



Rapid recognition and treatment of anaphylaxis

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INTRODUCTION — Anaphylaxis is a potentially fatal disorder. The rate of occurrence is increasing in industrialized countries [[1-5](#)] . All clinicians should be able to recognize anaphylaxis and treat it promptly and appropriately, although the diagnosis is not always readily apparent because anaphylaxis can mimic many other conditions and is variable in its presentation.

This topic discusses the recognition and treatment of anaphylaxis by clinicians working in healthcare settings, such as an emergency department (ED), surgical or obstetrical unit, hemodialysis facility, hospital ward, clinic, or clinician's office [[6-11](#)] .

The pathophysiology of this disorder is discussed separately. ([See "Pathophysiology of anaphylaxis"](#)).

DEFINITION AND DIAGNOSIS — Anaphylaxis is defined as a serious allergic reaction that is rapid in onset and may cause death [[12](#)] . The diagnosis of anaphylaxis is clinical and based primarily upon a detailed description of the acute episode, including antecedent activities and events.

Diagnostic criteria — New diagnostic criteria for anaphylaxis were published by a multidisciplinary group of experts in 2005 and 2006 [[12,13](#)] . These criteria were intended to help clinicians recognize the full spectrum of signs and symptoms that comprise anaphylaxis. Anaphylaxis is significantly underrecognized and undertreated [[1-3,5](#)] . This may partly be due to failure to appreciate anaphylaxis presenting without obvious cutaneous symptoms or overt shock. Anaphylaxis is a much broader syndrome than "anaphylactic shock" however, and the goal of therapy should be early recognition and treatment with epinephrine to prevent progression to life-threatening symptoms, including shock. Recognition of the variable and atypical presentations of anaphylaxis is therefore critical to providing effective therapy in the form of epinephrine, as well as reducing overreliance on less-effective medications, such as antihistamines and [glucocorticoids](#) [[14](#)] .

There are three criteria, each reflecting a different clinical presentation of anaphylaxis ([show table 1](#)) [[12](#)] . Anaphylaxis is highly likely when ANY ONE of the following criteria is fulfilled:

Criterion 1 — Acute onset of an illness (over 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)
- Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse] syncope, incontinence). ([See "Criterion 3" below](#) for definition of reduced BP in patients of different ages)

Note: Cutaneous symptoms are present in up to 90 percent of anaphylactic reactions. This criterion will therefore be used most frequently to make 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 (eg, hypotonia [collapse], syncope, incontinence)
- Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

Note: Ten to 20 percent of people with anaphylaxis lack skin symptoms. This criterion incorporates symptoms in other organ systems and is applied to patients with a known allergy.

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: This criterion is intended to detect episodes of anaphylaxis that consist of isolated cardiovascular symptoms and is applied to individuals with known exposure to an allergen.

Signs and symptoms — Anaphylaxis may present with various combinations of up to 40 potential symptoms and signs ([show table 2](#)) [[8-13,15-23](#)].

The most common signs and symptoms of anaphylaxis are the following:

- Cutaneous symptoms, which occur in up to 90 percent of episodes, including flushing, itching, urticaria, and angioedema (including periorbital edema and conjunctival swelling)
- Respiratory symptoms, which occur in up to 70 percent of episodes, including nasal discharge, nasal congestion, change in voice quality, sensation of throat closure or choking, cough, wheeze, and dyspnea
- Gastrointestinal symptoms, which occur in up to 40 percent of episodes, including nausea, vomiting, diarrhea, and crampy abdominal pain
- Cardiovascular symptoms, which occur in up to 35 percent of episodes, including dizziness, tachycardia, hypotension, and collapse

Anaphylaxis 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 [16,17] . Death from anaphylaxis usually results from asphyxiation due to upper airway edema or respiratory failure due to bronchial obstruction, and less commonly, from cardiovascular collapse [14,24-29] . (See "[Fatal anaphylaxis](#)").

Time course — Anaphylaxis is usually characterized by a defined exposure to a potential trigger, followed by rapid onset, evolution, and resolution of symptoms within minutes to hours.

Biphasic anaphylaxis — Biphasic anaphylaxis is defined as a recurrence of symptoms that develops following the apparent resolution of the initial anaphylactic event. Biphasic reactions have been reported to develop in 1 to 20 percent of anaphylactic reactions and typically occur within eight hours after resolution of the initial symptoms, although recurrences up to 72 hours later have been reported [30] .

Protracted anaphylaxis — Protracted anaphylaxis is defined as an anaphylactic reaction that lasts for hours, or even days in extreme cases [24] .

Pitfalls in making the diagnosis — 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 under-diagnosed and under-reported for a variety of reasons [3,6-10,17,19,20,31] :

- Some healthcare professionals remain reluctant to diagnose anaphylaxis in the absence of overt shock, even though changes in blood pressure are not required for the diagnosis by criterion 1 or 2 [12] . (See "[Diagnostic criteria](#)" above).
- Hypotension may go undetected, particularly in infants or young children, or when the initial blood pressure measurement is obtained after epinephrine administration.
- Many of the dramatic physical signs associated with hypotension and hypoxia in anaphylaxis are non-specific, such as confusion, collapse, unconsciousness, incontinence, sweating, presyncope, dyspnea, stridor, and wheeze ([show table 2](#)).
- Skin symptoms and signs (such as itching, flushing, and urticaria), which are helpful in

making the diagnosis, are absent or unrecognized in 10 to 20 percent of all episodes.

- Skin symptoms may be missed if an individual cannot describe itching, has recently taken an H1 antihistamine, or is not undressed and fully examined during the episode. The latter scenario may occur when anaphylaxis occurs in a public place such as a restaurant [17] .

- Skin symptoms may be missed in patients who are draped during surgery.

- Anaphylaxis may be difficult to recognize in certain specific clinical settings, such as during hemodialysis, surgery, or childbirth, because patients in these settings may experience dramatic physiologic shifts with consequent changes in vital signs [6-10,17,31] . In addition, the inability of the patient to communicate the presence of early symptoms (eg, during anesthesia) also impedes prompt recognition of anaphylaxis.
- Anaphylaxis in a known asthmatic may be mistaken for an asthma exacerbation if accompanying skin symptoms such as hives, or dizziness suggestive of impending shock, are overlooked [17] .
- Patients experiencing their first episode may not recognize the symptoms as a serious allergic reaction. As a result, they may not report symptoms fully, or may focus on one prominent symptom (eg, a patient presenting with vomiting may not report that the episode began with diffuse itching unless specifically asked).
- 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 impair cognition and judgment, making anaphylaxis particularly difficult to recognize in such patients ([show table 3](#)) [17,20,31] .

TRIGGERS AND MECHANISMS — Most anaphylaxis episodes are triggered through an immunologic mechanism involving IgE. Common allergens include foods, medications, and insect stings. The table provides a more comprehensive list of potential anaphylaxis triggers, categorized by causative mechanism ([show table 4](#)) [12,13,15-23] .

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

- Acute systemic reactions involving IgE-dependent mechanisms
- Acute systemic reactions involving other immunologic mechanisms (formerly called anaphylactoid reactions)
- Acute systemic reactions that occur independently of any immunologic mechanism, ie, involve direct release of histamine and other mediators from mast cells and basophils

The initial management of each of these acute reactions is the same, regardless of the trigger or mechanism involved [12,13] .

CONTRIBUTORY FACTORS — Co-morbidities and concurrent medications may impact the severity of symptoms and response to treatment in patients with anaphylaxis ([show table 5](#)) [16-

[18,20](#)] .

Comorbidities — Asthma and cardiovascular disease are the most important risk factors for a poor outcome from anaphylaxis. Other disorders may also increase risk.

- Persistent asthma, especially if not optimally controlled, is an important risk factor for death from anaphylaxis, especially in adolescents and young adults [[14,24-28](#)] .
- Cardiovascular disease is an important risk factor for death from anaphylaxis in middle-aged and older individuals [[29](#)] .
- Chronic obstructive pulmonary disease (COPD) and concurrent pneumonia are also risk factors for death from anaphylaxis in older adults [[29](#)] .
- Acute infection, psychologic stress, and other forms of systemic illness, although not systematically studied in the context of anaphylaxis, may also increase the risk [[16-18,20](#)] .

Concurrent medications — Concurrent administration of certain medications may impact the patient's ability to respond to both treatment and compensatory physiologic responses ([show table 5](#)) [[32](#)] .

- Beta-adrenergic blockers, administered orally, parenterally, or topically (eg, eye drops) may decrease the effects of endogenous or exogenous epinephrine at beta receptors and render patients less responsive to epinephrine [[33](#)] . ([See "Glucagon to counteract beta-blockers" below](#)).
- Angiotensin-converting enzyme inhibitors, and to a lesser extent, angiotensin II receptor blockers, may interfere with endogenous compensatory mechanisms, resulting in more severe or prolonged symptoms [[34](#)] .
- Alpha-adrenergic blockers may decrease the effects of endogenous or exogenous epinephrine at alpha receptors, rendering patients less responsive to epinephrine [[35](#)] .

LABORATORY TESTS — The clinical diagnosis of anaphylaxis can sometimes be supported by documentation of elevated concentrations of plasma histamine or serum or plasma total tryptase [[15,36-39](#)] . It is critical to obtain blood samples for measurement of these mast cell and basophil mediators as soon as possible after the onset of symptoms, as elevations are transient. Instructions for proper collection of samples are provided in the figure ([show figure 1](#)).

- 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 are more likely to be increased than are total serum tryptase levels. ([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, histamine levels will have returned to baseline by the time the patient reaches the emergency department. In addition, the blood samples require special handling. Thus, attempting to obtain this test is impractical in most cases of anaphylaxis occurring outside of the hospital. ([See "Laboratory tests to support the clinical diagnosis of anaphylaxis"](#)).

- Serum or plasma total tryptase - The test for measurement of total serum or plasma tryptase is widely available in clinical laboratories. Optimally, the blood sample for tryptase measurement needs to be obtained within three hours of symptom onset. An elevated total tryptase level (normal range 1 to 11.4 ng/mL, Phadia AB, Uppsala, Sweden; some experts use the range 1 to 15 ng/mL) supports the diagnosis of anaphylaxis. Tryptase elevations are more likely to be detected following reactions that involved hypotension.

Failure to document an elevation in total tryptase cannot be used to disprove the clinical diagnosis [15] . The history trumps the test results. As an example, in individuals with food-induced anaphylaxis, total tryptase levels are seldom elevated, even in optimally-timed blood samples obtained within three hours of symptom onset [24] .

Serial measurements of total tryptase in serum or plasma over several hours may increase the sensitivity and the specificity of the tests [38] . Comparison of a level obtained during the acute episode with a level obtained 24 hours after resolution of clinical signs and symptoms may be useful for confirming the clinical diagnosis [39] . ([See "Laboratory tests to support the clinical diagnosis of anaphylaxis"](#)).

- Potential future tests - The development of a rapid, sensitive, specific laboratory test that helps clinicians to confirm the diagnosis of anaphylaxis in real time remains an important goal [15] .

- 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 [37] . Testing for mature beta-tryptase is reviewed separately. ([See "Laboratory tests to support the clinical diagnosis of anaphylaxis"](#)).

- Other potential markers of mast cell and/or basophil degranulation, such as mast cell carboxypeptidase A3, chymase, basogranulin, and platelet-activating factor, are under investigation [15,40] .

DIFFERENTIAL DIAGNOSIS — Nearly 40 other diseases and conditions might need to be considered in the differential diagnosis of anaphylaxis ([show table 6](#)) [41-48] . These are reviewed in detail separately. ([See "Differential diagnosis of anaphylaxis in children and adults"](#)).

IMMEDIATE MANAGEMENT — Prompt assessment and treatment are critical in anaphylaxis, as death can ensue rapidly [14,22,24,26-29] . The cornerstones of initial management are the following [49-54] :

- Removal of the suspect inciting antigen (eg, stop infusion of a suspect medication)

- Call for help (summon a resuscitation team in the hospital setting, call 911 or an equivalent service in the community setting)
- Intramuscular injection of epinephrine
- Placement of the patient in the supine position (if tolerated)
- Supplemental oxygen
- Volume resuscitation

The median time interval between onset of symptoms and fatal cardiopulmonary arrest was less than 30 minutes in one series of over 200 anaphylactic deaths [[14](#)] . A more detailed review of fatal anaphylaxis is presented elsewhere. ([See "Fatal anaphylaxis"](#)).

Rapid overview table — The tables provide rapid overviews of the initial assessment and emergency management of anaphylaxis in adults ([show table 7](#)) and children ([show table 8](#)). These tables were intended to assist clinicians in emergency department and similar settings.

Initial assessment — A number of critical components in the initial management need to be instituted concomitantly:

- Initially, attention should focus on airway, breathing, and circulation, as well as adequacy of mentation. The skin should be examined.
- Epinephrine should be injected intramuscularly into the anterolateral thigh ([show table 7](#)) ([show table 8](#)) [[50-56](#)] . If symptoms are severe, an intravenous epinephrine infusion should be prepared. ([See "Dosing and administration" below](#)).
- The patient should be placed in the recumbent position with the lower extremities elevated to maximize perfusion of vital organs. This also helps prevent "empty ventricle syndrome," in which severe hypotension leads to inadequate cardiac filling and pulseless electrical cardiac activity [[54](#)] . Individuals with respiratory distress or vomiting may not tolerate the recumbent position. Empty ventricle syndrome is discussed in greater detail separately. ([See "Fatal anaphylaxis"](#)).
- Supplemental oxygen, 6 to 8 liters by face mask, up to 100 percent, should be administered.
- Two 14 to 16 gauge intravenous catheters should be inserted in preparation for rapid administration of fluids and medications.

- Normal saline should be infused (at a rate of 125 mL per hour) to maintain venous access in adults.

- In children, normal saline should be infused in boluses of 20 mL per kilogram, each over 5 to 10 minutes, and repeated as needed. Urine output should be monitored.

- Continuous monitoring of cardiopulmonary status, including heart rate, blood pressure, respiratory rate, and pulse oximetry is required for the duration of the episode.

Airway management — As noted above, the initial steps in anaphylaxis management involve a rapid assessment of the patient's airway:

- Intubation should be performed immediately if marked stridor or respiratory arrest is present.
- Preparations for possible intubation should be made if there is any airway involvement or significant edema of the facial or neck tissues.
- In a minority of cases, an emergency cricothyroidotomy may be required to secure the airway.

Intubation may be difficult in individuals in whom edema distorts the upper airway anatomical landmarks, and failed attempts can lead to complete airway obstruction and fatality. Therefore, upper airway closure in the setting of anaphylaxis should be managed by the most experienced clinician available. This may require (immediate) collaboration between an emergency medicine specialist and an anesthesiologist, otolaryngologist, or intensivist with training and experience in the management of the difficult airway. Hospitals and other healthcare facilities should have clear, written policies about how such situations will be handled.

Intravenous fluids — All patients with anaphylaxis require intravenous fluids. Massive fluid shifts can occur rapidly in anaphylaxis due to increased vascular permeability, with transfer of up to 35 percent of the intravascular volume into the extravascular space within minutes [50] . Any patient who does not respond promptly and completely to injected epinephrine should be assumed to have intravascular volume depletion causing persistent hypotension despite maximum vasoconstriction. These patients should receive large volume fluid resuscitation. The following should guide therapy:

- Normotensive adult patients should received normal saline at a rate of 125 mL per hour to maintain venous access. Normotensive children should receive maintenance fluid replacement. ([See "Maintenance fluid therapy in children"](#)).
- Larger volume fluid resuscitation should be initiated immediately in patients who present with orthostasis, hypotension, or incomplete response to intramuscular epinephrine.

- Adults should receive 1 to 2 liters of normal saline at a rate of 5 to 10 mL/per kilogram in the first minutes of treatment. Large volumes of fluid (eg, up to 7 liters) may be required.

- Children should receive normal saline in boluses of 20 mL per kilogram, each over 5 to 10 minutes, and repeated as needed. Large volumes of fluid (up to 100 mL per kilogram) may be required.

Normal saline is preferred initially for the first few liters, as Lactated Ringer's solution may potentially contribute to metabolic acidosis, and dextrose is rapidly extravasated from the circulation into the interstitial tissues.

Patients with histories of cardiovascular or renal disease must be monitored carefully for clinical response and for volume overload. In patients requiring larger volumes, colloid (albumin or

[hetastarch](#)) and crystalloid (normal saline) appear equally effective. ([See "Treatment of severe hypovolemia or hypovolemic shock in adults"](#) and [see "Hypovolemic shock in children: Initial evaluation and management"](#)).

PHARMACOLOGIC TREATMENT — Pharmacologic treatment of anaphylaxis is based upon extrapolation from therapies used in cardiac arrest and asthma, as well as from uncontrolled human trials of anaphylaxis during insect sting challenges and from studies of anaphylaxis in animal models [[50](#)] . Randomized, controlled studies that meet current standards have not been performed for any therapeutic interventions. Placebo-controlled trials for epinephrine have not been performed and will likely never be performed due to ethical considerations in a disease that can kill within minutes and mandates prompt intervention [[57](#)] .

Epinephrine — Epinephrine is the drug of choice for anaphylaxis. The pharmacologic actions of this agent address the pathophysiologic changes that occur in anaphylaxis better than any other single drug, as it is the only one that prevent or reverses bronchospasm and cardiovascular collapse ([show table 7](#)) ([show table 8](#)). Failure to administer epinephrine early in the course of treatment has been repeatedly implicated in anaphylaxis fatalities [[14,24-29,58](#)] .

Therapeutic actions and adverse effects — The therapeutic actions of epinephrine include the following ([show figure 2](#)) [[51](#)] :

- Alpha-1 adrenergic agonist receptor effects: increased vasoconstriction, increased peripheral vascular resistance, and decreased mucosal edema
- Beta-1 adrenergic agonist effects: increased inotropy and increased chronotropy
- Beta-2 adrenergic agonist effects: increased bronchodilation and decreased release of mediators of inflammation from mast cells and basophils

Epinephrine has a narrow toxic-therapeutic index (risk-to-benefit ratio). In therapeutic doses and by any route, it frequently causes transient adverse effects in individuals of all ages. These include anxiety, fear, restlessness, headache, dizziness, palpitations, pallor, and tremor [[51](#)] .

Rarely, and especially after overdose, it may lead to ventricular arrhythmias, angina, myocardial infarction, pulmonary edema, sudden sharp increase in blood pressure, and intracranial hemorrhage [[51](#)] . ([See "Situations requiring caution" below](#)).

Dosing and administration — Surveys suggest that there is persistent confusion among clinicians regarding the optimal epinephrine dose and route of administration for the treatment of anaphylaxis [[59](#)] .

- Intramuscular injection - Intramuscular injection is recommended over subcutaneous injection because it provides more rapid plasma and tissue concentrations of epinephrine [[52,53](#)] .

- For adults, the recommended dose of aqueous epinephrine (1 mg per mL) is 0.3 to 0.5 mg per single dose, injected intramuscularly into the anterolateral thigh (vastus lateralis muscle). This treatment may be repeated at 5 to 15 minute intervals [[18](#)] .

- For infants and children, the recommended dose of aqueous epinephrine (1 mg per mL) is 0.01 mg per kilogram, injected intramuscularly into the anterolateral thigh (vastus lateralis muscle). This treatment may be repeated at 5 to 15 minute intervals [18] .

If an ampoule of generic epinephrine is not readily available (eg, in a community clinician's office), epinephrine can be administered using a pre-filled adult or pediatric auto-injector, such as EpiPen® or Twin-ject®, intramuscularly into the anterolateral thigh. Children weighing less than 30 kilograms should receive the pediatric dose.

The needle used in adults should be of adequate length to reach the muscle beneath the subcutaneous adipose tissue over the vastus lateralis muscle (eg, 1.5 inches in a normal adult). Realistically, however, intramuscular injection into the thigh may be impossible in overweight or obese individuals, especially women [60] . Although the best approach in this situation has not been studied, we suggest as deep an injection as possible over the muscle, followed by intravenous infusion administration if there is an inadequate response to the initial dose.

- Intravenous infusion and indications - Patients who do not respond to an initial intramuscular injection of epinephrine and fluid resuscitation may not be adequately perfusing muscle tissues and should receive additional epinephrine by intravenous infusion. This most commonly occurs in individuals presenting with profound hypotension or symptoms suggestive of impending shock (dizziness, incontinence of urine or stool).

- For adults, the dose for intravenous epinephrine infusion is 2 to 10 micrograms per minute, titrated to effect on blood pressure with continuous hemodynamic monitoring.

- For infants and children, the dose for intravenous infusion of epinephrine is 0.1 to 1 microgram per kilogram per minute, titrated to effect on blood pressure with hemodynamic monitoring [61]

- Endotracheal dosing - If intravenous access cannot be obtained immediately, epinephrine can be delivered via the endotracheal tube. The efficacy of this delivery method is based upon small series of patients experiencing cardiac arrest [62] .

- For adults, 3 to 5 mL of aqueous epinephrine (of 0.1 mg per mL preparation), may be instilled endotracheally.

- For children, 0.2 mL per kilogram of aqueous epinephrine (of 0.1 mg per mL preparation), up to 5 mL, may be instilled endotracheally.

Situations requiring caution — There are NO absolute contraindications to epinephrine use in anaphylaxis [18,51] .

There are, however, subgroups of patients who might theoretically be at higher risk for adverse effects during epinephrine therapy, although formal risk-benefit analyses are not possible and clinical judgment is essential:

- Patients with cardiovascular diseases: reluctance to administer epinephrine due to fear of adverse cardiac effects should be countered by the awareness that myocardial ischemia and dysrhythmias can occur in untreated anaphylaxis [63,64] .
- Patients receiving monoamine oxidase inhibitors (which block epinephrine metabolism), or tricyclic antidepressants (which prolong epinephrine duration of action).
- Patients receiving stimulant medications (eg, amphetamines or [methylphenidate](#) used in the treatment of attention deficit hyperactivity disorder) or abusing cocaine
- Patients with certain preexisting conditions, such as recent intracranial surgery, aortic aneurysm, uncontrolled hyperthyroidism or hypertension, or other conditions that might place them at higher risk for adverse effects related to epinephrine.

To reiterate, there are no absolute contraindications to the use of epinephrine in the treatment of anaphylaxis because the risk of death or serious disability from anaphylaxis itself usually outweighs other concerns [18,51] . The authors believe that existing evidence clearly favors the benefit of epinephrine administration in most situations.

Glucagon to counteract beta-blockers — Patients receiving beta-blockers may be resistant to treatment with epinephrine and can develop refractory hypotension and bradycardia. [Glucagon](#) should be administered in this setting because it has inotropic and chronotropic effects that are not mediated through beta-receptors [65] . A dose of 1 to 2 mg in adults (in children, 20 to 30 micrograms per kilogram to a maximum of 1 mg) administered intravenously over 5 minutes is recommended, which may be repeated or followed by an infusion of 5 to 15 micrograms per minute. Rapid administration of glucagon can induce vomiting.

The further management of hypovolemic shock is discussed separately. ([See "Hypovolemic shock in children: Initial evaluation and management"](#) and [see "Treatment of severe hypovolemia or hypovolemic shock in adults"](#)).

Adjunctive agents — Adjunctive therapies for the treatment of anaphylaxis include antihistamines, bronchodilators, [glucocorticoids](#) , and other vasopressors.

Antihistamines — Epinephrine is first-line treatment for anaphylaxis and there is no equivalent substitute. Despite this, H1-antihistamines are the most commonly administered medications in the treatment of anaphylaxis, indicating over-reliance on these agents, which should be considered adjunctive [66-69] .

There is very limited evidence to support the use of H1 antihistamines in the emergency treatment of anaphylaxis. A systematic review of the literature failed to retrieve any randomized, controlled trials demonstrating efficacy [57] .

H1-antihistamines relieve itch and hives. These medications DO NOT relieve upper or lower airway obstruction, gastrointestinal symptoms, or shock, and (in standard doses) do not prevent mediator release from mast cells and basophils. It is probable that the improvement in non-cutaneous symptoms that is sometimes attributed to antihistamine treatment occurs instead because of endogenous production of epinephrine and other compensatory mediators, including

other catecholamines, angiotensin II, and endothelin I [17] .

Thus, H1 antihistamines should be used as adjunctive agents in anaphylaxis, for the purpose of relieving itching and hives. The following are commonly administered:

- For adults: [diphenhydramine](#) 25 to 50 mg intravenously; may be repeated up to a maximum daily dose of 400 mg
- For children: diphenhydramine 25 to 50 mg intravenously; may be repeated up to a maximum daily dose of 5 mg per kilogram or 300 mg

Second-generation H1-antihistamines (specifically [cetirizine](#) or [levocetirizine](#)) are preferred for oral therapy over first-generation agents (eg, [diphenhydramine](#), [chlorpheniramine](#), [hydroxyzine](#), and [promethazine](#)). These newer agents begin to work within one hour, and are less likely to cause sedation or impair psychomotor performance or the ability to drive [57,70] . These agents are not available for parenteral administration.

There is minimal evidence to support the use of H2 antihistamines in the emergency treatment of anaphylaxis, although there is no evidence of harm:

- If used, [ranitidine](#) (50 mg in adults) (12.5 to 50 mg [1 mg per kilogram] in children), may be diluted in 5 percent dextrose to a total volume of 20 mL and injected intravenously over 5 minutes.

Bronchodilators — For the treatment of bronchospasm not responsive to IM epinephrine, inhaled bronchodilators, such as [albuterol](#), should be used as needed. These agents do not prevent or relieve mucosal edema in the airway; mucosal edema is treated with the alpha-1 effects of epinephrine [51] . Thus, bronchodilators are considered to be an adjunctive therapy to IM epinephrine.

In most emergency care settings, nebulized therapy is more practical than metered-dose inhalers (with spacers) for patients with respiratory distress. Moreover, the effectiveness of [albuterol](#) delivery via nebulizer versus metered-dose inhaler (with spacer) remains uncertain for patients with severe respiratory distress. Therefore, we recommend albuterol administration via nebulizer in this setting.

Glucocorticoids — [Glucocorticoids](#) do not appear to be helpful in the treatment of acute anaphylaxis. However, these agents are sometimes given on an empirical basis with the rationale that they may help to prevent the biphasic or protracted reactions that occur in up to 20 percent of individuals. There is no satisfactory published evidence that they actually have this effect [30,71] .

If given, a dose of [methylprednisolone](#) of 1 to 2 mg per kilogram per day is sufficient. If corticosteroid treatment is instituted, it should be stopped after 3 or 4 days, since all biphasic reactions reported to date have occurred within 72 hours [30] . ([See "Time course" above](#)).

Refractory anaphylaxis — There are no published prospective studies on the optimal management of refractory anaphylactic shock. Admission to an intensive care unit should be

arranged without delay.

Vasopressors — Patients who have persistent hypotension despite the administration of epinephrine and intravenous fluids should receive additional vasopressor medications, titrated to effect. There is no compelling evidence to support one vasopressor over another in this clinical scenario. Options include the following:

- [Dopamine](#): 5 to 20 micrograms per kilogram per minute for adults
- [Norepinephrine](#): 0.5 to 30 micrograms per minute for adults
- [Phenylephrine](#): 30 to 180 micrograms per minute for adults

One report described a beneficial effect of the intravenous injection of [vasopressin](#) (10-40 IU) in a hypotensive adult with severe anaphylaxis unresponsive to epinephrine treatment [72] . Invasive hemodynamic monitoring is often required to guide vasopressor therapy [72,73] . ([See "Use of vasopressors and inotropes"](#) and [see "Swan-Ganz catheterization: Indications and complications"](#)).

Anaphylactic shock displays features of both distributive (vasodilatory) and hypovolemic shock, disorders that are reviewed separately. ([See "Management of severe sepsis and septic shock in adults"](#), [see "Septic shock: Initial evaluation and management in children"](#), [see "Treatment of severe hypovolemia or hypovolemic shock in adults"](#), and [see "Hypovolemic shock in children: Initial evaluation and management"](#)).

TREATMENT ERRORS — Important errors in the treatment of anaphylaxis include failure to administer epinephrine promptly and over-reliance on antihistamines and [albuterol](#) when epinephrine is indicated.

- Epinephrine should be administered as soon as possible once anaphylaxis is recognized. Delayed administration has been implicated in contributing to fatalities [14,24-29] . In a study of 13 fatal or near-fatal food-induced anaphylactic reactions in children, six of the seven children who survived received epinephrine within 30 minutes of ingesting the allergen, whereas only two of the six children who died received epinephrine within the first hour [24] .
- H1-antihistamines are useful only for relieving itching and urticaria, as mentioned previously. They do NOT relieve stridor, shortness of breath, wheezing, gastrointestinal symptoms, or shock, and should not be substituted for epinephrine [70] .
- Bronchodilator treatment with nebulized albuterol should be given in individuals with severe bronchospasm, as an adjunctive treatment with IM epinephrine. However, albuterol does not relieve airway edema and should not be substituted for IM epinephrine in the treatment of anaphylaxis.

CARE UPON RESOLUTION — Patients who have been successfully treated for anaphylaxis subsequently require confirmation of the anaphylaxis trigger, as well as anaphylaxis education in order to reduce the risk of recurrence.

Observation — There is no consensus regarding the optimal amount of time that a patient who has been successfully treated for anaphylaxis should be observed prior to discharge. We suggest the following:

- Some individuals with moderate anaphylaxis (especially if symptoms did not respond promptly to epinephrine treatment) and all individuals with severe anaphylaxis should be admitted to an observation unit or to hospital.
- For patients with anaphylaxis that resolved promptly and completely with treatment, we suggest a minimum observation period of two hours, and prefer a period of 8 hours (if possible). We also suggest that if patients are sent home after only two hours, that they be supplied with an actual epinephrine auto-injector (and training in its use), rather than simply a prescription. As noted previously, up to 20 percent of individuals may experience a recurrence of symptoms, which usually begin within 8 hours after the initial reaction, although symptom recurrence as late as 72 hours has been reported [30] . ([See "Biphasic anaphylaxis" above](#)).

Discharge care — All patients who have experienced anaphylaxis should be sent home with an Anaphylaxis emergency action plan, an epinephrine auto-injector(s), a plan for arranging further evaluation, and printed information about anaphylaxis and its treatment.

Anaphylaxis emergency action plan — Patients should be given a written Anaphylaxis Emergency Action Plan that contains information about self-injection of epinephrine prior to discharge ([show figure 3](#)) [17,74] .

Epinephrine auto-injector — Patients should also be supplied with an epinephrine auto-injector directly, or if this is not possible, provided with a prescription and advised to fill it immediately. Instructions in the proper use of epinephrine autoinjectors should be reviewed verbally and accompanied by written information. ([See "Information for patients" below](#) [See "Information for patients" below](#)).

Counseling — The mnemonic "SAFE" was developed to remind clinicians of the four basic action steps suggested for patients with anaphylaxis who have been treated and are subsequently leaving the emergency department or hospital [75] . The SAFE counseling is outlined below and has been incorporated into printable patient information materials. ([See "Information for patients" below](#) [See "Information for patients" below](#)).

- Seek support - Advise the patient that:
 - They have experienced anaphylaxis or "killer allergy", which is a life-threatening condition.
 - Symptoms of the current episode may recur up to three days after the initial onset of symptoms.
 - They should call an ambulance or get to the nearest emergency facility at the first sign of recurrence of symptoms, even if they have self-administered epinephrine already.
 - They are at risk for repeat episodes of anaphylaxis in the future.

Refer the patient to informational resources. ([See "Information for patients" below](#) [See "Information for patients" below](#)).

- Allergen identification and avoidance - The clinician should:

- Make efforts to identify the patient's trigger (either through history or in vitro testing) before the patient is discharged.

- Emphasize the importance of subsequent testing to determine and verify the trigger, so that it can be successfully avoided in the future.

- Follow-up with specialty care

- Advise the patient to follow up with his or her primary care clinician and obtain a referral to an allergist or to seek consultation directly with an allergist for testing, diagnosis, and ongoing management of the allergy.

- Epinephrine for emergencies

- Provide the patient with a prescription for self-injectable epinephrine (or supply the device directly) and verbal plus written instructions for its use.

- Explain the importance of carrying epinephrine at all times.

- Advise the patient to make sure that family and friends are aware of the risks of anaphylaxis, the patient's triggers, and how to administer epinephrine.

Information for patients — Educational materials about anaphylaxis and the correct use of epinephrine autoinjectors are available for patients. The SAFE counseling has been incorporated into these materials. We encourage clinicians to print or e-mail these topics, or to refer patients to the public web site, www.uptodate.com/patients, which includes these and other topics. ([See "Patient information: Use of an epinephrine autoinjector"](#)).

Other sources of accurate patient information, accessible through the Internet, include the American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology [[76,77](#)] .

LONG-TERM PROGNOSIS — Many patients with anaphylaxis will experience recurrent episodes unless long-term risk reduction measures are implemented [[17,75](#)] . Specifically, the trigger for the anaphylactic event should be verified, which is not always easily accomplished. In addition, extensive education is required in order to successfully avoid an allergen, and patients must be trained in self-treatment for recurrent episodes. For these reasons, patients with anaphylaxis would benefit from referral to an allergy specialist.

INFORMATION FOR PATIENTS — Educational materials on this topic are available for patients. ([See "Patient information: Anaphylaxis"](#) and [see "Patient information: Use of an epinephrine autoinjector"](#)). We encourage you to print or e-mail this topics, or to refer patients to our public web site www.uptodate.com/patients, which includes this and other topics.

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SUMMARY AND RECOMMENDATIONS — Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. Recognition is not always easy, because anaphylaxis can mimic many other disorders and can be variable in its presentation. ([See "Introduction" above](#)).

- Clinicians should not equate anaphylaxis with anaphylactic shock, as the latter represents the severe end of a spectrum, and the goal of therapy is early recognition and treatment with epinephrine to prevent progression to life-threatening symptoms. ([See "Definition and diagnosis" above](#)).

Clinical manifestations — Anaphylaxis may present with various combinations of up to 40 potential symptoms and signs ([show table 2](#)).

- There are three clinical criteria for the diagnosis of anaphylaxis, which reflect the different ways in which anaphylaxis may present ([show table 1](#)). Patients fulfilling ANY ONE criterion may be diagnosed with anaphylaxis. ([See "Diagnostic criteria" above](#)).
- Most anaphylaxis episodes are triggered through an immunologic mechanism involving IgE, although other mechanisms are possible. Common triggers include foods, medications, and insect stings, and there is a rapidly expanding number of novel and/or unusual triggers ([show table 4](#)). ([See "Triggers and mechanisms" above](#)).
- The clinical diagnosis of anaphylaxis can sometimes be supported by documentation of elevated concentrations of plasma histamine or serum or plasma total tryptase, although these elevations are transient and blood must be collected within minutes to hours of symptom onset ([show figure 1](#)). ([See "Laboratory tests" above](#)).

Treatment — Prompt recognition and treatment are critical in anaphylaxis. In fatal cases, death typically ensues within 30 minutes from exposure to the trigger. Initial management is summarized in a rapid overview table for adults ([show table 7](#)) and children ([show table 8](#)).

- Immediate management includes the following ([see "Immediate management" above](#)):
 - Assess airway, breathing, circulation, and adequacy of mentation
 - Call for help (summon a resuscitation team in the hospital setting, call 911 or an equivalent service in the community setting)
 - Stop/remove the inciting agent (if still present)
 - Place the patient in the supine position with legs elevated (if tolerated)
 - Administer intramuscular epinephrine
 - Establish intravenous access with two 14 to 16 gauge catheters
- Immediate intubation is indicated if stridor or respiratory arrest is present, and should be performed by the most experienced clinician available. The airway must be monitored throughout the duration of treatment. ([See "Airway management" above](#)).
- We recommend that all patients with anaphylaxis receive epinephrine. This should be administered as soon as possible after the onset of symptoms. Intramuscular injection into the anterolateral thigh is the preferred initial route of administration. We suggest the following intramuscular dosing. ([See "Dosing and administration" above](#)):

- For adults, the dose of aqueous epinephrine is 0.3 mg to 0.5 mg, injected intramuscularly into the anterolateral thigh. This treatment may be repeated at 5 to 15 minute intervals.

- For infants and children, the dose of aqueous epinephrine is 0.01 mg per kilogram, injected intramuscularly into the anterolateral thigh. This treatment may be repeated at 5 to 15 minute intervals.

- We recommend that all patients with anaphylaxis receive intravenous fluids. Patients with orthostasis, hypotension, or incomplete response to epinephrine should receive large volume fluid resuscitation with normal saline. Normotensive patients should receive normal saline to maintain venous access. ([See "Intravenous fluids" above](#)).
- For patients with profound hypotension or symptoms suggestive of impending shock (dizziness, incontinence of urine or stool) or those who do not respond to an initial intramuscular injection of epinephrine and fluid resuscitation, we suggest administration of epinephrine by continuous intravenous infusion. Immediate transfer to an intensive care setting should be facilitated. ([See "Refractory anaphylaxis" above](#)).
- H1 and H2 antihistamines help relieve cutaneous symptoms such as itching and hives. However, antihistamines cannot be used in place of epinephrine because these agents DO NOT relieve upper or lower airway obstruction, gastrointestinal symptoms, or shock, or prevent mediator release from mast cells and basophils. ([See "Antihistamines" above](#)).
- For patients with bronchospasm unresponsive to IM epinephrine, inhaled bronchodilators, such as [albuterol](#) , should be administered as needed by nebulization. ([See "Bronchodilators" above](#)).

Care after acute treatment — Patients successfully treated for anaphylaxis should be discharged with the following:

- An Anaphylaxis Emergency Action Plan ([show figure 3](#))
- An epinephrine auto-injector(s)
- Printed information about anaphylaxis and its treatment ([see "Information for patients" above](#) see ["Information for patients" above](#))
- A plan for arranging further evaluation

It is critical that patients be evaluated further to determine the trigger, as specific measures may be able to reduce the risk of recurrence. ([See "Care upon resolution" above](#) and [see "Long-term prognosis" above](#)).

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GRAPHICS

Diagnostic criteria for anaphylaxis

Anaphylaxis is highly likely when any ONE of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING

A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

B. Reduced BP* or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence)

2. TWO OR MORE OF THE FOLLOWING that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

A. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)

B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

C. Reduced BP* or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)

D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

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

A. Infants and children: low systolic BP (age specific)* or greater than 30 percent decrease in systolic BP

B. Adults: systolic BP of less than 90 mm Hg or greater than 30 percent decrease from that person's baseline

PEF: Peak expiratory flow; BP: blood pressure.

* Low systolic blood pressure for children is defined as:

- less than 70 mm Hg from 1 month to 1 year,
- less than (70 mm Hg + [2 x age]) from 1 to 10 years, and
- less than 90 mm Hg from 11 to 17 years.

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Signs and symptoms of anaphylaxis

Skin:

Feeling of warmth, flushing [erythema], itching [may begin on palms and soles], urticaria, angioedema, morbilliform rash, and "hair standing on end" [piloerection]

Oral:

Itching or tingling of lips, tongue, or palate

Edema of lips, tongue, uvula, metallic taste

Infants: drooling

Gastrointestinal:

Nausea, abdominal pain [colic, cramps], vomiting [large amounts of "stringy" mucus], and diarrhea

Difficulty swallowing*

Respiratory:

Laryngeal - pruritus and "tightness" in the throat, dysphagia, dysphonia and hoarseness, and sensation of itching in the external auditory canals

Lung - shortness of breath, dyspnea, chest tightness, deep or repetitive cough, and wheezing

Nose - itching, congestion, rhinorrhea, and sneezing

Cardiovascular:

Feeling of faintness or dizziness; syncope, chest pain, palpitations, and/or hypotension (tunnel vision, difficulty hearing)

Neurologic:

Anxiety, apprehension, sense of impending doom, seizures, headache*, confusion

Infants: lethargy, hypotonia

Ocular:

Periorbital itching, erythema and edema, tearing, and conjunctival erythema

Other:

Lower back pain due to uterine cramping in women

* Often occurs in association with throat tightness and other upper airway symptoms.

• Not common in anaphylaxis overall; however, reported in up to 30 percent of patients with exercise-induced anaphylaxis.

Comorbidities and concurrent medications that might interfere with recognition of trigger or symptoms

Comorbidities

Impairment of vision or hearing

Neurologic disease

Psychiatric disease (eg, depression, ADHD)

Developmental delay

Behavioral problems

Substance abuse

Concurrently administered medications

Sedatives (eg, sedating H₁-antihistamines)

Hypnotics

Alcohol (ethanol)

Recreational drugs

ADHD: Attention deficit-hyperactivity disorder.

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Triggers of anaphylaxis

Allergen triggers (IgE-dependent immunologic mechanism)

Foods, especially peanut, tree nut, seafood, finned fish, milk, egg
Insect stings and bites (eg, Hymenoptera venom)
Natural rubber latex
Medications (eg, beta-lactam antibiotics)
Biological materials, including allergens, vaccines, and hormones (eg, progesterone)
Food additives, including spices, insect-derived colorants (eg, carmine), and vegetable gums
Inhalants (eg, horse dander)
Seminal fluid
Occupational allergens
Immunologic triggers (IgE-independent immunologic mechanism)
Complement system activation
Coagulation system activation
Idiopathic anaphylaxis
Auto-immune mechanism in some patients
Clonal mast cell disorders
Non-immunologic triggers (direct action of mast cells and basophils)
Physical factors (eg, exercise*, cold, heat, sunlight/ultraviolet radiation)
Medications (eg, opiates)
Alcohol (ethanol)

Any food, medication or biological, or insect sting or bite may trigger anaphylaxis. Novel or unusual allergen triggers are frequently described. These include foods such as vegetables, fruits, lupin flour, mites, bird's nest soup, and seal, whale, and kangaroo meats. They also include insect saliva from mosquitoes, pigeon ticks, triatomid bugs, green ants, and pharaoh ants, and venoms from jellyfish, scorpions, and snakes. Medications include taxenes, platins, and other chemotherapy drugs; biologic agents, including monoclonal antibodies such as rituximab and omalizumab, and various other ingestants and injectants, including Botox, bee products, and herbal formulations.

Some triggers such as insect venom, radiocontrast media, and medications (such as non-steroidal anti-inflammatory drugs) act through more than one mechanism.

* Usually involves a co-trigger such as food, medication, or exposure to cold air or water.

Comorbidities and concurrent medications that may impact the severity and treatment of anaphylaxis

Comorbidities

Asthma

Other pulmonary diseases: COPD, pneumonia

Cardiovascular disease

Concurrently administered medications

β -Adrenergic blockers •

α -Adrenergic blockers •

Angiotensin-converting enzyme inhibitors Δ

Angiotensin II receptor blockers Δ

Tricyclic antidepressants \diamond

Monoamine oxidase inhibitors \diamond

ADHD medications \S (eg, amphetamines, methylphenidate)

COPD: Chronic obstructive pulmonary disease

ADHD: Attention deficit-hyperactivity disorder

• Potentially decrease epinephrine efficacy by blocking effects at adrenergic receptors (including topical eye drops).

Δ Potential interference with endogenous compensatory responses.

\diamond Potential increase in adverse effects of epinephrine because of prevention of epinephrine uptake at adrenergic receptors.

\S Side effects are similar to those of epinephrine.

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Instructions for optimal collection and handling of blood samples for measurement of histamine and tryptase following suspected anaphylaxis

Histamine (plasma)

When to collect the sample:

Plasma histamine should be collected as soon as possible after symptom onset: preferably within 30 min, and no later than 60 min.

How to collect the sample:

Pull blood manually (DO NOT use vacuum tubes) under gentle pressure through a 20 gauge or larger needle into a syringe containing either citrate or EDTA.

How to process the sample:

Anticoagulated blood should be placed on ice and centrifuged to separate plasma from cells as soon as possible, and then frozen until ready to be analyzed.

Tryptase (serum or plasma)

When to collect the sample:

Blood should be collected within the first one to three hours after symptom onset whenever possible.

How to collect the sample:

Blood can be drawn using normal technique. Collect blood for serum (red top tube) or plasma (tube with heparin, citrate or EDTA). A minimum of 1 mL is required.

For postmortem samples, blood is best collected from the femoral artery or vein.

How to process the sample:

Serum or plasma should be placed on ice and frozen as soon as possible. Samples should be shipped frozen by overnight courier if the assay cannot be performed on site.

Differential diagnosis of anaphylaxis

Common disorders

Vasovagal reaction (faint)
 Acute generalized urticaria
 Acute angioedema
 Acute asthma exacerbation
 Vocal cord dysfunction
 Other anxiety disorders
 Other causes of acute respiratory distress in children
 Myocardial infarction or stroke in adults
 Other forms of shock

Other disorders

Causes of flushing

Medications (including vancomycin, cephalosporins, griseofulvin, niacin, levodopa, amyl nitrate, and bromocriptine)
 Alcohol (ethanol)(alcohol-induced flushing may be exacerbated by certain medications)
 Menopause
 Tumors (carcinoid, intestinal tumors secreting VIP or substance P, pheochromocytoma, medullary carcinoma of the thyroid)

Food associated symptoms

Scombroidosis
 Anisakiasis
 Other (eg, sulfites)

Rare disorders

Histamine excess syndromes

Mastocytosis

Other clonal mast cell disorders

Certain leukemias

Hydatid cyst rupture

Capillary Leak Syndrome

The differential diagnosis in children and adults is shown. In infants, the differential diagnosis of anaphylaxis is unique.

Rapid Overview: Emergent management of anaphylaxis in adults

DIAGNOSIS IS MADE CLINICALLY:

Most common signs and symptoms are cutaneous (eg, urticaria, angioedema, flushing, pruritus). However, some patients have no skin findings.

Danger signs: Rapid progression of symptoms, respiratory distress (eg, wheezing, increased work of breathing, persistent cough, stridor), persistent vomiting, hypotension, syncope, dysrhythmia, chest pain

ACUTE MANAGEMENT:

The first and most important therapy in anaphylaxis is epinephrine. There are **no absolute contraindications** to epinephrine in the setting of anaphylaxis.

Airway: Immediate intubation if evidence of impending airway obstruction from angioedema; delay may lead to complete obstruction; intubation can be difficult; cricothyrotomy maybe necessary

IM Epinephrine: Give aqueous epinephrine 0.3 to 0.5 mg intramuscularly, preferably in the anterolateral thigh; can repeat every 3 to 5 minutes as needed. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below)

Place patient in recumbent position, if tolerated, and elevate lower extremities

Oxygen: Give 6 to 8 liters per minute via face mask, or up to 100 percent oxygen as needed

Normal saline rapid bolus: Treat hypotension with rapid infusion of 1 to 2 liters IV; repeat as needed; massive fluid shifts with severe loss of intravascular volume can occur

Albuterol: For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer; repeat as needed

Antihistamine (H1 blocker): Give diphenhydramine 25 to 50 mg IV

Antihistamine (H2 blocker): Consider giving ranitidine 50 mg IV

Corticosteroid: Consider giving methylprednisolone 125 mg IV

Hemodynamic and pulse oximetry monitoring should be performed continuously

TREATMENT OF REFRACTORY SYMPTOMS:

Epinephrine infusion: For patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion, 2 to 10 micrograms per minute, titrated to effect and with constant hemodynamic monitoring

Vasopressors: Patients may require large amounts of IV crystalloid to maintain blood pressure; if response to epinephrine and saline is inadequate, dopamine (5 to 20 micrograms per kilogram per minute) can be given by continuous infusion, titrated to effect and with constant hemodynamic monitoring

Glucagon: Patients on beta-blockers may not respond to epinephrine and can be given glucagon 1 to 2 mg IV over 5 minutes, followed by infusion of 5 to 15 micrograms per minute

Rapid Overview: Emergent management of anaphylaxis in infants and children

DIAGNOSIS IS MADE CLINICALLY

Most common signs and symptoms: cutaneous (eg, urticaria, angioedema, flushing, pruritus) and vomiting

Danger signs: Rapid progression of symptoms, evidence of respiratory distress (eg wheezing, increased work of breathing, retractions, persistent cough, stridor), signs of

poor perfusion*, syncope, dysrhythmia**ACUTE MANAGEMENT**

The first and most important therapy in anaphylaxis is epinephrine. There are **no absolute contraindications** to epinephrine in the setting of anaphylaxis

Airway: Immediate intubation if evidence of impending airway obstruction from angioedema; delay may lead to complete obstruction; intubation can be difficult and cricothyrotomy may be necessary

IM Epinephrine: Give epinephrine 0.01 mg per kilogram intramuscularly, preferably in the anterolateral thigh, can repeat every 3 to 5 minutes as needed. If signs of poor perfusion* are present or symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below)

Place patient in recumbent position, if tolerated, and elevate lower extremities

Oxygen: Give 6 to 8 liters per minute via face mask, or up to 100 percent oxygen as needed

Normal saline rapid bolus: Treat signs of poor perfusion* with rapid infusion of 20 mL per kilogram; re-evaluate and repeat fluid boluses (20 mL per kilogram) as needed; massive fluid shifts with severe loss of intravascular volume can occur; monitor urine output

Albuterol: For bronchospasm resistant to IM epinephrine, give albuterol 0.15 mg per kilogram (minimum dose: 2.5 mg) in 3 mL saline inhaled via nebulizer; repeat as needed

Antihistamine (H1 blocker): Give diphenhydramine 1 to 2 mg per kilogram (max 50 mg) IV; can give IM if symptoms are less severe

Antihistamine (H2 blocker): Consider giving ranitidine 1 to 2 mg per kilogram (max 50 mg) IV

Corticosteroid: Consider giving methylprednisolone 2 mg per kilogram (max 125 mg) IV

Hemodynamic and pulse oximetry monitoring should be performed continuously

TREATMENT OF REFRACTORY SYMPTOMS

Epinephrine infusion: Patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion at 0.1 to 1 microgram per kilogram per minute, titrated to effect and with constant hemodynamic monitoring

Vasopressors: Patients may require large amounts of IV crystalloid to maintain blood pressure; if response to epinephrine and saline is inadequate, dopamine (5 to 20 micrograms per kilogram per minute) can be given as continuous infusion, titrated to effect and with constant hemodynamic monitoring

* See the topic "Assessment of perfusion in pediatric resuscitation".

Physiologic effects and adverse effects of epinephrine in the treatment of anaphylaxis**Physiologic effects**

	<p>At alpha-1 receptor:</p> <ul style="list-style-type: none"> Increased vasoconstriction Increased peripheral vascular resistance Increased blood pressure Decreased mucosal edema (eg, in larynx) <p>At beta-1 receptor:</p> <ul style="list-style-type: none"> Increased heart rate (inotropy) Increased force of cardiac contraction (chronotropy) <p>At beta-2 receptor:</p> <ul style="list-style-type: none"> Decreased mediator release from mast cells and basophils Increased bronchodilation Increased vasodilation
Adverse effects*	
Common and transient	Anxiety, fear, restlessness, dizziness, headache, palpitations, pallor, tremor
Uncommon (occur more often in overdose)	Ventricular arrhythmias, angina, myocardial infarction, pulmonary edema, sudden sharp increase in blood pressure, intracranial

hemorrhage

* Risk of adverse effects may be increased in the following conditions:

- Use of cocaine, monoamine oxidase inhibitors, or tricyclic antidepressants
- Some preexisting cardiovascular, central nervous system, or thyroid diseases

Anaphylaxis Emergency Action Plan

NAME: _____		AGE: _____	
ALLERGY TO: _____			
Asthma <input type="checkbox"/> Yes (<i>high risk for severe reaction</i>)		<input type="checkbox"/> No	
Other health problems besides anaphylaxis: _____			
Concurrent medications, if any: _____			
SYMPTOMS OF ANAPHYLAXIS INCLUDE:			
MOUTH	itching, swelling of lips and/or tongue		
THROAT*	itching, tightness/closure, hoarseness		
SKIN	itching, hives, redness, swelling		
GUT	vomiting, diarrhea, cramps		
LUNG*	shortness of breath, cough, wheeze		
HEART*	weak pulse, dizziness, passing out		
<i>Only a few symptoms may be present. Severity of symptoms can change quickly. *Some symptoms can be life-threatening! ACT FAST!</i>			
WHAT TO DO:			
1. INJECT EPINEPHRINE IN THIGH USING (check one): <input type="checkbox"/> EpiPen Jr (0.15 mg) <input type="checkbox"/> Twinject 0.15 mg			
<input type="checkbox"/> EpiPen (0.3 mg) <input type="checkbox"/> Twinject 0.3 mg			
Other medication/dose/route: _____			
IMPORTANT: ASTHMA PUFFERS AND/OR ANTIHISTAMINES CAN'T BE DEPENDED ON IN ANAPHYLAXIS!			
2. CALL 911 or RESCUE SQUAD (BEFORE CALLING CONTACTS)!			
3. Emergency contact #1: home _____ work _____ cell _____			
Emergency contact #2: home _____ work _____ cell _____			
Emergency contact #3: home _____ work _____ cell _____			
DO NOT HESITATE TO GIVE EPINEPHRINE!			
COMMENTS: _____			

Doctor's Signature/Date		Parent's Signature (for individuals under age 18 yrs)/Date	

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