

Anaphylaxis

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.

THE ONE-LINE TRUTH

An allergen locks onto IgE antibodies sitting on mast cells all over your body, causing those cells to dump histamine (a chemical that widens blood vessels and makes them leak), leukotrienes (chemicals that squeeze airways shut), and other chemicals all at once—blood vessels widen and leak, blood pressure falls, and airways tighten.

The chain — how it unfolds

1. Allergen locks onto IgE on mast cells, triggering dump of stored chemicals. — why: 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. — why: 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). — why: 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). — why: 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. — why: 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. — why: 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. — why: 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. — why: 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.

Spot it — what you see, 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.

Red flags — act now

- 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

Treat it — in this order

1. 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.
2. 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.
3. 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.

4. 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.
5. 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.

Your top priorities at the bedside

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. — why: 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. — why: 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. — why: 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.