Food allergies are commonly seen by the practitioner, and managing these patients is often challenging. Recent epidemiologic studies report that as many as 1 in 13 children in the United States may have a food allergy, which makes this an important disease process to appropriately diagnose and manage for primary care physicians and specialists alike. Having a understanding of the basic immunologic processes that underlie varying presentations of food-induced allergic diseases will guide the clinician in the initial workup. This review will cover the basic approach to understanding the immune response of an individual with food allergy after ingestion and will guide the clinician in applying appropriate testing modalities when needed by conducting food challenges if indicated and by educating the patient and his or her guardian to minimize the risk of accidental ingestion. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:1-11)
Abbreviations used
AD-Atopic dermatitis
DBPCFC-Double-blind, placebo-controlled food challenge
FA-Food allergy
FALCPA-Food Allergy Labeling and Consumer Protection Act
FPIES-Food protein–induced enterocolitis syndrome
OFC-Oral food challenge
PA-Peanut allergy
SPT-Skin prick test

Key words: Food allergy; Anaphylaxis; Skin prick test; Oral food challenge; Label reading; Travel; Cross-contact; Autoinjectable epinephrine

IgE-mediated food allergies (FA) may be life-threatening, negatively impact the quality of life for affected individuals and their families, and require coordinated efforts among affected individuals and their caregivers to minimize the risk of accidental ingestion. The most recent epidemiologic studies show that approximately 1 in 13 US children has an FA, which makes FA an important disease process to be recognized, properly diagnosed, and effectively managed. This review primarily focuses on diagnosis and management of IgE-mediated FAs, with practical advice regarding avoidance and care of individuals with FA.

CLINICAL SPECTRUM
Specific food-induced allergic conditions
IgE-mediated FA occurs by cross linking of IgE on mast cells and basophils by allergenic proteins, which leads to the release of histamine and other mediators, and is the mechanism that underlies immediate hypersensitivity. Symptoms of IgE-mediated FA disease include urticaria, angioedema, vomiting, diarrhea, bronchospasm, and multisystem allergy that can result in anaphylaxis. A mild form of allergic disease, pollen-food syndrome, also referred to as oral allergy syndrome, occurs due to IgE cross-reactivity to PR10 proteins in fruits and nuts in patients with pollen allergies (Table I). These foods usually are tolerated in cooked or processed forms, and anaphylaxis is rarely seen in this condition. In more recent years, delayed food-induced anaphylaxis to meats has been described, which appears to be mediated via IgE specific for an oligosaccharide in red meat, galactose-alpha-1,3-galactose, and sensitization is associated with Lone Star tick exposure. The reason for the appearance of delayed symptoms is unclear.

A summary of the spectrum of food-induced allergic disease is provided in Table II. There are a number of non–IgE-mediated FA diseases. Perhaps with the exception of celiac disease, there is little mechanistic understanding of the pathologic processes that underpin such diseases. Food protein–induced enterocolitis syndrome (FPIES) specifically presents with acute recurrent vomiting and diarrhea that starts between 2 and 8 hours of ingestion of food, most commonly milk or soy. Although patients with FPIES are not at risk of anaphylaxis, they are at risk of developing shock and acidosis due to dehydration. Other non–IgE-mediated diseases of the gastrointestinal tract are typically characterized by eosinophilic inflammation of different segments of the gastrointestinal tract. Eosinophilic esophagitis may appear at any age, and symptoms vary by age of presentation. Younger children may present with failure to thrive and frequent vomiting; whereas older children and adults may have symptoms including food impaction, dysphagia, and heartburn. Eosinophilic proctocolitis presents with blood and mucus in the stools of young infants who are often exclusively breast fed but exposed to cow’s milk or soy proteins in maternal milk.

Mixed IgE FA diseases can occur, for example, in eosinophilic esophagitis or atopic dermatitis (AD), in which FA can be demonstrated by elimination and reintroduction diets, but IgE to the food may only be present a portion of the time. Some people refer to these conditions as IgE-associated conditions because it is unclear whether the IgE (when detected) plays a pathologic role. It may be that IgE is acting through antigen-presenting cells and driving facilitated antigen presentation to T cells, which drive Th2 responses and recruitment of eosinophils to the affected tissue. Frequently, eosinophilic gastrointestinal diseases may occur together with AD and that, indeed, individuals can be affected by both IgE-mediated FA and mixed or non-IgE allergic conditions.

EPIDEMIOLOGY
There are both study limitations and methodologic problems that influence our estimation of the incidence and prevalence of FAs. The majority of studies that document the prevalence of egg allergy, milk allergy, and peanut allergy (PA) occur in Western countries, and, to our knowledge, there are no published studies that examined FA at a global level. There is very little knowledge about FA in the developing world, although it seems to be reported far less frequently. There are methodologic differences that explain different results that have been obtained in different surveys. Whereas double-blind, placebo-controlled food challenges (DBPCFC) are the criterion standard, these are performed in few studies. Other surveys use FA questionnaires (generally unvalidated), skin prick test (SPT) responses, or IgE sensitization as markers of FA. However, neither correlates with FA, and it is remarkable that, in countries such as Ghana, for example, where the prevalence of PA is much lower, IgE positivity to peanut is extremely high compared with Western countries. This appears to be due to cross-reactive low-affinity antibodies to carbohydrate determinants.

In the United States, FAs are thought to occur in approximately 6% to 8% of infants and preschool children. Egg and milk allergies are the most common FAs in most countries and cultures. However, a meta-analysis of 51 articles from different countries showed that the self-reported prevalence of allergy varied from 0.2% to 7% for egg and from 1.2% to 17% for milk. Allergy determined by challenges was estimated to be much lower, which ranged from 0% to 1.7% for egg, and 0% to 3% for milk. The prevalence and rise of PA has been greatest in Western countries. PA is much less common in certain countries, for example, Israel, where sesame seed allergy is more common. Mustard allergy is more commonly reported in France, whereas buckwheat and wheat allergies are most commonly reported in Japan. Generally, the most common allergens in childhood include egg, milk, peanut, tree nuts, wheat, soy, fish, shellfish, and sesame. Fish and shellfish allergies do occur in childhood but are more prevalent in adolescents and adults. If pollen-food syndrome is included, in which IgE to pollens such as birch cross...
react with food allergens, then the prevalence of FA is considerably higher. A recent study showed that between 1.8% and 4.1% of adults in the United Kingdom may have pollen-food syndrome and that as many as 50% to 90% of those with birch pollen allergy may be affected. In general, the majority of children outgrow their milk, egg, soy, or wheat allergies, whereas peanut and tree nut allergies are typically more persistent. The age at which a child will outgrow a milk, egg, soy, or wheat allergy varies from study to study based on the phenotypes of the patients studied. For example, in tertiary care centers where children were seen with a more-severe phenotype of egg and milk allergies accompanied by much higher IgE titers, a much lower rate of cow’s milk and egg allergies resolution was seen, with substantial allergy that persisted into adolescence.

**PREVENTION**

Prevention of FA remains a controversial topic. Prolonged exclusive breast feeding has long been supported as a measure to prevent FAs, although there is little evidence that this strategy is effective. Given that careful elimination diets have failed to prevent the development of FAs in children, the strategy of exposing young infants to food allergens is now receiving attention. An ecological study that compared the prevalence of PA in Jewish children in the United Kingdom and Israel found a 10-fold increase in FA in the UK primary school children compared with the Israeli children. The study also found that UK infants were generally avoiding peanuts completely in the first year of life, whereas Israeli infants were consuming peanut snacks on a regular basis as of 4 to 6 months of age. Studies are now focusing on the early introduction of an allergen into the infant’s diet to induce oral tolerance and to prevent the development of FAs. The Learning Early About Peanut Allergy study is of 640 infants, ages 4 to 11 months, at high risk who are randomized to complete avoidance of or to high-level exposure to peanut protein until the age of 5 years to see which is the better strategy to prevent PA. The Enquiring About Tolerance study is randomizing infants who are both at normal risk and at high risk of developing FAs at 3 months of age into either continued exclusive breast feeding or continued breast feeding, together with the early introduction of complementary foods, including food allergens.

**DIAGNOSIS OF FA**

A detailed medical history is critical to the evaluation of the patient with suspected FA. The medical history can aid the proper identification of suspected food allergen(s) and limit the diagnostic evaluation to the allergen(s) most likely associated with symptoms. Foods that consistently elicit symptoms of FA should be the focus of diagnostic evaluations because foods that have been historically tolerated and have been eaten on multiple occasions are less likely to be causal foods. However, clinicians should also consider ingestion of hidden or unidentified food allergens as factors that may obscure the dietary history. Other historical factors, including patient characteristics such as underlying comorbid conditions (eg, asthma), activities proximate to ingestion of the causative food (eg, exercise), dose, and/or preparation of the causative food, may play a role in the clinical presentation and severity of reactions to foods.

**Diagnosis of IgE-mediated reactions**

IgE-mediated allergic reactions may involve 1 or multiple organ systems and typically occur immediately to a few minutes or hours after ingestion of the causative food. The majority of IgE-mediated food reactions involve skin manifestations, such as urticaria, erythema, or angioedema. Laboratory allergy testing,
including SPT and/or serum IgE testing, should be used to aid the accurate diagnosis of IgE-mediated FA; however, the clinician should be aware that a positive test does not equate to clinical reactivity.\textsuperscript{30,31} Also, the majority of IgE-mediated food reactions are caused by a limited number of foods; therefore, panel testing to a large number of allergens is not recommended.\textsuperscript{3} In an effort to reduce the risks of overdiagnosis and unnecessary dietary eliminations, allergy testing should be limited to specific foods that have been temporally related to acute symptoms or to foods that are suspected to exacerbate chronic symptoms (eg, AD). However, it has been recommended that infants who present with severe-to-moderate AD and a single FA (eg, milk, egg, peanut) should be tested for the other commonly associated food allergens\textsuperscript{14} because of the high cocreativity of milk, egg, peanut, and nut allergies in such infants.\textsuperscript{2}

**SPTs.** SPTs can be performed in the office setting and are a safe, effective method of detecting specific IgE antibodies.\textsuperscript{31,32} A positive SPT only reflects the presence of specific IgE bound to the surface of cutaneous mast cells, not clinical reactivity or disease severity. If positive, the wheal size may aid in medical decision making because a larger wheal size may be more likely to be clinically relevant. The mean diameter wheal size can help the clinician establish the probability of clinical reactivity versus oral tolerance and determine the need for further testing (eg, oral food challenge [OFC]) or dietary manipulations (Table III).\textsuperscript{34-41} A negative SPT can be particularly useful to rule out suspected food allergens due to the relatively high negative predictive value of SPT.\textsuperscript{30} However, the clinician should note that a negative SPT result does not guarantee clinical tolerance, and, when there is a high degree of clinical suspicion, further diagnostic procedures should be used.

**Serum-specific IgE tests.** Serum specific IgE testing is another important diagnostic tool that can aid in accurate identification of causal food allergens.\textsuperscript{42-47} Serum specific IgE testing is particularly useful for patients who cannot discontinue antihistamine therapy or for those with extensive skin disease or dermatographism.\textsuperscript{31} Although specific IgE results can neither definitively rule out nor rule in clinical FA, predictive values for a limited number of foods have been established (Table III). Generally, higher specific IgE levels are more likely to be associated with clinical reactivity, but the predictive value of specific IgE levels varies across patient populations and may be related to other factors, such as the patient’s age, race and/or ethnicity, and time since last ingestion of the suspected allergen.\textsuperscript{43,46-50} The history of clinical reactivity, along with results of other diagnostic tests are useful adjunctive tools when specific IgE testing is negative or below the established positive predictive value thresholds (Table III).\textsuperscript{21} It is important to note that the predictive curves have been established by using the ImmunoCAP platform (Phadia, Uppsala, Sweden) and that investigators have shown a discordance among specific IgE measurements when using other technologies.\textsuperscript{51}

**Component-resolved diagnostic testing.** Component-resolved diagnostic testing uses allergenic proteins derived from recombinant DNA technology or purification from natural sources to identify the patient’s specific IgE reactivity to recombinant allergenic proteins rather than whole allergens.\textsuperscript{72} Investigations of component-resolved diagnostic testing for a few allergens, such as peanut and hazelnut, have shown promising results.\textsuperscript{53-57} However, it is not routinely recommended for the diagnosis of FA. Analysis of results of recent investigations suggests that component-resolved diagnostic tests could potentially enhance diagnostic accuracy and provide insight regarding severity risks; however, studies have been limited to a few foods, and results have varied, depending on geographic region and population age.\textsuperscript{58-61} Whole blood basophil activation testing has recently been shown to enhance diagnostic accuracy for PA, which may substantially reduce the need for OFC.\textsuperscript{62}

**OFCs.** The types of OFCs include open (unmasked), single blind, with or without placebo, and DBPCFC. The DBPCFC is the criterion standard and is the most rigorous type of challenge. However, an open OFC is the criterion standard for establishing tolerance and should follow a negative DBPCFC.\textsuperscript{63} Although DBPCFCs reliably predict clinical reactivity, they are labor- and time-intensive procedures. Single-blind and open OFCs are frequently used for clinical use. For a diagnosis of IgE-mediated FA, graded dosing during OFC is recommended regardless of the type of challenge conducted. Graded dosing minimizes the risks of severe allergic reaction and identifies the lowest provoking dose (dose threshold). Example protocols for OFCs can be found in a recently published workgroup report and the PRACTicing ALLergology (PRACTALL) consensus report.\textsuperscript{63,64}

During the diagnostic evaluation, the decision to conduct an OFC should be determined by both the patient’s history of clinical reactivity and specific IgE testing.\textsuperscript{65,66} In many cases, OFC is not prudent or necessary if the patient has an unequivocal, convincing history of clinical reactivity to a known food allergen and positive specific IgE testing (SPT or serum specific IgE). Furthermore, the patient’s history may take priority over laboratory findings because results of specific IgE testing should not be interpreted as absolute indications or contraindications for conducting an OFC. OFCs can be used to determine clinical reactivity when the history is uncertain and results of specific IgE testing (SPT or serum specific IgE) are negative or when specific

**TABLE III. Predictive value of ImmunoCAP specific IgE testing in positive or negative OFCs**

<table>
<thead>
<tr>
<th>Food</th>
<th>Serum specific IgE (kU/L)</th>
<th>SPT wheal (mm)</th>
<th>Serum specific IgE (kU/L)</th>
<th>SPT wheal (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg white</td>
<td>≥7; ≥2 if &lt;2 y old</td>
<td>≥7</td>
<td>≤2</td>
<td>≤3</td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>≥15; ≥5 if &lt;1 y old</td>
<td>≥8</td>
<td>≤2</td>
<td>≤3</td>
</tr>
<tr>
<td>Peanut</td>
<td>≥14</td>
<td>≥8</td>
<td>≤2 if history of prior reaction; ≤5 if no history of prior reaction</td>
<td>≤3</td>
</tr>
<tr>
<td>Fish</td>
<td>≥20</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*From Refs 30-33, 35-37, 58.

†Serum specific IgE measurements are based on the ImmunoCAP platform.
IgE test results are positive but below established positive predictive cutoffs for the suspected food (Table II). OFCs also can be effective in determining the development of oral tolerance during the follow-up of patients with established FA.

A discussion regarding the risks-benefits of food challenge and informed consent should be obtained before OFCs. The risk of allergic reaction, including anaphylaxis, should factor into the decision making and the benefits of conducting OFC, such as the possibility of expanding the patient’s diet if the OFC is negative. Due to the risk of life-threatening symptoms or anaphylaxis, OFC should always be conducted under the supervision of trained medical staff in a health care facility equipped to treat anaphylaxis.

MANAGEMENT OF FA

Dietary management and allergen avoidance

Strict avoidance of the allergenic food is the cornerstone of management for individuals with FA. Although this is a seemingly straight-forward recommendation, adhering to strict avoidance may be challenging. In a 2-year period, accidental ingestion of peanut has been reported in as many as 50% of children with PA, and in up to 75% within 10 years. Children younger than 5 years old may be at particular risk of having a reaction, with a recent study that showed that 72% of participants in a national peanut and tree nut allergy registry. More recent surveys have further characterized reactions on airlines and identified areas of concern that may help in educating patients with FA who are planning to fly on commercial airlines. Consistent among the surveys is that individuals who experienced reactions did not commonly inform the flight crew that they were having a reaction and that epinephrine was underadministered. Therefore, it is of primary importance to review signs and symptoms of anaphylaxis and appropriate use of epinephrine with all individuals with FA who manufactured in the United States or packaged food imported for sale and subject to the US Food and Drug Administration regulation. The ingredient must be listed in either a “Contains” statement or the common name must be embedded in the ingredients label. FALCPA does not apply to “may contain” labeling, which is voluntary. Additional information regarding label reading may be found on the Food Allergy Research and Education Web site at www.foodallergy.org/food-labels.

Individuals allergic to foods outside of the 8 most common allergens may have more difficulty with ingredient label interpretation. Certain foods, for example, sesame seed, may not be listed directly on the ingredient label. “Spices” or “natural flavors” may include a multitude of foods or food products not included in FALCPA. It is especially important for individuals allergic to foods outside of those covered under FALCPA to contact manufacturers for clarification on products when listing is not certain.

Traveling

Traveling may also present a particular challenge. With individual differences in labeling laws and regulatory oversight around the world, it is important for individuals with FA to take special precautions when traveling abroad. It is recommended that patients and families learn the names of the food allergens in the foreign language, have a written statement, which is shown to the hotel and restaurant staff, that states that the individual cannot eat the named food(s) and that the food(s) can cause a severe reaction. Many embassies will provide this translation service.

Air travel also is a particular challenge for the patient with FA and creates significant anxiety for many individuals with FA and their families. Sicherer et al were the first to report on food-induced allergic reactions during commercial flight and presented self-reported data from participants in a national peanut and tree nut allergy registry. More recent surveys have further characterized reactions on airlines and identified areas of concern that may help in educating patients with FA who are planning to fly on commercial airlines. Consistent among the surveys is that individuals who experienced reactions did not commonly inform the flight crew that they were having a reaction and that epinephrine was underadministered. Therefore, it is of primary importance to review signs and symptoms of anaphylaxis and appropriate use of epinephrine with all individuals with FA who
are planning to travel and remind them to inform the flight crew in case of concern for an allergic reaction. Greenhawt et al\textsuperscript{2,4} reported that significantly fewer persons who had reactions on flights had the following characteristics: (1) had a personal source of epinephrine, (2) had made a specific request of the airline, and (3) had performed personal “risk-mitigating behaviors.” Although the “risk-mitigating behaviors” have not been proven to effectively minimize allergen exposure, the investigators suggest that these measures are likely to minimize passenger anxiety.\textsuperscript{3} The 8 “risk-mitigating behaviors” are (1) making any request of the airline, (2) requesting a buffer zone, (3) requesting an announcement that passengers not eat peanut and/or tree nut-containing foods, (4) requesting a peanut-and/or tree nut-free meal, (5) wiping their tray table, (6) bringing their own food from home, (7) avoiding use of an airline-provided pillow, and (8) avoiding use of an airline-provided blanket. Patients with FA who are traveling with an airline should be reassured that peanut is unlikely to aerosolize.

**Cross-contact.** Cross-contact may occur during meal preparation or food packaging, and refers to inadvertent transfer from a food that contains an allergen to a food that does not contain the allergen. Fleischer et al\textsuperscript{76} reported that 15.1% of reactions in their cohort of children younger that age 5 years occurred secondary to cross contact. Challenges for individuals with FA and their families include interpreting “may contain” statements, preparing safe foods at home, and eating food prepared by others (eg, school cafeteria, restaurant, relative’s house). The most common phrasing states “may contain [allergen],” “manufactured on shared equipment with [allergen],” and “manufactured in the same facility with [allergen].”\textsuperscript{67,74} Rather than informing the consumer that the ingredient is within the product, this labeling is often interpreted to mean that the food may or may not have inadvertently entered into the food product in question, which creates ambiguity and anxiety for some. One study showed that 17% of manufactured items in the United States contained precautionary labels\textsuperscript{75} and that 65% of products in Australia may carry such warnings.\textsuperscript{76} It has been reported that the labeling is often ignored,\textsuperscript{77,78} and there are results of studies that indicate that the type of wording used influences whether or not the product is avoided. Within the population with FA, adolescents and young adults may be least likely to avoid foods with such labeling, with 42% of participants stating that they purposefully ingest foods with a label that states “may contain.”\textsuperscript{79}

The significance of small amounts of cross-contact and the need for avoidance of foods with precautionary labeling rely on knowledge of threshold levels of reactivity for individual allergens. Reference doses for threshold levels of reactivity have been suggested,\textsuperscript{27} but standards have not been adopted by the US Food and Drug Administration. Investigators have tested products with “may contain” labeling for milk, egg, and peanut, and found that 5.3% of products with advisory labeling contained detectable amounts of these allergens.\textsuperscript{81} Products purchased from small companies versus large companies were more likely to have contaminated products (5.1% vs 0.75%). Given that individual threshold doses vary widely for consumers with allergy, the consensus expert recommendation is to avoid products with “may contain” labeling.\textsuperscript{27}

**Eating outside of the home.** Minimization of cross-contact at restaurants requires communication and vigilance on behalf of the individual with FA or his or her guardian. Cross-contact may be more common at a buffet, ice cream parlor, bakery, Asian restaurant (which commonly uses peanut and tree nut products), and seafood restaurant, and with deep-fried foods (oil may be reused for different foods, which leads to contamination).\textsuperscript{82} It is recommended to talk with the manager and the waiter, present a “chef card” (Figure 1), order simple foods (ie, few ingredients), and avoid fried foods. Preparing children and adolescents for FA management away from home starts with initiating supervised self-management techniques when developmentally appropriate.

**Dietary supplementation.** Avoidance and appropriate nutritional supplementation often require the coordinated efforts of a medical team, including a physician, nurse, and registered dietitian. Examples of overly restrictive diets that led to nutritional deficiency have been reported in the literature,\textsuperscript{63-65} which emphasizes the importance of appropriate use of currently available diagnostic tests and food challenges when needed to ensure appropriate diagnosis. Even in the absence of unnecessary avoidance, children with FA may be smaller than their peers without FA. Flammario et al\textsuperscript{85} followed children who received dietary education and appropriate supplementation, and found that, despite these interventions, children with FA were smaller for their age than were controls.\textsuperscript{86} There is no clear explanation for this difference, although the investigators hypothesize that intestinal absorption may differ based on ongoing allergic inflammation or higher protein and energy needs of children with moderate-to-severe AD, which is supported by findings from other investigators.\textsuperscript{87}

Although growth deficiency may be seen in any child with FA, children with cow’s milk allergy are particularly at high risk secondary to loss of a vital nutrient source for growth and development. Christie et al\textsuperscript{88} reported that children with a cow’s milk allergy or with 2 or more FAs were statistically shorter than their peers without FA and were at a greater risk of having inadequate calcium intake. Children allergic to cow’s milk also are at a higher risk for osteoporosis,\textsuperscript{89} are at risk for malnutrition without adequate supplementation,\textsuperscript{90} and are at higher risk of developing rickets.\textsuperscript{91,92} For these reasons, it is recommended that children with FAs have nutritional counseling and regular growth assessments,\textsuperscript{27} and evaluation and counseling by a registered dietitian should especially be considered for children with milk allergy or with 2 or more FAs.\textsuperscript{88}

**Heated milk and heated egg.** Exceptions to the rule for complete allergen avoidance have begun to take hold for foods such as milk and egg. There is evidence that ingestion of tolerated forms of allergenic food proteins might be beneficial and safe for some FAs. As outlined within this issue of *The Journal of Allergy and Clinical Immunology: In Practice*,\textsuperscript{93} ingestion of baked and extensively heated forms of milk and egg may hasten the development of tolerance to lesser cooked or raw forms of milk and egg for some individuals with allergy. Allergenicity appears to be affected by alterations in protein conformation\textsuperscript{94} and effects on gastrointestinal absorption.\textsuperscript{95} Controlled trials are lacking, and there is no universal agreement regarding the appropriate amount of protein to be ingested or frequency of ingestion required to make a noticeable difference in acquisition of tolerance. Regardless of these limitations, the introduction of extensively heated and baked milk and egg products for those able to tolerate them appears to be safe and intuitively may improve the
quality of life for the majority of children with egg and milk allergy.

**Treatment of acute FA reactions**

Food-induced anaphylaxis is a rapidly progressive, multiorgan allergic reaction that can result in death. Prompt recognition of signs and symptoms of an allergic reaction is essential for appropriate management. Symptoms may be uniphasic, biphasic, or protracted, and may involve all organ systems. 27,96,97 Food-induced fatalities are most commonly reported from exposure to peanuts and tree nuts, but severe and fatal reactions may occur with any culprit food allergen. Fatalities are often associated with a lack of, or delayed, treatment with epinephrine. Other risk factors associated with increased mortality include teen and young adult age groups, pre-existing and/or poorly controlled asthma, concomitant use of β-blocker medications, and a previously diagnosed FA. Other factors include an absence of skin symptoms, patient’s denial of symptoms, concomitant alcohol consumption, or reliance on oral antihistamines in place of epinephrine to manage symptoms. 27,96-100

Intramuscular epinephrine is the first-line treatment in all cases of anaphylaxis in both inpatient and outpatient situations, and repeated epinephrine dosing should be used when symptoms progress or response is suboptimal. 27,96,97 Self-injectable epinephrine must be readily available to patients with IgE-mediated FA, and patients must be instructed on the importance of its use and self-administration. Patients also must be educated on how and when to use an autoinjectable epinephrine device and when to seek immediate medical attention.

Adjunctive therapy for acute IgE-mediated allergic reactions includes bronchodilators and antihistamines (H1 blockers) in both inpatient and outpatient settings. Oxygen supplementation, volume replacement, pressors, corticosteroids, and H2 blockers also may be administered in inpatient or emergency department settings. 21,96 It is particularly important to note that bronchodilators should be prescribed and readily available to patients with concomitant asthma, regardless of severity because acute IgE-mediated allergic reactions may result in significant respiratory symptoms. Volume replacement is the recommended treatment for acute management of patients with FPIES, a medical emergency with up to a 15% risk of hypovolemic shock. Vigorous intravenous hydration with rapid normal saline solution boluses should be used. Epinephrine may be used in cases of severe hypotension but is not helpful as a first-line treatment. 101 A single dose of intravenous methylprednisolone 1 to 2 mg/kg may be used for some patients with protracted symptoms, although efficacy has not been established. In milder reactions, oral rehydration may be possible. 102 In protocollitis and enteropathy, symptoms are usually chronic, and there is low risk for acute reactions.

**Written emergency action plans and medical alert jewelry.** All patients with FA should have a written emergency treatment plan. 27,103 Treatment protocols should be designed to prevent delays in recognition and treatment of symptoms. These plans should be simple so that symptoms can be recognized and treated quickly and appropriately. Commonly used action plans are available at [http://www.foodallergy.org/document.doc?id=234](http://www.foodallergy.org/document.doc?id=234) and [http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Libraries/Anaphylaxis-Emergency-Action-Plan.pdf](http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Libraries/Anaphylaxis-Emergency-Action-Plan.pdf). FPIES is underrecognized and frequently mismanaged; therefore, a letter that describes manifestations of FPIES and management of acute reactions should be provided to patients. Patients should be instructed to present this letter to medical personnel on arrival to the medical facility. A template of an FPIES emergency letter may be found in an article by Sicherer et al. 101 Medical alert jewelry should be considered for patients at risk for severe allergic reactions and for certain populations, such as children or other individuals who may not be able to verbalize that they are experiencing an allergic reaction. Also, medical alert jewelry can potentially prompt first responders to initiate appropriate emergency medical treatment if the patient is found unconscious or unable to communicate.

**Care at school.** Caring for the child with FA includes having a familiarity with national and state laws regarding FA preparedness at school. In October of 2013, the Centers for Disease Control and Prevention published the first national comprehensive guidelines for school FA management. The voluntary national guidelines were developed to “provide practical information for parents, district administrators, school administrators and staff, and early childhood education program administrators and staff to develop or strengthen plans for food allergy management and prevention.” 104 A link to the guidelines may be accessed at [www.cdc.gov/healthyouth/foodallergies/](http://www.cdc.gov/healthyouth/foodallergies/). Many states have adopted guidelines for the care of children with FAs. A list of these states may be accessed at the Food Allergy Research and Education (FARE) website [www.foodallergy.org](http://www.foodallergy.org).

**TABLE IV. Web-based resources**

<table>
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<th>FA resources</th>
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<td>Eosinophilic esophagitis</td>
<td><a href="http://www.apfed.org">www.apfed.org</a></td>
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<td>The Children’s Hospital of Philadelphia Center for Pediatric Eosinophilic Disorders</td>
<td><a href="http://www.chop.edu/service/center-for-pediatric-eosinophilic-disorders">www.chop.edu/service/center-for- pediatric-eosinophilic-disorders</a></td>
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<td>Cincinnati Center for Eosinophilic Disorders</td>
<td><a href="http://www.cincinnatichildrens.org/service/c/eosinophilic-disorders/">www.cincinnatichildrens.org/service/c/eosinophilic-disorders/</a></td>
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<td>North American Society for Pediatric Gastroenterology, Hepatology and Nutrition</td>
<td><a href="http://www.naspgan.org">www.naspgan.org</a></td>
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<td>FPIES</td>
<td><a href="http://www.fpiesfoundation.org">www.fpiesfoundation.org</a></td>
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<td>The FPIES Foundation</td>
<td><a href="http://www.iaaffpe.org">www.iaaffpe.org</a></td>
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<td>International Foundation for Food Protein Enterocolitis</td>
<td><a href="http://www.foodproteinenterocolitis.org">www.foodproteinenterocolitis.org</a></td>
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<td>Celiac disease</td>
<td><a href="http://www.celiac.org">www.celiac.org</a></td>
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<td>Celiac Disease Awareness Campaign</td>
<td><a href="http://www.celiac.nih.gov">www.celiac.nih.gov</a></td>
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<td>Celiac Disease Foundation</td>
<td><a href="http://www.celiac.org">www.celiac.org</a></td>
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Education Web site (http://www.foodallergy.org/laws-and-regulations/guidelines-for-schools). Typical advice within the guidelines includes instructions on recognition of the signs and symptoms of anaphylaxis, safe and easy access to autoinjectable epinephrine, recommendations for minimizing food in the classroom, and proper cleaning techniques in the lunchroom to minimize inadvertent allergen contact. Schools should be encouraged to maintain usual cleaning techniques with a standard cleanser, and children should wash hands with either hand wipes or soap and water. Perry et al. showed that household cleaners and commercial wipes effectively remove peanut allergen, whereas tables washed with dishwashing liquid left residual low concentrations of peanut allergen. The same study showed that commercial wipes, liquid soap, and bar soap removed all traces of peanut protein from hands, whereas water alone or antibacterial hand sanitizer alone left detectable peanut residue.

Results of 2 studies showed that life-threatening reactions occur after ingestion rather than inhalation or contact in the overwhelming majority of cases. Therefore, attention should focus on minimization of ingestion. Foods such as peanut butter are not aerosolized, rather the odor results from airborne volatile organic compounds that are not allergenic. Aerosolization of food proteins may result with cooking or processing, which may lead to respiratory reactions and skin symptoms, which may more commonly occur with foods such as shellfish, finned fish, and milk.

The School Access to Emergency Epinephrine Act was signed into law on November 13, 2013. The law encourages schools to stock autoinjectable epinephrine at school that is not specifically labeled for 1 child. As many as 25% of food-induced allergic reactions at school may occur with children not previously diagnosed with an FA, and 16% to 18% of school-age children with FA experienced a reaction in the school setting, which underscores the importance of educating school personnel on the recognition of a life-threatening allergic reaction and having stock autoinjectable epinephrine at schools to use if needed.

Allowing children to self-carry autoinjectable epinephrine is typically left to the discretion of the guardian and the health care provider. There are no established guidelines that define when a child should be allowed to carry his or her own autoinjectable epinephrine, but, at a bare minimum, the child with an FA should verbalize understanding to the health care provider the following, without prompting, (1) symptoms of an allergic reaction and (2) symptoms that would require use of autoinjectable epinephrine; and should demonstrate (3) appropriate use of an autoinjectable epinephrine trainer. Managing FAs in college creates a new challenge and may be particularly anxiety provoking for the adolescent with FA who is preparing to leave home. Food Allergy Research and Education recommends communicating directly with the food services director, providing emergency treatment plans, discussing signs and symptoms of anaphylaxis with roommates, and consulting the campus health clinic. A list of numerous

### Food Allergy Patient/Provider Checklist

**Did we:**

- verify that the family and/or child had auto-injectable epinephrine at the visit?
- ask if the child is carrying auto-injectable epinephrine.
- verify the auto-injectable device is intact.
- double-check the expiration date on the auto-injectable device.
- double-check the dose of the auto-injectable device and the patient’s weight.

- demonstrate appropriate use of the auto-injectable epinephrine device?
- ask the child’s caregiver to demonstrate appropriate use of the auto-injectable epinephrine device?
- explain to the family their responsibility for always carrying auto-injectable epinephrine?
- have the child demonstrate how to use an auto-injectable epinephrine device (if developmentally appropriate)?
- ask the child to describe symptoms of anaphylaxis that would require the use of auto-injectable epinephrine?
  - the previous 2 questions are more important if:
    - the child has had more than 1 previous systemic allergic reaction.
    - the child has experienced severe of life-threatening anaphylaxis.
    - anaphylaxis is triggered by peanut or a tree nut.
    - the child had a severe reaction from a very small amount of ingested allergen.
    - the child has persistent asthma.
- if the child has asthma, specifically discuss the importance of control of asthma symptoms in order to reduce the likelihood of severe or fatal anaphylaxis.
- review a Food Allergy Action Plan?
- provide an updated Food Allergy Action Plan if it has been more than one year?
- verify and/or recommend a medical ID bracelet?
- provide avoidance handouts?
- refill prescriptions?

### FIGURE 2. Food Allergy Patient and/or Provider Checklist. Recommended items to review with new and follow-up patients with FA.
Web-based resources is given in Table IV; a comprehensive checklist of topics to be covered in a yearly visit for a child with FA is covered in Figure 2.

CONCLUSIONS

Although we are currently making advances in finding a cure for FA, safe and effective management relies on proper diagnosis and avoidance of food allergens that may trigger a reaction. Diagnosis is reliant on taking a complete and thorough history of the reaction of concern and ordering directed testing, led by clinical suspicion. OFCs are helpful in establishing the diagnosis of FA and should be performed when test results are inconclusive and/or it is believed that tolerance has developed. Providing comprehensive care to children with FA includes being knowledgeable about labeling laws, appropriate environmental control measures, and federal and state guidelines established for keeping children safe with FA in environments outside of the home. In addition, it is imperative that patients and guardians are educated regarding recognition of an allergic reaction and that they understand how to treat a reaction should accidental ingestion occur.

REFERENCES

44. Garcia-Ara MC, Boyano-Martinez MT, Diaz-Pena JM, Martin-Munoz MF, Martin-Esteban M. Cow’s milk-specific immunoglobulin E levels as predictors


