg protein and are contraindicated for patients who have egg allergy.

However, studies have supported a two-dose protocol for the administration of the influenza vaccine in egg-allergic patients. The two-dose protocol involves administering one tenth of the vaccine, observing the recipient for a period of time, and administering the rest of the vaccine, followed by a similar observation period.

In westernized countries, milk generally is regarded as the most common food allergen in infants, with an incidence of 2.5%, compared with an incidence of 1.5% for egg allergy.

5. A 10-year-old boy presents to the clinic complaining of tongue and mouth itching within a few minutes after eating apples. His mother states that he has not experienced these symptoms with other foods, but they occur every time he eats a fresh apple. He denies systemic symptoms, and the oral symptoms resolve within a few minutes. Other than allergic rhinitis in the spring months, he is healthy.
Of the following, you are MOST likely to advise his mother that
A. allergy skin testing to fresh apples probably will have negative results
B. cooking the apple will not alter its allergenicity
C. her son should avoid eating all fruits
D. her son should avoid milk products
E. her son’s symptoms are related to his allergic rhinitis

The boy described in the vignette is exhibiting a common form of food allergy called food pollen syndrome or oral allergy syndrome (OAS). OAS is seen in 30% to 40% of children who have allergic rhinitis. Certain foods contain proteins that are similar to airborne allergens, and patients who are allergic to an aeroallergen are at risk of developing reactions to the cross-reacting food protein.

In most cases, symptoms are isolated to the oropharynx, where food comes in contact with a mucosal surface, and include lip, tongue, and oral mucosal pruritus; tingling; and occasionally angioedema. Interestingly, because these food proteins are heat-labile, cooking the food (eg, apple pie) negates its antigenic properties. Although symptoms typically are mild, there are reports of severe reactions. In one recent review involving 1,361 patients who had OAS, 8.7% experienced systemic symptoms outside the gastrointestinal tract, 3% experienced symptoms other than oral symptoms, and 1.7% experienced anaphylactic shock.

Because OAS is relatively specific to particular cross-reacting food(s), patients do not need to avoid other fruits or vegetables to which they have not experienced reactions. Avoidance of unrelated foods (eg, milk, eggs) is not recommended unless the history suggests a previous reaction. The decision to avoid causative foods can be based on the severity of reaction.

Referral to an allergist typically is reserved for situations when skin testing is desired or if the child has experienced systemic symptoms. Skin testing is performed using a commercial extract or the fresh fruit or vegetable. When using fresh food, the sensitivity of skin testing with a history of reproducible reactions is close to 90%, while the negative predictive value is more than 90%. The skin prick device is pressed into the food and then pressed in the skin (so-called "prick-prick" skin test).

Other immunoglobulin (Ig) E food reactions include atopic dermatitis, eosinophilic esophagitis, and specific food allergy. In the United States, 85% of specific food allergies are due to egg, milk, wheat, soy, peanuts, tree nuts, fish, and shellfish. Most children who have IgE food allergies react to only one or two causative foods, although children who have tree nut allergy, atopic dermatitis, and eosinophilic esophagitis often have IgE-mediated reactions to multiple foods.