

Cushing Syndrome

Cushing syndrome is the whole picture of too-much-cortisol damage; it can come from your own glands going haywire or from taking steroid pills for a long time.

THE ONE-LINE TRUTH

Way too much cortisol flooding the body, no matter where it comes from.

The chain — how it unfolds

1. A tumor or medicine breaks the cortisol feedback loop, so cortisol floods the blood day and night at levels two to ten times higher than normal. — why: Cortisol is supposed to pulse—high in the morning (peak around 8 AM), low at night (nadir around midnight). In Cushing syndrome that circadian rhythm disappears; the level stays high around the clock, so there is never a rest period for the body to repair itself.
2. Every cell in the body has glucocorticoid receptors (proteins on the cell surface or inside that read the cortisol signal) and obeys the message—so when cortisol is always screaming, cells follow those loud orders even though the orders are wrong for the situation. — why: Cortisol normally helps in a short crisis: it raises blood sugar for quick energy, tightens blood vessels to keep pressure up during shock, and calms inflammation to prevent tissue damage. But when cortisol is high all the time, those helpful actions become toxic—sugar stays high and damages vessels (glycation of proteins, oxidative stress), pressure stays high and strains the heart and kidneys, and the immune system stays suppressed and lets infections in.

3. Fat moves from arms and legs into the face (moon facies), neck (supraclavicular fat pads fill in the hollows above the collarbones), upper back (buffalo hump), and deep belly; muscles waste; skin thins and bruises; and bones lose density—giving the classic 'Cushingoid' appearance. — why: Each feature comes from cortisol doing its normal job at the wrong intensity. Cortisol activates lipoprotein lipase in central fat depots and shifts fat storage from limbs to trunk and face (central obesity with thin extremities). It breaks down skeletal muscle protein (proteolysis) to supply amino acids for the liver to make glucose. It blocks fibroblasts from making collagen and elastin, so skin loses strength and capillaries break easily (easy bruising, bruises (ecchymoses)). It inhibits osteoblasts and stimulates osteoclasts, pulling calcium out of bone to keep serum calcium steady—so bone mineral density drops fast (T-score drops, fracture risk soars). The body is not trying to hurt itself—it is just following the hormone signal it is programmed to obey.
4. Blood sugar and blood pressure rise, and the heart and kidneys begin to suffer silently—setting up strokes, heart attacks, and chronic kidney disease over months to years. — why: High cortisol forces the liver to keep making glucose (hepatic gluconeogenesis runs constantly) even after meals, and it makes muscle and fat cells resist insulin (insulin receptor signaling is blunted), so blood sugar climbs and hemoglobin A1c rises. The pancreas tries to compensate by pumping out more insulin, but eventually beta cells tire and glucose control fails (secondary diabetes). High cortisol also keeps blood vessels clamped tight (increased vascular tone via catecholamine sensitization and direct smooth muscle effect) and raises blood volume (sodium and water retention via mineralocorticoid receptor activation in the kidney), so blood pressure stays elevated every hour of every day. The heart pumps against higher resistance every beat (increased afterload), the left ventricle thickens to handle the load (left ventricular hypertrophy), vessels stiffen (arterial stiffness, loss of compliance), and atherosclerotic plaques form faster (dyslipidemia, endothelial dysfunction)—so heart attack (myocardial infarction), stroke, and heart failure become the top causes of death if Cushing is not treated.

5. Infections become more common and more dangerous because white blood cells are suppressed, and mood crashes or thinking gets confused because brain chemistry and structure shift under the cortisol flood. — why: Cortisol normally damps down immune responses to prevent runaway inflammation after injury, but chronic excess cortisol leaves the immune system too weak to clear bacteria and fungi. Lymphocyte counts drop (lymphopenia), neutrophil migration to infection sites is impaired (reduced chemotaxis and phagocytosis), and cell-mediated immunity fails—so opportunistic infections like *Pneumocystis jirovecii* pneumonia, invasive fungal sinusitis, and disseminated tuberculosis can appear even without HIV. Skin and soft-tissue infections (cellulitis, abscesses) spread fast because wound healing is delayed. In the brain, too much cortisol causes the hippocampus (the memory and emotional regulation center) to shrink (neuronal atrophy, reduced neurogenesis in the dentate gyrus), the amygdala (the fear and alarm center) to become overactive, and the prefrontal cortex (the executive control center that plans and inhibits impulses) to lose volume. Neurotransmitter systems are disrupted: serotonin (the brain's mood-steadying messenger) drops, dopamine (the reward and motivation signal) is blunted, and GABA (the brain's main calming neurotransmitter) signaling is altered. The result is major depression (low mood, loss of interest, hopelessness) in 50 to 80 percent of patients, generalized anxiety, panic attacks, insomnia (cannot fall asleep or stay asleep because cortisol never drops at night), irritability, memory problems, and in severe cases psychosis (hallucinations, delusions, paranoia). Suicide risk is high and must be taken seriously—screening and psychiatric support are essential parts of care.
6. Once the source is removed—surgery to take out the pituitary or adrenal tumor (transsphenoidal resection for Cushing disease, unilateral adrenalectomy for adrenal adenoma, tumor resection for ectopic ACTH), or careful taper of steroid medicine—cortisol falls back toward normal and the damage slowly reverses. — why: Most clinical features improve over six to twelve months after successful treatment: blood pressure drops (often within weeks as vascular tone normalizes), blood sugar comes down (insulin sensitivity improves and diabetes may resolve or become easier to control), mood lifts (hippocampal volume can recover, serotonin normalizes, depression and anxiety improve), muscle strength returns (protein synthesis restarts, proximal myopathy resolves), and fat redistributes back toward a more normal pattern (moon facies and buffalo hump shrink). Skin heals and bruising lessens as collagen production restarts. Bone density takes much longer to rebuild—one to two years or more—and patients need calcium, vitamin D, and sometimes bisphosphonates (alendronate, risedronate) or other bone-strengthening treatment to prevent fractures during recovery. Some changes like wide purple striae fade to pale scars but do not disappear completely. The key is that the body can heal—but only if you match the treatment to the actual source (pituitary adenoma vs ectopic ACTH vs adrenal tumor vs exogenous steroids) and remove or block it before permanent damage (severe osteoporosis, heart failure, irreversible cognitive impairment) occurs.

7. If the source is not stopped, patients face deadly complications: severe infections (pneumonia, sepsis, fungal bloodstream infections), venous thromboembolism (blood clots in the deep veins of the legs that can break off and travel to the lungs as pulmonary embolism (a clot lodging in a lung artery)), heart failure, stroke, or suicide from unbearable depression. — why: Untreated Cushing syndrome has a mortality rate as high as 50 percent over five years because the cortisol flood damages so many systems at once. Even if blood pressure and blood sugar are controlled with pills (antihypertensives, metformin, insulin), the immune suppression, hypercoagulable state (cortisol increases clotting factors and platelet activation), cardiac strain, and severe psychiatric symptoms continue unabated. Opportunistic infections kill quickly once the immune system is too weak. Venous thromboembolism risk is five to ten times higher than in the general population. Cardiovascular events (myocardial tissue death from blocked blood flow (infarction), stroke) are the leading cause of death. Depression and psychosis can lead to suicide if psychiatric care is not provided. Finding and fixing the source is life-saving, not optional—it is the only way to stop the deadly cascade.
8. After surgery patients may swing into adrenal insufficiency (sudden cortisol deficiency) because the normal adrenal tissue or the normal pituitary-adrenal axis has been suppressed and asleep under the cortisol flood for months or years—so they need careful glucocorticoid replacement and slow weaning as their own glands wake up. — why: When the tumor is removed or steroid medicine is stopped, cortisol drops suddenly from sky-high to near zero. The hypothalamus and pituitary have been shut off by negative feedback for so long that they take weeks to months to restart making CRH and ACTH, and the normal adrenal tissue (in Cushing disease or ectopic ACTH cases) or the remaining adrenal gland (after unilateral adrenalectomy) takes time to wake up and respond. During that recovery window—sometimes six to twelve months or longer—patients must take physiologic-dose hydrocortisone (usually 15 to 25 milligrams per day in divided doses, mimicking the body's natural rhythm) to prevent adrenal crisis (life-threatening shock, low blood sugar, confusion, collapse). They must wear a medical alert bracelet, carry an emergency hydrocortisone injection kit, and know to double or triple their dose during illness, injury, or surgery (stress-dose steroids) because their body cannot make the extra cortisol needed to handle that stress. The dose is tapered slowly as the axis recovers, guided by morning cortisol levels and ACTH stimulation testing. Stopping glucocorticoid replacement too fast or skipping doses can cause acute adrenal insufficiency—severe weakness, nausea, vomiting, low blood pressure, shock, and death within hours if not treated with intravenous hydrocortisone and fluids. Patient education and close endocrine follow-up are essential to safely navigate this dangerous recovery phase.

Spot it — what you see, and why

- Weight gain in the center of the body (trunk obesity) with thin arms and legs: Too much cortisol (the body's main stress hormone) tells fat cells to grow and fill up around the belly, chest, and face, but at the same time it breaks down muscle and fat in the arms and legs—like a broken switch that puts all the padding in the middle and takes it away from the limbs.
- Round, full face (moon face) and fat pad on the back of the neck (buffalo hump): Extra cortisol makes fat pile up in specific spots: the cheeks swell and round out the face like a full moon, and fat builds up between the shoulder blades at the base of the neck, creating a visible hump.
- Purple or red stretch marks (striae) on the belly, thighs, breasts, or arms: High cortisol weakens collagen (the protein fibers that hold skin together and keep it strong), so when the skin stretches from weight gain it tears more easily—leaving wide, deep purple-red marks that look different from normal pale stretch marks.
- Thin skin that bruises easily and heals slowly: Cortisol breaks down collagen in the skin, making it fragile like tissue paper—even a light bump can cause a bruise, and cuts or scrapes take much longer to close up because the skin cannot rebuild itself quickly.
- High blood sugar or new diabetes: Cortisol signals the liver to make more glucose (sugar) and tells the body's cells to ignore insulin (the key that unlocks cells so sugar can get in), so sugar piles up in the blood instead of being used for energy.
- High blood pressure: Cortisol makes the walls of blood vessels squeeze tighter and tells the kidneys to hold onto salt and water, which increases the volume of fluid in the blood vessels and pushes blood pressure up—like overfilling a balloon.

Red flags — act now

- Sudden severe headache or vision changes (may mean a pituitary tumor is growing and pressing on the optic nerves near the brain)
- New bone fracture from a minor injury (sign that bones have become dangerously weak)
- Severe high blood pressure that does not come down with medicine (can lead to stroke or heart attack)
- Signs of infection that get worse quickly, such as fever and confusion (high cortisol weakens the immune system so the body cannot fight germs)
- Chest pain or trouble breathing (may signal a blood clot in the lungs, which is more common when cortisol is very high and blood clots more easily)

Treat it — in this order

1. Transsphenoidal surgery (going through the nose to remove the pituitary tumor) for Cushing disease → Cuts out the pituitary adenoma that is sending too much ACTH signal to the adrenal glands. Once the tumor is gone, ACTH drops, the adrenal glands stop overproducing cortisol, and cortisol levels return to normal within days to weeks. Cure rate is 70 to 90% if the tumor is found and completely removed by an experienced surgeon. Symptoms like high blood pressure, diabetes, and mood problems start improving within weeks to months.
2. Remove the ectopic tumor (lung, pancreas, thymus, or gut tumor making ACTH) → Cuts out the tumor that is making rogue ACTH outside the pituitary. Once the tumor is gone, ACTH and cortisol drop and the body can recover. This is curative if the tumor can be fully removed and has not spread. Small carcinoid tumors and early lung cancers can often be cured with surgery.
3. Unilateral adrenalectomy (remove one adrenal gland) if there is an adrenal tumor making cortisol on its own → Takes out the adrenal gland with the tumor, stopping the excess cortisol at its source immediately. The other healthy adrenal gland usually wakes up and takes over, making normal cortisol within weeks to months. This is curative for benign adrenal adenomas. Symptoms improve steadily as cortisol normalizes.
4. Medical therapy to block cortisol production — ketoconazole (200 to 400 mg twice daily), metyrapone (250 mg to 1 g every 6 hours), or osilodrostat (starting 2 mg twice daily) — while waiting for surgery or if surgery fails or is not possible → Blocks enzymes inside the adrenal gland that finish making cortisol (ketoconazole blocks CYP17A1 and other enzymes; metyrapone blocks 11-beta-hydroxylase; osilodrostat blocks 11-beta-hydroxylase very powerfully). This lowers blood cortisol toward normal even though the tumor or broken pituitary is still there. Helps control symptoms like high blood pressure, high blood sugar, and mood swings, and prepares the body for safer surgery by lowering surgical risk.
5. Bilateral adrenalectomy (remove both adrenal glands) if the source cannot be found or removed, if surgery fails, or if medical therapy does not work or cannot be tolerated → Takes out both adrenal glands completely, so the body can no longer make cortisol or aldosterone no matter what signal the pituitary or ectopic tumor sends. This cures the high cortisol immediately — 100% effective at stopping Cushing syndrome. Symptoms like high blood pressure, diabetes, and muscle weakness improve within weeks to months.

Your top priorities at the bedside

1. Monitor blood pressure every 4 hours and notify the provider immediately if systolic is above 180 or diastolic is above 110 — why: High cortisol causes the kidneys to hold sodium and water leading to high blood pressure (hypertension) (high blood pressure); uncontrolled high blood pressure can cause stroke or heart attack, especially in patients already at high risk
2. Check blood glucose (finger stick sugar) before meals and at bedtime, and give sliding scale insulin exactly as ordered — why: Cortisol tells the liver to make glucose and blocks insulin from working, causing high blood sugar (hyperglycemia) (high blood sugar); uncontrolled blood sugar leads to diabetic ketoacidosis (the acid crisis of missing insulin) (dangerous acid buildup) and slows wound healing
3. Inspect skin every shift for new bruises, tears, or pressure areas; use foam padding on bony areas and turn the patient every 2 hours if on bedrest — why: Excess cortisol destroys collagen (the protein that keeps skin strong) making the skin paper-thin and fragile; even small pressure or friction can cause skin tears or pressure ulcers (bedsores) that heal very slow