Anaphylaxis: acute diagnosis

Authors:

Ronna L Campbell, MD, PhD
John M Kelso, MD

Section Editor:

Ron M Walls, MD, FRCPC, FAAEM

Deputy Editor:

Anna M Feldweg, MD

Contributor Disclosures

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INTRODUCTION — Anaphylaxis is an acute, potentially life-threatening, multisystem syndrome caused by the sudden release of mast cell mediators into the systemic circulation. It most often results from immunoglobulin E (IgE)-mediated reactions to foods, drugs, and insect stings, but any agent capable of inciting a sudden, systemic degranulation of mast cells can produce it [1]. It can be difficult to recognize because it can mimic other conditions and is variable in its presentation. This topic will review the signs and symptoms of anaphylaxis, diagnostic criteria, and common causes and contributory factors. Laboratory tests that may be helpful in confirming the diagnosis are also briefly discussed.

The acute treatment of anaphylaxis, pathophysiology, and other related topics are reviewed separately.

- (See "Anaphylaxis: Emergency treatment".)
- (See "Pathophysiology of anaphylaxis".)
- (See "Fatal anaphylaxis".)
- (See "Anaphylaxis: Confirming the diagnosis and determining the cause(s)".)
- (See "Anaphylaxis in infants".)
- (See "Anaphylaxis in pregnant and breastfeeding women".)
- (See "Long-term management of patients with anaphylaxis".)

PREVALENCE — In industrialized countries, the lifetime prevalence of anaphylaxis from all causes has been estimated to be between 0.05 and 2 percent in the general population, and the rate of occurrence is increasing [2-7]. In the United States, the lifetime prevalence of anaphylaxis is reported to be 1.6 percent, based on strict clinical diagnostic criteria [8].

DEFINITION AND DIAGNOSIS — Anaphylaxis is defined as a serious allergic or hypersensitivity reaction that is rapid in onset and may cause death [9,10]. The diagnosis of anaphylaxis is based primarily upon clinical symptoms and signs, as well as a detailed description of the acute episode, including antecedent activities and events occurring within the preceding minutes to hours.

Diagnostic criteria — Diagnostic criteria for anaphylaxis were initially published by a multidisciplinary group of experts in 2005/2006 and intended to help clinicians recognize the full spectrum of symptoms and signs that constitute anaphylaxis [9,10].

Recognition of the variable and atypical presentations of anaphylaxis is critical to providing effective therapy in the form of epinephrine, as well as reducing over-reliance on second-line medications, such as antihistamines and glucocorticoids, that are not lifesaving in anaphylaxis [11]. In a retrospective cohort study of 214 emergency department patients, these criteria were found to have a sensitivity of 97 percent compared with an allergist's diagnosis upon review of the case, as well as a specificity of 82 percent, a positive predictive value of 69 percent, and a negative predictive value of 98 percent [12]. Thus, although the diagnostic criteria are helpful, they do not replace provider clinical judgment.

There are three diagnostic criteria for anaphylaxis, each reflecting a different clinical presentation (table 1) [9].

Anaphylaxis is highly likely when any **one** of the following three criteria is fulfilled:

Criterion 1 — Acute onset of an illness (minutes to several hours) involving the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)**and at least one of the following**:

- Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)

OR

- Reduced blood pressure (BP) or associated symptoms and signs of end-organ malperfusion (eg, hypotonia [collapse], syncope, incontinence)

Note that skin symptoms and signs are present in up to 90 percent of anaphylactic episodes. This criterion will therefore frequently be helpful in making the diagnosis.

Criterion 2 — Two 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, hypoxemia).
- Reduced BP or associated symptoms and signs of end-organ malperfusion (eg, hypotonia [collapse], syncope, incontinence).
- Persistent gastrointestinal symptoms and signs (eg, crampy abdominal pain, vomiting).

Note that skin symptoms or signs are absent or unrecognized in up to 20 percent of anaphylactic episodes. Criterion 2 incorporates gastrointestinal symptoms in addition to skin

symptoms, respiratory symptoms, and reduced BP. It is applied to patients with exposure to a substance that is a likely allergen for them.

Criterion 3 — Reduced BP after exposure **to a known allergen for that patient** (minutes to several hours):

- Reduced BP in adults is defined as a systolic BP of less than 90 mmHg or greater than 30 percent decrease from that person's baseline
- In infants and children, reduced BP is defined as low systolic BP (age-specific)* or greater than 30 percent decrease in systolic BP

* Low systolic BP for children is defined as:

  - Less than 70 mmHg from 1 month up to 1 year
  - Less than (70 mmHg + [2 x age]) from 1 to 10 years
  - Less than 90 mmHg from 11 to 17 years

Note that criterion 3 is intended to detect anaphylactic episodes in which only one organ system is involved and is applied to patients who have been exposed to a substance to which they are known to be allergic (for example, hypotension or shock after an insect sting).

There will be patients who do not fulfill any of these criteria but for whom the administration of epinephrine is appropriate. As an example, it would be appropriate to administer epinephrine to a patient with a history of near-fatal anaphylaxis to peanut who presents with urticaria and flushing that developed within minutes of a known or suspected ingestion of peanut [10].

SYMPTOMS AND SIGNS — Anaphylaxis may present with various combinations of approximately 40 potential symptoms and signs (table 2) [1,9,10,13-26].

Common symptoms and signs of anaphylaxis include the following:

- Skin and mucosal symptoms and signs, which occur in up to 90 percent of episodes, including generalized hives, itching or flushing, swollen lips-tongue-uvula, periorbital edema, or conjunctival swelling.
- Respiratory symptoms and signs, which occur in up to 70 percent of episodes, including nasal discharge, nasal congestion, change in voice quality, sensation of throat closure or choking, stridor, shortness of breath, wheeze, or cough.
- Gastrointestinal symptoms and signs, which occur in up to 45 percent of episodes, including nausea, vomiting, diarrhea, and crampy abdominal pain.
- Cardiovascular symptoms and signs, which occur in up to 45 percent of episodes, including hypotonia (collapse), syncope, incontinence, dizziness, tachycardia, and hypotension.

Death from anaphylaxis usually results from asphyxiation due to upper or lower airway obstruction or from cardiovascular collapse [11,27-34]. (See "Fatal anaphylaxis".)

Time course — Anaphylaxis is usually characterized by a defined exposure to a potential cause, followed usually within seconds to minutes but rarely up to hours later, by rapid onset, evolution, and ultimate resolution of symptoms and signs. However, anaphylaxis is unpredictable. It may be mild and resolve spontaneously due to endogenous production of compensatory mediators (eg, epinephrine, angiotensin II, endothelin, and others) or it may be severe and progress within minutes to respiratory or cardiovascular compromise and death [20]. At the onset of an anaphylactic episode, it is not possible to predict how severe it will become, how rapidly it will progress, and whether it will resolve promptly and completely or become biphasic or protracted, because the factors that determine the course of anaphylaxis in an individual patient are not fully understood. Thus, early administration of epinephrine is essential to prevent the progression to life-threatening manifestations. (See "Anaphylaxis: Emergency treatment".)

Death from anaphylaxis can occur within minutes. In a series of 164 cases of fatal anaphylaxis, the median time interval between onset of symptoms and respiratory or cardiac arrest was 5 minutes in iatrogenic anaphylaxis, 15 minutes in stinging insect venom-induced anaphylaxis, and 30 minutes in food-induced anaphylaxis [11]. A more detailed review of fatal anaphylaxis is presented elsewhere. (See "Fatal anaphylaxis".)

Biphasic anaphylaxis — Biphasic anaphylaxis is defined as a recurrence of symptoms that develops following the apparent resolution of the initial anaphylactic episode with no additional exposure to the causative agent. Biphasic reactions have been reported to develop in up to 21 percent of anaphylactic episodes (all ages) and in up to 15 percent of children with anaphylaxis [35,36]. They typically occur within 12 hours after resolution of the initial symptoms, although recurrences up to 72 hours later have been reported. (See "Biphasic and protracted anaphylaxis".)

Protracted anaphylaxis — Protracted anaphylaxis is defined as an anaphylactic reaction that lasts for hours, days, or even weeks in extreme cases [27].

Delayed anaphylaxis — Rarely, the onset of anaphylaxis will be delayed (ie, beginning hours rather than minutes after exposure to the causative agent) [37].

DIAGNOSTIC PITFALLS — Anaphylaxis is not always easy to recognize clinically. The patterns of target organ involvement are variable and may differ among individuals, as well as among episodes in the same individual. Anaphylaxis is likely underdiagnosed and under-reported for a variety of reasons [4,13-17,21-24,38]:

- Some health care professionals remain reluctant to diagnose anaphylaxis in the absence of hypotension or shock, even though changes in blood pressure (BP) are not required for the diagnosis according to criterion 1 or criterion 2 [9]. In fact, it is important to recognize anaphylaxis in its earlier stages because once shock has developed, anaphylaxis may be much more difficult to treat. (See "Anaphylaxis: Emergency treatment", section on 'Epinephrine'.)
- Hypotension may go undetected when measured very early in the course of the episode (when compensated by reflex tachycardia), when the initial BP measurement

is obtained after epinephrine administration, or when an inappropriately small BP cuff is used.

- Age-appropriate standards for normal BP must be used for children and infants.
- Many of the dramatic physical signs associated with hypoxia and hypotension in anaphylaxis are nonspecific, such as dyspnea, stridor, wheeze, confusion, collapse, unconsciousness, and incontinence (table 2).
- Skin symptoms and signs (such as hives, itching, flushing, and angioedema), which are helpful in making the diagnosis, are absent or unrecognized in up to 20 percent of all episodes. Skin symptoms and signs may be absent if a patient has taken an H1 antihistamine. They may also be missed if an individual cannot describe itching or is not undressed and fully examined during the episode or in patients who are draped during surgery [20]. (See "Perioperative anaphylaxis: Clinical manifestations, etiology, and management".)
- Anaphylaxis may be difficult to recognize or may not be considered in certain clinical situations, such as situations in which dramatic physiologic shifts are occurring (eg, hemodialysis, surgery, childbirth) [14-18,20,38,39]. In addition, the inability of the patient to communicate the presence of early symptoms (eg, if anesthetized, sedated, or unconscious) also impedes prompt recognition of anaphylaxis.
- Anaphylaxis in a known asthmatic may be mistaken for an asthma exacerbation if accompanying skin symptoms and signs, such as itching or hives, mucosal, tongue, or lip edema, or dizziness suggestive of impending shock, are overlooked [20].
- Patients experiencing their first episode may not recognize the symptoms as anaphylaxis. As a result, they may not report symptoms fully or may focus on one prominent symptom (eg, unless specifically asked, a patient presenting with vomiting may not report that the episode was preceded by diffuse itching).
- The above factors are further compounded in patients with neurologic, psychiatric, or psychologic problems or those who take medications or substances, such as a sedating H1 antihistamine, ethanol, or recreational drugs that potentially impair cognition and judgment, making anaphylaxis symptoms difficult to recognize (table 3) [20,23].

CAUSES AND MECHANISMS — Most anaphylactic episodes have an immunologic mechanism involving immunoglobulin E (IgE). Foods are the most common cause in children, while medications and insect stings are more common causes in adults. The table provides a more comprehensive list of potential anaphylaxis causes, categorized by causative mechanism (table 4) [9,10,13,19,21-24,40].

In this review, the term "anaphylaxis" applies to all of the following:

- Acute systemic reactions involving IgE-dependent mechanisms.
- Acute systemic reactions that occur due to direct (nonimmunologic) release of histamine and other mediators from mast cells and basophils, formerly called "anaphylactoid reactions" (eg, after exercise, exposure to cold, administration of radiocontrast media, etc).

●Acute systemic reactions without any obvious cause or mechanism (idiopathic anaphylaxis). (See "Idiopathic anaphylaxis".)

CONTRIBUTORY FACTORS — Comorbidities and concurrent medications may impact the severity of symptoms and signs and response to treatment in patients with anaphylaxis (table 5) [13,21-24,26,41].

Comorbidities — Asthma, cardiovascular disease, older age, and medication as a trigger are important risk factors for a poor outcome from anaphylaxis [27,42]. Other disorders may also increase risk.

●Persistent asthma is a risk factor for anaphylaxis [43,44]. Asthma is also associated with increased risk of death from anaphylaxis, especially in adolescents and young adults with poorly controlled disease [11,27-31].

●Cardiovascular disease is an important risk factor for death from anaphylaxis in middle-aged and older individuals [32].

●Other respiratory diseases (eg, chronic obstructive pulmonary disease [COPD], interstitial lung disease, or pneumonia) are also risk factors for severe or fatal anaphylaxis in older adults [32,45].

●Acute infection, such as an upper respiratory tract infection, fever, emotional stress, exercise, disruption of routine, and premenstrual status, may also increase the risk. With the exception of exercise, these amplifying factors have not been systematically studied in the context of anaphylaxis [21].

Concurrent medications — Concurrent administration of certain medications, such as beta-adrenergic blockers, angiotensin-converting enzyme (ACE) inhibitors, and alpha-adrenergic blockers, may increase the likelihood of severe or fatal anaphylaxis. These medications may also interfere with the patient's ability to respond to treatment and with the patient's compensatory physiologic responses (table 5) [46-49].

●Beta-adrenergic blockers are sometimes associated with severe anaphylaxis and may also potentially make anaphylaxis more difficult to treat. They can theoretically cause unopposed alpha-adrenergic effects, leading to paradoxical hypertension, as well as reduce the bronchodilator and cardiovascular responses to beta-adrenergic stimulation by endogenous or exogenous epinephrine [50]. (See "Anaphylaxis: Emergency treatment", section on 'Glucagon for patients taking beta-blockers'.)

●Alpha-adrenergic blockers may decrease the effects of endogenous or exogenous epinephrine at alpha-adrenergic receptors, potentially making anaphylaxis less responsive to the alpha-adrenergic effects of epinephrine [48].

●ACE inhibitors block the effect of angiotensin, a compensatory response, and also block the degradation of kinins, which are active in the production of symptoms and signs [49,50].

●In an emergency department study, use of antihypertensive medications in aggregate (beta-blockers, ACE inhibitors, calcium channel blockers, angiotensin-receptor blockers, or diuretics) by patients with anaphylaxis was associated with increased

organ system involvement and increased odds of hospital admission, independent of age, gender, suspected cause, or pre-existing lung disease [51].

●A study of anaphylaxis patients enrolled in a European national registry demonstrated that the combination of ACE inhibitors and beta-blockers increased the risk of more severe anaphylaxis [52].

●Ethanol, nonsteroidal anti-inflammatory drugs (NSAIDs), and opiates can exacerbate anaphylaxis symptoms by causing nonimmunologic mast cell activation [19].

LABORATORY TESTS — Anaphylaxis is a clinical diagnosis, and treatment cannot await laboratory confirmation. When the cause of the observed symptoms is in doubt, treatment for anaphylaxis is initiated. The clinical diagnosis can sometimes be retrospectively supported by documentation of elevated concentrations of serum or plasma total tryptase or plasma histamine, although the results of these tests are not immediately available to the treating clinician [41,53-56]. It is critical to obtain blood samples for measurement of these mast cell and basophil mediators soon after the onset of symptoms because elevations are transient. Instructions for proper collection of samples are provided in the table (table 6).

●**Serum or plasma total tryptase** – The standardized assay for measurement of total serum or plasma tryptase is widely available in clinical laboratories (normal range 1 to 11.4 ng/mL). In infants under age 6 months, normal baseline total tryptase concentrations are higher than they are in older infants, children, and adults [54,57]. Optimally, the blood sample for tryptase measurement needs to be obtained within 15 minutes to 3 hours of symptom onset. However, tryptase may remain elevated for 6 or more hours after the onset and therefore may still be informative if obtained after 3 hours.

Tryptase elevations are more likely to be detected in anaphylaxis from stinging insect venoms or medications and during reactions that involve hypotension [53,58].

A tryptase level that is within normal limits cannot be used to refute the clinical diagnosis of anaphylaxis [41]. The history is more important than the test results. As an example, in individuals with food-induced anaphylaxis or in patients who are normotensive, tryptase levels are seldom elevated, even in optimally timed blood samples obtained within 15 minutes to 3 hours of symptom onset [27].

Serial measurements of total tryptase in serum or plasma over several hours may increase the sensitivity and the specificity of the tests. In a prospective study, sequential serum tryptase concentrations were measured in 102 adults with anaphylaxis [59]. Tryptase levels 1 to 2 hours after onset of the episode were significantly elevated (19.3±15.4 mcg/L),compared with levels at 4 to 6 hours and at 12 to 24 hours after the onset and at baseline (all <11.4 mcg/L). However, tryptase was not elevated in 37 percent of cases. A rise in total tryptase levels above baseline may be more sensitive than a single measurement. In adults with venom-induced allergic reactions, an increase in tryptase of ≥2.0 mcg/L was 73 percent sensitive and 98 percent specific for anaphylaxis [60]. Sixty percent of children with anaphylaxis had an elevation of ≥2 + 1.2 x baseline tryptase levels [61]. (See "Laboratory tests to support the clinical diagnosis of anaphylaxis" and "Anaphylaxis: Confirming the diagnosis and determining the cause(s)".)

If a tryptase level obtained 24 or more hours after resolution of symptoms is still elevated, the patient should be referred to an allergy/immunology specialist for evaluation of possible systemic mastocytosis or a mast cell activation syndrome. Patients with mast cell disorders may have hypotensive reactions to insect stings, even in the absence of immunoglobulin E (IgE)-mediated allergy [62]. (See "Mast cell disorders: An overview".)

The real world utility of tryptase measurements was assessed in a study of 426 cases of suspected anaphylaxis admitted to three emergency departments over the course of one year [58]. Tryptase was obtained in 141 cases (33 percent), at a mean of 4.75 hours after estimated onset of symptoms and again after resolution in 23 cases. In this setting, a tryptase above 12.4 ng/mL had a high specificity (88 percent) and positive predictive value (0.93) and a low sensitivity (28 percent) and negative predictive values (0.17). Serum tryptase was more likely to be elevated in patients with hypotension, as has been observed in other studies.

●**Plasma histamine** – Plasma histamine levels typically peak within 5 to 15 minutes of the onset of anaphylaxis symptoms and then decline to baseline by 60 minutes due to rapid metabolism by N-methyltransferase and diamine oxidase. Elevated plasma histamine levels correlate with anaphylaxis symptoms and signs and are more likely to be increased than are total serum tryptase levels [56]. (See "Laboratory tests to support the clinical diagnosis of anaphylaxis".)

Measurement of this mediator may be useful in cases of anaphylaxis occurring in a hospital setting in which blood samples can be collected soon after the onset of symptoms. In many cases of anaphylaxis in the community, however, it is not practical to measure histamine, because often by the time the patient reaches the emergency department, levels have returned to baseline [41,53].

Histamine should be measured in plasma rather than serum because clotting may result in release of histamine that is artifactual and only occurs ex vivo due to compromised basophil cell membranes. Blood samples for histamine require special handling. Draw blood through a wide-bore needle, keep it cold at all times, centrifuge it immediately, and freeze the plasma promptly [41]. (See "Laboratory tests to support the clinical diagnosis of anaphylaxis".)

Histamine and histamine metabolites can sometimes be detected in the urine following anaphylaxis, and elevations are less fleeting than elevations in plasma histamine. However, a 24-hour urine collection started as soon as possible after the reaction begins is required. This is discussed separately. (See "Laboratory tests to support the clinical diagnosis of anaphylaxis", section on 'Histamine metabolites'.)

●**Potential future tests** – The development of a rapid, sensitive, specific laboratory test or panel of tests that helps clinicians to confirm the diagnosis of anaphylaxis in real time remains an important goal [19,41].

A laboratory test for mature beta-tryptase, a better marker of mast cell activation than total tryptase (which measures constitutively secreted alpha-tryptase in addition to beta-tryptase) has been developed, although it is not widely available [19]. Testing for mature beta-tryptase is reviewed separately. (See "Laboratory tests to support the

clinical diagnosis of anaphylaxis" and "Anaphylaxis: Confirming the diagnosis and determining the cause(s)".)

Other potential markers of mast cell and/or basophil degranulation, such as platelet-activating factor, mast cell carboxypeptidase A3, chymase, and basogranulin, are under investigation [41,56,63-65].

DIFFERENTIAL DIAGNOSIS — Approximately 40 other diseases and conditions might need to be considered in the differential diagnosis of anaphylaxis (table 7) [55,66-72]. The most common disorders in the differential diagnosis include acute generalized urticaria and/or angioedema, acute asthma exacerbations, syncope/faint, and anxiety/panic attacks. These are reviewed in detail elsewhere. (See "Differential diagnosis of anaphylaxis in children and adults" and "Anaphylaxis in pregnant and breastfeeding women", section on 'Differential diagnosis' and "Anaphylaxis in infants", section on 'Differential diagnosis'.)

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Anaphylaxis".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Anaphylaxis (The Basics)")
- Beyond the Basics topic (see "Patient education: Anaphylaxis symptoms and diagnosis (Beyond the Basics)")

Other sources of accurate patient information that are accessible through the internet include the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma & Immunology [73,74].

SUMMARY AND RECOMMENDATIONS

- Anaphylaxis is an acute, potentially life-threatening, multisystem syndrome caused by the sudden release of mast cell mediators into the systemic circulation. It most often results from immunoglobulin E (IgE)-mediated reactions to foods, drugs, and insect

stings, but any agent capable of inciting a sudden, systemic degranulation of mast cells can produce it. (See 'Definition and diagnosis' above.)

●There are three clinical criteria for the diagnosis of anaphylaxis, which reflect the different ways in which anaphylaxis may present. Anaphylaxis is highly likely when any **one** of the three criteria is fulfilled (table 1). These diagnostic criteria do not replace clinical judgment, particularly for a patient with a prior episode of anaphylaxis (see 'Diagnostic criteria' above):

- Although recognition of the clinical syndrome of anaphylaxis is generally straightforward, some cases may be difficult to diagnose because anaphylaxis can mimic many other disorders and can be variable in its presentation. Anaphylaxis may present with various combinations of as many as 40 potential symptoms and signs (table 2). (See 'Symptoms and signs' above.)
- Prompt recognition is critical in anaphylaxis. In fatal anaphylaxis, median times to cardiorespiratory arrest are 5 minutes in iatrogenic anaphylaxis, 15 minutes in stinging insect venom-induced anaphylaxis, and 30 minutes in food-induced anaphylaxis. Anaphylaxis is also unpredictable. It may be mild and resolve spontaneously due to endogenous production of compensatory mediators or it may be severe and progress within minutes to respiratory or cardiovascular compromise and death. At the onset of an anaphylactic episode, it is not possible to predict how severe it will become or how rapidly it will progress. For these reasons, early and definitive treatment of suspected anaphylaxis is indicated. (See 'Time course' above.)
- Patients and health care professionals commonly fail to recognize and diagnose anaphylaxis in its early stages when it is most responsive to treatment. In particular, there is a reluctance to diagnose anaphylaxis in the absence of hypotension, even though this sign is not required for the diagnosis and is uncommon in children with anaphylaxis or in food-induced anaphylaxis. (See 'Diagnostic pitfalls' above.)

●Anaphylaxis most often results from an IgE-mediated allergic reaction. Common causes include foods, insect stings, and medications, although there is a rapidly expanding list of novel and/or unusual causes (table 4). (See 'Causes and mechanisms' above.)

●The diagnosis of anaphylaxis is based on clinical criteria. The results of measurements of tryptase and other mediators are not available immediately at the point of care. However, detection of elevated total tryptase (in serum or plasma) or histamine (in plasma) can be helpful in excluding other disorders that do not involve activation of mast cells and basophils. Of note, elevations in these mediators are transient and are not detected in many patients. The blood sample for tryptase should be obtained within 15 minutes to 3 hours of symptom onset (table 6). (See 'Laboratory tests' above.)

●The differential diagnosis of anaphylaxis is broad (table 7). Common disorders that can mimic anaphylaxis include acute generalized urticaria and/or angioedema, acute asthma exacerbations, syncope/faint, and anxiety/panic attacks. (See 'Differential diagnosis' above.)

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