

Valproate Toxicity

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THE STORY IN ONE SENTENCE

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“Valproate blocks the liver's ammonia-cleaning system, so ammonia backs up into the brain and shuts down thinking.”

Normal anatomy — the body's job

The liver is the body's main detox factory. One of its most important jobs is turning ammonia—a toxic waste product made whenever cells break down protein—into urea, a harmless substance that leaves the body in urine. At the same time, the brain stays alert and thinking clearly because its neurons fire in a careful balance: excitatory signals (mainly glutamate) push activity up, and inhibitory signals (mainly GABA, the brain's brake pedal) hold it down. The pancreas makes digestive enzymes and insulin; it stays healthy when its ducts are open and enzymes flow smoothly into the small intestine.

BODY'S JOB

The liver cleans the blood every minute, catching ammonia before it can reach the brain. The brain uses GABA to keep seizures, anxiety, and racing thoughts under control. The pancreas digests food and keeps blood sugar steady. All three organs work together silently in the background to keep you awake, calm, and nourished.

1. You eat protein (meat, beans, eggs). As your body breaks it down, ammonia is released into the bloodstream.
2. Blood carrying ammonia flows straight to the liver through the portal vein.
3. Inside liver cells, an enzyme system called the urea cycle grabs ammonia and joins it with carbon dioxide to make urea.
4. Urea dissolves in blood, travels to the kidneys, and leaves the body in urine. Ammonia never reaches the brain.

5. Meanwhile, neurons in the brain release GABA to quiet overactive circuits, preventing seizures and calming mood.
6. The pancreas releases enzymes into the small intestine only when food arrives, keeping itself safe from self-digestion.

What breaks

Valproate poisons a key step in the liver's urea cycle, so ammonia piles up in the blood instead of being turned into urea and removed. At the same time, valproate can trigger the pancreas to digest itself, causing painful inflammation. High ammonia crosses into the brain, where it scrambles neurotransmitter balance, slows down the thinking centers (especially the cerebral cortex), and eventually shuts off the brainstem's wakefulness switch (the reticular activating system). The liver can also become directly inflamed and scarred by valproate, making the ammonia problem even worse. In rare cases, especially in young children or people with hidden mitochondrial disorders, valproate destroys so many liver cells that the organ fails completely.

CLINICAL TERM

Valproate inhibits carbamoyl phosphate synthetase I and depletes free carnitine, both of which are essential for hepatic ammonia detoxification via the urea cycle, leading to hyperammonemia. Concomitantly, valproate metabolites can cause mitochondrial dysfunction, oxidative stress, and direct hepatocellular injury, resulting in acute liver failure in susceptible individuals. Valproate also triggers acute pancreatitis through unclear mechanisms, possibly involving toxic metabolites or idiosyncratic immune reactions. Elevated ammonia disrupts astrocyte glutamate-glutamine cycling and impairs cortical and brainstem arousal networks.

How the body compensates

At first, the body tries to work around rising ammonia and mild liver injury. The kidneys excrete extra ammonia in urine. Muscles soak up some ammonia by turning it into glutamine. The brain's astrocytes try to buffer the toxin by converting ammonia into glutamine inside their cells. The pancreas, if only mildly inflamed, may still release enough enzymes to digest food. These workarounds can hide the problem for days or even weeks, so blood tests and alertness may look nearly normal even though ammonia is creeping up and liver cells are dying. This is

the dangerous window—when the patient feels only a little more tired than usual, but is actually on the edge of liver failure or coma.

1. {'what': 'Kidneys increase ammonia excretion', 'how': 'The kidneys sense high blood ammonia and pull more of it into urine, buying time for the liver to recover.', 'limit': 'Kidneys can only clear a small amount of ammonia compared to what the liver handles. If the liver stays broken, ammonia will keep rising.'}
2. {'what': 'Skeletal muscles absorb ammonia', 'how': 'Muscle cells use the enzyme glutamine synthetase to combine ammonia with glutamate, making glutamine, which is less toxic and can be stored temporarily.', 'limit': 'Muscle capacity is limited, and over time high glutamine levels can cause muscle weakness and fatigue.'}
3. {'what': 'Astrocytes in the brain buffer ammonia', 'how': 'Astrocytes (star-shaped support cells) try to detoxify ammonia by converting it into glutamine inside their own cytoplasm.', 'limit': 'Glutamine accumulation swells astrocytes (called Alzheimer type II astrocytes), which presses on neurons and disrupts brain architecture, worsening confusion and eventually causing cerebral swelling (edema) (brain swelling).')}
4. {'what': 'Liver tries to regenerate', 'how': 'Healthy liver cells divide to replace damaged ones. The liver can rebuild even after losing 70–80 % of its mass, as long as the poison is removed.', 'limit': 'If valproate continues, or if the person has a mitochondrial gene defect, regeneration cannot keep up with cell death, and the liver spirals into failure.'}
5. {'what': 'Pancreas walls off inflammation', 'how': 'The immune system sends white cells and fluids to surround the inflamed part of the pancreas, trying to contain the damage and prevent enzymes from leaking into the abdomen.', 'limit': 'If inflammation is severe, the pancreas can necrotize (tissue dies), leak enzymes into the bloodstream, and trigger a body-wide inflammatory storm (systemic inflammatory response syndrome, or SIRS), which can lead to shock and multi-organ failure.'}

Domino effect

1. Valproate blocks the liver's urea cycle and uses up carnitine, so ammonia starts to build in the blood instead of being cleared. — The enzyme carbamoyl phosphate synthetase I needs carnitine and a clear mitochondrial pathway to turn ammonia into urea. Valproate shuts down both, so ammonia accumulates like trash piling up when the garbage truck stops coming.
2. Rising ammonia crosses the blood-brain barrier and floods into astrocytes and neurons, especially in the cerebral cortex and brainstem. — Ammonia is small and uncharged enough to slip through the barrier. Once inside the brain, it disrupts glutamate recycling and mimics GABA's calming effect, over-sedating the circuits that keep you awake and thinking.

3. The person becomes unusually tired, confused, and clumsy. Speech may slur, hands may tremble, and they may vomit or stop eating. — The cerebral cortex (the outer brain layer responsible for reasoning and coordination) is slowing down because neurons are drowning in ammonia. The reticular activating system in the brainstem, which keeps you alert, is also suppressed, so the person feels like they are in a fog or falling asleep.
4. Astrocytes swell as they try to convert ammonia into glutamine; this swelling presses on surrounding neurons and blood vessels, raising pressure inside the skull. — Glutamine is osmotically active—it pulls water into astrocytes, making them balloon. This is the beginning of cerebral swelling (edema), which in severe cases can crush the brainstem and cause brain herniation (the brain gets pushed down through the skull opening, cutting off its own blood supply).
5. At the same time, valproate inflames the pancreas, causing severe upper belly pain, nausea, and vomiting. Pancreatic enzymes (lipase, amylase) spike in the blood. — The pancreas is digesting itself because enzymes meant for the intestine are activated too early. The pain and vomiting make the person even sicker, and they may stop taking fluids, worsening dehydration and ammonia buildup.
6. Liver cells begin dying from mitochondrial poisoning. Liver enzymes (ALT, AST) and bilirubin rise. The liver can no longer make clotting factors, so the person bruises easily or bleeds. — Valproate's breakdown products generate reactive oxygen species that kill hepatocytes. Without enough healthy liver tissue, the body cannot clot blood (because clotting factors are made in the liver), cannot regulate blood sugar, and cannot clear even more ammonia—so the spiral accelerates.
7. If valproate is not stopped, ammonia climbs even higher, the person slips into stupor or coma, and multi-organ failure begins (liver, brain, sometimes kidneys and heart). — The liver is no longer clearing toxins, the brain is swelling and shutting down, and the pancreas may leak enzymes that trigger body-wide inflammation. At this stage, only intensive care—stopping the drug, giving intravenous fluids, lactulose or rifaximin to lower ammonia, dialysis if needed, and sometimes a liver transplant—can save the person.
8. Early recognition and stopping valproate allows the liver to regenerate, ammonia to drop, and the brain to wake up, usually with full recovery. — The liver is one of the few organs that can regrow itself. Once the poison is removed, surviving hepatocytes divide, the urea cycle restarts, ammonia clears, astrocyte swelling resolves, and mental clarity returns—often within days to weeks.

Symptoms · what the patient feels, and why

- Nausea and vomiting: Valproate irritates the stomach lining directly and also triggers the brain's vomiting center (called the chemoreceptor trigger zone), making the person feel sick and throw up.

- **Confusion or drowsiness:** Too much valproate slows down the brain's normal electrical activity by boosting GABA (the brain's main calming signal) too much, making the person foggy, sleepy, or hard to wake up.
- **Tremor (shaking hands):** High valproate levels disrupt the signals between nerves and muscles, especially in the hands, causing fine shaking that the person cannot control.
- **Fast breathing (hyperventilation):** Valproate can build up ammonia (a waste chemical) in the blood, which the brain senses as dangerous, triggering faster, deeper breathing to try to blow off carbon dioxide and balance the blood.
- **Low blood pressure:** Valproate can relax blood vessel walls and slow the heart, so blood pressure drops because the vessels are wider and the pump is weaker.
- **Coma or very deep sleepiness:** At very high levels, valproate shuts down so much brain activity that the person stops responding and may need a breathing machine; the brain is too suppressed to wake up or protect the airway.
- **Liver damage (high liver enzymes, yellow skin or eyes):** Valproate is broken down in the liver; too much can overload and damage liver cells, causing them to leak enzymes into the blood and stop clearing bilirubin (the yellow waste from old red blood cells), which turns the skin and eyes yellow.
- **High ammonia level (hyperammonemia):** Valproate blocks one of the liver's enzymes (part of the urea cycle) that normally turns ammonia into urea for removal; ammonia builds up in the blood and can poison the brain.

Focused exam

- **Confusion, drowsiness, or lethargy that worsens over hours to days:** Valproate blocks the liver's ability to turn ammonia (a waste chemical from breaking down protein) into urea (the safe form you pee out). When ammonia builds up in the blood, it crosses into the brain and acts like a toxin—slowing down the signals that keep you awake and thinking clearly. This can progress to coma.
- **Tremor, trouble walking (ataxia), or slurred speech:** High ammonia poisons the cerebellum (the back part of the brain that fine-tunes balance and smooth movement) and the basal ganglia (deep brain clusters that coordinate muscle control). The brain's wiring for movement starts to misfire, so you shake, stumble, and slur words.
- **Nausea, vomiting, or upper belly pain:** Valproate can directly inflame the pancreas (the organ behind your stomach that makes digestive enzymes and insulin). When the pancreas swells, it hurts and the enzymes leak into surrounding tissue, causing nausea and pain. It can also signal liver injury.

- Yellowing of the skin and eyes (Jaundice) (yellowing of the skin or whites of the eyes): The liver normally breaks down old red blood cells into bilirubin (a yellow pigment) and flushes it out. When valproate damages liver cells, bilirubin backs up in the blood and stains the skin and eyes yellow. This is a sign of severe liver injury.
- Easy bruising, bleeding gums, or tiny red dots on the skin (petechiae): Valproate can lower platelets (the blood cells that plug holes and stop bleeding) or interfere with clotting factors made by the liver. Either way, your blood loses its ability to clot, so you bruise and bleed more easily.

Diagnostics · every test answers a question

- Serum ammonia → Is ammonia building up in the blood and poisoning the brain?
- Serum valproate level → Is the valproate dose too high, or is the drug piling up despite a normal dose?
- Liver enzymes (AST, ALT) and total bilirubin → Is the liver itself injured, or is this only an ammonia problem?
- Lipase and amylase → Is the pancreas inflamed?
- Complete blood count (CBC) with platelets → Are blood cells being suppressed or destroyed?
- Prothrombin time (PT) and INR → Can the blood still clot normally?
- Serum bicarbonate or venous blood gas → Is there metabolic acidosis (acid building up in the blood) from mitochondrial damage?
- Pregnancy test (urine or serum hCG) in anyone who can become pregnant → Is the patient pregnant, raising the stakes for both toxicity and fetal harm?

Treatment logic

- Stop valproate immediately → Removes the ongoing source of toxicity. Valproate has a half-life of 9–16 hours, so blood levels will fall by half each day once you stop the dose. Ammonia and liver enzyme levels can start to improve within 24–48 hours if the damage is not too severe.
- Give intravenous L-carnitine 100 mg/kg (max 6 g) loading dose, then 15 mg/kg every 4 hours until ammonia normalizes → L-carnitine is a helper molecule that shuttles fatty acids into mitochondria for energy. Valproate depletes carnitine and blocks the enzyme that clears ammonia. Giving carnitine back helps the liver restart the urea cycle (the ammonia-cleaning assembly line) and lowers blood ammonia within hours.

- Hemodialysis if serum valproate > 850 mg/L, ammonia stays very high despite L-carnitine, or the patient is in a coma or has severe liver failure → Dialysis physically pulls valproate and ammonia out of the bloodstream through a filter, bypassing the damaged liver. It can drop valproate levels by 50% or more in 4-6 hours and rapidly lower ammonia when the body cannot do it on its own.
- Activated charcoal 50 g by mouth or nasogastric tube if ingestion was within 1-2 hours and the patient can protect their airway → Charcoal binds valproate in the stomach and intestines before it absorbs into the blood, reducing the total dose that enters the body. Most effective when given early.
- Supportive care for liver failure: IV fluids, correct low blood sugar (dextrose if glucose < 70 mg/dL), give vitamin K 10 mg IV if INR > 1.5, monitor for encephalopathy, and stop all other potentially liver-toxic drugs → Keeps vital functions stable while the liver tries to regenerate. The liver has enormous healing capacity if you remove the toxin and support the patient through the critical window. IV fluids prevent dehydration from vomiting; dextrose prevents brain damage from low sugar; vitamin K helps clotting if the liver can still use it.
- Supportive care for pancreatitis: NPO (nothing by mouth), IV fluids, pain control, monitor for complications (fluid collections, shock, organ failure) → Resting the pancreas (no food to trigger enzyme release) and keeping the patient hydrated gives inflamed tissue time to calm down. Most valproate-induced pancreatitis resolves in 3-7 days once the drug is stopped.

Medications

Stop valproate immediately · Primary intervention (discontinuation of the offending drug)

Valproate is the poison causing the toxicity, so the first step is to stop giving it so no more toxicity builds up. The body can then start clearing what's already inside.

1. Valproate is stopped, so no new drug enters the bloodstream
2. The liver and kidneys begin breaking down and filtering out the valproate already in the body
3. Toxic levels in the blood start to fall, which reduces harm to the liver, pancreas, brain, and other organs
4. Symptoms like confusion, sleepiness, and high ammonia begin to improve as the drug clears

SAFETY WATCH

If the person was taking valproate for seizures, start a different anti-seizure medicine (like levetiracetam or phenytoin) right away to prevent breakthrough seizures · If valproate was for bipolar disorder, work with psychiatry to switch to a different mood stabilizer (like lithium or lamotrigine) to avoid a mood episode · Monitor closely for signs the toxicity is getting worse (deeper confusion, breathing slowing down, or liver function worsening) even after stopping the drug

L-carnitine · Metabolic cofactor and ammonia scavenger

Valproate toxicity drains the body's stores of L-carnitine, a helper molecule the liver needs to burn fat for energy and to clear ammonia (a brain poison). Giving L-carnitine IV replaces what's missing, helps the liver work again, and lowers dangerous ammonia levels in the blood.

1. L-carnitine is given through an IV so it reaches the bloodstream and liver quickly
2. It restocks the mitochondria's supply of carnitine, which they need to shuttle fatty acids inside to burn them for energy
3. The liver cells restart normal fat burning, which helps reverse the toxic buildup of fat and acid in the liver
4. L-carnitine also helps the urea cycle run again, so ammonia gets converted to urea and removed from the blood instead of building up and poisoning the brain
5. As ammonia drops, confusion and sleepiness improve; as the liver heals, liver enzyme levels start to fall

SAFETY WATCH

Dose is 100 mg/kg IV (up to 6 grams) as a loading dose, then 15 mg/kg IV every 4 hours until ammonia is normal and the person is alert · Watch for mild side effects like nausea or a fishy body odor (harmless but unpleasant) · Check ammonia levels every 6-12 hours to see if treatment is working · L-carnitine is safe and has very few serious side effects, so it should be started as soon as valproate toxicity with high ammonia is suspected — do NOT wait for lab confirmation

Activated charcoal · Gastrointestinal decontamination agent

Activated charcoal is a fine black powder that acts like a sponge in the stomach and intestines. It binds to valproate pills or liquid that haven't been absorbed yet and traps them, so they pass out in the stool instead of entering the bloodstream.

1. Activated charcoal is given by mouth (or through a tube into the stomach if needed) as a thick black drink

2. The charcoal's huge surface area sticks to valproate molecules in the gut
3. The charcoal-valproate bundle moves through the intestines and leaves the body in the stool
4. This lowers the total amount of valproate that gets absorbed into the blood, reducing toxicity

SAFETY WATCH

Only give if the overdose or last dose was within 1–2 hours — after that, it's too late and charcoal won't help · Do NOT give charcoal if the person is very drowsy, confused, or at risk of vomiting and breathing it into the lungs (aspiration), which can cause a dangerous pneumonia. Protect the airway first (intubate if needed) before giving charcoal in deeply sedated patients. · Dose is typically 50 grams for adults, 1 gram/kg (up to 50 grams) for children · Charcoal turns stool black (normal and harmless)

Hemodialysis · Extracorporeal drug removal (mechanical blood filtration)

Hemodialysis is a machine that filters the blood outside the body. It pulls valproate and other toxins out of the bloodstream much faster than the kidneys can, then returns the cleaned blood. This is life-saving when valproate levels are dangerously high or the person is so sick that waiting for the body to clear the drug naturally would take too long.

1. A large IV catheter (dialysis line) is placed in a neck or groin vein
2. Blood flows from the body into the dialysis machine
3. The machine's filter removes valproate, ammonia, and other small toxins from the blood
4. The cleaned blood flows back into the body
5. Valproate levels drop rapidly (often cut in half in 3–4 hours), which reduces toxicity faster than waiting for the liver and kidneys to clear it naturally

SAFETY WATCH

Reserve dialysis for severe cases: valproate level above 850–1000 mg/L (some guidelines say >850, others >1000; both are accepted thresholds), deep coma, severe metabolic acidosis (acid building up in the blood), liver failure, or life-threatening symptoms despite L-carnitine · Dialysis requires ICU-level monitoring because it involves a large catheter and blood pressure can drop during the procedure · Recheck valproate levels after dialysis because the drug can rebound (leak back out of tissues into the blood) — a second session may be needed · Watch for bleeding at the catheter site or dialysis-related electrolyte shifts (low calcium, low potassium)

Supportive care for liver injury · Organ support and monitoring (not a single drug, but a bundle of ICU interventions)

Valproate toxicity can damage the liver, causing it to swell, stop making clotting factors, and leak enzymes into the blood. Supportive care means watching the liver closely with blood tests, giving IV fluids to keep blood pressure up, replacing clotting factors if bleeding starts, and supporting other organs (like the brain and kidneys) while the liver heals. There is no specific antidote for liver damage — the goal is to keep the person stable until the liver repairs itself.

1. Check liver function tests (AST, ALT, bilirubin, INR) at admission and every 6–12 hours to see if injury is worsening or improving
2. Give IV fluids (normal saline or lactated Ringer's) to keep blood pressure normal and support the kidneys
3. If the INR is high (meaning blood won't clot well), give fresh frozen plasma or vitamin K to reduce bleeding risk
4. If the liver is failing badly (very high bilirubin, confusion from hepatic encephalopathy, or INR above 6), call the liver transplant team early — transplant may be life-saving in fulminant liver failure
5. Avoid acetaminophen, NSAIDs, and other drugs that stress the liver until recovery is confirmed

SAFETY WATCH

Fulminant liver failure (sudden, severe liver collapse) can happen even after valproate is stopped — watch for worsening yellowing of the skin and eyes (jaundice) (yellow skin), confusion, or bleeding that won't stop · Early transplant referral criteria: INR >6, hepatic encephalopathy (confusion from liver failure), rapidly rising bilirubin, or liver not improving after 48 hours · Monitor for low blood sugar (hypoglycemia) because the damaged liver can't make glucose well — check blood sugar every 4–6 hours and give IV dextrose if needed · Avoid sedating medications when possible (they can worsen confusion and make it hard to tell if the brain is being poisoned by ammonia or if it's just the drug)

Supportive care for pancreatitis · Organ support and pain management (not a single drug, but a bundle of interventions for inflamed pancreas)

Valproate can inflame the pancreas (pancreatitis), causing severe belly pain, nausea, and vomiting. The pancreas needs complete rest to heal, so the person is not allowed to eat or drink (NPO) and gets IV fluids to stay hydrated. Pain is controlled with IV medications, and the

pancreas is monitored with blood tests (lipase, amylase) and imaging (ultrasound or CT scan) to watch for complications like a fluid collection or infection.

1. Stop all food and drink by mouth (NPO) so the pancreas stops being stimulated to make digestive enzymes
2. Give aggressive IV fluids (lactated Ringer's is preferred) — typically 250–500 mL per hour initially — to keep the person hydrated and support blood flow to the pancreas
3. Control pain with IV medications (avoid NSAIDs because they can worsen pancreatitis; opioids like morphine or fentanyl are safer)
4. Check lipase and amylase every 12–24 hours to see if inflammation is improving
5. Get a CT scan if the person is not improving after 48–72 hours to look for complications like pancreatic tissue death (necrosis) (dead tissue) or a fluid collection

SAFETY WATCH

Severe pancreatitis can cause life-threatening complications: shock (low blood pressure from fluid leaking out of blood vessels), kidney failure, or infection of dead pancreas tissue (infected tissue death (necrosis)) · Watch for worsening pain, fever, or confusion — these may signal a complication that needs surgery or drainage · Once lipase is falling and pain is controlled, slowly restart eating with clear liquids, then advance to a low-fat diet as tolerated · Avoid alcohol, high-fat foods, and valproate forever after recovery — all can trigger pancreatitis again

Red flags

- Coma or cannot wake the person up
- Yellow skin or eyes (jaundice), which means the liver is failing
- Very fast breathing or gasping, which may signal high ammonia or acid in the blood
- Seizures that keep happening or will not stop
- Bleeding that will not stop (valproate can lower platelets, the blood cells that form clots)

Nursing priorities

1. Check level of consciousness every 15 to 30 minutes using the Glasgow Coma Scale (a scoring system that measures eye opening, speech, and movement) and immediately notify the provider if the score drops or the patient cannot be awakened. — High ammonia (a waste product that builds up when the liver fails) crosses into the brain and causes encephalopathy (brain poisoning), leading to confusion, then coma, so catching worsening sleepiness early allows time to give L-carnitine (a medicine that lowers ammonia) and start hemodialysis before brain swelling becomes irreversible.

2. Start two large-bore intravenous lines (IV catheters size 18 gauge or bigger) immediately and prepare to infuse L-carnitine 100 mg per kilogram (maximum 6 grams) over 30 minutes as ordered. — L-carnitine helps the body break down ammonia and protects liver cells from valproate damage, and giving the loading dose quickly through large IVs prevents veins from getting irritated and ensures the drug reaches the liver and brain fast.
3. Draw blood for ammonia level, complete blood count (a test that counts red cells, white cells, and platelets), liver enzymes (ALT and AST, which leak out when liver cells die), bilirubin (a yellow waste product that builds up in liver failure), and serum valproate level before giving any treatment. — Ammonia above 80 micromoles per liter and valproate above 850 milligrams per liter are thresholds for hemodialysis, and low platelets or high bilirubin tell us the liver is failing and bleeding risk is high, so these baseline labs guide all treatment decisions.
4. Place the patient on continuous pulse oximetry (a finger clip that measures oxygen) and capnography (a sensor that measures carbon dioxide in exhaled breath) if available, and watch for fast breathing rate above 20 breaths per minute. — Hyperventilation (fast breathing) happens when the body tries to blow off acid caused by high ammonia or liver failure, and tracking carbon dioxide shows whether the blood is becoming dangerously acidic—if it is, the patient may need a breathing tube and ventilator soon.
5. Hold all doses of valproate and check the medication administration record to make sure no nurse gives another dose by mistake. — Even one more dose adds to the poison load in the liver and blood, making ammonia and liver damage worse, so stopping the drug immediately is the first step in letting the body clear valproate and preventing further harm.
6. Monitor for signs of bleeding every 2 hours—check all IV sites, gums, nose, and skin for new bruises or pinpoint bleeding spots (petechiae) (tiny red dots from broken blood vessels)—and prepare to transfuse platelets if the count drops below 50,000 per microliter or if active bleeding starts. — Valproate lowers platelet production in the bone marrow and can also block platelet function, so counts below 50,000 raise bleeding risk, and transfusing platelets before procedures or if bleeding occurs prevents life-threatening bleeding (hemorrhage) (severe bleeding).
7. Insert a nasogastric tube (a flexible tube through the nose into the stomach) if the ingestion happened within 2 hours, the patient can protect their airway, and activated charcoal is ordered—give 50 grams mixed with water through the tube. — Activated charcoal binds to valproate in the stomach and gut, stopping more drug from entering the blood, but it only works if given early and if the patient will not vomit and breathe it into the lungs, which causes chemical pneumonia (lung inflammation from inhaled material).

8. Prepare the patient for urgent hemodialysis by notifying the dialysis team, ensuring IV access is secure, and explaining to the family that a temporary dialysis catheter (a large tube placed in the neck or groin vein) may be needed if valproate or ammonia levels stay dangerously high. — Hemodialysis removes valproate and ammonia directly from the blood when the liver cannot clear them, and it is the only treatment that works fast enough to save the brain and liver in severe toxicity, so preparing early avoids delays that can lead to permanent brain damage or death.

Sources

- American College of Medical Toxicology (ACMT) valproate guideline
- International League Against Epilepsy (ILAE) 2022
- UpToDate clinical review on valproate toxicity
- Cochrane systematic reviews on antiepileptic drug safety

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