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# Best Clinical Practice

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# ANAPHYLAXIS

Jeffrey Zilberstein, MD,* Michael T. McCurdy, MD,†‡ and Michael E. Winters, MD, FAAEM, FACEP†

*Department of Medicine, Division of Critical Care, Weiss Memorial Hospital, Chicago, Illinois, †Department of Emergency Medicine, and ‡Division of Pulmonary and Critical Care, Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland
*Reprint Address:* Michael E. Winters, MD, FAAEM, FACEP, Departments of Emergency Medicine and Medicine, University of Maryland School of Medicine, 110 S. Paca Street, 6th Floor, Suite 200, Baltimore, MD 21201

☐ **Abstract—Background: Anaphylaxis is the quintessential critical illness in emergency medicine. Symptoms are rapid in onset and death can occur within minutes. Approximately 1500 patients die annually in the United States from this deadly disorder. It is imperative, therefore, that emergency care providers be able to diagnose and appropriately treat patients with anaphylaxis. Any delays in recognition or initiation of therapy can result in unnecessary increases in patient morbidity and mortality. Discussion: Recent literature, including updated international anaphylaxis guidelines, has improved our understanding and management of this critical illness. Anaphylaxis is a multisystem disorder that can manifest signs and symptoms related to the cutaneous, respiratory, cardiovascular, and gastrointestinal systems. Epinephrine remains the drug of choice and should initially be administered intramuscularly, into the anterolateral thigh, as soon as the diagnosis is suspected. For patients unresponsive to repeated intramuscular injections, a continuous infusion of epinephrine should be started. Antihistamines and corticosteroids are second-line medications and should never be given in lieu of, or prior to, epinephrine. Aggressive fluid resuscitation should also be used to treat the intravascular volume depletion characteristic of anaphylaxis. Patient observation and disposition should be individualized, as there is no well-defined period of observation after resolution of signs and symptoms. Conclusions: For patients with anaphylaxis, rapid and appropriate administration of epinephrine is critical for survival. Additional therapy, such as supplemental oxygen, intravenous fluids, antihistamines, and corticosteroids should not delay the administration of epinephrine. © 2014 Elsevier Inc.**

☐ **Keywords—anaphylaxis; anaphylactic shock; allergic reaction; epinephrine; antihistamines; corticosteroids; hypovolemic shock; cardiogenic shock; distributive shock**

## INTRODUCTION

In 1902, Portier and Richet observed a deadly reaction in dogs after repeated injections of sea anemone toxin. Building off the existing term *prophylaxis*, they coined the word *aphylaxis*, which later became *anaphylaxis* (1). Anaphylaxis is often considered the quintessential emergency medicine disease: symptoms are rapid in onset, and death can occur within minutes. Therefore, every acute care provider must be able to diagnose and treat patients with anaphylaxis promptly to minimize morbidity and mortality rates.

Although numerous questions regarding anaphylaxis remain, recent publications, including updated international guidelines, have improved our understanding and management of this deadly disorder. This article serves to update the acute care provider on the recognition and management of patients with anaphylaxis.

## DISCUSSION

### *Definition*

No universally accepted definition for anaphylaxis exists. In an effort to provide a single definition and encourage higher rates of diagnosis, participants from the Second

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Symposium on the Definition and Management of Anaphylaxis, sponsored by the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network, defined anaphylaxis as "a serious allergic reaction that is rapid in onset and may cause death" (2).

*Epidemiology*

The true incidence of anaphylaxis is unknown due to its varying definitions, the lack of confirmatory laboratory values, as well as under-recognition and under-diagnosis by clinicians. However, studies estimate the lifetime prevalence of anaphylaxis to be 0.5% to 2% (3). For patients with severe anaphylaxis, mortality rates range between 0.65% and 2% (4). In the United States, anaphylaxis is estimated to account for approximately 1% of emergency department (ED) visits and 1500 deaths annually (5,6). Risk factors associated with fatal anaphylaxis include infancy, old age, and concomitant diseases such as asthma, chronic respiratory disease, cardiovascular disease, mastocytosis, and severe atopy (7).

*Clinical Features*

Anaphylaxis is a multisystem disorder that produces clinical signs and symptoms centered on the skin, respiratory, cardiovascular, gastrointestinal, and central nervous systems (Table 1). Importantly, up to 20% of patients with anaphylaxis do *not* manifest the characteristic cutaneous signs or symptoms (e.g., urticaria, angioedema). Cutaneous manifestations are commonly absent in people experiencing an allergic reaction to food (8). Gastrointestinal symptoms are associated with more severe reactions (9). The route of antigen exposure often determines how quickly symptoms manifest. In one case series, intravenous medications caused symptoms within 5 min, insect stings caused symptoms within 15 min, and ingestion caused symptoms within 30 min (10).

*Diagnostic Criteria*

Anaphylaxis is a clinical diagnosis. In addition to proposing a universal definition for anaphylaxis, participants from the Second Symposium on the Definition and Management of Anaphylaxis put forth formal diagnostic criteria to identify patients with anaphylaxis (11). These diagnostic criteria were recently incorporated into international guidelines, which are listed in Table 2 (7).

Traditional laboratory values (e.g., complete blood count, comprehensive metabolic panel) are unreliable and impractical in the identification of anaphylaxis; however, serum tryptase values can facilitate the diagnosis.

**Table 1. Signs and Symptoms of Anaphylaxis**

| |
|---|
| Skin, subcutaneous tissue, and mucosa (80–90%) |
| Urticaria |
| Angioedema |
| Flushing |
| Pruritus |
| Periorbital |
| Lips, tongue, palate |
| External auditory canal |
| Genitalia |
| Palms, soles |
| Morbilliform rash |
| Respiratory (70%) |
| Rhinorrhea, congestion, sneezing |
| Stridor |
| Dysphonia, hoarseness |
| Shortness of breath |
| Chest tightness |
| Bronchospasm |
| Cyanosis |
| Cardiovascular (45%) |
| Chest pain |
| Tachycardia |
| Bradycardia |
| Hypotension |
| Dysrhythmias |
| Cardiac arrest |
| Gastrointestinal (45%) |
| Abdominal pain |
| Nausea, vomiting |
| Diarrhea |
| Central nervous system (15%) |
| Sense of impending doom |
| Altered mental status |
| Dizziness |
| Confusion |
| Headache |

Tryptase, found in mast cells and basophils, is released after mast cell activation, peaks within 60 to 90 min after mast cell degranulation, and remains detectable for approximately 5 h (12). Interestingly, serum tryptase levels are elevated in patients experiencing anaphylaxis from insect stings and in those who are hypotensive, yet the levels can be normal in the setting of food-induced anaphylaxis. Serum histamine, another potential laboratory marker for anaphylaxis, can also be measured (13). Histamine levels can increase within 15 to 60 min after symptom onset. Because evidence regarding serum tryptase and histamine is limited, current guidelines emphasize that normal values for either laboratory parameter do not exclude anaphylaxis (7).

*Etiology*

Although any substance can elicit a hypersensitivity reaction severe enough to result in anaphylaxis, the three most common causes of anaphylaxis are food, medications, and insect stings and bites (14). For particular allergens, the time course and symptoms associated with the reaction often can be predicted.