

Anaphylaxis

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THE STORY IN ONE SENTENCE

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“Anaphylaxis happens when mast cells everywhere dump their chemical cargo at the same moment—blood vessels relax and leak fluid, blood pressure drops, and airways squeeze shut.”

Normal anatomy — the body's job

Mast cells live in tissues throughout your body—skin, lung lining, gut wall, blood vessel walls—and carry IgE antibodies on their surface like guards wearing specific alarm sensors. Each IgE molecule binds to one specific allergen. Normally, when a mast cell encounters its target, it releases chemicals like histamine (widens blood vessels and makes them leaky) and leukotrienes (tighten airways and drive swelling) in a small, controlled area to fight parasites or signal inflammation. This keeps the reaction local and limited—one patch of skin gets red and itchy, or one small area of lung tissue tightens, then the reaction stops. The chemicals are broken down quickly, blood vessels return to normal size, airways relax, and your body returns to baseline. Keep that picture in mind—anaphylaxis is what happens when this tightly controlled, local defense becomes a whole-body storm.

BODY'S JOB

If you do not understand the normal, controlled mast-cell response first, the explosive, multi-system cascade of anaphylaxis will seem like random chaos instead of one upstream break with predictable downstream effects.

1. Mast cells sit in tissues—skin, lung lining, gut wall, blood vessel walls—like guards waiting for trouble.
2. Each mast cell wears IgE antibodies on its surface like locks waiting for the right key.
3. Each IgE molecule recognizes only one specific allergen—a peanut protein, a bee venom peptide, a penicillin molecule.
4. When the allergen enters your body, it locks onto two or more IgE molecules sitting side-by-side on the mast cell, like a key turning two locks at once.
5. That cross-linking activates the mast cell membrane, triggering the cell to release granules—tiny storage sacks full of histamine, leukotrienes, tryptase (a tissue-breaking enzyme), and prostaglandins—into the nearby tissue.
6. Normally, this release stays local—one patch of skin gets red and itchy, or one small area of lung tissue tightens—then the reaction stops.
7. The chemicals are broken down quickly by enzymes in your blood and tissue, blood vessels return to normal size, airways relax, and your body returns to baseline.
8. This tight control keeps you safe: you fight off a parasite or a small infection without your whole body reacting.

What breaks

One upstream event—an allergen locking onto IgE on mast cells everywhere—explains every downstream finding you see at the bedside.

CLINICAL TERM

An allergen—food such as peanuts, tree nuts, shellfish, fish, milk, eggs, wheat, or soy; a drug such as penicillin, cephalosporins, nonsteroidal anti-inflammatory drugs, or neuromuscular blocking agents used in anesthesia; insect venom from bees, wasps, yellow jackets, hornets, or fire ants; or latex—locks onto IgE antibodies on mast cells throughout the body. Mast cells degranulate (dump their contents), releasing histamine (a chemical that widens blood vessels and makes them leaky by acting on H1 and H2 receptors on blood vessel walls), leukotrienes C4, D4, and E4 (powerful airway-squeezing chemicals that act on cysteinyl leukotriene receptors on airway smooth muscle), tryptase (an enzyme that breaks down tissue and serves as a marker of mast-cell activation, measurable in blood), and prostaglandin D2 (a fat-based chemical that drives blood vessel widening and inflammation) into the bloodstream. These chemicals cause blood vessels throughout the body to widen, vessel walls to leak fluid into surrounding tissues, smooth muscle in airways to contract and narrow the airway tube, and fluid to build up in tissues causing visible swelling. The response is no longer localized; it spreads through every organ system. The key downstream sign you will see is low blood pressure (hypotension)—low blood pressure—from widened blood vessels and fluid shift out of the blood vessels. Read every weird finding backward from that break: hives, wheezing, throat swelling, vomiting, rapid heart rate—all point upstream to widespread mast-cell dump.

How the body compensates

Vital signs can look deceptively stable while the body compensates. Your job is to recognize early warning signs before the patient crashes, because once shock or airway blockage is severe, the window to reverse it closes fast.

1. The body tries to keep blood pressure up by increasing heart rate and squeezing some vessels shut, so early vital signs may look near-normal even as the system is failing.
2. Baroreceptors—pressure sensors in the carotid artery in the neck and the aortic arch in the chest—detect the drop in blood pressure and signal the medulla oblongata in the brainstem (the control center for heart rate and blood pressure) to ramp up sympathetic activity (the fight-or-flight nervous system).
3. The sympathetic nervous system releases norepinephrine (a hormone and brain messenger that tells the heart to speed up and tells blood vessels in non-essential areas—skin, gut, kidneys—to squeeze shut, sending blood to the brain and heart).
4. This compensated phase is dangerous because it can fool you into underestimating severity or delaying epinephrine—a patient may have normal blood pressure and only mild fast heart rate while their airway is swelling or their blood vessel system is about to collapse.

5. The crash points to watch for are: upper airway swelling that blocks breathing, shock that does not respond to intravenous fluids, and biphasic reaction—symptoms return four to twelve hours later in five to twenty percent of cases.
6. Delaying epinephrine is the single biggest changeable risk factor for death in anaphylaxis. Current guidelines from the World Allergy Organization (2020), the American Academy of Allergy, Asthma & Immunology, and the European Academy of Allergy and Clinical Immunology say give intramuscular epinephrine right away at the first sign of anaphylaxis.
7. Give epinephrine at the first sign of anaphylaxis—do not wait for low blood pressure or breathing trouble. Dose is zero-point-three to zero-point-five milligrams intramuscular (inject into muscle, not a vein) using a one milligram per milliliter solution in the mid-antrolateral thigh—the outside middle of the thigh—for adults; zero-point-one-five milligrams for children under thirty kilograms (sixty-six pounds).
8. Monitor for at least four to six hours after symptoms go away in mild cases, longer—up to twenty-four hours—if the reaction was severe, if the patient takes a beta-blocker (a blood pressure medicine that blocks the body's speed-up response and reduces epinephrine effectiveness), if the allergen was eaten—because slower absorption and longer exposure increase risk—or if the patient has asthma, which raises the risk of breathing collapse.
9. Watch the trend—are symptoms getting worse, staying the same, or improving—not just a single snapshot of vital signs. Repeated measurements of blood pressure, heart rate, breathing rate, oxygen saturation, and clinical signs—skin appearance, airway sounds, mental status—guide your next move.
10. Place the patient lying flat or with feet elevated above the head if blood pressure is low to improve blood flow back to the heart. Sitting upright worsens low blood pressure by pooling blood in the legs. Exception: if severe breathing trouble or vomiting, allow the position of comfort to avoid breathing vomit into the lungs.
11. Repeat epinephrine every five to fifteen minutes if symptoms do not improve or come back—about ten to twenty percent of patients need a second dose; five percent need three or more doses.
12. Start high-flow oxygen by non-rebreather mask at fifteen liters per minute and prepare for advanced airway management—intubation (placing a breathing tube through the mouth into the windpipe) or cricothyrotomy (making a surgical hole in the front of the neck into the airway)—if a high-pitched noise on breathing in (stridor), drooling, or severe tongue or uvula swelling develops. Upper airway blockage can progress in minutes.
13. Give intravenous normal saline bolus—a rapid infusion of salt water—one to two liters in adults, twenty milliliters per kilogram in children, if low blood pressure continues despite epinephrine. Shock from widened blood vessels requires volume filling—pouring fluid into the widened blood vessel space.

14. Add H1 antihistamine such as diphenhydramine—brand name Benadryl—and H2 antihistamine such as famotidine—brand name Pepcid; ranitidine was removed from the U.S. market in 2020—after epinephrine to reduce histamine effects on skin and help prevent biphasic reaction, but these are helpers—never substitute for or delay epinephrine.
15. Consider glucocorticoid such as methylprednisolone or prednisone to reduce risk of biphasic reaction, though evidence is mixed. Give after epinephrine and acute stabilization. Steroids take four to six hours to work, so they do not help the immediate reaction.
16. If the patient is on a beta-blocker, standard epinephrine doses may be less effective because beta-blockers block the docking spots epinephrine uses to speed the heart and strengthen contraction. Consider intravenous glucagon—a hormone that bypasses beta-receptors—one to five milligrams bolus, then five to fifteen micrograms per minute infusion, as an alternative agent to strengthen heart contraction and squeeze blood vessels.

Domino effect

1. Allergen locks onto IgE on mast cells, triggering dump of stored chemicals. — When allergen molecules—such as peanut protein Ara h 1, bee venom phospholipase A2, or penicillin bound to a protein—bind to two or more IgE antibodies sitting side-by-side on a mast cell, the cell membrane is activated. Calcium ions rush into the cell through calcium channels (the gates that let calcium flood in), and the cell releases granules—tiny storage sacks—full of histamine (a chemical that widens blood vessels and makes them leaky), leukotrienes such as leukotriene C4, D4, and E4 (chemicals that squeeze airways shut and drive inflammation), tryptase (an enzyme that breaks down tissue), and prostaglandin D2 (a chemical that drives inflammation) into the bloodstream and surrounding tissue.
2. Blood vessels dilate—widen—and become leaky. — Histamine binds to H1 receptors (the main alarm-bell docking spots for histamine) on the endothelial cells that line blood vessel walls, causing smooth muscle in the vessel walls to relax—widening—and causing the tight junctions between endothelial cells to separate—increased leaking. Leukotrienes, especially leukotriene C4 and D4, are a thousand times more powerful than histamine at increasing blood vessel leaking. Fluid shifts out of the bloodstream into tissues.
3. Blood pressure drops—low blood pressure (hypotension). — Widening of blood vessels lowers the total squeeze on vessels throughout the body—like opening a dam and letting water spread into a wide, shallow pool. Fluid leaking into tissues reduces the amount of blood in the vessels. The heart pumps against less squeeze with less volume, so mean arterial pressure—the average pressure in the arteries during one heartbeat—falls. Blood pressure equals how much blood the heart pumps per minute times the total squeeze on vessels; both drop, so pressure falls.

4. Heart rate rises—a fast heart rate (tachycardia). — Baroreceptors—stretch sensors—in the carotid sinus in the neck and the aortic arch in the chest detect low blood pressure as less stretch on the vessel wall. They send signals via the glossopharyngeal nerve (the ninth cranial nerve) and vagus nerve (the tenth cranial nerve) to the medulla oblongata in the brainstem (the control center for heart rate and blood pressure), which increases sympathetic outflow—fight-or-flight signals—and decreases parasympathetic tone—rest-and-digest signals. The sinoatrial node—the heart's natural pacemaker in the right atrium—speeds up to try to restore how much blood the heart pumps, which equals heart rate times how much blood is pumped with each beat.
5. Airways constrict—bronchospasm—and breathing becomes difficult. — Leukotrienes, especially leukotriene D4, bind to cysteinyl leukotriene receptors (the docking spots on airway muscle that respond to leukotrienes) on bronchial smooth muscle cells in the walls of airways, causing the muscle to contract and narrow the airway tube—the open space inside. Histamine binds to H1 receptors on airway smooth muscle and also causes contraction. Mucus production from goblet cells in the airway lining increases, further blocking airflow. Airway resistance rises, and less air reaches the alveoli—the tiny air sacs where oxygen enters the blood.
6. Swelling—angioedema—develops in the face, lips, tongue, and upper airway. — Fluid leaks from widened, leaky capillaries—the smallest blood vessels—into loose connective tissue in the dermis of the face and the layers beneath the lining of the throat and larynx. Because these tissues have loose collagen fibers and few anchoring structures, fluid builds up rapidly, causing visible and feelable swelling that can block the airway by pushing the tongue backward, narrowing the pharynx, and swelling the epiglottis and aryepiglottic folds.
7. Skin develops hives—hives (urticaria)—and flushing. — Histamine causes tiny blood vessels in the skin to dilate and leak, producing raised, itchy welts—hives—as fluid collects under the skin and presses on nerve endings, triggering the sensation of itching. Widening of blood vessels increases blood flow to the skin, producing redness and a feeling of warmth, especially on the face, neck, and chest—flushing.
8. Gut symptoms appear: nausea, vomiting, cramping, diarrhea. — Mast cells in the lamina propria—the connective tissue layer beneath the gut lining—dump their chemicals, releasing mediators that increase intestinal smooth-muscle contraction, producing cramping pain, and increase fluid secretion into the intestinal tube, producing diarrhea. Histamine and other mediators stimulate the chemoreceptor trigger zone in the area postrema of the medulla oblongata in the brainstem (the brain's vomit sensor) via vagal sensory nerves, triggering nausea and activating the vomiting center.

Symptoms · what the patient feels, and why

- **Hives (urticaria) and skin flushing:** When an allergen enters the body, immune cells called mast cells burst open and release histamine (a chemical messenger that triggers allergic reactions). Histamine opens tiny gaps in blood-vessel walls, letting fluid leak into the skin. That leaked fluid makes raised, itchy welts (hives), and extra blood flow to the skin causes redness (flushing)—like a sponge soaking up water and swelling.
- **Angioedema (swelling of face, lips, tongue, or throat):** Histamine makes blood vessels leak fluid into the deeper layers of skin and mucous membranes (the soft lining of your mouth and throat). This swelling is deeper than hives. If it swells the tongue or larynx (voice box), it can squeeze the airway shut—like a garden hose getting pinched.
- **Difficulty breathing, wheezing, or a high-pitched noise on breathing in (stridor) (high-pitched sound when breathing in):** Mast cells also release leukotrienes (chemicals that make airways tighten). These make the smooth muscle around the bronchioles (tiny air tubes in your lungs) squeeze tight (bronchospasm), narrowing the path to your lungs. At the same time, the upper airway can swell. Both problems block airflow—like breathing through a straw that is squeezing tighter and tighter.
- **Low blood pressure (Hypotension) (low blood pressure) and dizziness or fainting:** Histamine makes blood vessels all over the body relax and widen (vasodilation), and fluid leaks out of the vessels into tissues. That means less blood stays inside the vessels to feed the brain and organs—like a water balloon with tiny holes losing water fast. Blood pressure drops, the brain gets less oxygen, and you feel dizzy or pass out.
- **A fast heart rate (Tachycardia) (fast heart rate):** When sensors called baroreceptors (pressure detectors in your blood vessels) notice low blood pressure, they send an emergency signal to the heart to beat faster. The goal is to pump more blood per minute to keep your organs alive—like a pump speeding up when it senses the tank is running low.
- **Nausea, vomiting, belly cramping, and diarrhea:** Mast cells in the lining of your stomach and intestines release histamine and other chemicals. These make the smooth muscle of your gut squeeze (causing cramps), speed up the movement of food (diarrhea), and trigger the chemoreceptor trigger zone (the brain's vomit center)—like a wave of squeezing pushing everything through too fast.
- **Sense of impending doom or severe anxiety:** Your brain senses that blood pressure is dropping and carbon dioxide is rising (because you cannot breathe well). This triggers the amygdala (the brain's alarm center that flags danger) and activates the fight-or-flight response. You feel a wave of terror or dread, even if you cannot explain why. It is your brain's way of saying something is very wrong.

- No skin findings in up to 20 out of 100 cases: Sometimes the mast-cell chemicals hit the heart, blood vessels, and lungs hard but skip the skin. You can have life-threatening anaphylaxis—low blood pressure and trouble breathing—without any hives or flushing. That is why doctors never rely on skin signs alone to diagnose or rule out anaphylaxis.

Focused exam

- Hives (raised, itchy red bumps) and flushed skin (sudden redness all over) appearing within minutes: When an allergen lands on immune cells called mast cells, the cells burst open and dump histamine (a chemical alarm signal) into the skin. Histamine makes tiny blood vessels swell and leak, creating raised bumps. This tells you a whole-body allergic storm has started, not just a rash in one spot.
- Swollen lips, tongue, or throat (you can see the puffiness or the patient feels the throat closing): Swelling inside the throat can squeeze the airway shut like a hand around a straw. Air cannot get in or out. The patient can die in minutes if the airway closes completely. This is the most dangerous sign in anaphylaxis and demands immediate action.
- Wheezing (a high whistle when breathing out) or a high-pitched noise on breathing in (stridor) (a harsh, loud sound when breathing in), plus trouble breathing: Histamine makes the smooth muscle rings around the lung's air tubes squeeze tight, like squeezing a garden hose. The tubes narrow and air cannot flow easily. A high-pitched noise on breathing in (Stridor) means the upper throat is swelling. Both are life-threatening because the patient is running out of air.
- Low blood pressure (systolic under 90 mmHg in adults or a drop more than 30% from baseline) and fast heart rate (over 100 beats per minute in adults): Histamine tells blood vessels all over the body to relax and open wide, like opening all the faucets in a house at once. Blood pressure drops because blood spreads out and leaks into tissues. The heart races to try to push blood to the brain and organs, but it cannot keep up. This is shock—organs are starving for blood.
- Cramping belly pain, nausea, vomiting, or diarrhea: Mast cells in the stomach and intestines also release histamine. It makes the gut muscles squeeze and the lining leak fluid, causing cramps and loose stools. These gut symptoms are part of the whole-body reaction and help confirm anaphylaxis is happening, not just a skin allergy.
- Dizziness, confusion, or fainting (loss of consciousness): The brain needs steady blood flow carrying oxygen. When blood pressure crashes, the brain does not get enough oxygen and starts to shut down. Confusion or fainting means shock is already here or arriving fast. The patient is in immediate danger.

Diagnostics · every test answers a question

- Clinical diagnosis at the bedside (no lab test needed to start treatment) → Does the patient have sudden-onset symptoms in two or more body systems (skin, breathing, heart and blood pressure, gut) after known allergen exposure?
- Serum tryptase level (a protein released when mast cells burst), drawn within 1 to 2 hours after symptoms start → Did mast cells release tryptase, proving they activated during the reaction?
- Electrocardiogram (ECG, a tracing of the heart's electrical rhythm) → Is the heart showing strain, abnormal rhythm, or signs of poor blood flow because of low blood pressure, lack of oxygen, or the epinephrine dose?
- Arterial blood gas (ABG, measuring oxygen, carbon dioxide, and acid levels in the blood) → Is the patient getting enough oxygen into the bloodstream, and is carbon dioxide building up because breathing is failing?
- Chest X-ray (picture of the lungs and heart) → Is there another reason for trouble breathing, like a collapsed lung (pneumothorax), fluid in the lungs (pulmonary swelling (edema)), or infection, that is not anaphylaxis?
- Allergy testing (skin prick test or blood test for allergen-specific IgE antibodies), done 4 to 6 weeks after the reaction → What specific allergen (food, venom, drug, latex) caused the reaction, so the patient can avoid it forever?

Treatment logic

- Intramuscular epinephrine 0.3 to 0.5 mg (1:1000 concentration) for adults, 0.01 mg per kg (max 0.5 mg) in children, injected into the outer mid-thigh muscle, repeated every 5 to 15 minutes if needed → Epinephrine is adrenaline—the body's emergency hormone. It squeezes blood vessels tight (raising blood pressure and stopping fluid leak), relaxes the smooth muscle around lung airways (opening the tubes so air flows), and tells mast cells to stop dumping histamine. It reverses all three deadly problems: low blood pressure, airway closure, and ongoing allergic storm. It works in 3 to 5 minutes. The thigh muscle absorbs it faster than the arm or under the skin.
- Intravenous fluid bolus—1 to 2 liters of normal saline (0.9% sodium chloride solution) given fast in adults (20 mL per kg in children), repeated if blood pressure stays low → Fluid fills up the blood vessels like pouring water into a leaky bucket. Even though vessels are leaking, adding volume keeps blood pressure up and pushes blood to the brain, heart, kidneys, and other organs. Some patients need several liters because so much fluid is leaking out into tissues. This buys time while epinephrine tightens the vessels.

- Lay the patient flat on the back with legs raised (unless the airway is swelling or the patient is vomiting or having trouble breathing) → Gravity pulls blood from the legs back toward the heart and brain, boosting blood pressure without any medication. Think of it like tipping a half-empty water bottle so the water pools at one end. This keeps the brain supplied with blood and can prevent fainting or worsening shock.
- H1 antihistamine (diphenhydramine 25 to 50 mg IV or IM, or cetirizine 10 mg by mouth), H2 antihistamine (famotidine 20 mg IV or ranitidine 50 mg IV), and corticosteroid (methylprednisolone 1 to 2 mg per kg IV or prednisone 1 mg per kg by mouth, max 60 to 80 mg)—all given after epinephrine → H1 blockers stop histamine from docking on receptors in blood vessels and skin, reducing hives, itching, and some vessel leakiness. H2 blockers hit histamine receptors in the gut and blood vessels for extra help. Corticosteroids (steroid hormones that calm inflammation) take 4 to 6 hours to work but calm the delayed wave of inflammation that can start hours later. Some experts think they may lower the chance of a biphasic reaction, though the evidence is still weak. These drugs support recovery but take 1 to 6 hours to work fully.
- Inhaled albuterol (2.5 to 5 mg by nebulizer, a machine that turns liquid medicine into a mist you breathe in) if wheezing or tight chest persists after epinephrine → Albuterol is a beta-2 agonist (a drug that attaches to receptors on smooth muscle). It makes the smooth muscle wrapped around the lung's small airways relax. The airways open wider and air flows more easily. It is the same medicine used for asthma. It works in 5 to 10 minutes.
- Glucagon 1 to 2 mg IV or IM every 5 minutes if the patient takes a beta-blocker (a blood pressure medicine like metoprolol or atenolol) and does not respond to epinephrine → Beta-blockers sit on the same receptors epinephrine needs to squeeze blood vessels and open airways. If those receptors are blocked, epinephrine cannot work well. Glucagon (a hormone made by the pancreas that raises blood sugar and also squeezes blood vessels) uses a different pathway and can raise blood pressure and heart rate even when beta-blockers are in the way. It works in 1 to 3 minutes.
- Observe the patient for at least 4 to 8 hours (longer if the reaction was severe, epinephrine was delayed, the patient has asthma, or the patient has had a biphasic reaction before). Discharge with two epinephrine auto-injectors (EpiPen, Auvi-Q) and a written emergency action plan. → Watching the patient allows you to catch and treat a second wave of symptoms (biphasic anaphylaxis), which usually happens within 8 hours but can occur up to 72 hours later. Patients with severe reactions, asthma, or delayed epinephrine are at higher risk and may need observation for 24 hours. Auto-injectors let the patient or family inject epinephrine immediately if symptoms return at home—into the outer thigh, through clothing if needed. A written plan teaches symptom recognition (hives, swelling, trouble breathing, dizziness), when to inject (at the first sign of a serious reaction), and when to call 911 (always, even after injecting).

Medications

Epinephrine (adrenaline) 0.3-0.5 mg IM into mid-outer thigh, repeat every 5-15 minutes if needed · Alpha-1 and beta-2 adrenergic agonist (turns on adrenaline switches in blood vessels, airways, and immune cells)

Epinephrine is the only life-saving drug in anaphylaxis because it fixes the three deadly problems at once. First, it squeezes blood vessels by turning on alpha-1 adrenergic receptors (switches on the muscle layer inside artery and vein walls). This pushes blood pressure back up and stops shock. Second, it opens airways by turning on beta-2 adrenergic receptors (switches on the muscle wrapped around breathing tubes). This relaxes the muscle so air can move freely again. Third, it tells mast cells—the cells that dumped the allergic chemicals—to stop releasing histamine (the main chemical that causes itching, swelling, and leaking) and other chemicals by turning on beta-2 adrenergic receptors on those cells. No other drug works this fast or fixes all three problems. It must go into muscle (IM), not under the skin, because muscle has more blood vessels. The drug reaches the bloodstream in 3 to 5 minutes instead of 20 to 30. The outer thigh (vastus lateralis muscle, the big muscle on the outside of your thigh) is the best spot because the muscle is big, close to the surface, and has great blood flow.

1. Epinephrine travels through the bloodstream to blood vessel walls and locks onto alpha-1 adrenergic receptors on vascular smooth muscle cells.
2. This alpha-1 signal turns on a pathway inside the muscle cell that raises calcium levels. The muscle squeezes. Vessels tighten, resistance goes up, and blood pressure climbs within minutes.
3. At the same time, epinephrine locks onto beta-2 adrenergic receptors on the smooth muscle wrapped around bronchioles (small airways). This beta-2 signal turns on a pathway that lowers calcium and raises cyclic AMP (cAMP, a chemical messenger inside the cell that tells muscle to relax). The muscle relaxes, airways open, wheezing stops, and oxygen can get in.
4. Epinephrine also locks onto beta-2 adrenergic receptors on mast cells and basophils. This shuts down the release of histamine, tryptase (an enzyme that breaks down tissue), leukotrienes (fat chemicals that tighten airways and make vessels leak), and prostaglandins (chemicals that cause pain and swelling). These are the chemicals that caused the blood vessels to leak and airways to close in the first place.
5. Beta-1 adrenergic receptors in the heart respond by making the heart beat faster and squeeze harder (positive chronotropy and inotropy). This boosts cardiac output (the volume of blood pumped per minute) and pushes blood pressure up even more.

SAFETY WATCH

Inject into the mid-outer thigh muscle (vastus lateralis), never into the buttock (gluteus muscle). Buttock shots often land in fat instead of muscle. Absorption is slow and unreliable. · Never give epinephrine into a vein (IV) as a single quick push in the field or emergency room unless the patient is in cardiac arrest or under continuous heart monitoring with an infusion pump. IV epinephrine can cause severe high blood pressure, irregular heart rhythms (arrhythmias), heart attack, or stroke. · Use the correct dose: 0.3 to 0.5 mg IM for adults and teens (using the 1:1,000 concentration, which is 1 mg per mL). Use 0.01 mg per kilogram IM (max 0.3 mg) for children (also 1:1,000). Double-check the concentration before drawing. Mixing up 1:1,000 with 1:10,000 can cause fatal underdosing. · Do NOT delay epinephrine to start an IV or give antihistamines first. Epinephrine is first, always. Every minute of delay increases the risk of death. · Patients on beta-blockers (such as metoprolol, atenolol, propranolol) may not respond fully to epinephrine because the beta-receptors are blocked. If epinephrine fails, give IV glucagon 1 to 2 mg (adults) or 20 to 30 micrograms per kilogram (children, max 1 mg). Glucagon bypasses the beta-receptor and can still open airways and support the heart. · Epinephrine can cause shaking (tremor), anxiety, feeling your heart pound (palpitations), headache, and pale skin because it turns on the sympathetic nervous system (the fight-or-flight system). These side effects are uncomfortable but not dangerous. They are far safer than untreated anaphylaxis. · After giving epinephrine, place the patient flat on their back (supine) with legs raised unless throat swelling (upper airway obstruction) or trouble breathing makes lying flat unsafe. Sitting or standing can cause cardiac arrest because blood pools in the legs and the brain does not get enough oxygen. · If the patient has coronary artery disease (clogged heart arteries) or is elderly, epinephrine can increase oxygen demand on the heart and rarely trigger a heart attack. You still give it. Anaphylaxis is immediately life-threatening and epinephrine is the only effective treatment. · Auto-injectors (such as EpiPen, Auvi-Q) deliver a fixed dose (0.3 mg for adults, 0.15 mg for children 15 to 30 kg). They are designed to be given through clothing if needed. After using an auto-injector, hold it in place for 3 seconds. Massage the site for 10 seconds to help absorption.

IV normal saline or lactated Ringer's, 1 to 2 liters rapid bolus (adults); 10 to 20 mL per kilogram bolus (children) · Isotonic crystalloid fluid (a salt-water solution that stays in blood vessels and replaces lost volume)

In anaphylaxis, histamine and other chemicals punch holes in capillaries (the tiniest blood vessels). Fluid leaks out of the bloodstream into the surrounding tissues. This is called third-spacing or capillary leak. The result is that the blood volume drops sharply. Blood pressure falls and organs do not get enough oxygen (distributive shock). Giving a large volume of IV fluid fast refills the blood vessels, raises the circulating volume, and brings blood pressure back up. Normal saline (0.9% sodium chloride, salt water with the same saltiness as blood) and

lactated Ringer's (a balanced salt solution with sodium, chloride, potassium, calcium, and lactate) are isotonic. This means they have the same concentration of particles as blood, so they stay in the vessels longer. They do not rush into cells or out of the body right away. Epinephrine tightens the vessels and IV fluids fill them. Together they reverse shock.

1. A large-bore IV catheter (14 to 18 gauge, a thick needle) is placed in a vein, usually in the forearm or antecubital fossa (inside the elbow), to allow fast fluid delivery.
2. Crystalloid fluid (normal saline or lactated Ringer's) flows into the vein and right away increases the volume of blood in circulation.
3. This increased volume stretches the heart chambers slightly. By the Frank-Starling mechanism (a built-in feature of heart muscle), this makes the heart contract more forcefully and pump more blood with each beat.
4. More blood flowing through arteries raises blood pressure. This restores blood flow (perfusion) (blood flow) to the brain, kidneys, heart, and other organs.
5. About 25 to 30% of the fluid you put in will leak out into the interstitial space over the next hour. You may need to give more boluses if blood pressure does not come up or drops again.

SAFETY WATCH

Use a large-bore IV (14 to 18 gauge) because narrow catheters slow the flow. You need to push fluid in fast. · Run the first liter wide open (as fast as gravity or a pressure bag allows) in adults. Do not run it slowly on a pump. Time matters in shock. · In children, give 10 to 20 mL per kilogram as a rapid bolus (push it in over 5 to 10 minutes using a syringe or pressure bag). Check the child again. Repeat the bolus if needed. Do not under-treat children out of fear of fluid overload. Anaphylactic shock kills faster than fluid overload in this setting. · Watch for fluid overload, especially in patients with heart failure or kidney disease. In anaphylaxis the immediate threat is shock, so you give the fluids and watch lung sounds and work of breathing closely. If you hear crackles (wet lung sounds) or the patient has trouble breathing that worsens after fluids, slow or stop fluids and think about giving a diuretic (a water pill). This is rare in the first hour. · If you cannot get IV access quickly (after two tries or 90 seconds), place an intraosseous line (IO, a needle into the bone marrow) in the proximal tibia (shinbone just below the knee) or humerus (upper arm bone). Give fluids and medicines through the bone marrow. Do NOT waste time trying over and over for an IV while the patient is crashing. · Some patients need 4 to 6 liters or more in the first hour if shock is severe. Keep giving boluses until blood pressure comes up and stays up. Do not stop after one liter if the patient is still in shock.

Diphenhydramine 25 to 50 mg IV or IM (adults); 1 mg per kilogram IV or IM, max 50 mg (children) · H1 antihistamine (blocks histamine type-1 receptors)

Diphenhydramine blocks H1 histamine receptors on blood vessels, airways, and skin.

Histamine—released by mast cells during anaphylaxis—normally locks onto these receptors and causes blood vessels to widen and leak, smooth muscle in airways to tighten, and skin to itch and swell. By sitting in the receptor and blocking histamine from binding, diphenhydramine reduces itching, hives, swelling, and some of the airway tightness. However, it works slowly (peak effect in 1 to 3 hours). It does NOT reverse life-threatening shock or severe airway closure. This is why it is only a helper drug and never replaces epinephrine.

1. Diphenhydramine enters the bloodstream and travels to tissues where histamine is binding to H1 histamine receptors.
2. It locks onto the H1 histamine receptor and physically blocks histamine from attaching. This is competitive antagonism. Diphenhydramine and histamine compete for the same spot, and diphenhydramine wins because you give a high dose.
3. With H1 histamine receptors blocked, histamine cannot tell blood vessels to widen or leak. Swelling (angioedema) and hives begin to improve over the next 30 to 60 minutes.
4. H1 histamine blockade in the airways reduces some of the bronchoconstriction (airway tightening), though this effect is small compared to epinephrine or albuterol.

SAFETY WATCH

Never give diphenhydramine first or instead of epinephrine. Epinephrine is first, always. · Diphenhydramine causes drowsiness, dry mouth, and trouble peeing (urinary retention) because it blocks acetylcholine receptors (anticholinergic effect). Warn the patient they will feel sleepy. · In elderly patients, diphenhydramine can cause confusion, agitation, or falls. Use it carefully and think about using a second-generation H1 antihistamine (such as cetirizine or loratadine) for follow-up instead, though those are pills and work slower. · Do NOT rely on oral diphenhydramine during active anaphylaxis. Absorption from the gut is slow and unreliable when blood pressure is low. Use IV or IM only. · Diphenhydramine can lower the seizure threshold slightly. Use carefully in patients with epilepsy, though in anaphylaxis the benefit far outweighs this small risk.

Methylprednisolone 125 mg IV or prednisone 40 to 60 mg by mouth (adults); methylprednisolone 1 to 2 mg per kilogram IV (children) · Corticosteroid (a steroid that reduces inflammation by turning off immune and inflammatory genes)

Corticosteroids enter immune cells (mast cells, basophils, T cells, macrophages) and travel into the nucleus (the cell's control center). There they turn on anti-inflammatory genes and turn off pro-inflammatory genes. This reduces the production of cytokines (inflammatory messenger

chemicals such as interleukin-5 and tumor tissue death (necrosis) factor-alpha), leukotrienes (fat chemicals that tighten airways and make vessels leak), and prostaglandins (chemicals that cause fever, pain, and swelling). The result is less inflammation over the next 4 to 12 hours. Corticosteroids are given in anaphylaxis to reduce the chance of a biphasic reaction (a second wave of symptoms 4 to 12 hours later, which happens in 5 to 20% of cases) and to calm down long-lasting inflammation. However, steroids take 4 to 6 hours to start working. They do NOT treat the immediate life-threatening symptoms and never replace epinephrine.

1. Methylprednisolone or prednisone enters the bloodstream and crosses cell membranes into immune cells.
2. Inside the cell, the steroid binds to a glucocorticoid receptor (a protein that acts as a switch).
3. The steroid-receptor pair moves into the nucleus and attaches to DNA at specific spots called glucocorticoid response elements.
4. This turns off genes that make pro-inflammatory cytokines (such as interleukin-5 and tumor tissue death (necrosis) factor-alpha), leukotrienes, and prostaglandins. It turns on genes that make anti-inflammatory proteins (such as lipocortin-1, which blocks phospholipase A2, an enzyme that makes inflammatory chemicals).
5. Over the next 4 to 12 hours, the immune system calms down. Inflammatory chemicals drop and the risk of a second wave of anaphylaxis goes down.

SAFETY WATCH

A single dose or short course (3 to 5 days) of corticosteroids is very safe. It does NOT cause the long-term side effects (weight gain, diabetes, weak bones, immune suppression) seen with months or years of steroid use. · High blood sugar (hyperglycemia) can happen within hours, especially in patients with diabetes. Check a fingerstick glucose if the patient has diabetes or symptoms of high blood sugar (thirst, peeing a lot). · Steroids can cause mood changes (feeling wound up, overly happy, trouble sleeping) even after one dose, but this is uncommon and goes away. · Do NOT skip steroids because you are worried about side effects. In anaphylaxis, the benefit of reducing biphasic reactions far outweighs the tiny risk of a short course. · If the patient cannot swallow or absorb oral prednisone (because of vomiting, low blood pressure, or confusion), give IV methylprednisolone instead. Do NOT give a pill to a patient in shock. It will not be absorbed.

Albuterol 2.5 to 5 mg nebulized or 4 to 8 puffs via inhaler with spacer, repeat every 20 minutes if needed · Short-acting beta-2 agonist (turns on beta-2 switches in the lungs to open airways)

Albuterol is added if wheezing or trouble breathing continues after epinephrine. It locks onto beta-2 adrenergic receptors on the smooth muscle that wraps around the breathing tubes

(bronchioles). This turns on a pathway inside the muscle cell that raises cyclic AMP (cAMP, a chemical messenger inside the cell). This lowers calcium and causes the muscle to relax. The airways widen (bronchodilation), air flows more easily, and wheezing goes down. Albuterol works only in the lungs. It does NOT raise blood pressure or stop mast cells from releasing histamine, so it is never a substitute for epinephrine. It is used as an add-on when airway tightness persists even after you give IM epinephrine.

1. Albuterol is breathed in as a mist (nebulizer) or spray (metered-dose inhaler with spacer) and lands directly on the lining of the airways.
2. It crosses into the smooth muscle cells wrapped around the bronchioles and binds to beta-2 adrenergic receptors on the cell surface.
3. This turns on an enzyme called adenylyl cyclase, which makes cyclic AMP inside the cell.
4. Rising cyclic AMP turns on protein kinase A, which pumps calcium out of the muscle cell and stops new calcium from coming in.
5. With less calcium available, the muscle cannot squeeze. It relaxes, the airway gets wider, and air moves in and out more easily. Wheezing goes down within 5 to 10 minutes.

SAFETY WATCH

Use a spacer (a tube attached to the inhaler) if giving albuterol by metered-dose inhaler. A spacer helps more drug reach the lungs and less land in the mouth. Without a spacer, most of the dose hits the back of the throat and is swallowed. · Albuterol can cause shaking (tremor), fast heart rate (tachycardia), and feeling your heart pound (palpitations) because beta-2 adrenergic receptors exist in small numbers in the heart and muscles. These side effects are mild and not dangerous in anaphylaxis. · In patients with severe coronary artery disease (clogged heart arteries), albuterol can make the heart need more oxygen and rarely trigger chest pain (angina). You still give it if wheezing is severe. The benefit is bigger than the risk. · Do NOT delay epinephrine to give albuterol first. Epinephrine treats the whole disease. Albuterol treats only one symptom (wheezing). · If the patient is too short of breath to breathe in deeply, the mist will not reach the small airways well. In this case, IM epinephrine (which works on the whole body through the bloodstream) is even more important.

Glucagon 1 to 2 mg IV or IM, repeat every 5 minutes if needed (for patients on beta-blockers who do not respond to epinephrine) · Hormone that raises blood sugar and turns on heart and smooth muscle through a pathway that skips beta-receptors

Glucagon is used when a patient on a beta-blocker (such as metoprolol, atenolol, propranolol) does not respond to epinephrine. Beta-blockers sit on beta-1 (heart) and beta-2 (lung, vessel) adrenergic receptors and stop epinephrine from binding, so epinephrine cannot raise heart

rate, boost the heart's pumping strength, or fully open airways. Glucagon works through a completely different receptor—the glucagon receptor—which turns on the same downstream pathway (raising cyclic AMP) without needing the beta-receptor. This allows glucagon to speed up the heart, strengthen heart squeezes, and relax airway smooth muscle even when beta-receptors are blocked. Glucagon also raises blood sugar by telling the liver to break down glycogen (stored sugar) into glucose. This can help if the patient has low blood sugar (hypoglycemia) from long-lasting shock.

1. Glucagon is injected IV or IM and travels through the bloodstream to the heart, lungs, and liver.
2. It binds to glucagon receptors (G-protein-coupled receptors) on cell surfaces.
3. This turns on adenyl cyclase, which raises cyclic AMP inside the cell—the same pathway that beta-2 drugs use, but starting from a different front door.
4. In the heart, rising cyclic AMP increases calcium entry into heart muscle cells. This makes the heart beat faster and harder. Cardiac output (the volume of blood pumped per minute) goes up and blood pressure rises.
5. In the lungs, cyclic AMP causes bronchial smooth muscle to relax. This opens the airways and reduces wheezing.
6. In the liver, cyclic AMP turns on enzymes that break glycogen into glucose. This is released into the blood and raises blood sugar.

SAFETY WATCH

Glucagon often causes nausea and vomiting within minutes, especially at doses above 1 mg. If the patient throws up, turn them on their side to protect the airway. Do NOT hold back glucagon because of this. Vomiting is common but not dangerous, and the drug may save the patient's life. · Give glucagon as an IV push (inject it over 1 to 2 minutes) or IM shot. If the patient does not respond after 5 minutes, give another dose. Some patients need a continuous IV drip (5 to 15 micrograms per minute) if symptoms continue. · Glucagon raises blood sugar, sometimes to 200 to 300 mg per deciliter or higher. This is not harmful in the short term, but check a fingerstick glucose and watch if the patient has diabetes. · Glucagon only works if the liver has glycogen stores. In patients with severe liver disease, long-term alcoholism, or long starvation, glucagon may not raise blood sugar well. It will still help the heart and lungs through the cyclic AMP pathway. · Glucagon is expensive and not stocked in all emergency rooms or ambulances. If you know a patient is on a beta-blocker and having anaphylaxis, ask pharmacy or EMS to bring glucagon right away.

Famotidine 20 mg IV (H2 antihistamine, optional add-on) · H2 antihistamine (blocks histamine type-2 receptors)

About 10 to 15% of histamine's effects in anaphylaxis happen through H2 histamine receptors (most happen through H1 histamine receptors). H2 histamine receptors are found on blood vessels, heart, and stomach. When histamine binds to H2 histamine receptors on blood vessels, it causes the vessels to widen and leak, which drops blood pressure. Blocking H2 histamine receptors with famotidine reduces this effect and may help steady blood pressure a bit when added to an H1 antihistamine blocker (such as diphenhydramine). However, H2 antihistamine blockers work slowly and are not essential. They are optional add-ons, never replacements for epinephrine or fluids.

1. Famotidine is given IV and travels to tissues where histamine is binding to H2 histamine receptors.
2. It sits in the H2 histamine receptor and blocks histamine from attaching (competitive antagonism).
3. With H2 histamine receptors blocked, histamine cannot widen blood vessels or make them leak as much. Blood pressure may steady a bit more than with an H1 antihistamine blocker alone.
4. The drug takes 30 to 60 minutes to reach peak effect, so it does not help in the first critical minutes.

SAFETY WATCH

Ranitidine (another H2 antihistamine blocker) was pulled from the U.S. market in 2020 because of contamination with NDMA (a probable cancer-causing chemical), so use famotidine instead. Some international guidelines still list ranitidine. If it is available and uncontaminated, it is safe for short-term use. · Famotidine is very safe. Side effects (headache, dizziness, constipation) are rare and mild. · Do NOT give an H2 antihistamine blocker instead of an H1 antihistamine blocker. Always give diphenhydramine (H1) first, and only add an H2 antihistamine blocker if your protocol includes it. · H2 antihistamine blockers can be given by mouth for follow-up after anaphylaxis, but in the emergency use IV to make sure it is absorbed.

Red flags

- A high-pitched noise on breathing in (Stridor), hoarseness, or trouble swallowing—signs the upper airway is swelling and may close off completely
- Low blood pressure (Hypotension) or fainting—the cardiovascular system is collapsing into distributive shock

- Severe trouble breathing, blue skin (cyanosis), or oxygen saturation below 90 percent—the lungs are failing to get enough oxygen into the blood
- Confusion, loss of consciousness, or seizure—the brain is not getting enough blood or oxygen
- Symptoms coming back 4 to 12 hours after the first wave improves (biphasic reaction)—up to 20 out of 100 people have a second round that can be just as dangerous

Nursing priorities

1. Give intramuscular epinephrine 0.3 to 0.5 mg (1:1000 concentration) in the outer mid-thigh immediately, then prepare to repeat every 5 to 15 minutes if symptoms do not improve. — Epinephrine (also called adrenaline) reverses every deadly part of anaphylaxis—it squeezes blood vessels to raise blood pressure, opens airways by relaxing bronchial smooth muscle, and stops mast cells from dumping more histamine. The thigh muscle absorbs it fast. Delaying epinephrine is the number-one cause of death in anaphylaxis.
2. Assess and support the airway—look for a high-pitched noise on breathing in (stridor), hoarseness, drooling, or tongue swelling; sit the patient upright if they are having trouble breathing, and prepare suction and bag-valve-mask ventilation equipment at the bedside. — Angioedema can close the upper airway within minutes. A high-pitched noise on breathing in (Stridor) (a high-pitched sound when breathing in) means the larynx is already narrowing. Upright positioning uses gravity to reduce swelling and makes breathing easier. If the airway closes, you will need to force air in with a bag-valve mask or the patient will need emergency intubation (a breathing tube) or cricothyrotomy (a surgical airway through the neck).
3. Start two large-bore intravenous lines and give a rapid bolus of 1 to 2 liters of normal saline in adults (20 mL per kg in children), repeating boluses if blood pressure stays below 90 systolic. — Histamine and other mediators (chemicals released from mast cells) make blood vessel walls leaky, so plasma (the liquid part of blood) leaks out into tissues. This drops the blood volume inside vessels and causes distributive shock. Rapid IV fluid refills the vascular space and supports blood pressure so the brain, heart, and kidneys get enough blood flow.
4. Lay the patient flat and elevate the legs unless they are vomiting or having severe trouble breathing, in which case keep the head of the bed up 30 to 45 degrees. — The flat position with legs raised helps blood drain from the legs back to the heart, increasing venous return (blood flow into the heart) and cardiac output (blood the heart pumps out). This simple position raises blood pressure. Do not lay a vomiting patient flat because they may aspirate (breathe stomach contents into the lungs). Do not lay flat a patient in respiratory distress because it makes breathing harder.

5. Place the patient on continuous pulse oximetry and cardiac monitoring, checking oxygen saturation and heart rate and rhythm every 1 to 2 minutes during the emergency phase. — Oxygen saturation shows whether the lungs are getting enough air in and oxygen into the blood—levels below 90 percent mean severe low oxygen in the blood (hypoxemia) (low blood oxygen) and possible respiratory failure. A fast heart rate (Tachycardia) (fast heart rate over 100) is an early sign of shock as the heart tries to pump faster to make up for low blood pressure. Arrhythmias (irregular heart rhythms) can happen if the heart does not get enough oxygen or if you give too much epinephrine.
6. Give supplemental oxygen by non-rebreather mask at 15 liters per minute if oxygen saturation is below 94 percent or the patient looks short of breath. — Bronchospasm (squeezing of small airways), upper airway swelling, and low blood pressure all reduce oxygen delivery to tissues. High-flow oxygen increases the amount of oxygen in each breath and helps prevent low oxygen (hypoxia) (oxygen starvation) in the brain and heart while you treat the anaphylaxis.
7. Prepare second-line medications at the bedside—H1 antihistamine (diphenhydramine 25 to 50 mg IV), H2 antihistamine (famotidine 20 mg IV), corticosteroid (methylprednisolone 125 mg IV or equivalent), and if the patient takes a beta-blocker, draw up glucagon 1 to 2 mg IV. — Antihistamines block histamine receptors (docking ports for histamine on cells) and reduce itching, hives, and some airway swelling, but they work slowly—over 30 to 60 minutes—so they do not save lives like epinephrine does. Corticosteroids (steroids that calm immune system inflammation) may prevent a biphasic reaction hours later. Glucagon raises blood pressure and heart rate in patients on beta-blockers when epinephrine does not work well.
8. Monitor the patient for at least 4 to 6 hours after symptoms resolve, and arrange longer observation or admission if the reaction was severe, involved low blood pressure (hypotension), or required more than one dose of epinephrine. — Biphasic anaphylaxis (a second wave of symptoms without new allergen exposure) happens in 5 to 20 percent of cases, typically 4 to 12 hours after the first reaction. Patients with severe initial reactions, slow response to treatment, or a history of biphasic reactions are at highest risk and need extended monitoring in a setting where you can give epinephrine and airway support immediately.

Sources

- World Allergy Organization Anaphylaxis Guidance 2020
- American Academy of Allergy, Asthma & Immunology Practice Parameter 2020
- Resuscitation Council UK Emergency Treatment of Anaphylaxis Guidelines 2021
- UpToDate

Last reviewed: 2026-07-07