Adrenal insufficiency

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 STORY IN ONE SENTENCE

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).

“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.”

Normal anatomy — the body's job

The hypothalamus (a control center deep in your brain that senses stress, low blood sugar, and danger) sends a chemical signal to the pituitary gland (a pea-sized gland hanging just below your brain). The pituitary responds by releasing ACTH (a messenger hormone that travels through your bloodstream like a letter in the mail) to the adrenal glands. ACTH lands on the adrenal cortex (the outer shell of the adrenal gland, wrapped around the top of each kidney like a cap) and tells it to make cortisol. The adrenal cortex also makes aldosterone, but aldosterone production is controlled by a different system called the renin-angiotensin system —sensors in your kidneys that detect when blood volume drops or sodium runs low and send a signal to the adrenal glands to make more aldosterone. Cortisol does three big jobs: it makes blood vessel walls squeeze tight when adrenaline hits them (so your blood pressure does not drop when you stand up), it tells your liver to build new glucose molecules from protein and fat (a process called gluconeogenesis, so your brain always has fuel even if you skip a meal), and it keeps your immune system from overreacting and causing inflammation that damages your own tissues. Aldosterone tells the last part of the kidney tubules (tiny tubes where urine is fine-tuned) to grab sodium and water from the urine and pull them back into your blood, while dumping potassium into the urine to leave your body. Picture this normal assembly line in your

head—every weird symptom and lab result you will see in adrenal insufficiency is a direct consequence of losing these two hormones.

> **BODY'S JOB**
> If you do not understand the normal job first, the clinical findings look like random noise instead of a clear chain of cause and effect that you can see and predict.

1. Stress (infection, surgery, low blood sugar, fear) hits the hypothalamus in your brain.
2. Hypothalamus sends a signal (CRH, corticotropin-releasing hormone) down to the pituitary gland sitting just below it.
3. Pituitary releases ACTH into the bloodstream—ACTH is the traveling messenger that finds the adrenal glands.
4. ACTH binds to receptors on the adrenal cortex (the outer layer of the adrenal gland, on top of each kidney) and tells it to make cortisol.
5. Cortisol floods into the blood and does three things: makes blood vessels squeeze tight (keeps blood pressure up), tells the liver to make glucose from stored protein and fat (keeps blood sugar up), and tells immune cells to calm down (stops too much inflammation).
6. At the same time, the renin-angiotensin system (a separate alarm in the kidneys) senses low blood volume or low sodium and signals the adrenal cortex to make aldosterone.
7. Aldosterone travels to the kidney tubules and tells them to hold onto sodium and water (keeps blood volume and pressure up) and dump potassium into urine (keeps potassium from building up and stopping your heart).
8. When cortisol levels rise high enough, cortisol loops back to the hypothalamus and pituitary and says 'enough'—this negative feedback shuts off the ACTH signal so you do not make too much cortisol.
9. This whole cycle runs every day, with cortisol peaking in the early morning (to wake you up) and falling at night (so you can sleep).

What breaks

One broken piece upstream—either the adrenal glands themselves die, or the pituitary gland stops sending the ACTH signal—and every downstream finding at the bedside (low blood pressure, low sodium, high potassium, bronze skin, crushing fatigue) flows logically from that single break.

CLINICAL TERM

Primary adrenal insufficiency means the adrenal glands themselves are destroyed, so they cannot make cortisol or aldosterone no matter how loud the ACTH signal screams. The most common cause in the United States and Europe is autoimmune adrenalitis (Addison disease), where your own immune system attacks and kills the adrenal cortex—about 70 to 90 percent of cases, often linked to other autoimmune diseases like type 1 diabetes or autoimmune thyroid disease. Worldwide, tuberculosis is the leading cause—the TB bacteria seed into the adrenal glands and destroy them. Other causes include adrenal bleeding (hemorrhage) (bleeding into the glands from overwhelming infection like meningococcemia, blood clots from antiphospholipid syndrome, or blood thinners), metastatic cancer (lung cancer, breast cancer, or melanoma that spreads to the adrenals and replaces normal tissue), and rarely genetic enzyme defects (congenital adrenal hyperplasia) or drugs that poison the adrenal cortex (like mitotane or ketoconazole at high doses). Secondary adrenal insufficiency means the pituitary gland fails to make ACTH, so the adrenal glands get no signal and shrink from lack of use—cortisol production stops, but aldosterone production continues because it does not depend on ACTH. The most common cause of secondary disease is suddenly stopping long-term glucocorticoid therapy (prednisone, dexamethasone, or hydrocortisone taken for months or years for asthma, rheumatoid arthritis, or lupus)—the outside steroid shuts down the pituitary's ACTH factory, and when you stop the pills abruptly, the pituitary cannot restart quickly enough, leaving you with no cortisol for weeks to months. Other causes include pituitary tumors (adenomas that crush normal pituitary tissue), pituitary surgery or radiation, traumatic brain injury, and pituitary tissue death from blocked blood flow (infarction) (Sheehan syndrome, where the pituitary dies from blood loss during childbirth). Tertiary adrenal insufficiency means the hypothalamus fails to make CRH, so the pituitary never gets the wake-up call—clinically it looks just like secondary disease and is managed the same way. The break does not stay local. The downstream signals you will see at the bedside are crushing fatigue (the patient feels exhausted even after a full night of sleep), weight loss (5 to 15 pounds over months without trying), nausea and vomiting (the gut stops moving normally), low blood pressure (often systolic below 100, with dizziness when standing up), low serum sodium (hyponatremia, often 125 to 132 mEq/L), and high serum potassium (hyperkalemia, often 5.5 to 6.5 mEq/L). In primary disease, high ACTH also causes hyperpigmentation—bronze or tan patches on sun-exposed skin, elbows, knuckles, palmar creases, old scars, and dark spots inside the mouth on the gums and cheeks. Read every weird lab and symptom backward—they all point to this one broken organ or signal upstream.

How the body compensates

The body can hide how sick it really is for weeks or months by cranking up ACTH, making you crave salt (so you drink and eat more sodium), and forcing you to rest (so you burn fewer calories). Vital signs can look almost normal while the patient is one infection or one stressful event away from total collapse. Your job is to recognize the patient heading toward adrenal crisis before they crash, because once blood pressure drops below 90 and glucose drops below 60, the window to save their life shrinks to hours.

1. In the early weeks or months, the body holds blood pressure and blood sugar near-normal by cranking up ACTH (which weakly stimulates aldosterone in primary disease), triggering intense salt craving (patients eat pickles, chips, and add salt to everything, which pulls water into the bloodstream and props up blood volume), and down-regulating all non-essential activity (patients feel exhausted and spend more time lying down, which lowers the body's demand for cortisol).
2. This compensation phase is the most dangerous window because normal vital signs and normal labs today can hide a patient who is one stressor away from crisis—the team may discharge them home thinking they are stable, when in reality homeostasis (the body's balance) is hanging by a thread.
3. The decompensation point is adrenal crisis, triggered when any stressor (infection like pneumonia or flu, surgery, trauma, severe vomiting or diarrhea, heat stroke, or even emotional stress) demands a surge in cortisol that the failing adrenal glands or suppressed pituitary cannot provide. Blood pressure crashes (systolic below 90 mmHg, often below 70 mmHg, refractory to intravenous fluids because blood vessels have lost cortisol-dependent tone and cannot squeeze), blood glucose plummets (often below 60 mg/dL, sometimes into the 30s, because the liver cannot make new glucose without cortisol), and the patient develops confusion or loss of consciousness (from low glucose and low blood flow to the brain), severe nausea and vomiting (gut stops moving), abdominal pain (can mimic appendicitis or bowel obstruction), fever (from infection or from the crisis itself), and cardiovascular collapse leading to death within hours if intravenous hydrocortisone and saline are not given immediately.
4. Watch for the decompensation point before it happens, because once the patient tips into crisis, the window to reverse shock narrows to hours and mortality climbs to 5 to 10 percent even with aggressive treatment. A delay in diagnosis—because the team thinks it is just sepsis or gastroenteritis or a surgical abdomen—can be fatal.

5. Look at the trend over days to weeks—worsening fatigue (patient who used to work full-time now naps twice a day), increasing nausea (patient who used to eat normal meals now picks at food), rising serum potassium (from 4.5 to 5.2 to 5.8 mEq/L over weeks), falling serum sodium (from 138 to 132 to 126 mEq/L), weight loss (5 to 15 pounds without trying), and orthostatic low blood pressure (hypotension) (blood pressure drops more than 20 mmHg systolic when standing up, with dizziness or near-fainting (syncope))—not just a single snapshot in time.
6. A patient with stable vital signs today but a downward trajectory (progressive fatigue, progressive weight loss, progressive lab derangements) is not truly stable—they are in compensated shock, and intervention (starting hydrocortisone replacement, teaching sick-day rules, giving a medical alert bracelet and emergency injection kit) must happen before crisis, not during it.

Domino effect

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. — 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. — 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. — 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. — 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. — 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. — 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.

Symptoms · what the patient feels, 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.
- Low sodium (Hyponatremia) (serum sodium below 135 mEq/L) and high potassium (hyperkalemia) (serum potassium above 5.0 mEq/L): In primary disease, loss of aldosterone makes your kidneys dump sodium and water while holding onto potassium, so lab values show low sodium, high potassium, and often rising creatinine (a kidney number that goes up when blood flow to the kidneys is low)—secondary insufficiency usually shows only low sodium (because cortisol loss blocks your kidneys from getting rid of extra water) without high potassium.
- Low blood sugar (Hypoglycemia) (blood sugar below 70 mg/dL): Cortisol drives the liver to make new glucose from protein and fat; without it, blood sugar falls during fasting or stress, especially in children, causing shakiness, confusion, and hunger—adults are more likely to show low blood sugar during adrenal crisis (a sudden collapse) than at rest.
- Refractory low blood pressure (hypotension) (blood pressure below 90 mmHg systolic that does not respond to intravenous fluids alone): In adrenal crisis, loss of cortisol means your blood vessels cannot squeeze tight anymore and your blood volume is critically low from aldosterone loss, so blood pressure collapses into a combined shock (your vessels are too loose and your tank is too empty)—fluids alone will not restore pressure without intravenous hydrocortisone.

- Altered mental status, confusion, or loss of consciousness: Severe low blood pressure reduces blood flow to the brain, low blood sugar starves brain cells of fuel, and severe low sodium causes the brain to swell, so the patient becomes confused, sleepy, or unresponsive—this is a sign of adrenal crisis and the heart and circulation are about to collapse.

Focused exam

- Dark patches of skin on elbows, knuckles, scars, gum line, and creases of the palms: When the adrenal glands fail, the pituitary gland releases extra ACTH (a hormone that tells the adrenal glands to make cortisol). ACTH also accidentally turns on the pigment-making cells in your skin, causing dark patches called hyperpigmentation. This darkening happens most on areas that already have pigment or get rubbed (like elbows and knuckles). Hyperpigmentation is the biggest clue that the adrenal glands themselves are broken, not the pituitary. If the pituitary were the problem, ACTH would be low and skin would stay normal.
- Blood pressure below 90 over 60 mmHg that stays low or drops further when the patient stands up: Cortisol keeps blood vessels firm so they can squeeze and push blood around the body. Without cortisol, the vessels relax like a deflating balloon and blood pressure falls. When you stand, gravity pulls blood into your legs; normally your vessels squeeze tighter to keep blood flowing to your brain, but in adrenal insufficiency they cannot respond. Low blood pressure that does not rise when standing (called orthostatic low blood pressure (hypotension)) means the body has lost its ability to adjust—this is dangerous and can lead to fainting or shock.
- Blood sodium below 135 mEq/L and blood potassium above 5.0 mEq/L: Aldosterone is a hormone from the outer layer of the adrenal glands that tells your kidneys to hold onto sodium and get rid of potassium. When the whole adrenal gland is damaged, aldosterone disappears. Sodium leaks out in your urine and potassium piles up in your blood. This pattern—low sodium plus high potassium—only happens when the adrenal glands themselves are failing, not when the pituitary fails. It is a fingerprint of primary adrenal insufficiency.
- Severe tiredness that rest does not fix, even after a full night of sleep: Cortisol helps your body make glucose (sugar for energy) from stored protein and fat, and it helps your cells use that glucose. Without enough cortisol, your body runs out of fuel. You feel exhausted because your muscles, brain, and organs cannot get the energy they need. This is not normal tiredness—it is a deep fatigue that sleep does not repair.

- Weight loss, constant nausea, vomiting, and no desire to eat: Low cortisol slows down the movement of your stomach and intestines and increases signals in your body that make you feel sick. You lose your appetite, feel nauseated, and may throw up. Because you are not eating and your body cannot use food normally, you lose weight. These gut symptoms are common and can last for weeks before anyone realizes the adrenal glands are the problem.
- Signs of shock: blood pressure below 90 over 60 mmHg, heart rate above 100 beats per minute, confusion, cold clammy skin, and blood sugar below 70 mg/dL: When the body faces stress—like an infection, injury, or surgery—it normally floods the bloodstream with cortisol to keep blood pressure up and glucose steady. In adrenal insufficiency, that surge cannot happen. Blood vessels collapse, blood sugar crashes, and organs do not get enough blood flow. This is called adrenal crisis and it is a life-threatening emergency. The patient needs IV hydrocortisone and fluids within minutes or they can die.

Diagnostics · every test answers a question

- Morning serum cortisol at 8 AM → Is the adrenal gland making any cortisol when it should be making the most? Cortisol levels are naturally highest in the early morning. If cortisol is very low even at 8 AM, the adrenal glands are failing.
- ACTH stimulation test with cosyntropin 250 mcg IV or IM, measure cortisol at 0 and 30 or 60 minutes → Can the adrenal glands respond when you give them a big dose of synthetic ACTH (cosyntropin)? A healthy adrenal gland will produce a surge of cortisol. A damaged gland will not respond.
- Plasma ACTH level → Is the pituitary gland screaming for cortisol (high ACTH) or is it silent (low ACTH)? High ACTH with low cortisol means the adrenal glands are broken. Low ACTH with low cortisol means the pituitary or hypothalamus is broken.
- Serum sodium and potassium → Is the adrenal gland also failing to make aldosterone? Low sodium plus high potassium only happens in primary adrenal insufficiency because aldosterone comes from the adrenal gland, not the pituitary.
- 21-hydroxylase autoantibodies (also called adrenal cortex antibodies) → Is the immune system attacking the adrenal glands? Positive antibodies mean the cause is autoimmune adrenalitis, also called Addison disease.
- Adrenal CT scan or MRI → If antibodies are negative, is there structural damage—infection like tuberculosis, bleeding, cancer that has spread to the adrenal glands, or infiltration by another disease? Imaging shows whether the glands are enlarged, shrunken, calcified, or replaced by abnormal tissue.
- Blood glucose → Is the body able to maintain normal blood sugar? Cortisol is needed to make glucose from protein and fat. Without cortisol, blood sugar drops, especially during fasting or stress.

- Renin and aldosterone levels (if electrolyte abnormalities are present) → Is the renin-aldosterone system working? In primary adrenal insufficiency, aldosterone is low but renin is high because the kidneys are trying to signal the adrenal glands to make more aldosterone. In secondary insufficiency, aldosterone is usually normal because the kidneys can still make it independently.

Treatment logic

- 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.
- 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.
- 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.
- 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.

- 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.
- Treat the underlying cause if it can be reversed: give anti-tuberculosis therapy (rifampin, isoniazid, pyrazinamide, and ethambutol for 6 to 9 months per CDC guidelines) if TB is found; remove or radiate a pituitary tumor if secondary insufficiency is from an adenoma; support blood pressure and stop anticoagulation if adrenal bleeding (hemorrhage) is found. → Stops the process destroying the adrenal glands (infection, tumor, or bleeding). In some cases—especially tuberculosis—treating the cause early may allow partial recovery of adrenal function over many months, though most patients still need replacement.
- Patient education: teach the patient to recognize early signs of crisis (vomiting, severe weakness, confusion, low blood pressure), when to double or triple the dose, when to use the emergency injection, and when to go to the emergency department. → Empowers the patient to prevent crises by adjusting doses during minor illness and to seek help early during major illness. Education reduces hospitalizations and deaths from adrenal crisis, which still occurs in 5 to 10 percent of patients with adrenal insufficiency each year.

Medications

Hydrocortisone · Glucocorticoid (cortisol replacement)

Hydrocortisone is a man-made copy of cortisol, the stress hormone your adrenal glands normally make. When you take it, it acts like the missing cortisol in your body. It tells your liver to make glucose (sugar that fuels your brain and muscles), tells your blood vessels to tighten when needed (to keep blood pressure up), and calms down the immune system so it doesn't overreact. Without it, your body can't handle stress, your blood sugar drops dangerously low, and your blood pressure crashes.

1. You swallow the hydrocortisone pill, and it dissolves in your stomach and small intestine.
2. The medicine enters your bloodstream and travels to cells all over your body.
3. It slips through the cell's outer wall and finds a special docking site inside called the glucocorticoid receptor.
4. The receptor grabs the hydrocortisone and together they move into the nucleus, the cell's control room where DNA lives.
5. They land on specific genes and turn them on, like flipping a light switch.
6. Those genes tell the cell to make enzymes—proteins that do jobs like turning protein into glucose or breaking down fat for fuel.

7. Your blood glucose rises, giving your brain and muscles the energy they need.
8. Your blood vessels become more sensitive to adrenaline and tighten up, raising blood pressure.
9. Your immune cells quiet down, reducing fever and inflammation.

SAFETY WATCH

Too much hydrocortisone over time causes Cushing syndrome: your face and belly get puffy with fat, your arms and legs stay thin, your skin gets fragile and bruises easily, purple stretch marks appear, bones weaken (osteoporosis), blood sugar rises (can cause diabetes), and blood pressure climbs. · Too little hydrocortisone or skipping doses during stress (fever, infection, surgery, injury) triggers adrenal crisis—a life-threatening emergency where blood pressure drops so low that organs shut down, blood sugar falls dangerously, you feel confused or pass out, and you can die within hours if not treated. · Never stop hydrocortisone suddenly after taking it for weeks or months—your adrenal glands need time to wake up and start working again. Stopping cold causes adrenal crisis. · During any illness with fever, vomiting, or diarrhea, double or triple your dose and call your doctor. If you vomit and cannot keep pills down, you need an emergency injection or IV hydrocortisone. · Carry an emergency injection kit of hydrocortisone at all times and wear a medical alert bracelet that says 'adrenal insufficiency' so paramedics and doctors know to give you hydrocortisone immediately if you are unconscious or in shock. · Your doctor will check your blood pressure, weight, blood sugar, and how you feel to adjust the dose—everyone needs a slightly different amount.

Prednisone · Glucocorticoid (cortisol replacement, alternative to hydrocortisone)

Prednisone is another man-made form of cortisol. Your liver turns prednisone into prednisolone, which then works exactly like cortisol: it raises blood sugar, keeps blood pressure steady, and controls the immune system. It lasts longer in your body than hydrocortisone, so you can take it once a day instead of splitting doses. It replaces the cortisol your adrenal glands cannot make.

1. You swallow the prednisone tablet.
2. In your liver, enzymes convert prednisone into prednisolone, the active form.
3. Prednisolone enters cells throughout your body and binds to the glucocorticoid receptor inside.
4. The receptor carries it into the nucleus, where it attaches to DNA.
5. Genes are switched on to produce enzymes that make glucose, raise blood sugar, and break down fat and protein for energy.

6. Your blood vessels become more responsive to signals that tighten them, raising blood pressure.
7. Your immune cells dial down their activity, reducing fever and swelling.

SAFETY WATCH

Too much prednisone causes the same problems as too much hydrocortisone: round puffy face, weight gain in the belly, high blood sugar, high blood pressure, thin fragile skin, easy bruising, weak bones, and muscle weakness. · Too little or missing doses during stress causes adrenal crisis—dangerously low blood pressure, confusion, collapse, and death within hours without emergency treatment. · Never stop prednisone suddenly after long-term use—taper the dose slowly under your doctor's guidance to let your adrenal glands recover, or you will go into adrenal crisis. · During illness, injury, or surgery, double or triple your dose and notify your doctor. If you cannot swallow pills, you need IV hydrocortisone immediately. · Carry an emergency hydrocortisone injection kit and wear a medical alert bracelet. · Your doctor will monitor your blood pressure, weight, and blood sugar to make sure the dose is right.

Fludrocortisone · Mineralocorticoid (aldosterone replacement)

Fludrocortisone replaces aldosterone, the hormone that tells your kidneys to hold onto sodium (salt) and water and get rid of potassium. When you take it, it travels to the kidney's collecting duct—the final tube where urine is fine-tuned before leaving your body. There it tells the cells lining the tube to pull sodium out of the urine and back into your blood. Water follows the sodium by osmosis (water always follows salt), so your blood volume goes up. Higher blood volume raises your blood pressure and keeps you from getting dizzy when you stand up. At the same time, it pushes potassium into the urine so your potassium level stays normal.

1. You swallow the fludrocortisone pill and it enters your bloodstream.
2. It travels to the kidneys and enters the principal cells lining the collecting duct.
3. Inside the cell, it binds to the mineralocorticoid receptor.
4. The receptor moves into the nucleus and turns on genes that make sodium channels (called ENaC) and sodium-potassium pumps.
5. The sodium channels open on the side of the cell facing the urine, allowing sodium to flow from urine into the cell.
6. The sodium-potassium pumps on the other side of the cell push sodium into the blood and pull potassium out of the blood into the cell.
7. Potassium flows into the urine and is lost in urine.
8. Water follows sodium back into the blood by osmosis, increasing blood volume.
9. Blood pressure rises and stays steady, so you don't feel dizzy or weak.

SAFETY WATCH

Too much fludrocortisone makes your body hold onto too much sodium and water, causing swelling (edema) in your legs and lungs, high blood pressure, and dangerously low potassium (hypokalemia). Low potassium makes your heart rhythm unstable and can cause life-threatening arrhythmias, muscle weakness, and cramping. · Too little fludrocortisone causes your body to lose too much sodium and water in urine, leading to low blood pressure, dizziness when standing (orthostatic low blood pressure (hypotension)), intense salt cravings, fatigue, and dangerously high potassium (hyperkalemia). High potassium can stop your heart. · Your doctor will check your blood pressure sitting and standing, measure sodium and potassium levels in your blood regularly, and ask about swelling or dizziness to adjust the dose. · If you get diarrhea, vomiting, or heavy sweating, you may need more fludrocortisone temporarily to replace the extra salt and water you lose. · Fludrocortisone dose is usually stable and does not need to be increased during stress or illness (unlike hydrocortisone), but your doctor may adjust it based on your blood tests and symptoms.

Red flags

- 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

Nursing priorities

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. — 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. — 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. — 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.
4. Administer IV hydrocortisone exactly on time every 6 to 8 hours as ordered, and never delay or skip a dose even if patient is eating or seems stable. — The body has zero cortisol reserve in adrenal insufficiency, so missing even one dose during stress or illness can trigger life-threatening adrenal crisis within hours.
5. Monitor serum sodium and potassium levels at least daily, watching for low sodium (hyponatremia) (sodium below 135 mEq/L) and high potassium (hyperkalemia) (potassium above 5.0 mEq/L). — Low aldosterone causes the kidneys to dump sodium and hold onto potassium, creating dangerous electrolyte imbalances that can cause seizures from low sodium or deadly heart rhythms from high potassium.
6. Assess for nausea, vomiting, or abdominal pain every 4 hours, give antiemetics as ordered, and keep patient NPO (nothing by mouth) if vomiting until IV hydrocortisone stabilizes the gut. — Cortisol deficiency irritates the gastrointestinal tract, and vomiting worsens dehydration and prevents oral steroid absorption, so controlling nausea is essential to recovery.
7. Teach the patient and family to recognize sick-day rules: double or triple the home steroid dose during fever, infection, vomiting, or diarrhea, and go to the emergency room if unable to keep pills down. — The body needs 2 to 3 times more cortisol during physical stress, but damaged adrenal glands cannot respond, so patients must increase replacement doses themselves or risk adrenal crisis.

8. Ensure the patient wears a medical alert bracelet stating adrenal insufficiency and carries an emergency injection kit of hydrocortisone 100 mg (Solu-Cortef Act-O-Vial) before discharge. — In emergencies like car accidents or sudden collapse, bystanders and paramedics must know to give IV steroids immediately, because delay of even 30 to 60 minutes in adrenal crisis can cause irreversible shock and death.

Sources

- Endocrine Society Clinical Practice Guideline on Diagnosis and Treatment of Primary Adrenal Insufficiency (2016)
- UpToDate Clinical Overview: Adrenal Insufficiency in Adults (2024)
- National Institute for Health and Care Excellence (NICE) guideline on Addison Disease (2024)
- Cochrane systematic review on Glucocorticoid Replacement for Adrenal Insufficiency (2022)

Last reviewed: 2026-07-07