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Anaphylaxis and Emergency Treatment

Hugh A. Sampson, MD

ABSTRACT. Food anaphylaxis is now the leading known cause of anaphylactic reactions treated in emergency departments in the United States. It is estimated that there are 30 000 anaphylactic reactions to foods treated in emergency departments and 150 to 200 deaths each year. Peanuts, tree nuts, fish, and shellfish account for most severe food anaphylactic reactions. Although clearly a form of immunoglobulin E-mediated hypersensitivity, the mechanistic details responsible for symptoms of food-induced anaphylaxis are not completely understood, and in some cases, symptoms are not seen unless the patient exercises within a few hours of the ingestion. At the present time, the mainstays of therapy include educating patients and their caregivers to strictly avoid food allergens, to recognize early symptoms of anaphylaxis, and to self-administer injectable epinephrine. However, clinical trials are now under way for the treatment of patients with peanut anaphylaxis using recombinant humanized anti-immunoglobulin E antibody therapy, and novel immunomodulatory therapies are being tested in animal models of peanut-induced anaphylaxis. *Pediatrics* 2003;111:1601–1608; *anaphylaxis, immunoglobulin E, anti-IgE antibodies, food hypersensitivity, elimination diet, EpiPen.*

ABBREVIATION. IgE, immunoglobulin E.

Although the death of the Pharaoh Menes in 2640 BC may be the first documented case of anaphylaxis, Portier's and Richet's work aboard the yacht of Prince Albert of Monaco is cited as the seminal work on this phenomenon.¹ Instead of observing the anticipated protective "anti-toxic" effect after the immunization of dogs with the stinging fluid of the sea anemone tentacles, the dogs died within minutes of receiving the second injection, a phenomenon that Richet termed "anaphylaxis." Only 3 years later, Scholssman reported the first case of food-induced anaphylaxis in the United States,² but it was not until 1969 that the first series of food-induced anaphylaxis in human was published.³ Now food anaphylaxis is the leading single known cause of anaphylaxis treated in emergency departments in the United States,^{4,5} a change that many believe has come about in the last 10 to 20 years.

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Food-induced anaphylaxis is a form of immunoglobulin E (IgE)-mediated hypersensitivity manifested by an abrupt onset of symptoms within minutes to hours of ingesting a food. The symptom complex results from the generation and release of a variety of potent biologically active mediators and their combined effects on target organs, including the skin, gastrointestinal tract, respiratory tract, and cardiovascular system. The majority of food anaphylactic reactions in the United States and Europe are the result of allergic reactions to peanuts, tree nuts, fish, or shellfish.

In clinical practice and the literature, the term "anaphylaxis" is used variably to connote the acute constellation of symptoms after exposure to an allergen that may or may not include hypotension, or to indicate the immunopathogenic mechanism consisting of an "immediate" IgE-mediated hypersensitivity response. The American Academy of Allergy, Asthma and Immunology defines anaphylaxis as "a collection of symptoms [see Table 1] affecting multiple systems in the body. The most dangerous symptoms include breathing difficulties and a drop in blood pressure or shock, which are potentially fatal."⁶ In this review, the term "anaphylaxis" refers to the symptom complex resulting from an IgE-mediated response to an allergen. For avoiding the confusion over the extent of symptoms that constitutes the term "anaphylaxis," a grading system is proposed to indicate "severity" (see Table 2), a concept proposed by others.⁷

PREVALENCE

The prevalence of food-induced anaphylaxis seems to vary with the dietary habits of a region. In Denmark, Sorensen et al⁸ reported 3.2 cases of ana-

TABLE 1. Clinical Signs and Symptoms of Anaphylaxis

Oral: pruritus of lips, tongue, and palate and edema of lips and tongue; metallic taste in the mouth
Cutaneous: flushing, pruritus, urticaria, angioedema, morbilliform rash, and pilor erecti
Gastrointestinal: nausea, abdominal pain (colic), vomiting (large amounts of "stringy" mucus), and diarrhea
Respiratory (major shock organ): laryngeal: pruritus and "tightness" in the throat, dysphagia, dysphonia and hoarseness, dry "staccato" cough, and sensation of itching in the external auditory canals; lung, shortness of breath, dyspnea, chest tightness, "deep" cough, and wheezing; nose, pruritus, congestion, rhinorrhea, and sneezing
Cardiovascular: feeling of faintness, syncope, chest pain, dysrhythmia, hypotension
Other: periorbital pruritus, erythema and edema, conjunctival erythema, and tearing; lower back pain and uterine contractions in women; aura of "doom"

TABLE 2. Grading of Food-Induced Anaphylaxis According to Severity of Clinical Symptoms

Grade	Skin	GI Tract	Respiratory Tract	Cardiovascular	Neurological
1	Localized pruritus, flushing, urticaria, angioedema	Oral pruritus, oral "tingling," mild lip swelling			
2	Generalized pruritus, flushing, urticaria, angioedema	Any of the above, nausea and/or emesis x's 1	Nasal congestion and/or sneezing		Change in activity level
3	Any of the above	Any of the above plus repetitive vomiting	Rhinorrhea, marked congestion, sensation of throat pruritus or tightness	Tachycardia (increase >15 beats/min)	Change in activity level plus anxiety
4	Any of the above	Any of the above plus diarrhea	Any of the above, hoarseness, "barky" cough, difficulty swallowing, dyspnea, wheezing, cyanosis	Any of the above, dysrhythmia and/or mild hypotension	"Light headedness," feeling of "pending doom"
5	Any of the above	Any of the above, loss of bowel control	Any of the above, respiratory arrest	Severe bradycardia and/or hypotension or cardiac arrest	Loss of consciousness

All symptoms are not mandatory. The severity score should be based on the organ system most affected, eg, if grade 3 respiratory symptoms are present but only grade 1 GI symptoms, then the anaphylaxis severity score would be "grade 3." **Boldface symptoms** are absolute indications for the use of epinephrine; use of epinephrine with other symptoms will depend on patient's history.

phylaxis per 100 000 inhabitants per year with a fatality rate of ~5%. In a more recent US survey, Yocum et al⁵ reported an annual incidence of food-induced anaphylaxis of 7.6 cases per 100 000 person-years and a food-induced anaphylaxis occurrence rate of 10.8 per 100 000 person-years. The figures were based on a review of the medical records of Olmsted County inhabitants followed in the Rochester Epidemiology Study from 1983 to 1987. Assuming that the prevalence of food allergy has not increased since the late 1980s and given that the US population is now 280 million, one could estimate that 30 000 food-induced anaphylactic episodes occur in the United States each year, resulting in ~2000 hospitalizations and 150 to 200 deaths. Food-induced anaphylactic reactions account for more than one third of the anaphylactic reactions treated in emergency departments and are most often attributable to peanut, tree nuts, fish, or shellfish. Pumphrey and Stanworth⁹ and Moneret-Vautrin and Kanny¹⁰ reported similar findings in the United Kingdom and France, respectively. In Italy, Novembre et al¹¹ reported that food allergy was responsible for approximately one half of severe anaphylactic episodes in children treated in emergency departments. Similarly, a survey of South Australian preschool- and school-aged children revealed a parent-reported food-induced anaphylaxis rate of 0.43 per 100 school children, which accounted for more than one half of all cases of anaphylaxis in this age group.¹² Whereas food-induced anaphylaxis accounts for one third to one half of anaphylaxis cases treated in emergency departments in North America, Europe, and Australia,^{5,9,11-15} it seems to be uncommon in countries in which people do not consume a "westernized" diet, eg, China.¹⁶

In 1988, Yunginger et al¹⁷ reported 7 cases of fatal food anaphylaxis evaluated during a 16-month period, and in 1992, 6 fatal and 7 near-fatal (required intubation and vasopressor support) food-induced anaphylactic reactions that occurred in children

(ages 2–17 years) from 3 metropolitan areas during a 14-month period were reported.¹⁸ Common risk factors were identified and included the following: asthma (even if well-controlled), failure to identify the responsible food allergen in the meal, and previous allergic reactions to the incriminated food, although in most cases symptoms had been much milder. All patients developed some immediate symptoms with approximately half experiencing a quiescent period before a major respiratory collapse. In both series, no patient who received adrenaline immediately died, but in more recent reports, 7% to 10% of patients died despite the prompt administration of epinephrine.^{19,20} In the series of 48 fatal cases reviewed by Pumphrey,¹⁹ 3 patients died despite receiving epinephrine from a self-administration kit appropriately at the onset of their reaction. Of 32 fatal food anaphylaxis cases reported by Bock et al,²⁰ 2 of 32 individuals who died had received intramuscular epinephrine immediately but failed to respond. It is interesting that in most cases of fatal food anaphylaxis in which serum tryptase was measured, no significant increase in tryptase was found, raising some question about the exact mechanism involved in food anaphylaxis.¹⁸

Reports of food-induced anaphylaxis associated with exercise (food-associated exercise-induced anaphylaxis) have been reported with increasing frequency. Two forms of food-induced anaphylaxis associated with exercise have been described: the most common involves reactions after the ingestion of specific foods (eg, celery, shellfish, wheat),²¹⁻²³ and rarely such reactions occur after the ingestion of any food.^{24,25} In most cases, anaphylaxis occurs when exercise takes place within 2 to 4 hours of ingesting a specific food. Otherwise, the patient can ingest the food without any apparent reaction and can exercise without any apparent reaction as long as the specific food has not been ingested within the past several hours. This disorder seems to be twice as common in female individuals, and >60% of cases occur in in-

dividuals younger than 30 years. In a survey of 199 individuals who experienced exercise-induced anaphylaxis, ingestion of food within 2 hours of exercise was believed to be a factor in the development of attacks in approximately one half of the cases.²⁴ Symptoms often start with pruritus about the scalp that becomes more generalized. Urticaria and flushing are common, followed by respiratory obstruction and sometimes cardiovascular collapse. Patients with specific food anaphylaxis associated with exercise usually have positive skin tests to the food that provokes symptoms and occasionally have a history of reacting to the food when they were younger.

The prevalence of fatal food-induced anaphylactic reactions is unknown. A recent report from the United Kingdom suggested that the incidence of fatal reactions in children ≤ 15 years was 0.006 deaths per 100 000 children per year.²⁶ The authors based their conclusion on death certificates and clinical reports, both of which have been shown to underestimate the true prevalence of anaphylaxis.^{8,27}

FOODS IMPLICATED IN ANAPHYLAXIS

The list of foods implicated in anaphylactic reactions is unlimited, although a few foods seem to provoke the vast majority of severe anaphylactic reactions (see Table 3). In westernized countries, peanuts and tree nuts,^{4,9,17,18,20} fish (eg, cod, whitefish), and shellfish (shrimp, lobster, crab, scallops, oyster)¹³ are most often implicated in fatal or near-fatal reactions. Of note, these foods also tend to induce "persistent sensitivity" in the vast majority of patients, in contrast to other foods such as milk, eggs, and soybeans, which are frequently associated with milder allergic reactions and are usually "outgrown."

Signs and Symptoms of Food Anaphylaxis

Symptoms of food anaphylaxis (Table 1) may develop within seconds to a few hours after the ingestion of a food allergen, with the vast majority of reactions developing within the first hour. In general, the longer it takes for anaphylactic symptoms to develop, the less severe the overall reaction. Up to one third of children with grade 4 or 5 anaphylactic reactions (see Table 2) will experience a biphasic response.¹⁸ In such cases, patients develop classical symptoms of anaphylaxis, seem to recover (and may become asymptomatic), and then experience a recurrence of symptoms. Bronchospasm is often severe and largely refractory to β -agonists and can lead to

severe hypoxia. Although initial symptoms tend to be more severe preceding biphasic reactions, this is not always the case. Fatal reactions have been reported after premature discharge from an emergency department as a result of the second-phase response. The intervening "quiescent" period typically lasts for up to 1 to 3 hours, so patients should be observed for 4 hours after initial symptoms subside. In our report of 7 cases of near-fatal food anaphylaxis, 3 experienced protracted anaphylaxis with symptoms lasting from 1 day to 3 weeks.¹⁸ Most reports suggest that the earlier epinephrine is administered in the course of anaphylaxis, the better the chance of a favorable outcome.

The symptoms of anaphylaxis are generally related to the skin, gastrointestinal tract, respiratory tract, and cardiovascular systems (Table 1). The time of onset of symptoms, the sequence in which symptoms develop, and severity of symptoms frequently vary among individuals and may even vary in the same individual during repeated episodes or in response to different foods. As children get older and develop other atopic symptoms, such as asthma, it is not uncommon for them to experience more severe symptoms if they do not outgrow their food allergy. For example, a peanut-allergic toddler, who reacted with minimal cutaneous and gastrointestinal symptoms before developing asthma, not infrequently experiences a more severe anaphylactic reaction after ingesting peanut in later years. However, subsequent allergic reactions are highly variable and may manifest as milder, similar, or more severe reactions.²⁸

The first symptoms experienced in food anaphylaxis often involve the oral cavity and throat. Symptoms may include a "metallic" taste in the mouth; a tingling sensation; and pruritus and edema of the lips, oral mucosa, palate, and pharynx. Young children may be seen scratching at their tongue, palate, anterior neck, or external auditory canals. Similar symptoms may be seen in up to one third of children with "hayfever" as a result of birch, ragweed, grass, or mugwort pollen sensitivity after ingesting certain raw fruits and vegetables, a disorder known as pollen-food allergy syndrome (or oral allergy syndrome). The symptoms are attributable to IgE antibodies that are generated against the inhaled pollen but that also recognize similar (homologous) proteins in certain raw vegetables and fruits, eg, birch pollen, raw apple, carrots, potato, hazel nut, kiwi. This cross-reactivity typically provokes mild symptoms in the mouth and oropharynx and should not be confused with the initial symptoms of an anaphylactic reaction. Evidence of laryngeal edema includes a "dry staccato" or "barky" cough and/or dysphonia and dysphagia. Although severe upper airway edema was considered the cause of death in $\sim 10\%$ of cases in 1 series,²⁹ this seems less frequent in other series. Gastrointestinal symptoms frequently follow, including nausea, colicky abdominal pain, vomiting, and diarrhea. Emesis may contain large amounts of "stringy" mucus. Skin symptoms during anaphylaxis may include flushing, urticaria, angioedema, and/or an erythematous macular rash, but may be absent in severe reactions.¹⁸ Respiratory symptoms

TABLE 3. Foods Most Frequently Implicated in Food Anaphylaxis

Peanut	
Tree nuts	(walnut, hazel nut [filberts], Brazil nuts, pistachios, pecans, pine nuts, cashews, almonds, macadamia nuts)
Fish	(salmon, cod, less often tuna)
Shellfish	(shrimp, crab, lobster, oyster, scallop)
Milk	(cow, goat, sheep)
Chicken egg	
Seeds	(sesame seed, mustard seed, psyllium, cotton seed)
Fruits	(kiwi)

often consist of a deep repetitive cough, stridor, dyspnea, and/or wheezing. The development of cardiovascular symptoms along with airway obstruction is of greatest concern in anaphylactic reactions. In the second phase of the biphasic response, extreme bronchospasm often makes it extremely difficult to ventilate patients, and tension pneumothoraces are a frequent complication of high ventilatory pressure. Cardiovascular symptoms may include syncope, a feeling of faintness, palpitations, and/or chest pain. Hypotension or shock may be the result of vascular collapse, cardiac arrhythmia, or asphyxia. Anaphylaxis may be complicated by myocardial ischemia.

Other signs and symptoms reported frequently in food-induced anaphylaxis include periocular and nasal pruritus, sneezing, diaphoresis, disorientation, fecal or urinary urgency or incontinence, and uterine cramping in women (lower back pain). Patients often report a "sense of doom." In some instances, the initial manifestation of anaphylaxis may be the loss of consciousness. Death may ensue in minutes but has been reported to occur days to weeks after anaphylaxis.³⁰ In 6 cases of fatal food-induced anaphylaxis,¹⁸ initial symptoms developed within 3 to 30 minutes and severe respiratory symptoms within 20 to 150 minutes. Symptoms involved the lower respiratory tract in all children, the gastrointestinal tract in 5 of 6, and the skin in only 1 of 6 children. It should be stressed that skin symptoms may be absent in food-induced anaphylaxis.

Several factors seem to predispose individuals to more severe food anaphylaxis, including a personal history of atopy, adolescence (especially late teens), the presence of asthma, and the particular food to which they are allergic.^{18,20,31,32} In the reports of Yunginger et al,¹⁷ Sampson et al,¹⁸ and Bock et al,²⁰ individuals were highly atopic and all had histories of asthma. Although atopy reportedly does not predispose individuals to an increased risk of anaphylaxis,³³ it does tend to predispose to more severe reactions.

DIAGNOSTIC FEATURES

In light of its abrupt and dramatic nature, the diagnosis of food anaphylaxis is generally readily apparent. Occasionally, disorders such as scombroid poisoning, aspiration with upper airway obstruction, myocardial infarction, a vasovagal response, or a panic reaction must be differentiated from food-induced anaphylaxis. In the majority of cases in which a food is implicated, the responsible food is evident from the temporal relationship between the ingestion and the onset of symptoms. When evaluating the cause of anaphylaxis, a careful history is essential, especially when the cause of the episode is not apparent. Specific questions should include whether any other precipitating factors seem to be involved, such as exercise. In cases in which the cause of the anaphylactic reaction is not clear, a dietary history should review all ingredients of the suspected meal, including any possible concealed ingredients or food additives. The food provoking the reaction may be a minor ingredient in the meal or a contaminant.³⁴

The laboratory evaluation of food-induced ana-

phylaxis is generally focused on the identification of specific IgE antibodies to the suspected food(s). Limited prick skin testing or radioallergen sorbent tests are necessary to demonstrate whether the patient possesses IgE antibodies to the suspected food. In individuals with a negative prick skin test to a suspected food, some allergists will perform an intradermal skin test because of its perceived increased sensitivity. However, a positive intradermal skin test after a negative prick test is unlikely to reflect clinical sensitivity.³⁵ In addition, anaphylactic reactions (including fatal reactions) have been reported after intradermal skin tests to foods.³⁶ In typical anaphylactic reactions, massive activation of mast cells during anaphylaxis results in a dramatic rise in plasma histamine and somewhat later a rise in plasma or serum tryptase.³⁷⁻³⁹ After the onset of symptoms in a food anaphylactic reaction, plasma histamine rises during the first several minutes of a reaction and generally remains elevated for only a few minutes.³⁷ Because of the lability of histamine, quantification of plasma histamine requires special collection techniques not generally available in emergency departments. Whether measurement of urinary methyl-histamine is useful for confirming anaphylaxis remains to be demonstrated. Serum tryptase has been shown to rise during the first hour and may remain elevated for up to 12 hours in bee-sting and drug-induced anaphylaxis.^{38,39} It is stable at room temperature and can be obtained from postmortem specimens. However, serum tryptase is rarely elevated in food anaphylaxis.¹⁸ The reason for this is not clear but suggests that other cells, such as basophils or monocytes/macrophages, may be more important in the pathogenesis of food-induced anaphylaxis.

Diagnostic food challenges are usually contraindicated in patients with a clear-cut history of anaphylaxis after the isolated ingestion of a food to which they have IgE antibodies. However, in some cases, patients have ingested a number of foods before the onset of their anaphylactic reaction and have positive skin tests to several foods. In such cases, it is essential that the responsible food be identified, and physician-supervised food challenges are warranted. Many young children who experience food anaphylaxis eventually outgrow their clinical reactivity (except to peanuts, tree nuts, fish, and shellfish), so an oral challenge is appropriate after an extended period of food elimination with no history of adverse reactions. In these patients, quantifying their level of food-specific IgE antibodies may be useful in determining when they have "outgrown" their sensitivity and it is safe to challenge them.^{40,41}

TREATMENT OF FOOD-INDUCED ANAPHYLAXIS

Acute Management of Food Anaphylaxis

Treatment of food-induced anaphylaxis is similar to treatment of anaphylaxis as a result of other causes. A review of fatal anaphylactic reactions caused by bee stings indicated that the longer the initial therapy is delayed, the greater the incidence of complications and fatalities.³⁰ Reports of fatal food anaphylaxis have suggested similar findings.^{9,17,18,20}

TABLE 4. Management of Food-Induced Anaphylaxis

Assess the adequacy of oxygenation, cardiac output and tissue perfusion

Therapeutic management

In the Field:

Injectable epinephrine (dependent on history and symptoms)

<10 kg—ampule of epinephrine (1:1000) 0.01 mg/kg/dose with syringe

10–20 kg—EpiPen Jr (0.15 mg epinephrine)

20–28 kg—EpiPen Jr or EpiPen dependent on history

>28 kg—EpiPen (0.3 mg epinephrine)

Oral liquid diphenhydramine (most readily absorbed) 1–1.5 mg/kg up to 75 mg

Transport to emergency facility

Emergency medical facility:

Supplemental oxygen and airway management

IM epinephrine (IV–1:10,000 in case of severe hypotension)

IV fluid expansion

H₁ antagonist (diphenhydramine)—oral, IM, or IV

Corticosteroids—oral prednisone (1–2 mg/kg up to 75 mg) or IV solumedrol

(1–2 mg/kg up to 125 mg)

Nebulized albuterol: every 20 mins or continuous

H₂ antagonist (ranitidine: 1–2 mg/kg up to 150 mg)Glucagon for refractory hypotension: 5–15 μ g/min

Discharge therapy: Antihistamine—cetirizine, fexofenadine, or loratidine for 3 d

Prednisone—1 mg/kg (up to 75 mg) daily for 3 d

Appointment for evaluation by an allergist, if not previously evaluated

IM indicates intramuscular; IV, intravenous.

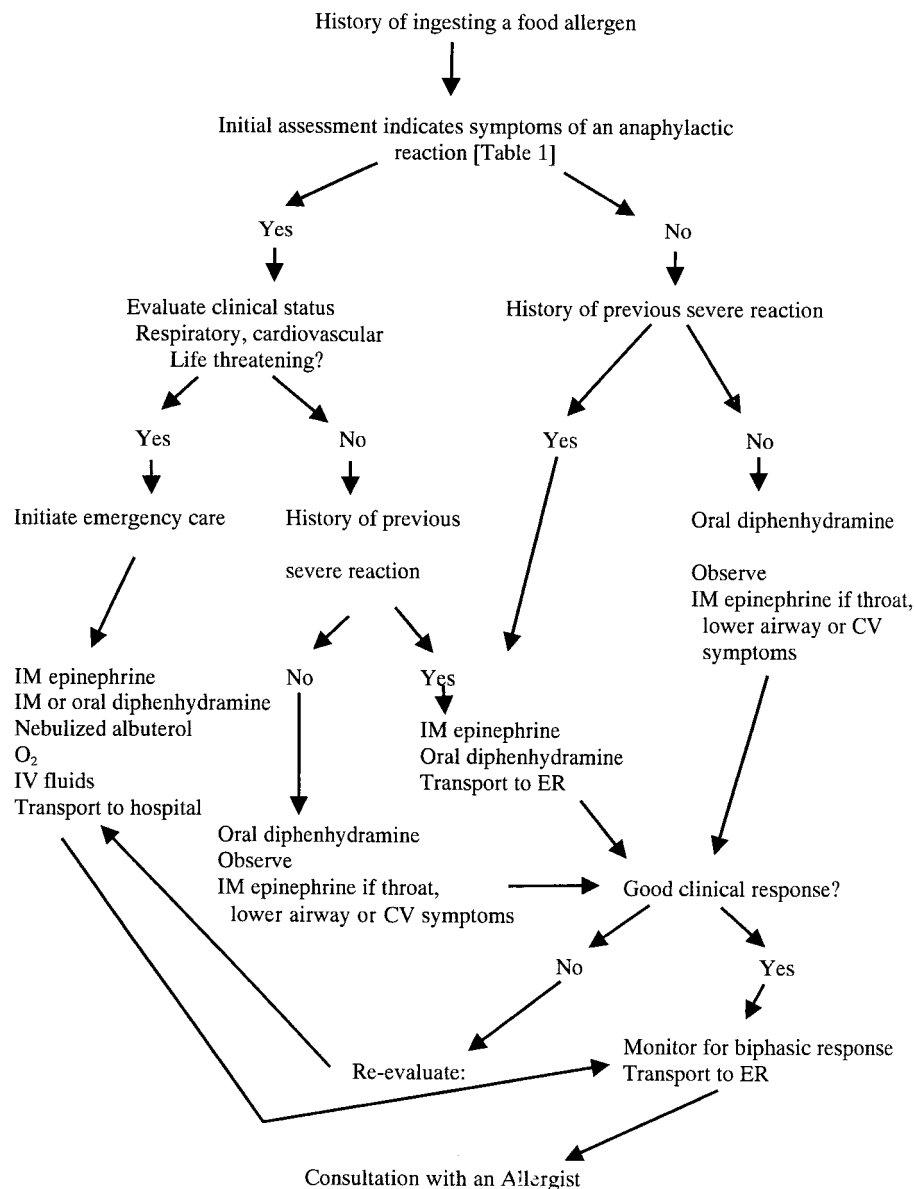
Initial treatment must be preceded by a rapid assessment to determine the extent and severity of the reaction, the adequacy of oxygenation, cardiac output, tissue perfusion, any potential confounding medications, and the suspected cause of the reaction (see Table 4).⁴² Initial therapy should be directed at the maintenance of an effective airway and circulatory system. Intramuscular epinephrine (adrenaline) is the drug of choice in the treatment of anaphylaxis (0.01 mL/kg aqueous epinephrine 1:1000 [maximum dose 0.3–0.5 mL, or 0.3–0.5 mg]).^{43,44} Although published reports suggest that inhalation of racemic epinephrine may be an effective alternative form of therapy for anaphylaxis,^{45,46} a recent controlled trial failed to confirm the efficacy of this therapeutic approach in children.⁴⁷ In patients with pulmonary symptoms, supplemental oxygen should be administered.

Although no specific guidelines exist, epinephrine for self-administration (EpiPen; Dey, Napa, CA) should be prescribed to any individual at high risk for severe food-induced anaphylactic reactions. This would include food-allergic patients who have asthma (regardless of the severity) or who have experienced a previous reaction involving the airway or cardiovascular systems (Table 2, grades 3–5). In addition, many allergists recommend providing an EpiPen to any patient who is allergic to peanuts, tree nuts, fish, or shellfish; any patient who has food allergy and has wheezed during a respiratory illness even if they are not considered to have asthma; and any food-allergic child from a family in which another family member has experienced a severe reaction. In addition, the child's family members and other care providers should be instructed in the administration of epinephrine. Preloaded syringes with epinephrine generally are recommended for use in emergency situations, because both the patient and caregivers are typically distraught and the scene is often chaotic. In the United States, the EpiPen provides a disposable drug delivery system with a

spring-activated, concealed needle used for a single intramuscular injection. It is available in 2 forms: the EpiPen (0.3 mg, which is recommended for individuals who weigh >66 lb) and the EpiPen Jr (0.15 mg for individuals who weigh 33–66 lb). The recommended dose of epinephrine for treatment of anaphylaxis is 0.01 mg/kg/dose. Therefore, the EpiPen Jr is ideal for children who weigh 15 kg (33 lb) and the EpiPen is ideal for children who weigh 30 kg (66 lb). Most allergists will prescribe the EpiPen Jr for children who weigh from 10 kg to 20 kg (22 lb–44 lb) and the EpiPen for children $\geq$ 28 kg (62 lb). In some cases, patients who weigh <10 kg (22 lb) may need self-injectable epinephrine. In these cases, the caregivers should be taught how to draw up and administer the appropriate dose of epinephrine (1:1000) in a syringe. In children who weigh 21 kg to 28 kg, the use of the EpiPen or the EpiPen Jr will depend on the physician's judgment as to the risk of the patient's experiencing a severe anaphylactic reaction. Simons et al⁴⁸ found that 5 of 5 children who weighed an average of 25.4 kg (56 lb) developed pallor, tremor, anxiety, and palpitations or other cardiovascular effects after using the 0.3 mg EpiPen, and several developed headache and nausea. In general, if a patient in this weight range has experienced a severe anaphylactic reaction previously and/or is at high risk for such a reaction, ie, history of asthma or allergic to peanut, tree nut, or seafood, then the 0.3 mg EpiPen is probably the appropriate choice. However, if the patient has never experienced a severe allergic reaction and is not in the higher risk group, then the physician may continue the 0.15 mg EpiPen Jr until the patient is $\geq$ 28 kg (62 lb). Sustained-release preparations of epinephrine are not appropriate treatment for acute anaphylaxis. Inhaled epinephrine may be beneficial to reverse laryngeal edema or persistent bronchospasm but should not be considered first-line therapy.

Studies suggest that the combination of H₁ antihistamines (ie, diphenhydramine, 1 mg/kg up to 75 mg)

Fig 1. Management of acute anaphylaxis.



and H₂ antihistamines (eg, 4 mg/kg up to 300 mg of cimetidine) may be more effective than either administered alone.⁴⁹ Patients who are at risk for food anaphylaxis should be provided with liquid diphenhydramine for use in case of a reaction resulting from an accidental allergen ingestion. In patients with a history of near-fatal reactions, it may be prudent to provide an H₁ antihistamine for immediate use in case an inadvertent ingestion is suspected. Many authorities recommend giving prednisone (1 mg/kg orally) for mild to moderate episodes of anaphylaxis and solumedrol (1–2 mg/kg intravenously) for severe anaphylaxis in an attempt to modulate the late-phase response. If wheezing is prominent, then an aerosolized β -adrenergic agent (eg, albuterol) is recommended intermittently or continuously, depending on the patient's symptoms and the availability of cardiac monitoring. Hypotension may be severe and prove refractory to epinephrine and antihistamines. Depending on the blood pressure, large volumes of crystalloid (eg, lactated Ringer's solution or normal

saline) may need to be infused rapidly to reverse hypotension, and alternative vasopressors, eg, glucagon, may be needed. Given the possibility of a biphasic response, all patients should be observed for at least 4 hours before discharge. If a patient has had a previous severe reaction or if there is some question about the patient's ability to return in case of relapsing symptoms, then he or she should be admitted to the hospital for observation.

Long-Term Management of Food Anaphylaxis

The life-threatening nature of anaphylaxis makes prevention the cornerstone of therapy. The central focus of prevention necessitates appropriate identification and complete dietary avoidance of the responsible food allergen. Certain factors place some individuals at increased risk for more severe anaphylactic reactions: 1) history of an anaphylactic reaction; 2) history of asthma, especially if poorly controlled; 3) allergy to peanuts, nuts, fish, and shellfish; 4) teenage patients, and 5) patients on β -blockers or

angiotensin-converting enzyme inhibitors. Education is imperative to ensure that the patient and his or her family understands how to avoid all forms of the food allergen and the potential severity of a reaction if the food is inadvertently ingested. Accidental food ingestion is likely despite avoidance measures, so immediate treatment should be available for such emergencies. Treatment protocols should be prescribed by the patient's physician, and caregivers and/or school staff should have written instructions by the physician and signed by the parents. A sample plan can be downloaded from the Food Allergy and Anaphylaxis Network's web page: www.foodallergy.org. "Epinephrine is the first drug that should be used in the emergency management of a child having a potentially life-threatening allergic reaction. There are no contraindications to the use of epinephrine for a life-threatening allergic reaction."⁶ Children who are at risk for anaphylaxis should carry medical information concerning their condition, eg, Medic Alert bracelet, emergency medications (EpiPen and liquid diphenhydramine), and their treatment plan with them at all times. This information may be lifesaving, because it can expedite the diagnosis and appropriate treatment of a patient who is experiencing an anaphylactic reaction.

When to Give Epinephrine

Most authorities agree that any food-allergic child who has experienced a life-threatening anaphylactic reaction (Table 2, grades 4–5) or who is experiencing severe symptoms (Table 2, bolded symptoms) should be given intramuscular epinephrine and transported to a hospital immediately if a food allergen ingestion is suspected. In other situations, opinions differ. Overall, how aggressive a suspected anaphylactic event is treated depends on the symptoms that the patient is experiencing, the type of reactions that the child has experienced in the past, whether the child has asthma, who is with the child, where the reaction is occurring, and, to some extent, the food suspected of causing the reaction. Table 4 provides a list of medications and dosages for treatment of anaphylaxis, and Fig 1 provides 1 algorithm for managing suspected food-allergic reactions. If a food-allergic child has experienced only mild cutaneous or oral symptoms in the past, eg, grade 1 (see Table 2), and has no history of wheezing, then it may be appropriate to have the parents administer diphenhydramine and bring the child to the office or local emergency department for observation. However, if the child is experiencing more generalized cutaneous symptoms, eg, grade 2, and has a history of asthma, then it would be more appropriate to administer diphenhydramine and send them to the emergency department with instructions to administer epinephrine if other symptoms develop. A number of factors may lower the threshold for when to administer epinephrine (eg, if nonmedical personnel are caring for the child; if the child is >15 minutes from a medical facility; if the reaction is provoked by peanut, tree nuts, or seafood). As noted above, a comprehensive plan should be written in conjunction with the child's allergist. In a school or child care

setting, an EpiPen should be readily available and not locked away where only 1 or 2 individuals have access.^{6,50,51} Additional epinephrine should be available during transport and may be administered every 15 to 20 minutes if necessary.

New immunomodulatory therapies are being evaluated for their efficacy in the treatment of food allergy. Anti-IgE therapy and "desensitization" with modified recombinant proteins look promising, as discussed elsewhere in this supplement. In the meantime, education about strict avoidance of food allergens and treatment of accidental ingestions are the mainstays of therapy. Pediatricians are often the first to diagnose food allergy in young infants. As discussed elsewhere in this supplement, a child with an IgE-mediated food allergy will often develop other food allergies (approximately one third of cases) and atopic disease. Early referral to an allergist who is knowledgeable about food allergies may be useful in fully evaluating a child's atopic potential and educating the family in potential prophylactic measures. In addition, it is generally prudent to refer any child who has a food allergy and history of wheezing or who is allergic to "life-long" allergens such as peanut, tree nuts, fish, or shellfish to an allergist to ensure that the extent of the child's food allergies are fully evaluated and extensive education regarding avoidance and treatment strategies are undertaken.

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