

Lithium Toxicity

Lithium saves lives in bipolar disorder, but the gap between 'just right' and 'too much' is razor-thin—dehydration, a new medicine, or a stomach bug can tip you over.

THE ONE-LINE TRUTH

Lithium's safe window is narrow (0.6–1.2 mEq/L), and anything that drops your body's water or raises sodium—dehydration, diuretics, NSAIDs, kidney trouble—can push lithium into the danger zone fast.

The chain — how it unfolds

1. Trigger: something reduces lithium clearance or increases intake. — why: Dehydration (vomiting, diarrhea, sweating, not drinking enough) shrinks blood volume → kidneys respond by reabsorbing more sodium and water in the proximal tubule and loop of Henle → lithium uses the same sodium transporters, so it gets reabsorbed back into the blood instead of leaving in urine → serum lithium climbs above 1.2 mEq/L. Alternatively, starting an NSAID (ibuprofen, naproxen) or a diuretic (hydrochlorothiazide, furosemide) does the same thing by cutting kidney blood flow or boosting sodium reabsorption.
2. Lithium enters neurons and disrupts the inositol recycling pathway. — why: Inside the nerve cell, lithium blocks enzymes (inositol monophosphatase) that recycle inositol, a building block for the PIP₂ signaling system neurons use to pass messages. Without enough inositol, the neuron's internal 'volume dial' for excitement jams—some signals are too weak (slurred speech, confusion), others misfire (tremor, twitching). This is why neurotoxicity shows up even before lithium reaches lethal levels: the brain's fine-tuning breaks first.
3. Early signs: GI upset (nausea, vomiting, diarrhea) and worsening hand tremor. — why: Lithium irritates the gut lining directly, triggering nausea and loose stools (which then worsen dehydration and push lithium higher—another vicious loop). The hands shake because lithium disrupts the cerebellum and basal ganglia's control of smooth movement; a fine tremor you already had on lithium turns coarse and rhythmic as levels rise.

4. Moderate toxicity: loss of coordination (ataxia) (staggering walk), slurred speech (dysarthria), confusion, muscle twitches (myoclonus). — why: The cerebellum (the brain's balance and coordination computer at the back of the skull) is exquisitely sensitive to lithium—once poisoned, it can't smooth out movement commands, so you lurch and stumble. The brainstem and cortex also misfire, scrambling speech and clouding thought. Muscle jerks (myoclonus) mean motor neurons are firing randomly because lithium has jammed their off-switches.
5. Severe toxicity: seizures, decreased level of consciousness (lethargy → stupor → coma), arrhythmias. — why: Lithium floods the whole brain, and excitatory neurons (using glutamate) fire out of control while inhibitory neurons (using GABA) are overwhelmed—this electrical storm is a seizure. The brainstem's alertness centers shut down to protect themselves, dropping you into a coma. Meanwhile, lithium disrupts the heart's SA and AV nodes, slowing the pulse (bradycardia), blocking conduction (first-degree or higher AV block), or causing pauses—any of which can lead to cardiac arrest.
6. Kidney damage: acute kidney injury (AKI) and, if chronic, irreversible nephrogenic diabetes insipidus and chronic kidney disease. — why: High lithium is directly toxic to the kidney tubule cells, causing cell death and scarring (interstitial nephritis). Acutely, the kidney can't filter waste, so creatinine and BUN rise (AKI). Chronically, the collecting duct loses its aquaporin-2 channels permanently, leaving you unable to concentrate urine—you pee dilute urine all day (nephrogenic DI), stay dehydrated, and need lithium stopped or the dose cut way down. Some people never recover full kidney function.
7. Outcome: with early recognition (stop lithium, IV fluids, sometimes hemodialysis if level >4.0 mEq/L or severe symptoms), most recover fully; delay or missed diagnosis can leave permanent loss of coordination (ataxia), cognitive slowing, or kidney failure. — why: Lithium takes hours to days to clear from brain and kidney cells even after blood levels drop, so the faster you stop the drug and flush it out (fluids, dialysis), the less time it has to kill cells. Hemodialysis physically pulls lithium out of the blood in 6–8 hours, preventing further buildup in tissues. Every hour of delay at high levels means more neurons and nephrons die—hence the push for immediate treatment and close monitoring until lithium is safely below 1.0 mEq/L and symptoms resolve.

Spot it — what you see, and why

- Shaking hands (tremor): Too much lithium disrupts the cerebellum (the brain's balance and coordination center) and irritates muscles, making them twitch and shake even when you're trying to hold still.
- Confusion or slurred speech: High lithium levels poison nerve cells in the cerebral cortex (the thinking part of the brain), slowing down signals so thoughts get foggy and words come out jumbled.

- Nausea, vomiting, or diarrhea: Lithium irritates the stomach and intestines directly, triggering the gut to empty itself as if it were trying to get rid of poison.
- Muscle twitching or jerking movements: Lithium disrupts sodium and calcium channels in muscle cells, causing random, uncontrolled firing—like a car engine misfiring.
- Feeling very drowsy or sluggish: Lithium slows down the reticular activating system (the brain's wake-up switch), making you feel like you're stuck in slow motion or half asleep.
- Peeing far more than usual (polyuria): Lithium blocks vasopressin (the hormone that tells kidneys to save water), so the kidneys let huge amounts of water leak out into urine—sometimes gallons a day.

Red flags — act now

- Confusion, slurred speech, or not making sense
- Seizures or uncontrollable muscle jerking
- Very slow, fast, or irregular heartbeat
- Barely able to stay awake or unresponsive
- New kidney failure (very little urine or swelling)

Treat it — in this order

1. Stop lithium immediately → Stopping lithium prevents any more of the drug from entering the bloodstream and gives the kidneys a chance to start clearing what is already there. This is the first mandatory step in every case of suspected toxicity.
2. Start intravenous normal saline (0.9% NaCl) to restore volume and sodium → IV saline rehydrates the body and raises sodium levels, which makes the kidneys start excreting lithium again instead of holding onto it. Saline also dilutes the lithium concentration in the blood, slowing further toxicity.
3. Hemodialysis if lithium level ≥ 2.5 mEq/L OR severe symptoms (seizures, coma, confusion, arrhythmias) OR acute kidney injury → Hemodialysis physically removes lithium from the blood using a machine that filters it out—this is the fastest way to lower lithium when kidneys cannot do the job. Dialysis can drop lithium levels by 1 to 2 mEq/L per session.
4. Stop any medications that raise lithium levels: thiazide diuretics (hydrochlorothiazide), NSAIDs (ibuprofen, naproxen, indomethacin), ACE inhibitors (lisinopril, enalapril), and ARBs (losartan, valsartan) → These drugs reduce kidney excretion of lithium or cause dehydration and salt loss, trapping lithium in the body. Stopping them restores normal kidney clearance.

5. Monitor lithium level every 4 to 6 hours until it falls below 1.0 mEq/L and symptoms resolve → Frequent monitoring catches rebound (lithium leaking back out of cells into the blood after initial treatment) and guides whether more dialysis or IV fluids are needed. It also confirms when it is safe to stop intensive treatment.

Your top priorities at the bedside

1. Stop all lithium doses immediately and hold any medications that raise lithium levels (thiazide diuretics, NSAIDs, ACE inhibitors, ARBs) — why: Lithium has a narrow therapeutic window (safe range of 0.6 to 1.2 mEq/L), and even one more dose can push levels higher while the kidneys struggle to clear the drug already in the body; medications like hydrochlorothiazide and ibuprofen block kidney lithium elimination and must be stopped to prevent further accumulation.
2. Start intravenous normal saline (0.9% sodium chloride) at 100 to 150 mL per hour to restore fluid volume and enhance kidney lithium clearance — why: Normal saline rehydrates the patient and provides sodium, which competes with lithium in the kidney tubules (tiny filters); when sodium is plentiful, the kidneys excrete lithium instead of reabsorbing it, lowering blood levels naturally and preventing further brain and heart damage.
3. Draw stat serum lithium level, basic metabolic panel (BMP) for sodium, potassium, creatinine (kidney function), and obtain 12-lead ECG — why: The lithium level tells us severity (levels above 2.5 mEq/L require hemodialysis); creatinine shows if the kidneys are failing and trapping lithium; sodium and potassium affect heart rhythm; the ECG detects life-threatening arrhythmias like a slow heart rate (bradycardia), QT prolongation, or T-wave flattening caused by lithium's effect on cardiac muscle cells.