

Acute Liver Failure

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THE STORY IN ONE SENTENCE

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“When something kills most of your liver cells fast—acetaminophen overdose, a virus, or a toxin—your liver stops making the proteins that stop bleeding and stops cleaning ammonia (a brain poison), so you bleed and get confused at the same time, usually within days to weeks.”

Normal anatomy — the body's job

Your liver makes clotting factors (proteins II, V, VII, IX, and X that stop bleeding) and albumin (a protein that holds fluid inside your blood vessels). It detoxifies ammonia into urea, a safer waste your kidneys can remove. It breaks down medications and toxins. It stores glycogen (chains of sugar) and releases glucose (blood sugar) between meals to keep your brain fed. In health, these jobs keep your blood clotting normal, your brain ammonia low, and your energy supply steady.

BODY'S JOB

Understanding what the liver normally does—making clotting factors, clearing ammonia, and keeping blood sugar stable—is essential. Every clinical finding in acute liver failure reflects the sudden loss of one or more of these core jobs.

1. Blood flows into the liver through two vessels: the hepatic artery (bringing oxygen-rich blood from the heart) and the portal vein (bringing nutrient-rich blood from the intestines, stomach, and spleen).

2. Inside the liver, blood passes through sinusoids—tiny channels lined by hepatocytes (liver cells)—where hepatocytes pull nutrients, toxins, and ammonia out of the blood and release clotting factors, albumin, and glucose back into it.
3. Hepatocytes convert ammonia (made when gut bacteria digest protein) into urea via the urea cycle, a series of chemical reactions that happens only in liver cells; urea is water-soluble and safe, so kidneys can filter it into urine.
4. Hepatocytes synthesize (make) clotting factors from amino acids and vitamin K; these proteins are released into the blood and travel to injury sites to stop bleeding.
5. Hepatocytes store glucose as glycogen (long chains of sugar molecules) after meals and break glycogen back into glucose between meals (glycogenolysis) or make new glucose from lactate, amino acids, and glycerol (gluconeogenesis) to keep blood sugar between 70 and 100 mg/dL.
6. Clean, processed blood exits the liver through hepatic veins that flow into the inferior vena cava (the large vein carrying blood back to the heart), while bile (a digestive fluid made by hepatocytes) drains into bile ducts and flows to the gallbladder and intestines to help digest fats.

What breaks

Massive sudden death of liver cells from a toxin, virus, or immune attack stops the liver from making clotting factors and clearing ammonia, so blood clotting fails and the brain becomes confused.

CLINICAL TERM

Acute liver failure is hepatocyte tissue death (necrosis) (liver cell death) severe enough to cause impaired blood clotting (coagulopathy)—INR at or above 1.5, meaning blood takes at least 50% longer to clot than normal—plus any degree of hepatic encephalopathy (altered mental status from ammonia and other brain toxins) within 26 weeks of first symptoms in a patient with no preexisting cirrhosis (chronic liver scarring).

How the body compensates

Early in acute liver failure, vital signs may look stable because your body increases cardiac output (the volume of blood your heart pumps per minute) and redistributes blood flow. But

this compensation hides the rising risk of brain swelling, organ failure, and death. Your job is to recognize the trajectory toward collapse before it becomes irreversible.

1. The heart increases cardiac output by 30–50% and heart rate rises (tachycardia, often 100–120 beats per minute) to maintain mean arterial pressure (the average pressure in arteries during one heartbeat) above 65 mmHg, even though blood vessels throughout the body are widening (systemic vasodilation) from nitric oxide and inflammatory cytokines (immune signaling proteins) released by dying liver cells.
2. This early cardiovascular compensation masks the severity of liver injury—patients may have normal or near-normal blood pressure and appear stable even as encephalopathy grade and INR climb rapidly; a normal blood pressure does NOT mean the patient is stable.
3. The critical crash points to anticipate are cerebral swelling (edema) (brain swelling) with intracranial pressure rising above 20–25 mmHg, causing brain herniation (brain tissue forced through skull openings, compressing the brainstem and causing death); sepsis (bloodstream infection) from bacteria or fungi; hepatorenal syndrome (kidney failure triggered by liver failure and splanchnic vasodilation, meaning blood vessels in the gut and spleen widen, stealing blood flow from the kidneys); acute respiratory distress syndrome (ARDS, severe lung injury from systemic inflammation); and multiorgan dysfunction syndrome.
4. Monitor trajectory markers closely—worsening encephalopathy grade (I → II → III → IV), rising ammonia (above 100–150 $\mu\text{mol/L}$, normal is below 35), rising INR (above 2.0, then 3.0, then 4.0), falling platelet count (thrombocytopenia from the spleen holding onto platelets and decreased thrombopoietin production), rising creatinine (above 1.5 mg/dL indicates acute kidney injury, normal is 0.6–1.2), falling urine output (below 0.5 mL/kg/hr for more than 6 hours, called low urine output (oliguria)), and rising lactate (above 4 mmol/L indicates tissues are not getting enough oxygen, normal is below 2 mmol/L)—because these trends predict collapse hours to days before vital signs crash.
5. A patient with stable blood pressure but worsening encephalopathy (grade II advancing to grade III), rising lactate, or rising ammonia is deteriorating rapidly, not stable, and requires immediate escalation of care to the intensive care unit.
6. Once grade III–IV encephalopathy, cerebral swelling (edema), or multiorgan failure is established, the window for emergency liver transplantation or spontaneous recovery narrows to hours; early ICU transfer, intubation (placing a breathing tube) to protect the airway, and urgent transplant center evaluation are life-saving interventions that must happen within the first 24–48 hours after encephalopathy begins.

Domino effect

1. Impaired blood clotting (Coagulopathy) (blood clotting failure) develops. — Massive hepatocyte death stops synthesis of vitamin K-dependent clotting factors (II, VII, IX, X) and factor V, so prothrombin time (PT, the time it takes blood to clot in a lab test) and INR (international normalized ratio, a standardized clotting score) rise above 1.5 within days. Bleeding risk increases from every needle stick, from the lining of the stomach and intestines (gastrointestinal mucosa), from the nose and gums, and from any site of trauma.
2. Hepatic encephalopathy (altered mental status and brain dysfunction) begins and progresses. — The dying liver cannot run the urea cycle to convert ammonia—produced in the gut by bacteria breaking down protein—into urea. Ammonia rises in the blood, crosses the blood-brain barrier, and poisons astrocytes (star-shaped brain support cells). Astrocytes swell and release glutamine, which further raises osmotic pressure inside the skull. Clinically this produces confusion (grade I), lethargy and asterixis, a flapping tremor of the hands (grade II), stupor, meaning very hard to wake (grade III), and coma (grade IV) over hours to days.
3. Low blood sugar (Hypoglycemia) (dangerously low blood sugar) occurs. — The liver normally maintains blood glucose between meals by breaking down stored glycogen into glucose (glycogenolysis) and making new glucose from lactate, amino acids, and glycerol (gluconeogenesis). When hepatocytes die, both pathways shut down and blood glucose drops below 70 mg/dL, sometimes to below 40 mg/dL, starving the brain of its primary fuel and worsening encephalopathy and risk of seizures.
4. Cerebral swelling (edema) (brain swelling) and intracranial high blood pressure (hypertension) (high pressure inside the skull) develop in severe cases. — High serum ammonia—often above 150–200 $\mu\text{mol/L}$ —plus inflammatory cytokines (tumor tissue death (necrosis) factor-alpha, interleukin-6) and astrocyte swelling cause the brain to swell. Intracranial pressure rises above 20–25 mmHg (normal is 5–15). If unchecked, this compresses the brainstem through the foramen magnum (the opening at the base of the skull), causing brain herniation, loss of brainstem reflexes (pupil response to light, gag reflex, cough reflex), and death.
5. Low blood pressure (Hypotension) (low blood pressure) and circulatory shock emerge. — Systemic vasodilation from nitric oxide and prostacyclin (vasodilator molecules released by dying hepatocytes) combined with third-spacing—fluid leaking from blood vessels into tissues—from low albumin (below 2.5 g/dL, normal is 3.5–5.0) drops systemic vascular resistance (the resistance arteries provide to blood flow). Mean arterial pressure falls below 65 mmHg. The heart initially compensates by increasing cardiac output, but eventually myocardial depression (heart muscle dysfunction from circulating toxins) and hypovolemia (low blood volume) cause distributive shock (from vasodilation) and hypovolemic shock (from fluid loss).

6. Acute kidney injury (AKI) develops. — Low blood pressure (Hypotension) reduces renal blood flow (perfusion) pressure (blood pressure reaching the kidneys) below the autoregulation threshold—around 80 mmHg systolic—causing prerenal waste buildup in the blood (azotemia) (rising blood urea nitrogen and creatinine from inadequate kidney blood flow). In 40–50% of cases, hepatorenal syndrome type 1 develops: intense renal vasoconstriction (kidney blood vessel narrowing) triggered by splanchnic vasodilation and activation of the renin-angiotensin-aldosterone and sympathetic nervous systems. Creatinine rises above 1.5–2.0 mg/dL and urine output falls below 400 mL per day.
7. Infection and sepsis become common complications. — Loss of liver synthesis of complement proteins (C3, C4), opsonins (immune proteins that tag bacteria for destruction), and acute-phase reactants (infection-fighting proteins) plus increased gut permeability (leaky gut allowing bacteria to enter the bloodstream via the portal vein) plus invasive lines—central venous catheters, urinary catheters, breathing tubes—create the perfect environment for pneumonia, spontaneous bacterial bloodstream infection, urinary tract infection, and invasive fungal sepsis, especially from *Candida* species. This occurs in 25–50% of patients and often worsens shock and triggers multiorgan failure.

Symptoms · what the patient feels, and why

- Yellowing of the skin and eyes (Jaundice) (yellow skin, eyes, and under the tongue): When liver cells die suddenly, they can no longer attach a sugar molecule (glucuronic acid) to bilirubin—a yellow-orange waste from broken-down old red blood cells—and cannot push it into bile. Both forms of bilirubin (the unattached and the attached) pile up in the blood. Once bilirubin levels go above about 3 (measured in mg/dL), the yellow waste spills into body tissues, staining the skin, the whites of the eyes, and the tissue under the tongue a yellow-orange color.
- Confusion, sleepiness, or coma (hepatic encephalopathy): The dying liver cannot clean poisons—especially ammonia from digested protein, sulfur-containing compounds called mercaptans, and metals like manganese—out of the blood. These toxins cross into the brain, poison the support cells (astrocytes) and nerve cells (neurons), and scramble the brain's chemical signals. At first the person gets confused and may sleep during the day and stay awake at night (grade I). Next comes extreme sleepiness and a flapping hand tremor (grade II). Then stupor—the person only wakes up if you cause pain (grade III). Finally, coma—no response at all (grade IV).

- Easy bruising, tiny red spots on the skin, bleeding gums, nosebleeds, or blood in vomit or stool: The liver makes most of the proteins (clotting factors II, V, VII, IX, and X) that stop bleeding. When the liver fails, these proteins vanish from the blood. Blood tests show the prothrombin time (PT) and INR (international normalized ratio) climb above 1.5—often as high as 2 to 6 or more. Now even tiny injuries—brushing teeth, inserting an IV, placing a feeding tube—cause bleeding that won't stop. Platelet counts also drop (often below 100,000 per microliter) because the spleen traps them and the liver stops making thrombopoietin (the hormone that tells bone marrow to make platelets), adding even more bleeding risk.
- Pain or tenderness below the right rib cage: When liver cells die quickly and the liver swells up with inflammation, the outer fibrous bag around the liver (called Glisson's capsule) stretches tight. This capsule is packed with pain nerves. The stretch causes a constant dull ache or sharp tenderness just below the right ribs. Taking a deep breath or pressing on the area makes the pain worse.
- Nausea, vomiting, and complete loss of appetite: Poisons like ammonia and waste products that should have been cleared by the liver, plus inflammatory messenger molecules (interleukin-1 and tumor tissue death (necrosis) factor-alpha), flood the bloodstream. These chemicals directly trigger the vomiting center in the brainstem (the chemoreceptor trigger zone in a spot called the area postrema) and shut down the appetite control centers in the hypothalamus (a deep brain region). The result is persistent nausea, frequent vomiting, and zero desire to eat.
- Flapping hand tremor when arms are held out (asterixis): High ammonia levels in the blood (usually above 100 micromol per liter) disrupt the circuits in the deep brain (thalamus and basal ganglia) that keep muscles contracted steadily. When you ask the person to hold their arms straight out with wrists bent back (like stopping traffic), the hands suddenly flap downward and then jerk back up every one to two seconds. This repeating flap is a sensitive sign that hepatic encephalopathy has reached grade II or higher.
- Fast heart rate (over 100 beats per minute) and low blood pressure (top number under 90 or mean arterial pressure under 65 mmHg): The failing liver releases chemicals (like nitric oxide) that make blood vessels relax and widen all over the body, dropping the resistance that normally keeps blood pressure up. At the same time, low albumin (a protein the liver makes, now under 2.5 grams per deciliter) lets fluid leak out of blood vessels into tissues (third-spacing), shrinking the volume of blood circulating in the vessels. The heart tries to fix this by beating faster (tachycardia) to pump enough blood to organs. But eventually the heart cannot keep up and blood pressure drops into the dangerous low range.

- Very little urine (less than 400 mL in 24 hours or less than 0.5 mL per kilogram of body weight per hour for six hours or more): Low blood pressure and a condition called hepatorenal syndrome—where blood vessels in the gut dilate and kidneys respond by clamping down their own blood vessels through the renin-angiotensin-aldosterone system and sympathetic nerves—cut the kidneys' filtering power (glomerular filtration rate) to 30–50 percent of normal or less. The kidneys make almost no urine. Creatinine (a waste product) climbs above 1.5 mg/dL, often reaching 2 to 3 or higher. Wastes like urea, potassium, and phosphate pile up in the blood.
- Rapid, deep breathing (Kussmaul respirations) or shortness of breath: Severe metabolic acidosis (acid building up in the blood) (blood pH dropping below 7.35) from lactic acid buildup—because dying liver cells and oxygen-starved tissues switch to anaerobic metabolism—stimulates the brainstem's respiratory center to blow off carbon dioxide and compensate. The person breathes fast and deeply. Additionally, fluid overload or acute respiratory distress syndrome (ARDS) from systemic inflammation can flood the lungs, making oxygen exchange difficult and causing shortness of breath even at rest.
- Swelling of the abdomen (ascites) or swelling of the ankles and legs (peripheral swelling (edema)): The liver stops making albumin (a protein that normally holds water inside blood vessels). With low albumin, fluid leaks out of blood vessels into the abdominal cavity (ascites) and into tissues of the legs and ankles (peripheral swelling (edema)). Portal high blood pressure (hypertension)—high pressure in the portal vein that carries blood from the gut to the liver—further pushes fluid into the belly. Kidney retention of salt and water (from activation of aldosterone and antidiuretic hormone) compounds the swelling.

Focused exam

- Yellow skin and whites of eyes: The liver normally removes bilirubin — a yellow waste product left over when old red blood cells break down — from the blood. When huge numbers of liver cells die suddenly, the liver stops this job. Bilirubin piles up in the bloodstream and stains the skin and eyes yellow, a sign called yellowing of the skin and eyes (jaundice). Seeing yellowing of the skin and eyes appear in hours or days means liver cells are dying right now.
- Bleeding or big bruises from tiny bumps: The liver makes clotting factors — proteins that let blood form clots and stop bleeding. When liver cells die, production stops. Blood cannot clot normally, a problem called impaired blood clotting (coagulopathy). A person may bleed from a small cut or get a big purple bruise from barely touching something. This is the most dangerous complication of acute liver failure.

- Confusion, slurred words, or getting sleepier: The liver normally removes ammonia and other brain poisons from the blood. When the liver fails, these toxins build up and damage the brain — a condition called hepatic encephalopathy. If confusion gets worse hour by hour, pressure inside the skull may be rising because the brain is swelling. That is a life-threatening emergency.
- Pain or tenderness under the right rib cage: The liver sits under the right ribs. When liver cells die fast and the organ swells, it stretches the thin outer covering around the liver. That stretch makes the area sore to touch. This tenderness tells you massive numbers of liver cells are dying quickly.
- Sweet or musty smell on the breath: When the liver fails, it cannot break down certain chemicals that evaporate and come out in the breath. This creates a sweet, musty odor called fetor hepaticus — liver breath. Smelling it suddenly means severe liver failure and a pile-up of toxic waste products.
- Hand tremor or flapping when arms are held out straight: When brain poisons accumulate because the liver cannot clear them, they disrupt the signals between brain and muscles. This produces a flapping tremor of the wrists when you hold your arms out — called asterixis. It signals advanced brain dysfunction from liver failure and warns that pressure inside the skull may be rising.

Diagnostics · every test answers a question

- INR (international normalized ratio) and PT (prothrombin time) → How badly has the liver lost its ability to make clotting factors? Is the problem getting worse?
- Total and direct bilirubin → How much bilirubin is piling up because the liver cannot process and remove it?
- ALT (alanine aminotransferase) and AST (aspartate aminotransferase) → How many liver cells have died and spilled their inside enzymes into the blood?
- Arterial blood gas with lactate → Is the liver failure causing lactic acidosis (acid from oxygen-starved tissues) — acid buildup from cells not getting enough oxygen or not burning fuel correctly?
- Serum ammonia → How much ammonia is building up because the liver cannot convert it to urea — a waste product normally removed in urine?
- Blood glucose → Can the dying liver still keep blood sugar steady, or is it dropping dangerously low?
- Acetaminophen level → Is acetaminophen (Tylenol) poisoning the cause, and should the antidote be started immediately?
- Hepatitis A IgM, hepatitis B surface antigen and core IgM, hepatitis E IgM; HSV and CMV PCR → Is a virus causing the liver failure?

- Ceruloplasmin and 24-hour urine copper (if age under 40 and no clear cause) → Could this be Wilson disease — a genetic disorder where copper piles up and poisons the liver?
- Abdominal ultrasound with Doppler of liver blood vessels → Is a blood clot blocking the veins draining the liver — Budd-Chiari syndrome — or the artery feeding it?

Treatment logic

- N-acetylcysteine (NAC) intravenous infusion → NAC refills glutathione — the liver's main shield against acetaminophen breakdown products — cuts down damage from reactive oxygen molecules, and helps liver cells survive in acetaminophen overdose. It works best when started within 8-10 hours of taking the drug, but still helps even when started late. Per AASLD guidelines, NAC also improves survival without transplant in early-stage (grade I-II) brain dysfunction from non-acetaminophen acute liver failure.
- Fresh frozen plasma, prothrombin complex concentrate, or cryoprecipitate — only for active bleeding or before procedures → These blood products replace clotting factors — proteins like II, VII, IX, X, and fibrinogen — that the dead liver cannot make, temporarily fixing the clotting problem to stop bleeding or allow safe procedures like placing a central IV line or brain pressure monitor.
- Hyperosmolar therapy: mannitol 0.5-1 g/kg IV or 3% saline bolus for brain swelling → These agents increase the concentration of dissolved particles in blood, pulling water out of swollen brain tissue back into the bloodstream by osmosis — water moving from low to high concentration. This lowers pressure inside the skull and reverses brain compression temporarily. Target serum sodium 145-155 mEq/L and serum osmolality below 320 mOsm/kg per AASLD guidelines.
- Urgent liver specialist consultation and transplant evaluation (King's College Criteria or MELD score) → Early transplant evaluation finds patients who meet criteria for listing. Per King's College Criteria for acetaminophen cases: pH below 7.30 after resuscitation, or INR above 6.5 plus creatinine above 3.4 mg/dL plus grade III-IV brain dysfunction. For non-acetaminophen cases: INR above 6.5, or any three of — age under 10 or over 40, non-A non-B hepatitis or drug reaction, yellowing of the skin and eyes (jaundice) over 7 days before confusion started, INR above 3.5, bilirubin above 17.4 mg/dL. Listing before irreversible multi-organ failure improves survival after transplant.
- Continuous IV dextrose (D10 or D20) to keep blood glucose above 70 mg/dL → IV sugar replaces the glucose the failing liver cannot produce, preventing low blood sugar from injuring the brain and worsening confusion. Check blood glucose every 1-2 hours.

- ICU monitoring and organ support: infection surveillance, antibiotics for sepsis, dialysis for kidney failure, breathing tube for airway protection in grade III–IV brain dysfunction → Preventing and treating infection stops bacterial and fungal bloodstream invasion, which worsens inflammation and blocks liver regrowth. Dialysis or continuous kidney replacement therapy fixes waste buildup, acid overload, and fluid overload from kidney failure. A breathing tube protects the airway when confusion impairs consciousness and the gag reflex.
- Cause-specific therapy: acyclovir for herpes virus hepatitis, chelation (penicillamine or trientine) for Wilson disease, delivery for HELLP syndrome or acute fatty liver of pregnancy → Treating the root cause stops ongoing liver cell injury at its source. Acyclovir (an antiviral drug) halts herpes virus copying; chelators (drugs that bind and remove metals) pull out excess copper in Wilson disease; delivering the baby removes the placental trigger in pregnancy-related liver failure — HELLP syndrome (breakdown of red cells, high liver enzymes, low platelets) or acute fatty liver of pregnancy.

Medications

N-acetylcysteine (NAC) — for acetaminophen (Tylenol) poisoning and some other forms of sudden liver failure · Antidote and glutathione precursor (it supplies the raw ingredient that helps liver cells rebuild their detox shield)

Your liver uses a chemical called glutathione to neutralize poisons. Think of glutathione as a tiny sponge inside each liver cell that soaks up and disarms toxins before they can punch holes in the cell. When you take too much acetaminophen, your liver turns it into a toxic chemical called NAPQI (picture a sharp spike). Normally glutathione grabs every spike and makes it safe. But an overdose floods the liver with so many spikes that the glutathione sponges run out. Once the sponges are gone, free spikes stab liver cells and kill them. N-acetylcysteine gives your liver cysteine, the one ingredient your body cannot make fast enough on its own. With fresh cysteine, liver cells quickly build new glutathione sponges in an hour or two. Those new sponges mop up the leftover spikes, so no more liver cells die, and the liver can start healing.

1. When you swallow acetaminophen, most of it leaves your body safely through urine. But a small amount is processed by liver enzymes called cytochrome P450 (mainly CYP2E1), which turn it into NAPQI — a very reactive, toxic molecule shaped like a tiny spike.
2. In a normal dose, liver cells have plenty of glutathione. Each glutathione molecule grabs one NAPQI spike, wraps it up, and the harmless bundle is flushed out in your pee.
3. In an overdose (more than 150 milligrams per kilogram of body weight, or roughly 10 grams in an adult), the liver churns out so much NAPQI that glutathione is completely used up within a few hours.

4. Once glutathione runs out, free NAPQI spikes stick to the inside machinery of liver cells — proteins, membranes, and the power plants. This direct attack causes hepatocyte tissue death (necrosis) (the cell swells, breaks open, and dies).
5. When you give N-acetylcysteine, it is absorbed into the blood, travels to the liver, and slips into hepatocytes. Inside, the cell uses NAC's cysteine to build new glutathione molecules within one to two hours.
6. The fresh glutathione immediately grabs any NAPQI still floating around, stopping the killing. With the toxin neutralized, surviving liver cells begin to multiply and repair the damage over the next few days to weeks.

SAFETY WATCH

Anaphylactoid reactions (the body releases histamine, causing flushing, a red itchy rash, wheezing, and a dangerous drop in blood pressure) happen in 10 to 20 out of every 100 people getting NAC through an IV, usually during the first fast dose. If this occurs, slow down or pause the drip and give diphenhydramine (Benadryl) to block histamine. If breathing becomes difficult or blood pressure crashes, give epinephrine right away. · Nausea and vomiting are very common with NAC pills or liquid because it smells and tastes like rotten eggs (sulfur). Give an anti-nausea medicine like ondansetron (Zofran). If the person keeps vomiting and cannot keep NAC down, switch to the IV form. · Dilutional low sodium (hyponatremia) (blood sodium drops too low because NAC is mixed in water without enough salt) can happen if you dilute IV NAC in the wrong fluid. Always mix it in 5% dextrose in water (D5W) and check blood sodium levels often in anyone with liver failure. · Monitor INR (a blood test that measures how long it takes blood to clot; the liver makes clotting factors, so INR rises when the liver fails), creatinine (a waste product cleared by the kidneys; when it climbs, the kidneys are failing too), and mental status (alertness, confusion, or coma) every 12 to 24 hours. If INR keeps rising, creatinine climbs, or the person becomes more confused despite NAC, transfer to a liver transplant center urgently. · Start NAC within 8 hours of swallowing the acetaminophen overdose for the best chance of preventing liver death. After 24 hours, it is much less effective — but still give it if any acetaminophen is detectable in the blood or if liver enzymes (ALT and AST) are elevated, because some benefit remains even late.

Red flags

- Stupor (arousable only to painful stimuli) or coma (no response to pain)—this is grade III or IV hepatic encephalopathy and signals high risk of brain swelling (cerebral swelling (edema)), pressure inside the skull rising above 20 mmHg, and the brain herniating (getting squeezed through the skull base). The person needs a breathing tube placed immediately, transfer to the ICU, and (in transplant centers) a device to monitor brain pressure.

- INR above 4.0 or active bleeding from the gut (vomiting blood, black tarry stool, or bright red blood from the rectum)—this means the blood has almost no clotting ability and bleeding can be deadly. Fresh frozen plasma, prothrombin complex concentrate, or recombinant factor VIIa must be given, and if bleeding is ongoing, a camera scope (endoscopy) must look inside the gut to find and stop the source.
- Blood sugar below 60 mg/dL despite continuous IV dextrose (sugar solution)—this means the liver has lost almost all ability to make new glucose (gluconeogenesis) or release stored glucose (glycogenolysis). Less than 10 percent of liver cells are still working. Without an emergency liver transplant, death is imminent.
- Creatinine above 2.0 mg/dL or climbing more than 0.3 mg/dL per day, plus very little urine —this strongly suggests hepatorenal syndrome type 1 or death of kidney tubule cells (acute tubular tissue death (necrosis)). Both mean multiple organs are failing. Without a liver transplant, 70 to 80 percent of patients will die.
- Blood pressure so low that it requires vasopressor drugs (norepinephrine or vasopressin) through an IV to keep mean arterial pressure at or above 65 mmHg—this is distributive shock and multiorgan dysfunction syndrome. The person must go to the ICU immediately for close monitoring and be evaluated urgently for emergency liver transplant. Without transplant, fewer than 20 out of 100 patients survive.

Nursing priorities

1. Check mental status every 1 to 2 hours using the Glasgow Coma Scale and document hepatic encephalopathy grade—alert (grade 0), confused (grade I–II), stuporous or only responding to pain (grade III), or no response to pain (grade IV)—and call the provider immediately if the grade worsens. — The brain swells (cerebral swelling (edema)) in 75 percent of people with grade III or IV encephalopathy because ammonia and other toxins leak through the blood-brain barrier, pulling water into brain cells. Swelling raises intracranial pressure (pressure inside the skull) above 20 mmHg, cutting off blood flow and causing brain herniation (the brainstem gets squeezed through the skull base), which stops breathing and heartbeat within minutes.
2. Keep the head of the bed elevated 30 degrees at all times, avoid tight cervical collars or neck flexion, keep the room quiet and lights dim, and give sedation medicines only as ordered—never give benzodiazepines like lorazepam or diazepam because they worsen encephalopathy. — Elevating the head 30 degrees helps venous blood (blood returning from the brain) drain by gravity, lowering intracranial pressure by 5 to 10 mmHg. Neck flexion kinks the jugular veins (large neck veins), trapping blood in the skull and raising pressure. Loud noise and bright light trigger agitation, which increases brain oxygen demand and worsens swelling. Benzodiazepines (sedative medicines) cannot be cleared by the failing liver and build up, deepening coma and making it impossible to assess mental status.

3. Check blood glucose by fingerstick every 1 to 2 hours and hang continuous IV dextrose (D10 or D20 solution) to keep glucose between 100 and 150 mg/dL—never let it drop below 60 mg/dL. — The liver stores glucose as glycogen (a starch) and releases it between meals to keep blood sugar steady. When liver cells die, glycogen stores run out within 12 hours, causing low blood sugar (hypoglycemia) (low blood sugar below 60 mg/dL). The brain uses glucose as its only fuel, so low blood sugar triggers seizures, more brain swelling, and permanent brain damage within 30 minutes.
4. Inspect skin, gums, and all puncture sites every 2 to 4 hours for new bruises, pinpoint bleeding spots (petechiae) (tiny red dots), oozing, or active bleeding; use the smallest-gauge needles possible; apply pressure for 5 minutes after any blood draw or IV insertion; avoid rectal temperatures, suppositories, and intramuscular injections completely. — The liver makes clotting factors (proteins II, VII, IX, X, fibrinogen) that plug holes in blood vessels. Without them, the INR (international normalized ratio, a clotting test) rises above 1.5 and often above 3, meaning blood takes three times longer to clot. Even tiny trauma—a needle stick, brushing teeth, a rectal thermometer—can cause uncontrolled bleeding into the brain, abdomen, or lungs, leading to shock (blood pressure dropping below 90/60 mmHg) and death.
5. Measure and record all urine output hourly with a Foley catheter, target at least 0.5 mL per kilogram per hour (about 30 to 40 mL per hour for an average adult), hang IV normal saline to match losses, and notify the provider if urine output drops below 0.3 mL/kg/hour for 2 hours in a row. — Acute liver failure triggers hepatorenal syndrome (the kidneys shut down even though they are structurally normal) in 50 percent of cases because the dying liver releases toxins that constrict (squeeze) kidney blood vessels. Low urine output (oliguria) means the kidneys are failing, creatinine (a kidney waste marker) rises above 1.5 mg/dL, and toxins like ammonia build up faster, worsening encephalopathy. Catching kidney failure early allows time to start dialysis (a blood-filtering machine) before potassium rises above 6 mEq/L and stops the heart.
6. Hang the N-acetylcysteine (NAC) IV infusion exactly as ordered—loading dose 150 mg/kg over 1 hour, then 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours—and watch for anaphylactoid reactions (flushing, rash, wheezing, low blood pressure) in the first hour. — NAC is the antidote for acetaminophen poisoning—it replaces glutathione (an antioxidant the liver uses to neutralize acetaminophen's toxic byproduct NAPQI). Even when acetaminophen is not the cause, NAC improves survival in all acute liver failure patients by protecting remaining liver cells from oxidative stress (damage from free radicals) and improving blood flow to the liver. Anaphylactoid reactions happen in 15 percent of patients during the loading dose but resolve when you slow or pause the infusion—true anaphylaxis (throat swelling, airway closing) is rare.

7. Place the patient on contact-plus-droplet isolation (gown, gloves, mask) until hepatitis A, hepatitis B, and hepatitis E serology results return negative, and list the patient as NPO (nothing by mouth) with a bowel regimen (lactulose 30 mL every 6 hours by mouth or rectal enema) to produce 2 to 3 soft stools per day. — Hepatitis A and E spread through stool (fecal-oral route), and hepatitis B spreads through blood—isolation protects other patients and staff until viral tests confirm the person is not contagious. Lactulose (a synthetic sugar) traps ammonia in the colon as ammonium ions and flushes it out in stool, lowering blood ammonia from over 200 micrograms per deciliter to under 100. Lowering ammonia slows encephalopathy progression and reduces brain swelling, buying time for the liver to regenerate or for transplant.
8. Avoid giving any unnecessary medicines—especially sedatives, opioids, NSAIDs like ibuprofen, antibiotics like tetracycline or sulfa drugs, and herbal supplements—and double-check every ordered dose with pharmacy because the failing liver cannot metabolize (break down) most drugs, causing toxic buildup. — The liver uses cytochrome P450 enzymes to convert medicines into inactive forms that the kidneys can eliminate. Without these enzymes, drug levels rise 5 to 10 times higher than intended, causing overdose toxicity. For example, morphine (an opioid) normally lasts 4 hours but accumulates for days, deepening coma. NSAIDs (nonsteroidal anti-inflammatory drugs like ibuprofen) block prostaglandins that protect the stomach lining, causing bleeding ulcers in patients who already cannot clot. Only essential medicines—adjusted to kidney function and given at reduced doses—should continue.

Sources

- American Association for the Study of Liver Diseases (AASLD) 2023 Guidance on Acute Liver Failure
- European Association for the Study of the Liver (EASL) Clinical Practice Guidelines: Acute Liver Failure 2017
- American College of Gastroenterology (ACG) Clinical Guideline: Diagnosis and Management of Acute Liver Failure 2020
- U.S. Acute Liver Failure Study Group (ALFSG)

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