CHEST

Anaphylaxis

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Anaphylaxis is a systemic, life-threatening disorder triggered by mediators released by mast cells and basophils activated via allergic (IgE-mediated) or nonallergic (non-IgE-mediated) mechanisms. It is a rapidly evolving, multisystem process involving the integumentary, pulmonary, gastrointestinal, and cardiovascular systems. Anaphylaxis and angioedema are serious disorders that can lead to fatal airway obstruction and culminate in cardiorespiratory arrest, resulting in hypoxemia and/or shock. Often, these disorders can be appropriately managed in an outpatient setting; however, these conditions can be severe enough to warrant evaluation of the patient in the ED and in some cases, hospitalization, and management in an ICU. Reports suggest that underdiagnosis and undertreatment of anaphylaxis are common. Several new syndromes have been described recently including bird-egg, pork-cat, delayed allergy to mammalian meat and a diverse group of mast cell activation disorders. Conditions such as postural orthostatic tachycardia syndrome, carcinoid syndrome, Munchausen stridor, and factitious anaphylaxis can present similarly and need to be included in the differential diagnosis. Anaphylaxis is a clinical diagnosis, but plasma tryptase and urinary histamine levels are often elevated, allowing diagnostic confirmation; however, diagnostic testing should not delay treatment as results may not be immediately available. The sine qua non of treatment is avoidance of any known triggers and epinephrine, which should never be delayed if this disorder is suspected. Secondary treatments include fluids, bronchodilators, antihistamines, and glucocorticoids. Patients with cardiopulmonary arrest or airway or vascular compromise require mechanical ventilation, vasopressors, and other advanced life support in the ICU.

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Anaphylaxis and angioedema are serious disorders that can lead to fatal airway obstruction and culminate in cardiorespiratory arrest, resulting in hypoxemia and/or shock, requiring management in an ICU setting.[1-3] Reports suggest that underdiagnosis and undertreatment of anaphylaxis are common.[4] Anaphylaxis is presumably an ancient disease, although several developments in the past century have led to enormous insights and treatment advances.[5] In the early 20th century, the French physiologist, Charles Richet, along

ABBREVIATIONS: alpha-gal = alpha-galactose; ECLS = extracorporeal life support; IA = idiopathic anaphylaxis; IO = intraosseous; NSAID = nonsteroidal antiinflammatory drug; PAF = platelet-activating factor; VLM = vastus lateralis muscle

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with Paul Portier, undertook a study of hypnotoxin, an urticaria-inducing toxin and other toxins derived from Physalia (Portuguese man of war or "floating terror" found in the Atlantic, Indian, and Pacific oceans) extracts.[6] An important series of experiments were conducted on the dog, Neptune, wherein an initial injection of toxin was followed by a second injection 22 days later. Within minutes of the second injection, Neptune began to gasp, wheeze, and collapsed with bloody emesis, only to die within 25 min. Richet termed the condition "anaphylaxis" as opposed to prophylaxis and was awarded the Nobel Prize in Medicine for this work in 1913.[5] e-Table 1 provides a historical perspective of events leading to our current understanding of anaphylaxis.

Anaphylaxis has been defined as a systemic, immediate hypersensitivity reaction mediated by IgE and resulting in mast cell and basophil mediator release. This results in multiple clinical effects leading to the diagnosis (Table 1). Anaphylactic reactions result from release of mediators by mast cells and basophils activated either by IgE, termed "immunologic," or by direct activation of these cells by certain agents, termed "nonimmunologic anaphylaxis."[1,7-10] Although the term "anaphylactoid" was previously used to describe non-IgE-mediated anaphylaxis, this terminology is no longer recommended.[11]

Anaphylaxis Patterns: Uniphasic, Biphasic, and Protracted

Three patterns of anaphylactic syndromes have been described based on disease expression: uniphasic, biphasic and protracted. Uniphasic type accounts for 70% to 90% of anaphylaxis cases, peaks at 30 to 60 min, and resolves over the next hour with no recurrence of symptoms. Biphasic anaphylaxis is defined by recurrence of symptoms hours after resolution of the initial event in the absence of re-exposure to the trigger.[12] Biphasic type has been variably reported to occur in <1[13] to up to 23% of reactions, with a recent report suggesting that 3% of adults and up to 15% of children experience biphasic anaphylaxis.[12] Early administration of epinephrine may be beneficial in preventing biphasic reactions; the role of glucocorticoids in preventing this type is unclear but physiologically reasonable. Protracted or persistent anaphylaxis refers to the rare reaction lasting for days or even weeks.[14]

Fatal Anaphylaxis and Time to Death

Jerschow et al[15] examined rates of fatal anaphylaxis in the United States between 1999 and 2010. Using International Classification of Diseases, version 10, diagnostic codes on death certificates, they identified 2,458 anaphylaxis-related deaths over an 11-year period with a prevalence of 0.69 people per million. In this study population (>96% adult), medication-induced anaphylaxis fatalities were the most frequent (58.8%), followed by "unspecified" (19.3%), venom (15.2%), and food (6.2%). Fatal anaphylaxis in the outpatient setting was most commonly food-induced anaphylaxis, whereas drug-induced anaphylaxis was most frequent in the inpatient setting. Two case series reported median time from clinical manifestation to death as 30 to 35 min for food, 10 to 15 min for insect venom, and 5 min for IV medications.[16,17]

TABLE 1] Criteria for Diagnosis of Anaphylaxis

Anaphylaxis is highly likely if any *one* of the following three conditions is satisfied.	
1.	Acute onset of illness with:
	Mucocutaneous involvement (pruritus, flushing, urticaria, angioedema) *and* one of the following:
	A. Respiratory complications (wheezing, stridor, hypoxemia/cyanosis)
	B. Hypotension[a] or end-organ damage (encephalopathy, kidney injury, etc.)
2.	Two or more of the following occurring rapidly after exposure to *known* or *likely* allergen:
	• Mucocutaneous involvement (pruritus, flushing, urticaria, angioedema)
	• Respiratory complications (wheezing, stridor, hypoxemia/cyanosis)
	• Hypotension[a] or evidence of end organ hypoperfusion (encephalopathy, kidney injury, etc.)
	• Persistent gastrointestinal symptoms (pain, nausea, vomiting)
3.	Reduced BP soon after exposure to a *known* allergen.

[a]Hypotension in adults is regarded as systolic BP of <90 mm Hg or greater than a 30% decrease in systolic BP from the patient's baseline. Hypotension in infants and children: systolic BP <70 mm Hg (1-12 months); <(70 mm Hg + [2x age]) (1-10 years); <90 mm Hg (11-17 years); or >30% decrease in systolic BP.