NIAID-Sponsored 2010 Guidelines for Managing Food Allergy: Applications in the Pediatric Population

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KEY WORDS

food allergy, food hypersensitivity, infants, children, guidelines, anaphylaxis

ABBREVIATIONS

NIAID—National Institute of Allergy and Infectious Diseases

IgE—immunoglobulin E

DBPCFC—double-blind, placebo-controlled food challenge

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abstract

Data from many studies have suggested a rise in the prevalence of food allergies during the past 10 to 20 years. Currently, no curative treatments for food allergy exist, and there are no effective means of preventing the disease. Management of food allergy involves strict avoidance of the allergen in the patient's diet and treatment of symptoms as they arise. Because diagnosis and management of the disease can vary between clinical practice settings, the National Institute of Allergy and Infectious Diseases (NIAID) sponsored development of clinical guidelines for the diagnosis and management of food allergy. The guidelines establish consensus and consistency in definitions, diagnostic criteria, and management practices. They also provide concise recommendations on how to diagnose and manage food allergy and treat acute food allergy reactions. The original guidelines encompass practices relevant to patients of all ages, but food allergy presents unique and specific concerns for infants, children, and teenagers. To focus on those concerns, we describe here the guidelines most pertinent to the pediatric population. *Pediatrics* 2011;128:955–965

Food allergy is a serious public health problem that affects people of all ages, but the natural history of the disease creates considerations exclusive to the pediatric population. Examples of such considerations are introduction of solid foods in infants and development of tolerance during childhood. Data from many studies have indicated a rise in the prevalence of food allergies during the past 10 to 20 years.^{1,2} Currently, no treatment for food allergy exists. Managing the disease involves strict dietary avoidance of the allergen and treatment of symptoms. Diagnosis and management of the disease can vary between clinical practice settings.

To harmonize best clinical practices across medical specialties, the National Institute of Allergy and Infectious Diseases (NIAID) sponsored development of clinical guidelines for the diagnosis and management of food allergy in the United States.³ An expert panel and coordinating committee representing 34 professional organizations (including the American Academy of Pediatrics), federal agencies, and patient advocacy groups developed the guidelines during a 2-year period. The guidelines were drafted by using a comprehensive, independent literature review and evidence report on the state of the science in food allergy in combination with expert clinical opinion.

Here we summarize the content of the guidelines most pertinent to the pediatric population. Readers of this summary are encouraged to review the original guidelines document,³ which has a comprehensive reference list and explicitly defines the evidence levels of individual recommendations. The guidelines did not address public health issues such as managing food allergy in schools or restaurants.⁴

FOOD ALLERGY: DEFINITION, PREVALENCE, AND COEXISTING CONDITIONS

A food allergy is an adverse health effect arising from a specific immune response that occurs reproducibly after exposure to a given food. Food allergy includes conditions associated with immunologic reactivity that may be either immunoglobulin E (IgE)-mediated or non-IgE-mediated. In contrast, reproducible but nonimmunologic adverse reactions, such as the inability to digest lactose, are food intolerances. A diagnosis of IgE-mediated food allergy requires both sensitization, meaning the presence of allergen-specific IgE, and clinical symptoms after exposure to the allergen.

The incidence and prevalence of food allergy is difficult to measure, in part because methods for reporting food allergy vary. In a meta-analysis by Rona et al,⁵ the overall prevalence of food allergy to cow's milk, egg, peanut, fish, or crustacean shellfish was 12% in children and 13% in adults when assessed by self-reported symptoms. This figure compares to a much lower value of 3% for adults and children combined when assessed by self-reported symptoms plus sensitization or by double-blind, placebo-controlled food challenge (DBPCFC).

Children with food allergy are ~2 to 4 times more likely to have related conditions such as asthma (4.0-fold), atopic dermatitis (2.4-fold), and respiratory allergies (3.6-fold) compared with children without food allergy.¹ However, estimates of comorbidities can be subject to selection bias. Food allergy may coexist with eosinophilic esophagitis or exercise-induced anaphylaxis.

In patients with asthma, coexistence of food allergy may be a risk factor for severe asthma exacerbations.⁶⁻⁹ Moreover, a high prevalence of asthma has

been reported among people who died as a result of food-induced anaphylaxis.^{10,11}

RISK FACTORS FOR DEVELOPING FOOD ALLERGY AND SEVERITY OF REACTIONS

Patients defined as at risk for food allergy have a biological parent or sibling with a history of allergic rhinitis, asthma, atopic dermatitis, or food allergy.¹²⁻¹⁴ Children at high risk for developing food allergy have preexisting severe allergic disease (significant atopic dermatitis or asthma) or family history of food allergy.³

Up to 37% of children younger than 5 years with moderate-to-severe atopic dermatitis have IgE-mediated food allergy.¹⁵ Whether or how food allergy can exacerbate atopic dermatitis is unclear.

The severity of allergic reactions to foods is multifactorial and variable.^{9,11,16,17} The severity of a reaction cannot be accurately predicted by the severity of past reactions, by food-specific IgE level, or by wheal size in a skin-prick test.³ The factor most commonly identified with severe reactions is coexistence of asthma, especially with peanut or tree nut allergy.

Diet in At-Risk Children

Patients at risk for developing food allergy do not need to limit exposure to potential nonfood allergens (eg, dust mites or pollen), and they do not need to limit exposure to foods that may be cross-reactive with the 8 major food allergens in the United States (cow's milk, egg, peanut, tree nuts, soy, wheat, fish, and crustacean shellfish). There is insufficient evidence to recommend routine food allergy testing before introducing highly allergenic foods (such as cow's milk, egg, and peanut) in children at high risk of developing food allergy.³ Nevertheless, there may be value in food allergy eval-

uations that include some diagnostic testing and an oral food challenge for patients with certain risk factors, such as having a sibling with peanut allergy^{18,19} or evidence of another food allergy.

Although conclusive data on the subject are lacking, if a child is younger than 5 years and has persistent atopic dermatitis, there can be benefit to determining whether the child is allergic to a food. Early diagnosis can lead to better management of food allergy and reduce the risk of exposure to food antigens. However, testing can be time-consuming and costly. Children younger than 5 years with moderate-to-severe atopic dermatitis should be considered for food allergy evaluation for cow's milk, egg, peanut, wheat, and soy if the child has persistent atopic dermatitis despite optimized management and topical therapy or the child has a reliable history of an immediate reaction after ingestion of a specific food. However, because false-positive tests for food allergy are common, care should be taken to ensure that children are clinically allergic and not just sensitized (as judged by the presence of a positive skin-prick test result or specific IgE level) to a food before dietary removal.

Diet During Pregnancy and Infancy

Restricting maternal diet during pregnancy or lactation is not recommended as a strategy for preventing the development or clinical course of food allergy. Because of the benefits of breastfeeding, it is recommended that all infants, including those with a family history of atopic disease, be exclusively breastfed until 4 to 6 months of age unless breastfeeding is contraindicated for medical reasons. Using soy infant formula instead of cow's milk infant formula is not recommended as a strategy for preventing food allergy in at-risk infants.

Use of hydrolyzed infant formulas, as opposed to cow's milk formula, may be considered as a strategy for preventing the development of food allergy in at-risk infants who are not exclusively breastfed. Cost and availability of extensively hydrolyzed infant formulas may be weighed as prohibitive factors. The preventive effects of hydrolyzed infant formulas on allergy in infants and children have varied considerably between studies. Evidence from a small number of large-population studies indicates that feeding hydrolyzed versus cow's milk infant formulas to at-risk infants may reduce, albeit to a small extent, allergy in infants and children and cow's milk allergy in infants. None of the studies showed reduction in allergy to foods other than cow's milk.^{20–23} There is no evidence to suggest that exclusive feeding with a hydrolyzed infant formula is more likely to prevent atopic disease than exclusive breastfeeding.

In infants, solid-food introduction should occur by 4 to 6 months of age. Potentially allergenic foods may be introduced any time afterward. These guidelines are in agreement with those in the American Academy of Pediatrics 2008 clinical report.²⁴

Development of Tolerance

The time course of food allergy resolution in children varies according to food and may occur during the teenage years. Most children with food allergy eventually tolerate cow's milk, egg, soy, and wheat; far fewer will eventually tolerate peanuts, tree nuts, fish, and shellfish. Generally, risk factors for persistence of food allergy are the presence of high initial levels of specific IgE antibodies, additional atopic disease, or allergy to more than 1 food. For many food-allergic patients, specific IgE antibodies to foods appear within 2 years after birth. Levels may increase or decrease. In children, a de-

crease in food-specific IgE levels is often a marker for the onset of tolerance, although with some foods, allergy persists despite a decrease in specific IgE. Similarly, a reduction in wheal size after a skin-prick test may be a marker for the onset of tolerance, although skin-prick test response can remain positive long after the food is safely consumed.³

DIAGNOSIS OF IgE-MEDIATED FOOD ALLERGY

IgE-mediated food allergy should be suspected in children who have experienced anaphylaxis or the symptoms listed in Table 1 within minutes to hours of ingesting food, especially if the symptoms occur repeatedly or in young children.³ Food allergy should also be suspected in infants, young children, and selected older children who have been diagnosed with moderate-to-severe atopic dermatitis, eosinophilic esophagitis, gastritis, enteritis or enterocolitis, enteropathy, or allergic proctocolitis. With IgE-mediated food allergy, allergic reactions can occur within minutes to a few hours.³ Mixed IgE- and non-IgE-mediated food allergy, such as eosinophilic esophagitis, should be suspected when symptoms affect the gastrointestinal tract, are of a more chronic nature, do not resolve rapidly, and are not closely associated with ingestion of an offending food.

Although medical history and physical examination are mainstays in diagnosing food allergy, they are not sufficient for diagnosis and should be considered in combination with diagnostic testing. Skin-prick tests or measurement of specific IgE level are recommended for identifying foods that may provoke allergic reactions, but the tests (either alone or in combination) are not diagnostic of food allergy. Neither intradermal testing nor measurement of total serum IgE level is recom-

TABLE 1 Symptoms of Food-Induced Allergic Reactions

Target Organ	Immediate Symptoms	Delayed Symptoms
Cutaneous	Erythema	Erythema
	Pruritus	Flushing
	Urticaria	Pruritus
	Morbilliform eruption	Morbilliform eruption
	Angioedema	Angioedema
Ocular		Ecematous rash
	Pruritus	Pruritus
	Conjunctival erythema	Conjunctival erythema
	Tearing	Tearing
	Periorbital edema	Periorbital edema
Upper respiratory	Nasal congestion	
	Pruritus	
	Rhinorrhea	
	Sneezing	
	Laryngeal edema	
	Hoarseness	
	Dry staccato cough	
Lower respiratory	Cough	Cough, dyspnea, and wheezing
	Chest tightness	
	Dyspnea	
	Wheezing	
	Intercostal retractions	
	Accessory muscle use	
	Angioedema of the lips, tongue, or palate	
Gastrointestinal (oral)	Oral pruritus	
	Tongue swelling	
Gastrointestinal (lower)	Nausea	Nausea
	Colicky abdominal pain	Abdominal pain
	Reflux	Reflux
	Vomiting	Vomiting
	Diarrhea	Diarrhea
		Hematochezia
		Irritability and food refusal with weight loss (young children)
Cardiovascular	Tachycardia (occasionally bradycardia in anaphylaxis)	
	Hypotension	
	Dizziness	
	Fainting	
	Loss of consciousness	
Miscellaneous	Uterine contractions	
	Sense of "impending doom"	

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mended for use in diagnosing food allergy. The atopy patch test should not be used in the routine evaluation of food allergy.

Verification of clinical reactivity requires well-designed oral food-challenge testing.^{25–31} The DBPCFC is the gold standard for diagnosis, particularly in research studies. DBPCFC can be useful for ruling out foods that do not cause allergy; in several studies that used DBPCFC, only approximately

one-third of the suspected foods were confirmed to be allergenic. Open food challenges can help identify which food(s) are causing an allergic reaction if the patient's history and results from diagnostic tests are not clear. Open food challenges can also be used if the child is likely outgrowing the food allergy. In older children, single-blind food challenges or DBPCFCs might be necessary to minimize patient and physician bias. In the case of postprandial

exercise-induced reactions, food challenge should be followed by exercise.³² Because of the inherent risk, an oral food challenge must be conducted at a medical facility that has onsite medical supervision and appropriate medicines and devices (Table 2).

DIAGNOSIS OF NON-IgE-MEDIATED FOOD ALLERGY

Before a diagnostic workup, it may be difficult to distinguish an IgE-mediated allergy from a non-IgE-mediated allergy on the basis of medical history and physical examination alone. A number of diagnostic tools have been suggested for use in diagnosing non-IgE-mediated reactions, including food challenges, contact dermatitis patch testing, and atopy patch tests. Food challenges are recommended for diagnosis if the clinical history and laboratory studies are not definitive and for determining when the disease has been outgrown.³ The other diagnostic tests have not been validated and are not recommended.

Eosinophilic Gastrointestinal Diseases

Skin-prick tests, specific IgE tests, and atopy patch tests may be helpful in identifying foods that are associated with eosinophilic esophagitis, but these tests alone are not sufficient for diagnosing food allergy. The role of these tests in diagnosing other eosinophilic gastrointestinal diseases has not been established.

Food Protein–Induced Enterocolitis Syndrome

Medical history and oral food challenge should be used to diagnose food protein–induced enterocolitis syndrome. However, when infants or children have experienced hypotensive episodes or multiple reactions to the same food, a diagnosis may be made on the basis of a convincing history

TABLE 2 Conducting an Oral Food Challenge⁵

Before the challenge
Suspected foods should be eliminated from the diet for 2 to 8 wk
Length of time will depend on the type of food-induced allergic reaction being examined (eg, urticaria vs eosinophilic esophagitis)
In infants, diet can be limited to a hypoallergenic formula
For exclusively breastfed infants, the suspected food can be eliminated from the mother's diet
Document any significant improvements as a result of dietary elimination
If dietary elimination has led to significant improvement, the challenge test may be carried out while the patient is on minimal or no medication for treating allergy symptoms
The test should be designed with supervision from medical personnel with experience in carrying out challenges
During the challenge
The challenge should be carried out by medical personnel with experience in performing food challenges
Oral food challenge begins with a low dose (intended to be lower than a dose that can induce a reaction)
While monitoring for any allergic symptoms, the dose is gradually increased until a cumulative dose at least equivalent to a standard portion for age is consumed
Treatment for reactions, including anaphylaxis, must be available for immediate administration

and absence of symptoms after eliminating the trigger food.

Food Protein–Induced Allergic Proctocolitis

The diagnosis of allergic proctocolitis should be made on the basis of medical history, resolution of symptoms after eliminating the causative food, and/or recurrence of symptoms after oral food challenge.

MANAGEMENT OF FOOD ALLERGY

Dietary Avoidance

Children with documented IgE-mediated or non-IgE-mediated food allergy should avoid ingesting their specific allergens. Carefully planned allergen-free diets can provide sufficient nutrients to maintain a healthy and active life. For children without documented or proven food allergy, avoiding potentially allergenic foods is not recommended as a means of managing atopic dermatitis, asthma, or eosinophilic esophagitis.

Nutritional counseling and regular growth monitoring are recommended for all children with food allergy. Children with food allergy and their caregivers should receive education and training on interpreting food labels

and recognizing food-allergen ingredients. Products with precautionary labeling, such as “this product may contain trace amounts of allergen,” should be avoided because of the small but significant risk of actual food contamination. The Food Allergy and Anaphylaxis Network (www.foodallergy.org) provides practical information on recognizing and avoiding food allergens.

Retesting

Tolerance to cow's milk and egg generally occurs at an earlier age than to peanut and tree nuts.^{33–41} Insufficient data exist to recommend specific optimal intervals for food-allergy follow-up testing. The interval depends on the food, the child's age, and the intervening medical history. Annual testing in younger children is often done for cow's milk, egg, soy, or wheat allergy. The testing interval is more commonly every 2 to 3 years for older children or those with allergy to peanut, tree nuts, fish, or crustacean shellfish.

Medications

There are currently no recommended medications for preventing IgE- or non-IgE-mediated food-induced aller-

gic reactions. Epinephrine is the mainstay for the treatment of acute, systemic allergic reactions. Use of antihistamines remains the mainstay of managing symptoms of nonsevere allergic reactions.⁵ Allergen-specific oral and sublingual immunotherapy have been used for inducing clinical desensitization to foods (for review see ref ⁴²), but this approach carries the risk of severe reactions and is not recommended for clinical practice at this time. Immunotherapy with cross-reactive allergens is not recommended for treating IgE-mediated food allergy.

Quality-of-Life Issues

Food allergy can increase anxiety and diminish quality of life for patients and their families.^{43,44} Patients and caregivers should be provided culturally and age-appropriate information on food-allergen avoidance and emergency management. As children transition into adolescence and adulthood, they have increased responsibility regarding food selection and should be counseled on strategies for avoiding potentially allergenic foods in various settings. Patients can be referred to the Consortium of Food Allergy Research's online educational program (<https://web.emmes.com/study/cofar/EducationProgram.htm>).

Egg-Containing Vaccines

Several vaccines are grown in chick embryos or embryonic tissues and contain egg protein (Table 3). However, some of these vaccines, such as measles, mumps, and rubella (MMR), are safe for patients with egg allergy. Others are either contraindicated or may be used after testing with the vaccine. There have been limited studies with results that indicate that influenza vaccines may be administered to persons with severe egg allergy under appropriate supervision depending on the ovalbumin content.⁴⁵ Approaches in-

TABLE 3 Recommendations for Administering Egg-Containing Vaccines to Egg-Allergic Patients⁵

Vaccine	Recommendation	Notes
MMR or MMRV	Safe for children with egg allergy, even those with a history of severe reactions	—
Influenza (inactivated or live-attenuated)	Not recommended for patients who have a history of severe reactions to egg or egg protein; severe reactions include a history of hives, angioedema, allergic asthma, or systemic anaphylaxis to egg or chicken proteins; less-severe or local manifestations of allergy to egg or feather are not contraindications	Live-attenuated vaccine is not licensed for use in patients with asthma ⁷²
Yellow fever	Do not administer to patients with a history of hives, angioedema, allergic asthma, or systemic anaphylaxis to egg proteins unless an allergy evaluation and testing with the vaccine are performed first	—
Rabies	Do not administer to patients with a history of hives, angioedema, allergic asthma, or systemic anaphylaxis to egg proteins unless an allergy evaluation and testing with the vaccine are performed first	1 rabies vaccine (Imovax [Sanofi Pasteur, Swiftwater, PA]) is not made in chick embryos and does not contain egg protein; this vaccine is not contraindicated in egg-allergic people

MMR indicates measles, mumps, and rubella; MMRV, MMR with varicella.

clude full or split dosing, possibly with vaccine testing.^{46–49} There have been a number of study reports that have been published or are coming that will likely change these recommendations in the next few years.

DIAGNOSIS AND MANAGEMENT OF FOOD-INDUCED ANAPHYLAXIS

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.^{50,51} IgE-mediated food-induced anaphylaxis is believed to involve systemic mediator release from

sensitized mast cells and basophils.⁵² Although prompt recognition and management of anaphylaxis are essential for a good treatment outcome,⁵³ anaphylaxis is significantly underrecognized and undertreated.^{50,54–56}

Diagnosis of Anaphylaxis

Diagnostic criteria for anaphylaxis are detailed in Table 4. The signs and symptoms of food-induced anaphylaxis are the same as those of anaphylaxis in general^{53,57–61}:

- Cutaneous symptoms such as flushing, pruritus, urticaria, and angioedema: cutaneous symptoms occur in most patients, but 10% to 20% of cases (including many fatal and near-fatal reactions) involve no cutaneous manifestations.
- Respiratory symptoms such as nasal congestion and rhinorrhea, throat pruritus and laryngeal edema, stridor, choking, wheeze, cough, and dyspnea: up to 70% of cases involve respiratory symptoms.
- Gastrointestinal symptoms such as cramping, abdominal pain, nausea, emesis, and diarrhea: up to 40% of cases involve gastrointestinal symptoms.
- Cardiovascular symptoms such as dizziness, tachycardia, hypotension, and hypotonia: up to 35% of cases involve cardiovascular symptoms.
- Anxiety, mental confusion, lethargy, and seizures.

Time Course of Food-Induced Anaphylaxis

In food-induced anaphylaxis, exposure to a food allergen is followed by a rapid onset of symptoms over minutes to several hours. Death caused by food-induced anaphylaxis can occur within 30 minutes to 2 hours of exposure^{10,11,62}

TABLE 4 Diagnostic Criteria for Anaphylaxis³

The presence of any 1 of these 3 criteria indicates that anaphylaxis is highly likely:

1. Acute onset of an illness (over minutes to several hours) involving skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula) and at least 1 of the following:
 - Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow rate, hypoxemia)
 - Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia [circulatory collapse], syncope, incontinence) or
2. ≥ 2 of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
 - Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
 - Respiratory compromise (eg, dyspnea, wheeze, bronchospasm, stridor, reduced peak expiratory flow rate, hypoxemia)
 - Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence)
 - Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting) or
3. Reduced blood pressure after exposure to a known allergen for that patient (minutes to several hours); in infants and children, reduced blood pressure is defined by the following:
 - Low systolic blood pressure (age-specific) or $>30\%$ decrease in systolic blood pressure
 - Low systolic blood pressure is defined as follows:
 - <70 mm Hg for ages 1 mo to 1 y
 - $<(70 \text{ mm Hg plus twice the age})$ for ages 1–10 y
 - <90 mm Hg for ages 11–17 y

Note that in infants and young children, hypotension may be a late manifestation of hypovolemic shock. Tachycardia, in the absence of hypotension, also may indicate shock.⁷³

and usually results from cardiorespiratory compromise.⁵⁸ Food-induced anaphylaxis also can have a milder course and resolve spontaneously.

The time course of an anaphylactic reaction may be uniphasic, biphasic, or protracted. A uniphasic reaction occurs immediately after exposure, resolves with or without treatment within the first minutes to hours, and does not recur. In a biphasic reaction, a recurrence of symptoms develops after apparent resolution of the initial reaction. Biphasic reactions have been reported to occur in 1% to 20% of anaphylaxis episodes, and they typically occur ~8 hours after the first reaction, although they have been reported to occur up to 72 hours later.^{11,63,64} A protracted reaction is any anaphylaxis episode that lasts for hours or days after the initial reaction.¹¹

Risk Factors for Anaphylaxis and Resulting Fatality

Those at the highest risk for life-threatening food-induced anaphylaxis are adolescents and young adults; people with known food allergy and a previous history of anaphylaxis; and people with asthma, especially with poorly controlled symptoms. Peanuts and tree nuts cause the majority of fatalities from food-induced anaphylaxis.^{10,11,62} Fatalities are also associated with delayed use or improper dosing of epinephrine.

MANAGEMENT OF PATIENTS AT RISK FOR ANAPHYLAXIS

Patients with the following should be prescribed an epinephrine autoinjector: a previous systemic allergic reaction; food allergy and asthma; or a known food allergy to peanut, tree nuts, fish, or crustacean shellfish. In addition, some consideration should be given to prescribing an epinephrine autoinjector for all patients with food allergy who have IgE-mediated reac-

tions, because it is impossible to predict the severity of subsequent reactions.

Patients should be verbally instructed on the proper use of epinephrine autoinjectors. They should also receive an instructional video, if available, and a written anaphylaxis emergency action plan. Patients should be instructed on the value of medical identification jewelry for easy recognition of their potential for anaphylaxis and food-allergen triggers. Patients should be told the importance of carrying epinephrine at all times and of making sure that family and friends are aware of the risks of anaphylaxis, the patient's triggers, and how to administer epinephrine. If allowed by state law, students should be advised to carry their epinephrine autoinjector at school and at all school-related events.

Patients and family members should be advised to regularly check the epinephrine autoinjector expiration dates (which expire after 1 year) and to verify that the liquid remains clear. Ideally, the prescribing physician's office should see patients annually or notify patients (or their parents or guardians) by telephone or mail that their autoinjector will soon reach its expiration date. Patients can be encouraged to register for automated pharmacy reminders for epinephrine renewal. Epinephrine autoinjectors are temperature sensitive and should be stored at room temperature to prevent degradation of the medication.

Treatment of Acute, Life-Threatening, Food-Induced Allergic Reactions

For food-induced anaphylaxis, prompt and rapid treatment with epinephrine is paramount. Delayed administration of epinephrine has been implicated in contributing to fatalities.^{10,11,16,62} Initial management of anaphylaxis should include elimination of the allergen and

intramuscular injection of epinephrine (Table 5). Autoinjector dosing for epinephrine is 0.15 mg for children who weigh 10 to 25 kg and 0.3 mg for those who weigh >25 kg. These steps should be followed by a call for an emergency medical team, placement of the patient in a recumbent position with lower extremities elevated (if tolerated), and adjunctive therapy (Table 5). If a patient responds poorly to the initial dose of epinephrine or has ongoing or progressive symptoms, repeated dosing may be required after 5 to 15 minutes.

Given their anti-inflammatory properties, systemic corticosteroids are often recommended for preventing biphasic or protracted food-induced allergic reactions, but evidence to support their use is lacking.⁶⁵

Observation Period After Food-Induced Anaphylaxis

There is no consensus in the literature regarding the optimal time duration for observing a patient who has been successfully treated for anaphylaxis before discharge. All patients who receive epinephrine for food-induced anaphylaxis should proceed to an emergency facility for observation and possibly additional treatment. A reasonable length of time for observation of most patients who have experienced anaphylaxis is 4 to 6 hours; a prolonged observation time or hospital admission is reasonable for patients with severe or refractory symptoms.^{51,61}

Discharge Plan After Treatment for Food-Induced Anaphylaxis

All patients who have experienced anaphylaxis should be sent home with (1) an anaphylaxis emergency action plan, (2) an epinephrine autoinjector (2 doses), (3) a plan for monitoring autoinjector expiration dates, (4) a plan for arranging further evaluation, and (5)

TABLE 5 Pharmacologic Management of Anaphylaxis

With the exception of epinephrine as first-line treatment, these treatments often occur concomitantly and are not meant to be sequential.

In an outpatient setting**● First-line treatment**

- Epinephrine, IM; auto-injector or 1:1000 solution
 - Weight 10 to 25 kg: 0.15 mg epinephrine autoinjector, IM (anterior-lateral thigh)
 - Weight >25 kg: 0.3 mg epinephrine autoinjector, IM (anterior-lateral thigh)
 - Epinephrine (1:1000 solution) (IM), 0.01 mg/kg per dose; maximum dose, 0.5 mg per dose (anterior-lateral thigh)
- Epinephrine doses may need to be repeated every 5–15 minutes

● Adjunctive treatment

- Bronchodilator (β_2 -agonist): albuterol
 - MDI (child: 4–8 puffs; adult: 8 puffs) or
 - Nebulized solution (child: 1.5 mL; adult: 3 mL) every 20 minutes or continuously as needed
- H_1 antihistamine: diphenhydramine
 - 1 to 2 mg/kg per dose
 - Maximum dose, 50 mg IV or oral (oral liquid is more readily absorbed than tablets)
 - Alternative dosing may be with a less-sedating second generation antihistamine
- Supplemental oxygen therapy
- IV fluids in large volumes if patient presents with orthostasis, hypotension, or incomplete response to IM epinephrine
- Place the patient in recumbent position if tolerated, with the lower extremities elevated

In a hospital-based setting**● First-line treatment**

- Epinephrine IM as above, consider continuous epinephrine infusion for persistent hypotension (ideally with continuous non-invasive monitoring of blood pressure and heart rate); alternatives are endotracheal or intra-osseous epinephrine

● Adjunctive treatment

- Bronchodilator (β_2 -agonist): albuterol
 - MDI (child: 4–8 puffs; adult: 8 puffs) or
 - Nebulized solution (child: 1.5 mL; adult: 3 mL) every 20 minutes or continuously as needed
- H_1 antihistamine: diphenhydramine
 - 1 to 2 mg/kg per dose
 - Maximum dose, 50 mg IV or oral (oral liquid is more readily absorbed than tablets)
 - Alternative dosing may be with a less-sedating second generation antihistamine
- H_2 antihistamine: ranitidine
 - 1 to 2 mg/kg per dose
 - Maximum dose, 75 to 150 mg oral and IV
- Corticosteroids
 - Prednisone at 1 mg/kg with a maximum dose of 60 to 80 mg oral or
 - Methylprednisolone at 1 mg/kg with a maximum dose of 60 to 80 mg IV
- Vasopressors (other than epinephrine) for refractory hypotension, titrate to effect
- Glucagon for refractory hypotension, titrate to effect
 - Child: 20–30 mcg/kg
 - Adult: 1–5 mg
 - Dose may be repeated or followed by infusion of 5–15 mcg/min
- Atropine for bradycardia, titrate to effect
- Supplemental oxygen therapy
- IV fluids in large volumes if patients present with orthostasis, hypotension, or incomplete response to IM epinephrine
- Place the patient in recumbent position if tolerated, with the lower extremities elevated

To instruct to patients at discharge**● First-line treatment**

- Epinephrine auto-injector prescription (2 doses) and instructions
- Education on avoidance of allergen
- Follow-up with primary care physician
- Consider referral to an allergist

● Adjunctive treatment

- H_1 antihistamine: diphenhydramine every 6 hours for 2–3 days; alternative dosing with a non-sedating second generation antihistamine
- H_2 antihistamine: ranitidine twice daily for 2–3 days
- Corticosteroid: prednisone daily for 2–3 days

IM indicates intramuscular; IV, intravenous; MDI, metered-dose inhaler.

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printed information about anaphylaxis and its treatment⁶⁶ (Table 5). Advice should be provided to the patient regarding follow-up with his or her primary health care professional within 1 to 2 weeks after a food-induced anaphylaxis event. The patient may be referred to a specialist such as an allergist or immunologist for further evaluation.

Management of Milder Acute Food-Induced Allergic Reactions in Health Care Settings

Milder forms of allergic reactions, such as flushing, urticaria, isolated mild angioedema, and symptoms of oral allergy syndrome, can be treated with H_1 and H_2 antihistamine medications.^{67,68} When antihistamines alone are given, ongoing observation and monitoring are warranted to ensure a lack of progression to more significant symptoms of anaphylaxis. If progression or increased severity is noted, epinephrine should be administered immediately. If there is history of a previous severe allergic reaction, epinephrine should be administered promptly and earlier in the course of treatment (eg, at the onset of even mild symptoms).

KNOWLEDGE GAPS AND RESEARCH PRIORITIES

In developing these guidelines, the expert panel noted several knowledge gaps and priority areas of research related to pediatric care. Published data on remission rates for specific food allergies are lacking and even contradictory. For example, Sampson³⁵ has estimated that milk tolerance develops in 80% of patients by the age of 5 years, whereas Skripak et al⁴¹ concluded that only 5% of patients were tolerant by the age of 4 and that 21% were tolerant by the age of 8. A better understanding of remission rates and time frames would help determine optimal intervals for follow-up testing. The expert

panel noted that the quality of evidence was low in regards to whether exclusive breastfeeding can help prevent atopic disease, the optimal timing of introduction of potentially allergenic foods to infants, and whether food allergy testing should precede introducing allergenic foods to children at high risk.

Both peanut allergy⁶⁹ and atopic dermatitis^{70,71} have been associated with loss-of-function mutations in the epidermal barrier protein filaggrin, which indicates that impaired skin barrier function has a role in atopic diseases. However, whether filaggrin mutations are common among pa-

tients with both atopic dermatitis and food allergy is unknown.

Although not noted in the guidelines, transitions in care, such as an adolescent leaving a pediatric clinic or a child leaving an academic center, are points of concern for the pediatric population, because continuous care is crucial for the safety of patients with food allergy.

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