

Hepatic Encephalopathy

Hepatic encephalopathy means ammonia and other toxins are getting into the brain and confusing it—sometimes to the point of coma.

THE ONE-LINE TRUTH

The liver is not cleaning ammonia and other toxic waste from the blood, so poison reaches the brain.

The chain — how it unfolds

1. Ammonia and other toxins (mercaptans, manganese, inflammatory cytokines) build up in the blood because the liver cannot detoxify them. — why: In cirrhosis, scar tissue replaces working liver cells, so the urea cycle slows or stops. In portosystemic shunts, blood skips the liver entirely. Either way, ammonia that should be turned into urea stays in the bloodstream and rises.
2. Ammonia crosses the blood-brain barrier and enters the brain. — why: Ammonia is a small molecule that slips easily from blood into brain tissue. Once inside, it is taken up by astrocytes (the brain's support cells), which try to detoxify it by converting ammonia to glutamine.
3. Astrocytes swell with water (cytotoxic swelling (edema)) as glutamine accumulates inside them. — why: Glutamine is osmotically active—it pulls water into the cell. Swollen astrocytes press on neurons (the brain's signal cells) and disrupt normal brain chemistry, especially in the cortex (the outer thinking layer) and basal ganglia (deep motor-control centers).
4. Early encephalopathy appears: subtle confusion, poor attention, personality changes, sleep-wake reversal (awake at night, sleepy during the day). — why: The prefrontal cortex (front of the brain, responsible for focus and judgment) and the reticular activating system (brainstem network that controls wakefulness) are sensitive to ammonia. Even modest levels disrupt their signaling, causing mild cognitive slips and flipped sleep cycles (West Haven grade I-II).
5. Asterixis (flapping hand tremor) and slurred speech develop; confusion deepens. — why: Ammonia interferes with the basal ganglia and motor cortex, causing brief lapses in muscle tone—seen as the flapping tremor when the patient holds their arms out. As more neurons misfire, speech becomes slurred and confusion worsens (grade II-III).

6. The patient becomes lethargic, then stuporous, then unresponsive (coma). — why: High ammonia levels and swollen astrocytes disrupt the thalamus (the brain's relay station) and brainstem, shutting down consciousness. The brain cannot maintain normal electrical activity, and the patient slips into coma (grade IV).
7. In acute liver failure, cerebral swelling (edema) (brain swelling) and intracranial high blood pressure (hypertension) (high pressure inside the skull) develop rapidly. — why: Without time to adapt, ammonia-driven astrocyte swelling happens fast and globally. The skull is a rigid box, so swelling raises pressure inside. High pressure crushes blood vessels (reducing oxygen delivery) and can push the brainstem downward (herniation), causing sudden death.
8. Every sign—confusion, asterixis, coma, and brain swelling—is the brain's direct reaction to ammonia toxicity, not a separate disease. — why: This is one chain of injury. Lowering ammonia (with lactulose to trap it in the gut, rifaximin to reduce ammonia-producing bacteria, and treating triggers like infection or bleeding) can reverse early stages and prevent progression. Liver transplant is the only cure when the liver is too damaged to recover.

Spot it — what you see, and why

- Confusion and trouble thinking clearly: When the liver is damaged, it cannot clean ammonia (a toxic waste from breaking down protein) out of the blood. That ammonia travels to the brain and poisons the neurons (brain cells), making it hard to think, remember, or focus.
- Sleeping during the day but awake at night (flipped sleep schedule): The ammonia and other toxins confuse the brain's internal clock (the part that tells you when to sleep and wake). This flips the normal day-night pattern so the person feels sleepy during the day and restless at night.
- Hand tremor or flapping (asterixis): The toxins disrupt the brain's motor cortex (the region that controls smooth muscle movements) and the basal ganglia (deep brain structures that coordinate motion). The muscles in the wrists and hands lose steady control, causing a jerky flapping motion when the person holds their arms out.
- Slurred speech or mumbling: Ammonia damages the neurons in the brain areas that plan and coordinate speech. The tongue and lips do not move precisely, so words come out unclear or jumbled.
- Personality changes (irritability, apathy, or acting out of character): The prefrontal cortex (the front of the brain that manages emotions and social behavior) is especially sensitive to ammonia. When it is poisoned, the person may lose their usual self-control, becoming short-tempered, withdrawn, or behaving strangely.
- Slow responses or seeming 'out of it': Ammonia slows the electrical signals between neurons all over the brain. Messages take longer to travel, so the person reacts late to questions or events and seems distant or 'foggy.'

Red flags — act now

- Sudden deep confusion or inability to wake the person (coma) — the brain is being poisoned fast and may swell or stop working.
- New seizures or uncontrolled shaking — extremely high ammonia or swelling in the brain can trigger abnormal electrical storms.
- Vomiting blood or black tarry stools in a person with liver disease — bleeding inside the gut dumps more protein (which becomes ammonia) into the system and can trigger or worsen brain poisoning.
- Fever and worsening confusion together — may signal an infection (like spontaneous bacterial peritonitis) that is pushing the sick liver over the edge.
- Very slow breathing or gasping — the brainstem centers that control breathing may be shutting down from severe toxin buildup.

Treat it — in this order

1. Identify and treat the trigger — bleeding, infection, dehydration, low potassium, constipation, sedating drugs, or high protein load → The liver or shunt was already broken, but the trigger pushed ammonia over the edge. Removing the trigger stops the ammonia spike. For example, stopping a GI bleed removes the protein flood in the gut; treating infection lowers inflammation and metabolic stress; fixing dehydration and low potassium restores kidney function so ammonia can be cleared.
2. Lactulose by mouth (15–30 mL every 1–2 hours initially, then adjust) or rectal enema to achieve 2–3 soft bowel movements per day → Lactulose is a synthetic sugar that gut bacteria ferment into acid. The acid traps ammonia in the colon (turning it into ammonium, which cannot be absorbed) and speeds it out in stool. It also feeds beneficial bacteria that produce less ammonia.
3. Rifaximin 550 mg by mouth twice daily (added to lactulose for moderate to severe or recurrent encephalopathy) → Rifaximin is a non-absorbed antibiotic that kills ammonia-producing bacteria in the gut, lowering the ammonia source. It works without wiping out bacteria throughout the body because it stays in the intestines.
4. Correct electrolytes — replace potassium (goal > 4.0 mEq/L) and restore normal hydration with IV fluids if needed → Low potassium and dehydration worsen kidney function, which traps ammonia in the blood. Correcting them helps the kidneys clear ammonia and removes common metabolic triggers.

5. Stop or reverse any bleeding — transfuse blood if hemoglobin < 7 g/dL, perform urgent upper endoscopy for varices, and give octreotide and ceftriaxone if variceal bleeding is suspected → Blood in the gut is a massive protein load — bacteria break it down into ammonia. Stopping the bleed and clearing blood from the intestines with lactulose removes the ammonia source. Octreotide lowers portal pressure, and antibiotics prevent infection.

Your top priorities at the bedside

1. Check airway and breathing every 15 to 30 minutes in confused or sleepy patients; place patient on their side; have suction ready; check oxygen saturation — why: High ammonia slows brain signals to breathing muscles and patients can vomit and breathe it into their lungs causing aspiration pneumonia; patients in grade 3 or 4 coma may need a breathing tube
2. Give lactulose every hour until the first bowel movement, then adjust to get two to three soft stools per day; give by mouth, feeding tube, or enema if patient cannot swallow — why: Lactulose turns into acid in the colon which traps ammonia as ammonium and pulls it out in stool; also works as a laxative to speed removal of ammonia-making bacteria and protein
3. Look for and report bleeding signs including checking all stools for black color or blood, measuring blood pressure and heart rate every 2 to 4 hours, and watching for pale skin or low hemoglobin — why: Gastrointestinal bleeding releases protein that becomes ammonia and is the number one trigger; needs urgent blood transfusion and endoscopy to stop bleeding and remove blood from intestines