

## Authors and Disclosures

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## From Medscape Allergy & Clinical Immunology Food Allergy in the ED: The Patient With Anaphylaxis

### Highlights of the NIAID Guidelines

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### Food Allergy in the Emergency Department

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Children and adults who are having adverse reactions to food often present or are transported to emergency departments (EDs) and urgent care centers. Some of these reactions turn out to be nonallergic "food intolerances"; some are true allergic (immunoglobulin [Ig]E-mediated) reactions; and some are food-induced anaphylaxes -- the most serious and potentially deadly allergic reactions to food.

The latest data have revealed that more than 200,000 visits to EDs annually are for food-related acute allergic reactions -- or 1 visit every 3 minutes.<sup>[1]</sup> An estimated 90,000 ED visits are made each year for food-induced anaphylaxes<sup>[1]</sup>; a number that is 3 times higher than previous estimates.<sup>[2-4]</sup> Fewer data are available for prehospital emergency care settings. One study estimated that 0.5% of emergency medical services (EMS) runs were for acute allergic reactions or anaphylaxes.<sup>[5]</sup> Data from multiple sources also show that ambulatory visits, including EDs, for food allergy concerns in children are increasing.<sup>[6]</sup>

For many reasons, precise numbers for the incidence and prevalence of food allergies and food-induced allergic reactions such as anaphylaxes are not known.<sup>[7]</sup> However, evidence does show wide variances in the *management* of food-induced allergic reactions, particularly in emergency care settings.

When a multidisciplinary expert panel developed the [Guidelines for the Diagnosis and Management of Food Allergy in the United States](#) for the National Institute of Allergy and Infectious Diseases (NIAID),<sup>[8]</sup> an important goal was to standardize the diagnosis and management of food allergies and food-allergic reactions across clinical settings, including emergency care, where the most severe and life-threatening consequences of food allergies are managed. The NIAID-sponsored guidelines were approved by the American College of Emergency Physicians. For emergency care clinicians the most valuable content in the new guidelines is that which deals with anaphylaxis, an often underrecognized and suboptimally managed food-induced reaction. For more information about the NIAID guidelines, see [Food Allergy: The Definitive Guide to Clinical Practice](#).

### Food-Induced Anaphylaxis

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Food is the most common cause of anaphylaxis in the community. Food-induced anaphylaxis is a potentially fatal reaction if not recognized and managed promptly.<sup>[8]</sup> Anaphylaxis follows a previous sensitization to a food allergen: most commonly peanuts, tree nuts, fish, shellfish, cow's milk, soy, eggs, or sesame seeds. The allergen induces IgE production, and these antibodies bind to the surface of mast cells in the tissues and basophils in the bloodstream. Upon re-exposure to the allergen, proinflammatory mediators are released from these mast cells and basophils including preformed mediators such as histamine and tryptase as well as newly synthesized mediators such as leukotrienes, which

stimulate the inflammatory process that produces an array of clinical symptoms on target organs: the skin, mucous membranes, gastrointestinal tract, respiratory tract, and the cardiovascular system.

Anaphylaxis can go unrecognized in the ED setting, according to Joseph Wood, Assistant Professor Emergency Medicine, Mayo Medical School, Rochester, Minnesota, and member of the NIAID Guidelines Coordinating Committee. Dr. Wood suggests that the lack of a universally accepted definition of anaphylaxis is partly to blame. If one has preconceived notions about what must be present for a reaction to be considered anaphylaxis -- such as hives or shock -- the likelihood of failing to recognize anaphylaxis is high. "Clinicians have tended to think that if the patient isn't in cardiovascular collapse, it's not anaphylaxis," explains Dr. Wood.

Cutaneous manifestations -- the urticaria, itching, and flushing commonly associated with anaphylaxis -- can be absent in as many as 20% of cases,<sup>[8]</sup> and severe anaphylaxis can occur without any appreciable cutaneous manifestations. The currently accepted definition of anaphylaxis does not mandate that reduced blood pressure or shock be present; indeed, evidence has shown that in patients who die of anaphylaxis their initial signs and symptoms were more likely to involve respiratory distress than circulatory collapse.<sup>[9,10]</sup>

## Diagnosis of Anaphylaxis

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A healthy adolescent presents to the ED with nausea, vomiting, itching, and hives about 2 hours after eating at a school potluck. He has never experienced a severe reaction to food, although he is known to be allergic to seafood. Is this just a severe allergic reaction? Could this patient have anaphylaxis?

Unlike many other medical emergencies food-induced anaphylaxis often affects very young, otherwise healthy individuals. The onset of anaphylaxis is often rapid, and its course can be unpredictable. A continuum of symptoms from mild to severe is possible. Target organ involvement and accompanying signs and symptoms vary from person to person.<sup>[11]</sup>

Invariably, patients will present to the ED who do not have apparently life-threatening symptoms, and many of these reactions will be self-limited. Clark and associates found that of 678 patients presenting to the ED with food-related allergic reactions, 51% met the criteria for anaphylaxis.<sup>[2]</sup> The difficulty faced by clinicians lies in determining which patients have anaphylaxis or are progressing toward anaphylaxis. True anaphylaxis is a medical emergency and must be promptly and appropriately managed to reduce the risk for fatality.

Clinical findings and a detailed history, including a medical history of confirmed food allergy or previous anaphylactic reactions, and a detailed history of all foods consumed during the previous 6 hours are the chief means of diagnosing food-induced anaphylaxis.<sup>[12]</sup> However, although more common in children, a first episode of anaphylaxis can occur at any age.<sup>[8]</sup> Fewer than half of patients presenting to the ED with acute food-induced allergic reaction had a history of an allergic reaction to the food that precipitated anaphylaxis.<sup>[2]</sup>

## A Definition for Anaphylaxis

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Patients with anaphylaxis are often diagnosed with "acute allergic reaction" rather than anaphylaxis, resulting in a delay of appropriate treatment and poorer outcomes.<sup>[13]</sup> In a retrospective review of ED documentation as many as 1 in 4 patients were not identified as having anaphylaxis, although it was clear from their medical records that they had met the criteria for anaphylaxis.<sup>[14]</sup> Other studies have found similarly high levels of failure to diagnose anaphylaxis in the ED.<sup>[2]</sup>

In response to the challenges of recognizing anaphylaxis in some patients, the NIAID and The Food Allergy & Anaphylaxis Network (FAAN) convened consensus meetings to develop a clinically useful definition of food-induced anaphylaxis. The outcome of these meetings was a universally accepted definition of anaphylaxis and a set of clinical criteria that would accurately identify cases of anaphylaxis.<sup>[11]</sup> The "short" definition of anaphylaxis is "a serious allergic reaction that is rapid in onset and may cause death."<sup>[11]</sup>

More helpful for clinicians are the new consensus clinical criteria for diagnosing anaphylaxis.<sup>[11]</sup> *The presence of any 1 of these criteria indicates that anaphylaxis is highly likely.*<sup>[8]</sup> The index of suspicion must be immediately raised if the patient has hypotension, reports exposure to a known allergen, or has had a previous anaphylactic reaction.<sup>[15]</sup>

Anaphylaxis is highly likely when any 1 of the 3 following criteria are present<sup>[8]</sup>:

- Acute onset of illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (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 symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence)
- 2 or more 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 symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence)
  - Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
- Reduced blood pressure after exposure to a known allergen for that patient (minutes to several hours) defined as
  - Adults: systolic blood pressure: < 90 mm Hg or > 30% from that person's baseline
  - Infants and children: Low age-specific blood pressure or > 30% decrease in systolic blood pressure

Atypical presentations can be problematic especially when the manifestations include respiratory signs and symptoms, such as in a patient with asthma. In some cases, patients who died of anaphylaxes were misdiagnosed as having fatal asthma attacks.<sup>[10]</sup> Asthma is an important risk factor for death from food-induced anaphylaxis, but Dr. Wood pointed out that an asthma attack as the sole reaction to food allergen exposure is uncommon. "If a patient with asthma has other manifestations, we would give some consideration to food allergy as a possible trigger for the asthma attack," explains Dr. Wood.

NIAID guidelines also emphasize that hypotension can be a late manifestation of shock in infants and young children, and that tachycardia even without low blood pressure could indicate shock.<sup>[8]</sup>

## Characteristics of Food-Induced Anaphylaxis

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### Signs and Symptoms

Food-induced anaphylaxis typically involves more than a single organ system, and frequency of these symptoms varies.<sup>[8]</sup>

**Cutaneous.** Cutaneous symptoms occur in 80%-90% of patients and include flushing, pruritus, urticaria, and angioedema. Cutaneous signs are often believed, mistakenly, to be essential components of "textbook anaphylaxis." However, studies of anaphylaxis fatalities demonstrate that -- if anything -- the lack of cutaneous signs can be a marker of severity of the anaphylactic reaction. Whether this is a reflection of the length of time required for mucocutaneous signs to develop is not known but suggests that clinicians should not depend on these signs in making the diagnosis of anaphylaxis.<sup>[16]</sup>

**Respiratory.** Up to 70% of patients have nasal congestion, rhinorrhea, throat pruritus, laryngeal edema, stridor, choking, wheeze, cough, or dyspnea.<sup>[8]</sup>

**Gastrointestinal.** Diarrhea, cramping, abdominal pain, nausea, or emesis occurs in up to 40% of patients.

**Cardiovascular.** Up to 35% of patients have dizziness, tachycardia, and hypotension. The vascular permeability induced by anaphylaxis can permit transfer of a large proportion of a patient's intravascular volume into the extravascular space, producing hemodynamic collapse in as few as 10 minutes.<sup>[12]</sup>

**Other symptoms.** Anxiety, mental confusion, lethargy, hypotonia, and seizures are all possible accompaniments to food-induced anaphylaxis.

### Time Course

Food-induced anaphylaxis is a progressive reaction that begins rapidly after ingestion of the allergen, with symptoms that evolve over minutes to hours. Mild anaphylaxis can resolve spontaneously. Anaphylaxis can be either uniphasic, biphasic, or protracted.

- *Uniphasic:* Reaction occurs immediately after allergen ingestion and does not recur after resolution (whether spontaneous or treated).
- *Biphasic:* Symptoms recur 8-72 hours after apparent resolution; up to 25% of fatal/near-fatal anaphylactic episodes are biphasic.<sup>[12]</sup>

- *Protracted*: Episode lasts hours or days (up to 72 hours) after the initial reaction despite attempts to treat.

### Risk Factors for Fatal Anaphylaxis

Patients at greatest risk of dying from anaphylaxis are adolescents and young adults, patients with diagnosed food allergies (especially tree nuts or peanuts) and a history of anaphylaxis, and those with asthma.<sup>[8]</sup> Comorbid diseases that are associated with a higher risk for food-induced anaphylaxis or death from anaphylaxis include asthma, cardiovascular disease, and chronic pulmonary disorders. Certain medications (beta-adrenergic antagonists, angiotensin-converting enzyme inhibitors, alpha-adrenergic blockers) can contribute to the severity of symptoms. Rapidly developing symptoms and delayed or insufficient treatment also predispose patients experiencing anaphylaxis to fatality.<sup>[8]</sup>

### Laboratory Indicators of Anaphylaxis

During the acute anaphylactic reaction, laboratory tests such as levels of mast cell and basophil mediators have limited clinical value and do not aid in making a diagnosis of anaphylaxis.<sup>[8]</sup> Histamine levels peak about 5 minutes after the start of the reaction, and with a short half-life of about 15-30 minutes this blood sample must be drawn within 15 minutes: a nearly impossible undertaking unless the ingestion takes place in the ED waiting room. Total tryptase levels are not generally elevated in food-induced anaphylaxis and lack specificity. A negative total tryptase level does not rule out food-induced anaphylaxis.<sup>[8]</sup> With all of these limitations laboratory tests to confirm food-induced anaphylaxis or to seek the specific cause of food-induced anaphylaxis are not generally conducted during the ED visit.

### Management of Food-Induced Anaphylaxis in the ED

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Anaphylaxis is a medical emergency for which emergency care settings must be prepared, and their responses well rehearsed.<sup>[17]</sup>

In addition to epinephrine, NIAID makes the following recommendations for observation, education, discharge prescriptions, and follow-up for patients treated in the ED for possible food-induced anaphylaxis:

- *Dosing* with intramuscular epinephrine
- *Adjunctive/supportive* measures
- *Observation* for 4-6 hours
- *Education* for patient and family
  - Allergen avoidance
  - Early recognition of anaphylaxis
  - Anaphylaxis emergency plan
  - Administration of intramuscular epinephrine
  - Medical alert jewelry or identification
- *Prescription* for epinephrine autoinjector
- *Continuation* of adjunctive treatments
- *Follow-up*
  - Primary care
  - Allergist/immunologist

Recent studies revealed that, like epinephrine use, these measures are inconsistently applied in the ED management of these patients.

### Initial Management

**Epinephrine.** Allergy experts have contended for many years that the only first-line measure for food-induced anaphylaxis is intramuscular epinephrine. However, explains Dr. Wood, "The use of epinephrine is not as high as it should be. Many physicians are quicker to use antihistamines such as diphenhydramine (Benadryl®) and even steroids such as prednisone or methylprednisolone (Solu-Medrol®). They are hesitant to use epinephrine unless the patient is in cardiovascular collapse, but it's safer than people think."

Indeed, the benefits of immediate administration of epinephrine far outweigh any risk associated with giving epinephrine to the patient whose symptoms might resolve spontaneously. Also, the consequences of not using epinephrine are grave. *Failure to promptly administer epinephrine has been repeatedly implicated in anaphylaxis fatalities.*<sup>[8]</sup>

NIAID recommends a dose of 0.01 mg/kg of a 1:1000 concentration aqueous epinephrine given intramuscularly in the anterolateral thigh (maximum dose, 0.5 mg). Children should receive 0.01 mg/kg with a maximum dose of 0.3 mg.

The effects of epinephrine include:

- Alpha<sub>1</sub>-adrenergic effects: vasoconstriction, increased peripheral vascular resistance, and decreased mucosal edema;
- Beta<sub>1</sub>-adrenergic effects: inotropic and chronotropic; and
- Beta<sub>2</sub>-adrenergic effects: bronchodilation and reduced inflammatory mediators.

These therapeutic actions begin within minutes, but the drug is rapidly metabolized necessitating repeat dosing. If the symptoms do not apparently resolve or if symptoms progress, epinephrine should be repeated every 5 minutes, if necessary, to increase blood pressure and control symptoms. A frequent error in the use of epinephrine is waiting too long to redose the patient or moving on to adjunctive pharmacologic agents in patients who respond suboptimally to the first dose of epinephrine rather than repeating the epinephrine.<sup>[8]</sup> Other agents, such as antihistamines, are not lifesaving because they do not relieve upper airway obstruction (laryngeal edema), hypotension, or shock.<sup>[17]</sup>

Although epinephrine is being prepared and administered, other personnel should institute additional measures as listed below. In the hospital setting, when multiple staff members and resources are available, these measures are implemented more or less concurrently.<sup>[8,17]</sup>

**Airway.** Assess the patient's respiratory status and oxygen saturation. Establish an airway if needed, and administer supplemental oxygen and ventilatory assistance.

**Positioning.** Place the patient in a recumbent position with lower extremities elevated. This maximizes perfusion of vital organs but might not be tolerated in patients with respiratory distress or vomiting.

**Intravenous access.** Persistent hypotension may require a continuous epinephrine infusion; therefore, obtaining intravenous access is important. Moreover, the increased vascular permeability that can accompany anaphylaxis can result in the transfer of large volumes of intravascular fluid into extravascular spaces exacerbating hypotension. Fluid replacement may therefore be indicated in the patient whose circulating blood volume is inadequate to maintain blood pressure. Such patients may not respond to epinephrine until blood volume is restored.

**Adjunctive therapies.** Second-line pharmacologic agents include bronchodilators (via metered-dose inhaler or nebulizer), antihistamines (H<sub>1</sub>, H<sub>2</sub>), corticosteroids, vasopressors, glucagon, and atropine depending on patient symptoms, comorbid conditions, progression of anaphylaxis, and other individual factors.

## Observation

The NIAID guidelines recommend that patients be observed for 4-6 hours following resolution of anaphylaxis (considered, by consensus, to be a "reasonable" duration of observation). A biphasic reaction can occur without warning. The duration and location of observation must be individualized. If the patient leaves the hospital before a satisfactory period of observation has been completed, it should be only in the company of a reliable adult who is capable of recognizing and responding to a possible biphasic reaction, and the patient should remain in a location that has rapid access to emergency care until the time period of risk has passed. The guidelines do not offer specific recommendations for patient disposition following treatment for anaphylaxis except that reliable supervision and observation should be ensured.

## Discharge Planning

The NIAID guidelines recommend the following for patients discharged from the ED after treatment for anaphylaxis<sup>[8]</sup>:

- An anaphylaxis emergency plan;
- An epinephrine autoinjector with 2 doses;
- Plan for monitoring epinephrine expiration dates;
- Plan for arranging further evaluation for food allergy; and
- Printed information about anaphylaxis and its treatment.

Patients who have experienced food-induced anaphylaxis should be instructed to avoid the allergen, and depending on the allergen may need instruction in how to read food labels. The signs and symptoms of anaphylaxis should be reviewed and provided in print form as well. The patient or family should develop an anaphylaxis action plan for use if the reaction

recurs, which includes wearing or carrying medical alert information, calling 911/seeking emergency care without delay, and carrying 2 doses of autoinjectible epinephrine.<sup>[17]</sup>

"Patients who have been treated for anaphylaxis should be discharged *with* epinephrine autoinjectors," emphasizes Dr. Wood. Education on using the autoinjector must be provided along with prescription refills and reminders about checking expiration dates on and replacing their epinephrine autoinjectors.

The [Food Allergy & Anaphylaxis Network](#) has numerous resources for download including a video demonstration of how to use an epinephrine autoinjector, sample anaphylaxis action plans, and handouts on how to read food labels for the identification of allergens.

### Follow-up

Upon discharge from the ED, patients should be instructed to make an appointment with their primary care provider. Patients who are having a first severe food-induced allergic reaction should also be referred to an allergist/immunologist for further consultation and ongoing management. Additional counseling on effective avoidance of the allergen will be necessary.

### Management of Milder Food-Induced Allergic Reactions

Not every patient presenting with food-induced allergic reaction has anaphylaxis, stresses Dr. Wood. "Some patients will have acute reactions that might not reach the threshold of anaphylaxis."

In these circumstances ED clinicians may elect to treat patients presenting with milder allergic symptoms, such as flushing or urticaria, with antihistamines. NIAID suggests that patients managed this way should be observed and monitored to ensure lack of progression to anaphylaxis. Epinephrine should be used earlier in patients who have a history of previous severe allergic reactions.

### Think Anaphylaxis

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In most age groups except the elderly, food is the most common trigger for anaphylaxis. When a patient presents to the ED with signs and symptoms of acute food-induced allergic reaction, the most important decision to be made is whether the patient could be progressing toward anaphylaxis, and caregivers must keep this possibility in mind when triaging and assessing patients. Until recently, the lack of a universally accepted definition of anaphylaxis hampered the diagnosis of anaphylaxis except in the most extreme circumstances of cardiovascular collapse and shock. The new NIAID guidelines on food allergy have simplified the diagnosis of anaphylaxis by providing a set of criteria that can be applied in each situation and giving clinicians confidence to "reach for the epi" and possibly save a life.

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