Adrenal insufficiency

When the adrenal glands fail, the body cannot fight back against stress—an infection, surgery, or even vomiting can trigger a crash in blood pressure and blood sugar that kills within hours if you do not get emergency steroids.

THE ONE-LINE TRUTH

Adrenal insufficiency means the adrenal glands make too little cortisol (the hormone that keeps your blood pressure steady and your blood sugar normal when you are stressed) and often too little aldosterone (the hormone that holds onto salt and water so your blood pressure does not drop).

The chain — how it unfolds

1. The adrenal cortex cannot make cortisol (because the gland is destroyed in primary disease, or because the pituitary stops sending the ACTH signal in secondary disease), and the pituitary responds by pumping out very high levels of ACTH trying to wake up the unresponsive adrenal glands. — why: Low cortisol removes the normal negative feedback brake on the pituitary, so ACTH climbs—often above 200 pg/mL in primary adrenal insufficiency (normal is under 46 pg/mL). ACTH is made from a large precursor molecule called POMC (pro-opiomelanocortin), which is also the precursor for melanocyte-stimulating hormone (MSH, the hormone that tells skin cells to make pigment). High ACTH cross-activates melanocyte receptors in the skin and mucous membranes, causing hyperpigmentation—bronze or tan patches show up on sun-exposed areas (face, neck, arms), pressure points (elbows, knuckles), skin creases (palmar creases, axillae), old scars (scars turn darker than the surrounding skin), and mucous membranes (dark spots on the gums and inside the cheeks, called buccal mucosa). This hyperpigmentation is the visual clue that separates primary from secondary disease—if ACTH is low (secondary disease), the skin stays normal.

2. Without cortisol, blood vessel walls lose their ability to squeeze tight, the liver stops making new glucose, and the immune system loses its brake and starts overreacting. — why: Cortisol is required for vascular smooth muscle (the muscle layer in artery and vein walls) to respond to catecholamines (adrenaline and noradrenaline, the hormones that make blood vessels constrict). Without cortisol, blood vessels stay floppy and dilated even when adrenaline floods the system, so blood pressure drifts downward—patients develop orthostatic low blood pressure (hypotension) (blood pressure drops more than 20 mmHg systolic when they stand up, causing dizziness or near-fainting). Cortisol also drives gluconeogenesis (the liver's process of building new glucose molecules from amino acids and fatty acids), so without cortisol, blood glucose falls, especially during fasting, overnight, or when the patient is sick and not eating—low blood sugar (hypoglycemia) (blood glucose below 70 mg/dL, sometimes into the 40s or 30s) causes confusion, shakiness, sweating, and can lead to seizures or coma. Finally, cortisol normally dampens the immune system's inflammatory response by blocking cytokine production (chemical signals like IL-1, IL-6, and TNF-alpha that tell immune cells to attack). Losing cortisol lifts that brake, so patients have persistent low-grade inflammation, which explains chronic nausea, a run-down, unwell feeling (malaise) (feeling generally unwell and achy), and increased susceptibility to autoimmune flares if they have other autoimmune diseases.
3. In primary adrenal insufficiency, aldosterone production also fails because the adrenal cortex is destroyed, so the kidney loses its signal to hold onto sodium and water. — why: Aldosterone normally acts on the distal convoluted tubule and collecting duct (the last parts of the kidney's filtering system) and tells them to pull sodium and water out of the urine and back into the bloodstream, while dumping potassium into the urine. Without aldosterone, sodium and water spill into the urine and leave the body, so serum sodium falls (hyponatremia, often 120 to 132 mEq/L, normal is 135 to 145 mEq/L)—low sodium causes confusion, nausea, muscle cramps, and seizures if it drops below 120. At the same time, the kidneys hold onto potassium instead of dumping it, so serum potassium rises (hyperkalemia, often 5.5 to 6.5 mEq/L, normal is 3.5 to 5.0 mEq/L)—high potassium makes the heart's electrical system unstable and can cause fatal arrhythmias (peaked T waves on ECG, then wide QRS, then ventricular fibrillation and cardiac arrest if potassium climbs above 7.0 mEq/L). Losing sodium and water shrinks the blood volume (hypovolemia), which drops blood pressure further (orthostatic low blood pressure (hypotension) worsens) and reduces blood flow to the kidneys, causing prerenal waste buildup in the blood (azotemia) (creatinine and BUN rise because the kidneys are not getting enough blood flow to filter waste). Patients crave salt intensely because volume receptors in the kidneys and blood vessels sense dehydration and trigger thirst and salt-seeking behavior—patients report eating handfuls of potato chips, drinking pickle juice, or adding salt to every meal.

4. Chronic cortisol deficiency causes loss of appetite, nausea, vomiting, abdominal pain, and progressive weight loss over weeks to months. — why: Cortisol normally stimulates appetite (it is one reason why people on prednisone gain weight) and maintains the integrity of the gut lining and normal gut motility (the rhythmic squeezing that moves food through the intestines). Losing cortisol causes gastrointestinal dysmotility (the gut stops moving food smoothly), which triggers nausea, vomiting, constipation or diarrhea, and vague abdominal pain that can mimic ulcers, gastritis, or even appendicitis. Patients lose their desire to eat (anorexia, not the eating disorder but the medical term for loss of appetite), and food tastes unappealing or makes them feel sick. Weight loss is multifactorial: reduced calorie intake (patients eat less because they feel nauseated), ongoing muscle breakdown (catabolism—without cortisol's anabolic support, the body breaks down muscle protein for energy), and loss of sodium and water (which accounts for several pounds of the weight loss). Patients often lose 5 to 15 pounds over months without trying, and family members notice they look thinner and more tired.
5. Patients experience profound, unrelenting fatigue and muscle weakness that worsens as the day goes on and never improves with rest. — why: Low cortisol means low blood glucose (the brain and muscles do not have enough fuel), impaired mitochondrial energy production (cortisol is needed for cells to efficiently burn glucose and fat for ATP, the energy currency of the cell), and loss of the normal cortisol circadian rhythm (cortisol normally peaks at 6 to 8 AM to wake you up and give you energy, then falls at night so you can sleep—without that peak, patients feel exhausted even after a full night of sleep and never feel refreshed). Muscle weakness also comes from high potassium (hyperkalemia) (high potassium depolarizes muscle cell membranes, making them less responsive to nerve signals so muscles feel weak and heavy) and from low sodium (hyponatremia) (low sodium reduces the electrical gradient across nerve and muscle cells, blunting neuromuscular excitability). Patients describe the fatigue as crushing—they cannot climb stairs without stopping, they fall asleep in meetings, they need naps multiple times a day, and even simple tasks like grocery shopping feel exhausting.

6. When a patient with chronic adrenal insufficiency (diagnosed or undiagnosed) faces a physiologic stressor—infection (flu, pneumonia, gastroenteritis, urinary tract infection), surgery, trauma (broken bone, car accident), severe vomiting or diarrhea, heat exposure, or major emotional stress—adrenal crisis erupts: refractory low blood pressure (hypotension), altered mental status, severe low blood sugar (hypoglycemia), and cardiovascular collapse. — why: Physiologic stress normally triggers a 5 to 10 fold surge in cortisol production (from a baseline of 10 to 20 mg per day up to 100 to 200 mg per day) to maintain vascular tone (so blood vessels stay tight and blood pressure stays up), ramp up glucose production (so the brain and muscles have fuel to fight infection or heal injury), and modulate the immune response (so inflammation helps fight infection but does not spiral out of control and damage tissues). A patient with adrenal insufficiency cannot produce that surge—the adrenal glands are dead (primary disease) or the pituitary signal is missing (secondary disease). Without the cortisol surge, blood vessels dilate and stay floppy (distributive shock—blood pools in the veins and does not return to the heart), blood volume drops further from vomiting, diarrhea, or third-spacing of fluid into tissues (hypovolemic shock), and blood pressure crashes—systolic pressure often falls below 90 mmHg, sometimes below 70 mmHg, and does not respond to intravenous fluids alone because the vessels cannot constrict without cortisol. Blood glucose plummets because the liver cannot make new glucose (no cortisol-driven gluconeogenesis)—glucose often drops below 60 mg/dL, sometimes into the 30s or 40s, causing confusion, loss of consciousness, seizures, or coma. The brain becomes confused from both low blood sugar (hypoglycemia) (not enough fuel) and low blood pressure (hypotension) (not enough blood flow delivering oxygen). Patients develop severe nausea and vomiting (gut shuts down), abdominal pain so severe it can mimic a surgical emergency (appendicitis, bowel obstruction, perforated ulcer), fever (from the underlying infection or from the crisis itself), and loss of consciousness. Death follows within hours if intravenous hydrocortisone (100 mg bolus, then 50 to 100 mg every 6 to 8 hours) and aggressive normal saline resuscitation (1 to 2 liters in the first hour, often 4 to 6 liters in the first 24 hours) are not given immediately. Even with treatment, mortality is 5 to 10 percent if diagnosis is delayed. This is why every patient with known adrenal insufficiency must carry an emergency hydrocortisone injection kit, wear a medical alert bracelet, double or triple their oral hydrocortisone dose during illness (sick-day rules), and go to the emergency room immediately if they cannot keep pills down or if they feel weak and dizzy.

Spot it — what you see, and why

- Fatigue and generalized weakness: Low cortisol reduces blood sugar (because the liver cannot make new glucose from protein and fat anymore), flattens the normal morning cortisol peak that wakes you up, and slows down how your cells make energy, so your body feels exhausted all day and your muscles feel weak.

- Weight loss and loss of appetite: Cortisol normally makes you hungry; losing it triggers nausea and makes food unappealing, while your muscles slowly break down and you lose sodium and water through your kidneys, causing steady weight loss over weeks to months.
- Hyperpigmentation (darkened skin on elbows, knuckles, palms, scars, gums, and inside the cheeks): In primary adrenal insufficiency (when the adrenal glands themselves are damaged), your pituitary gland pumps out very high levels of ACTH (a signal hormone, often above 200 pg/mL) trying to wake up the dead adrenal glands; ACTH accidentally turns on melanocytes (the cells that make skin color), causing bronze or tan patches in sun-exposed and rubbed areas—this does NOT happen in secondary insufficiency (when the pituitary itself is the problem) because ACTH is low.
- Salt craving: Loss of aldosterone (the hormone that tells your kidneys to hold onto sodium) in primary disease makes your kidneys dump sodium into urine, shrinking your blood volume and triggering an intense craving for salt as your body tries to restore volume.
- Orthostatic low blood pressure (hypotension) (blood pressure drops when you stand) and dizziness: Low aldosterone causes sodium and water loss (your blood volume is too low), and low cortisol weakens your blood vessels so they cannot squeeze tight when you stand up; blood pressure falls, especially when standing, causing lightheadedness or fainting.
- Nausea, vomiting, and belly pain: Low cortisol disrupts how your gut moves (normal squeezing motion) and damages the protective lining of your stomach and intestines, causing cramping, nausea, vomiting, and sometimes diarrhea—these gut symptoms can look like an emergency belly problem and lead doctors down the wrong path.

Red flags — act now

- Refractory low blood pressure (hypotension) (blood pressure below 90 mmHg systolic despite intravenous fluids) or shock—adrenal crisis requires immediate intravenous hydrocortisone 100 mg bolus and aggressive fluid resuscitation
- Altered mental status, confusion, or loss of consciousness—sign of severe low blood sugar, not enough blood reaching the brain, or severe low sodium; check fingerstick glucose and give dextrose if needed
- Severe low sodium (hyponatremia) (serum sodium below 120 mEq/L) with confusion or seizures—requires cautious saline infusion and stress-dose hydrocortisone, not rapid correction alone
- High potassium (Hyperkalemia) above 6.5 mEq/L with EKG changes (peaked T waves, widened QRS)—life-threatening heart rhythm risk; treat high potassium emergently while replacing cortisol and aldosterone
- Recent stop of chronic steroid therapy (prednisone, dexamethasone) in a patient with low blood pressure or low blood sugar—secondary adrenal insufficiency from HPA axis suppression (the body's own cortisol system shut down); restart steroids immediately

Treat it — in this order

1. In adrenal crisis: give IV hydrocortisone 100 mg immediately, then 50 to 100 mg IV every 6 to 8 hours. At the same time, give IV normal saline 1 to 2 liters rapidly in the first hour, then continue maintenance fluids with dextrose 5 percent to raise blood sugar. → IV hydrocortisone replaces the missing cortisol so blood vessels can tighten again, blood pressure rises, and the body can make glucose from stored fuel. IV fluids restore blood volume (the amount of liquid in your blood vessels) and dextrose directly raises blood sugar. Together these reverse shock (when organs are not getting enough blood flow) and prevent death. Most patients improve within hours.
2. For chronic replacement: give oral hydrocortisone 15 to 25 mg daily in 2 to 3 divided doses (for example 10 mg in the morning, 5 mg at lunch, and 5 mg in late afternoon), or prednisone 5 to 7.5 mg once daily in the morning. → Replaces the cortisol the adrenal glands can no longer make, restoring energy, appetite, normal blood pressure, and the body's ability to make and use glucose. Divided dosing copies the body's natural rhythm: cortisol is highest in the morning and lowest at night. This schedule prevents symptoms and keeps metabolism steady.
3. For primary adrenal insufficiency only: give oral fludrocortisone 0.05 to 0.2 mg once daily. → Replaces aldosterone, which tells the kidneys to hold onto sodium and release potassium. This brings sodium and potassium back to normal and keeps blood pressure stable. The dose is adjusted based on blood pressure, sodium, and potassium levels. Most patients need 0.1 mg daily.
4. Stress-dose steroids: double or triple the daily hydrocortisone dose during fever, infection, or minor illness. Give hydrocortisone 50 to 100 mg IV or IM if the patient is vomiting, having major surgery, or is severely ill and cannot take pills. → Meets the body's surge in cortisol need during physical stress so blood pressure and blood sugar stay normal and the heart and blood vessels can respond to adrenaline. Prevents the patient from slipping into adrenal crisis. Stress dosing mimics what healthy adrenal glands do automatically.
5. Prescribe an emergency intramuscular hydrocortisone injection kit (100 mg) and a medical alert bracelet or card that says 'adrenal insufficiency—needs hydrocortisone in emergencies.' → Lets the patient, a family member, or a paramedic inject hydrocortisone immediately if the patient cannot swallow (because of vomiting or unconsciousness). This buys time before an IV can be started in the hospital and can prevent progression to full shock. The medical alert tells emergency responders what is wrong and what to do.

Your top priorities at the bedside

1. Check blood pressure lying down and standing every 15 minutes if patient is unstable, and immediately notify the provider if systolic blood pressure is below 90 mmHg or drops more than 20 mmHg when standing. — why: Low blood pressure (Hypotension) from low cortisol and aldosterone can progress to shock (adrenal crisis), and catching early drops allows prompt IV hydrocortisone and fluid resuscitation before organs lose blood flow.
2. Establish large-bore IV access and prepare to give normal saline 1 to 2 liters rapidly in the first hour if adrenal crisis is suspected, while waiting for hydrocortisone order. — why: Volume depletion from aldosterone deficiency causes severe low blood pressure (hypotension), and rapid saline infusion restores blood volume and blood pressure while steroids take time to work.
3. Check fingerstick blood glucose immediately and every 1 to 2 hours in unstable patients, and give dextrose 50 percent (D50) IV per protocol if glucose is below 70 mg/dL. — why: Low cortisol impairs the liver from making new glucose, causing low blood sugar (hypoglycemia) that can lead to seizures, confusion, or coma if not corrected quickly.