

Lithium Toxicity

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THE STORY IN ONE SENTENCE

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“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.”

Normal anatomy — the body's job

Lithium is a positively charged metal ion (like sodium or potassium) that your body treats almost like salt. Your kidneys filter it from your blood into urine and flush it out. A healthy kidney keeps lithium blood levels steady by balancing how much it reabsorbs (takes back) and how much it throws away.

BODY'S JOB

In the brain, lithium slips into nerve cells and gently lowers the volume on excitatory signals—the bursts of electricity that neurons use to talk to each other. It does this by tweaking the recycling of a messenger chemical called inositol and by calming down overactive glutamate (the brain's main 'go' signal) and boosting the effect of GABA (the brain's main 'stop' signal). The result: mood swings flatten, racing thoughts slow, and impulsive behavior settles. Meanwhile, your kidneys watch the sodium and water balance in your blood; if sodium or lithium goes up, the kidney tries to hold on to water to dilute it, but lithium gets caught in that same current and can pile up.

1. You swallow a lithium pill → it dissolves in your stomach and small intestine → lithium enters your bloodstream.
2. Blood carries lithium everywhere: brain, heart, kidneys, muscles.

3. In the brain, lithium slowly crosses into neurons and turns down the 'volume knob' on excitatory signals, smoothing out the wild electrical storms that cause mania.
4. Your kidneys filter all your blood about 50 times a day, pulling lithium into tiny tubes (nephrons) and deciding how much to pee out versus reabsorb back into the blood.
5. Normally your kidneys dump most lithium into urine, keeping blood levels in the safe 0.6–1.2 mEq/L range.
6. If you lose water (sweat, vomit, diarrhea, not drinking enough), your blood volume shrinks → kidneys panic and grab back MORE sodium and water to protect blood pressure → lithium hitchhikes along and gets reabsorbed too → lithium blood level climbs.

What breaks

Lithium toxicity happens when lithium builds up in your blood faster than your kidneys can clear it. The three big triggers: (1) losing too much water (dehydration from heat, exercise, vomiting, diarrhea); (2) starting a medicine that makes your kidneys hold on to lithium (diuretics like hydrochlorothiazide or furosemide, pain pills like ibuprofen or naproxen, ACE inhibitors for blood pressure); (3) your kidneys getting weaker (from age, diabetes, or years of lithium itself). When lithium floods into brain cells, it jams the brakes on nerve signaling so hard that neurons misfire—causing shaking, confusion, muscle twitches, seizures, and coma. In the heart, too much lithium disrupts the electrical rhythm. In the kidneys, it can punch holes in the system that concentrates urine, leaving you peeing gallons of dilute urine (nephrogenic diabetes insipidus) and making dehydration even worse—a vicious circle.

CLINICAL TERM

Lithium toxicity results from decreased renal clearance or increased intake, raising serum lithium above the therapeutic range (0.6–1.2 mEq/L). Risk factors include volume depletion, NSAIDs, thiazide or loop diuretics, ACE inhibitors, reduced GFR, and sodium restriction. Lithium competes with sodium for reabsorption in the proximal tubule and loop of Henle; hypovolemia or diuretics trigger avid sodium (and lithium) reabsorption. Chronic lithium also impairs aquaporin-2 expression in the collecting duct, causing nephrogenic diabetes insipidus and excessive urination (polyuria), which worsens dehydration. Neurotoxicity manifests as tremor, loss of coordination (ataxia), slurred speech (dysarthria), altered mental status, myoclonus, seizures, and coma due to intracellular lithium disrupting inositol metabolism and neurotransmitter release. Cardiotoxicity includes sinus node dysfunction, AV block, and QT prolongation.

How the body compensates

At first, your body hides lithium toxicity by working overtime. Your kidneys try to flush extra lithium by making more urine, your heart speeds up to keep blood pressure normal despite dehydration, and your brain soldiers through mild confusion or shaking. But these fix-it tricks cost energy and water, so the system runs down. Once kidneys can't keep up, lithium shoots higher, the tremor turns coarse, balance goes, and confusion deepens—all while labs may still look 'okay' if checked too early. By the time symptoms are obvious, lithium has already flooded cells and damage is underway.

1. {'what': 'Kidneys ramp up urine output (polyuria) to try to wash out rising lithium.', 'cost': "You lose liters of water every day, which triggers thirst and dehydration if you can't drink enough—and dehydration then makes the kidneys reabsorb MORE lithium, fueling a vicious cycle."}
2. {'what': 'Heart rate climbs (mild a fast heart rate (tachycardia)) to keep blood pressure up when blood volume drops from excessive urination (polyuria).', 'cost': "The heart works harder, masking early volume depletion; you might feel 'fine' even as lithium climbs, until suddenly the SA or AV node gets poisoned and the heart rhythm crashes."}
3. {'what': "Brain neurons fire less to protect themselves from too much excitation, so you feel 'foggy' or slow before confusion sets in.", 'cost': 'Mild cognitive slowing and a fine hand tremor are easy to ignore or blame on stress, giving lithium more time to build up before anyone catches it.'}
4. {'what': 'Cerebellum (balance computer) tries to recalibrate shaky signals, keeping you upright despite mild nerve misfires.', 'cost': "Once lithium saturates the cerebellum, compensation fails all at once—you go from 'slightly unsteady' to uncoordinated (ataxic) (staggering, unable to walk) fast."}
5. {'what': "If lithium keeps rising, the brain's last-ditch defense is to shut down consciousness (coma) to lower metabolic demand and stop runaway electrical activity (seizures).", 'cost': 'Coma and seizures mean the brain is already severely poisoned; even if you survive, permanent damage to kidneys (chronic kidney disease) or brain (persistent loss of coordination (ataxia), cognitive deficits) is possible.'}

Domino effect

1. Trigger: something reduces lithium clearance or increases intake. — 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. — 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. — 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). — 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. — 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. — 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. — 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.

Symptoms · what the patient feels, 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.
- **Seizures:** Very high lithium levels cause massive, chaotic electrical storms in the brain by throwing off the balance of sodium, potassium, and calcium that nerve cells need to fire in an orderly way.

- Slow or irregular heartbeat: Lithium can interfere with the sinoatrial node (the heart's natural pacemaker) and potassium channels, disrupting the electrical rhythm that keeps the heart beating steadily.

Focused exam

- Tremor that gets worse with movement (coarse tremor): Lithium toxicity starts with a fine tremor in the hands; when it turns coarse (big, jerky shakes), it means lithium has climbed high enough to interfere with the cerebellum (the brain's movement-control center). Coarse tremor signals moderate to severe toxicity.
- Confusion, slurred speech, or drowsiness: Lithium at toxic levels disrupts electrical signals across the brain. Confusion or slurred words mean the cerebral cortex (the thinking and speaking part of the brain) is malfunctioning—this is a sign of moderate to severe toxicity and can progress to coma.
- Nausea, vomiting, or diarrhea: The gut feels lithium toxicity early because lithium irritates the stomach and intestines. Vomiting and diarrhea cause dehydration and sodium loss, which make the kidneys hold onto even more lithium—this creates a vicious cycle that worsens toxicity fast.
- Loss of coordination (Ataxia) (stumbling, unsteady gait, or trouble coordinating movements): Loss of coordination (Ataxia) signals that lithium has poisoned the cerebellum (the brain's balance center). This finding means toxicity is moderate to severe and requires urgent treatment to prevent permanent brain damage.
- Muscle twitching (fasciculations) or increased deep tendon reflexes (hyperreflexia): Lithium toxicity overexcites nerves and muscles. Twitching and brisk reflexes show that the nervous system is irritated and at risk for seizures if toxicity continues to climb.
- Decreased urine output or signs of dehydration (dry mouth, low blood pressure, fast heart rate): The kidneys filter lithium out of the blood. Dehydration or kidney failure means lithium cannot leave the body and will keep building up. Low urine output is both a cause and a consequence of lithium toxicity.

Diagnostics · every test answers a question

- Serum lithium level → How much lithium is in the blood right now, and does the level match the symptoms?
- Serum creatinine and blood urea nitrogen (BUN) → Are the kidneys working well enough to clear lithium, or is kidney failure trapping lithium in the body?
- Serum sodium and osmolality → Is dehydration or low sodium causing the kidneys to reabsorb lithium instead of flushing it out?
- Electrocardiogram (ECG) → Is lithium toxicity affecting the heart's electrical rhythm?

- Serum calcium → Is lithium toxicity causing high calcium (hypercalcemia), which makes confusion and kidney problems worse?
- Thyroid-stimulating hormone (TSH) and free T4 → Has chronic lithium use damaged the thyroid and slowed metabolism, which can worsen toxicity?
- Urinalysis and urine output monitoring → Are the kidneys concentrating urine normally, or has lithium caused nephrogenic diabetes insipidus (kidneys cannot hold onto water)?

Treatment logic

- 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.
- 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.
- 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.
- 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.
- 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.
- Correct electrolyte imbalances (sodium, potassium, calcium) and support the kidneys with fluids and close urine output tracking → Restoring normal sodium and hydration helps the kidneys excrete lithium normally. Tracking urine output catches early kidney failure, which would require dialysis.
- Address the cause: dehydration, infection, medication changes, or missed doses. Provide education, stable housing, mental health support, and regular follow-up before restarting lithium at a lower dose. → Fixing the root cause (e.g., teaching the person to drink water during illness, stopping a conflicting drug, ensuring stable access to food and shelter) prevents the same toxicity from happening again. Restarting lithium at a lower dose with close monitoring allows safe mood stabilization.

Medications

Stop lithium immediately · Discontinuation of the offending agent

Lithium is the poison causing the problem, so the first step is to stop it right away. This lets the body start clearing out the extra lithium through the kidneys. While the body works to get rid of it, doctors give intravenous (IV) normal saline (salt water through a vein) to help the kidneys flush lithium faster. If the lithium level is very high (2.5 mEq/L or above), or if the person has serious brain symptoms (confusion, seizures, coma) or kidney failure, hemodialysis is needed. Dialysis is a machine that cleans the blood directly when the kidneys cannot do it fast enough. Doctors also stop any other medicine that was raising lithium levels – like thiazide diuretics (water pills that reduce how much lithium the kidney removes), NSAIDs such as ibuprofen (pain pills that slow kidney clearance of lithium), and ACE inhibitors (blood pressure pills that can reduce kidney blood flow). Lithium levels are checked frequently (every 4–6 hours at first, then every 12–24 hours) until they are safe and falling. Once the person recovers, lithium may be restarted at a lower dose if it is still needed, and the cause of the toxicity (dehydration, drug interaction, too-high dose) is fixed to prevent it from happening again.

1. Stop lithium tablets or liquid right away so no new lithium enters the body.
2. Start IV normal saline (0.9% sodium chloride) to expand blood volume and increase urine flow, which helps the kidneys excrete lithium faster.
3. Stop thiazide diuretics (they make the kidney hold onto lithium), NSAIDs (they reduce kidney blood flow and lithium clearance), and ACE inhibitors or ARBs (they can also reduce kidney filtration).
4. Check serum lithium level every 4–6 hours until it is clearly falling and below 1.5 mEq/L, then space checks to every 12–24 hours.
5. If lithium level is ≥ 2.5 mEq/L, or if severe symptoms are present (altered mental status, seizures, coma, acute kidney injury with rising creatinine), start hemodialysis immediately. Dialysis removes lithium directly from the blood much faster than the kidneys can.
6. Continue hemodialysis sessions (usually 4–6 hours each) until lithium level is safely below 1.0 mEq/L and symptoms are improving. Watch for rebound (lithium moving back into blood from cells after dialysis stops) and recheck levels 6–12 hours after stopping dialysis.
7. Support vital signs and treat complications: give fluids for dehydration, control seizures with benzodiazepines if needed, monitor heart rhythm.
8. Once lithium is cleared and the person is stable, identify and fix the cause (dose too high, dehydration, drug interaction, kidney problem). If lithium is still needed for bipolar disorder, restart at a lower dose with close monitoring.

SAFETY WATCH

Lithium levels must be rechecked frequently (every 4–6 hours at first) because they can stay high or even rise for hours after stopping the drug, especially if the person took a large dose or has kidney damage. · Watch for rebound: lithium stored in cells can leak back into the blood after dialysis stops, so recheck levels 6–12 hours post-dialysis and repeat dialysis if needed. · Monitor kidney function (creatinine, urine output) closely – acute kidney injury from lithium toxicity can worsen even after stopping the drug, and dialysis may be needed for kidney failure as well as for lithium removal. · Watch for seizures, which can happen with severe toxicity; have benzodiazepines ready. · Check electrolytes (sodium, potassium) during IV saline and dialysis to keep them balanced. · Do NOT restart lithium until the cause is fixed, kidney function is stable, and a safe lower dose is calculated. Measure levels 5–7 days after restarting to make sure they stay in the safe range (0.6–1.0 mEq/L for maintenance). · Educate the patient and family: report early warning signs (nausea, tremor, confusion) immediately, avoid dehydration, do not start NSAIDs or diuretics without telling the prescriber, and get regular lithium level checks as scheduled.

Red flags

- 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)

Nursing priorities

1. Stop all lithium doses immediately and hold any medications that raise lithium levels (thiazide diuretics, NSAIDs, ACE inhibitors, ARBs) — 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 — 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 — 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.
4. Place patient on continuous cardiac monitoring and pulse oximetry, and perform hourly neurologic checks (level of consciousness, speech clarity, tremor severity, muscle twitching) — Lithium toxicity causes cardiac conduction delays and arrhythmias that can lead to sudden cardiac arrest; continuous monitoring catches dangerous rhythms early; neurologic deterioration (worsening confusion, seizures, or coma) signals severe brain toxicity requiring emergency hemodialysis to remove lithium before permanent damage occurs.
5. Measure strict intake and output every hour, and report urine output below 30 mL per hour or 0.5 mL per kilogram per hour immediately — The kidneys are the only way lithium leaves the body—there is no other elimination pathway; low urine output means acute kidney injury, which traps lithium and creates a toxic cycle; catching low urine output (oliguria) (low urine) early lets us escalate to hemodialysis before lithium levels climb even higher.
6. Notify the provider immediately if lithium level is 2.5 mEq/L or higher, or if patient shows confusion, seizures, unresponsiveness, or arrhythmias, because these require emergency hemodialysis — Hemodialysis is the only way to rapidly remove lithium when the kidneys fail or toxicity is severe; waiting for the kidneys to clear lithium naturally in severe cases allows continued brain and heart damage; patients with levels above 2.5 mEq/L or life-threatening symptoms need dialysis within hours to prevent permanent neurologic injury or death.
7. Keep the patient NPO (nothing by mouth) if neurologic status is declining or if hemodialysis is being arranged, and maintain seizure precautions with padded side rails up — Worsening confusion or drowsiness increases aspiration risk (breathing in vomit or fluids); seizures occur in severe lithium toxicity when the drug excites brain neurons excessively; padded rails and a clear airway prevent injury during seizures, and NPO status prepares the patient for possible urgent dialysis catheter placement under sedation.
8. Recheck serum lithium level every 4 to 6 hours until levels are steadily falling and patient symptoms improve, because lithium redistributes from tissues back into blood after initial clearance — Lithium stored in body tissues (muscle, brain, bone) slowly leaks back into the bloodstream after the first blood level drops; this rebound effect can cause a second wave of toxicity hours or days later; serial levels catch this redistribution early so we can continue IV fluids or repeat hemodialysis if needed.

Sources

- American College of Medical Toxicology (ACMT) lithium position statement 2018
- UpToDate clinical guideline on lithium toxicity
- Kidney Disease: Improving Global Outcomes (KDIGO) lithium guidance
- American Academy of Clinical Toxicology practice guidelines

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