

APAP Toxicity

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THE STORY IN ONE SENTENCE

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“Acetaminophen overdose floods the liver with NAPQI, a poison that your liver normally catches with glutathione. Too much NAPQI uses up all the glutathione, then kills liver cells. NAC (the antidote) gives your liver fresh glutathione so it can stop the damage—but only if you give it early.”

Normal anatomy — the body's job

Your liver breaks down acetaminophen through three pathways. The two main pathways—glucuronidation (sticking a sugar molecule onto the drug) and sulfation (sticking a sulfate molecule onto it)—turn acetaminophen into harmless, water-soluble waste that your kidneys filter out in your pee. About 5 to 10 percent goes through a third pathway that uses enzymes called cytochrome P450 to make NAPQI, a toxic chemical. Your liver keeps a supply of glutathione, a protective molecule that grabs NAPQI instantly and turns it into something harmless that leaves in your urine.

BODY'S JOB

The liver's job is to turn acetaminophen into safe, water-soluble products that your kidneys can get rid of. Glutathione acts like a safety net, catching and neutralizing any NAPQI before it can hurt liver cells.

1. Acetaminophen enters your liver through the bloodstream.
2. About 90 percent goes through glucuronidation and sulfation pathways, which attach molecules to the drug and make it harmless and water-soluble.
3. Your kidneys filter out these harmless products in your urine.

4. About 5 to 10 percent goes through the cytochrome P450 pathway (enzymes CYP2E1 and CYP3A4), which makes NAPQI, a reactive, poisonous chemical.
5. Glutathione (stored in liver cells) immediately binds to NAPQI, neutralizing it into a harmless compound.
6. The neutralized product leaves your body in your urine.
7. As long as glutathione supply is plentiful, NAPQI never builds up and never harms liver cells.

What breaks

Overdose completely fills up the two safe breakdown pathways, forcing most of the acetaminophen through the NAPQI pathway. NAPQI is made faster than glutathione can neutralize it, so all the glutathione gets used up within a few hours. Free NAPQI—poison with nothing to stop it—sticks to proteins inside liver cells and kills them by damaging their energy-making parts (mitochondria) and triggering cell death.

CLINICAL TERM

Acetaminophen overdose (greater than 7.5 to 10 grams in adults or greater than 150 milligrams per kilogram in children) saturates glucuronidation and sulfation pathways. Excess acetaminophen is shunted to CYP2E1 and CYP3A4 enzymes, producing NAPQI faster than hepatic glutathione stores can conjugate it. Glutathione depletion occurs within 2 to 4 hours. Unbound NAPQI covalently binds to hepatocyte macromolecules, causing mitochondrial dysfunction, oxidative stress, and centrilobular tissue death (necrosis) (death of liver cells in zone 3 around the central vein). Peak hepatic injury occurs 48 to 72 hours post-ingestion.

How the body compensates

Vital signs may stay normal for 24 to 48 hours while liver damage is already happening. The danger is missing the silent progression from no symptoms to sudden, severe liver failure.

1. {'what': 'Normal vital signs in the first 24 hours', 'why': '"The liver has backup capacity (functional reserve). Early cell death is localized to zone 3 (around the central vein), so most of the liver is still working. Blood pressure, heart rate, and mental status stay normal because the liver hasn't lost enough function yet to affect the whole body.'}
2. {'what': 'Silent window (latent period)', 'why': '"Patients feel fine or just nauseated in the first 24 hours. This is dangerous because you and the doctor might think everything is okay when liver cells are already dying. The lack of symptoms creates false reassurance.'}

3. {'what': 'Rising liver enzymes (ALT and AST)', 'why': 'Dead liver cells break open and spill their enzymes into the bloodstream. ALT and AST levels rise into the thousands (normal is under 40), peaking at 24 to 72 hours. This is the first measurable sign of liver damage.'}
4. {'what': 'Rising INR (clotting time)', 'why': 'The damaged liver cannot make clotting factors (proteins that help blood clot). INR rises (normal is around 1; INR greater than 1.5 means clotting is slow). Higher INR means worse liver damage and higher bleeding risk.'}
5. {'what': 'Watch for the crash point: fulminant hepatic failure', 'why': "If more than 70 percent of liver cells die, the liver loses the ability to do its jobs. This causes encephalopathy (confusion from ammonia buildup), impaired blood clotting (coagulopathy) (inability to clot blood), acute kidney injury (hepatorenal syndrome, kidney failure triggered by liver failure), and low blood sugar (hypoglycemia) (low blood sugar, under 70, because the liver can't make glucose)."}}
6. {'what': 'Cerebral swelling (edema) (brain swelling)', 'why': 'Ammonia crosses from the blood into the brain, causing brain cells to swell. This leads to confusion, asterixis (flapping hand tremor when you hold your arms out), stupor, and coma.'}
7. {'what': 'Track serial measurements', 'why': 'A patient who looks stable but has worsening lab trends—rising ALT, AST, INR, creatinine (kidney waste product, normal under 1.2), and falling mental status—is decompensating (losing the ability to compensate) and needs urgent intervention.'}
8. {'what': "Transplant evaluation criteria (King's College Criteria)", 'why': 'pH less than 7.3 after giving fluids, or INR greater than 6.5 plus creatinine greater than 3.4 plus grade III or IV encephalopathy (deep confusion or coma). If any of these are met, refer for liver transplant immediately—do not wait for all criteria.'}

Domino effect

1. Hours 0 to 24: no symptoms or mild nausea, vomiting, feeling unwell. — NAPQI is building up and glutathione is being used up, but liver cells are just starting to die. Not enough liver damage has happened yet to release big amounts of enzymes or cause the liver to lose function. Nausea and vomiting come from acetaminophen irritating your stomach and triggering the vomiting center in your brain.
2. Hours 24 to 72: pain under your right ribs, sky-high liver enzymes (ALT and AST in the thousands), rising INR. — Liver cells around the central vein (zone 3) are dying and breaking open, spilling ALT and AST into your bloodstream. Pain happens because your liver is swelling and stretching its outer covering (the capsule). INR rises because your liver can't make clotting factors anymore.

3. Hours 72 to 96: peak liver damage with yellowing of the skin and eyes (jaundice) (yellow skin and eyes), confusion (encephalopathy), bleeding problems (coagulopathy), kidney failure, lactic acidosis (acid from oxygen-starved tissues) (acid buildup in the blood). — So many liver cells are dead that the liver stops doing its jobs. It can't clear bilirubin (a yellow pigment from broken-down red blood cells), so you turn yellow. It can't convert ammonia to urea, so ammonia builds up in your blood, crosses into your brain, and causes confusion, flapping hand tremor, and coma. It can't make clotting factors, so you bleed and bruise easily, sometimes with serious GI bleeding. It can't keep blood flowing to your kidneys (hepatorenal syndrome), so your kidneys fail and creatinine rises. It can't clear lactic acid or make energy properly (mitochondria are broken), so acid builds up in your blood.
4. Hours 96 and beyond: recovery (liver grows new cells) or death from multiorgan failure (liver, kidneys, brain, clotting all collapse). — The liver can grow back if less than half of its cells are dead. Surviving liver cells divide (mitosis) and replace the dead ones over 1 to 3 months. If more than 70 percent of the liver is destroyed, the liver can't regenerate fast enough and you die unless you get a liver transplant.
5. Every clinical finding is a direct result of NAPQI killing liver cells and using up glutathione. — Nothing is random. Nausea is the toxin irritating your gut and brain. Pain is your swollen liver stretching its capsule. High liver enzymes are dead cells spilling their insides. Bleeding is lost clotting factors. Confusion is ammonia poisoning your brain. Kidney failure is lost blood flow from a failing liver. Low blood sugar is lost ability to make glucose. Yellow skin is bilirubin buildup. All trace back to one upstream break: NAPQI overwhelming glutathione and killing liver cells.
6. Treatment is time-sensitive: NAC (N-acetylcysteine) restores glutathione if given within 8 hours (nearly 100 percent effective); it still helps after 24 hours but works less well. — NAC is the building block your liver uses to make glutathione. It refills your liver's glutathione stores so your liver can neutralize remaining NAPQI. NAC also improves blood flow and oxygen delivery to liver cells and calms down inflammation. Early NAC prevents liver damage. Late NAC reduces severity but cannot reverse cells that are already dead.
7. Diagnosis: measure blood acetaminophen level at 4 hours after you took the drug and plot it on the Rumack-Matthew nomogram. Levels greater than 150 micrograms per milliliter at 4 hours or greater than 75 at 8 hours predict liver damage. — The nomogram is a chart that compares your blood acetaminophen level to the time since you took the drug. It tells the doctor how likely you are to get liver damage before any symptoms show up. If your level is above the line, you get NAC treatment immediately, even if you feel fine.

8. Risk factors that make toxicity worse: chronic alcohol use (induces CYP2E1, making more NAPQI), malnutrition (depletes glutathione), medications that induce P450 enzymes (phenytoin, rifampin, carbamazepine), and fasting (lowers glutathione stores). — Chronic alcohol use turns on the enzymes that make NAPQI, so you make more poison from the same dose. Malnutrition and fasting mean you have less glutathione to start with, so NAPQI overwhelms your liver faster. Enzyme-inducing drugs also ramp up NAPQI production. These patients can get severe liver damage from lower acetaminophen doses (as low as 4 grams per day).

Symptoms · what the patient feels, and why

- Nausea and vomiting (first 24 hours): Acetaminophen (the pain medicine) and the toxic byproduct NAPQI (a poison made when the liver tries to break down too much acetaminophen) irritate the stomach lining and trigger a special zone in the brainstem called the chemoreceptor trigger zone—the brain's 'vomit switch'—causing nausea and vomiting even before the liver is badly damaged.
- Right upper quadrant pain—sharp or aching pain under the right ribs (24–72 hours): As liver cells die from the poison, they swell up like water balloons. This stretches the liver's outer wrapper (the hepatic capsule), which has pain nerves. Think of it like a balloon stretching inside a tight box—it hurts.
- Yellowing of the skin and eyes (Jaundice)—yellowing of the skin and whites of the eyes (48–96 hours): The damaged liver cannot process bilirubin (a yellow pigment left over when old red blood cells are broken down). Bilirubin piles up in the blood and seeps into the skin and the whites of the eyes, turning them yellow—like staining a white shirt with mustard.
- Confusion, sleepiness, or coma—hepatic encephalopathy (72–96 hours): The failing liver cannot clean ammonia (a toxic waste from gut bacteria and digested protein) out of the blood. Ammonia crosses into the brain and poisons brain cells, causing confusion, disorientation, a flapping hand tremor called asterixis, and eventually coma—like trying to think clearly in a room full of toxic fumes.
- Easy bruising, bleeding gums, or blood in vomit or stool (72–96 hours): The liver makes clotting factors (special proteins like II, VII, IX, and X that help blood form clots). When the liver fails, it stops making these proteins, so the blood cannot clot properly. Even small bumps cause bruises, gums bleed, and bleeding can start inside the stomach or intestines.
- Decreased urine output and dark urine (72–96 hours): The kidneys can fail in two ways: hepatorenal syndrome (blood vessels in the kidneys squeeze shut because the liver is failing) and direct tubular injury (the kidney's filter tubes are poisoned by toxins the liver cannot clear anymore). Less urine is made, creatinine (a kidney waste marker) rises in the blood, and urine turns dark like cola.

- Rapid breathing and severe fatigue (72–96 hours): Lactic acidosis (acid from oxygen-starved tissues) (acid buildup in the blood) happens because the liver cannot clear lactate (a normal byproduct of muscle work) and because the cell's energy factories (mitochondria) are poisoned. The body tries to fix the acid by breathing faster to blow off carbon dioxide, and the whole system feels exhausted—like running uphill while holding your breath.
- Low blood sugar (Hypoglycemia)—shakiness, sweating, and confusion from low blood sugar (72–96 hours): The damaged liver cannot make new glucose through a process called gluconeogenesis (building glucose from amino acids and lactate). Blood sugar drops below 70 mg/dL. This causes shakiness and sweating (the body's alarm bells) and confusion or even seizures (the brain runs on glucose—when it runs low, the brain shuts down like a phone with a dead battery).

Focused exam

- No belly pain and feeling completely fine in the first 24 hours after taking too much acetaminophen: Acetaminophen poisoning is sneaky. While the person feels well and acts normal, a toxic breakdown product called NAPQI is quietly killing liver cells inside. This calm period is the danger zone—the best window to start treatment before massive liver damage happens.
- Pain or tenderness under the right ribcage (right upper belly) after 24 hours: Your liver sits tucked beneath your right ribs. Pain here means the liver is swelling as thousands of liver cells die and spill their contents. It is the liver's first cry for help—a warning that NAPQI has caused real damage.
- Skin and the whites of the eyes turning yellow (jaundice) after 48 hours: Healthy liver cells grab bilirubin (a yellow waste product from old red blood cells) out of the blood and get rid of it. When acetaminophen kills those cells, bilirubin piles up in the blood and stains the skin yellow. Yellowing of the skin and eyes (Jaundice) is visible proof the liver is failing.
- Confusion, sleepiness, or strange behavior by day 3: A failing liver cannot clean ammonia and other poisons out of the blood anymore. These toxins float up to the brain and cause swelling and confusion (doctors call this hepatic encephalopathy). It means the liver is nearly gone and time is running out.
- Easy bruising, bleeding gums, or nosebleeds after day 2: Your liver makes special proteins called clotting factors that stop bleeding. When acetaminophen destroys the liver, clotting factors disappear and blood cannot clot properly. Bleeding anywhere on the body is a red flag that the liver has stopped working.
- Nausea and throwing up in the first 24 hours: The stomach and intestines react to the poisonous dose. This clue is not specific—it happens with many overdoses—but combined with the timing and other signs, it fits the acetaminophen pattern.

Diagnostics · every test answers a question

- Serum acetaminophen level (drawn at least 4 hours after the person swallowed the pills) → How much acetaminophen is in the blood right now, and does that amount predict liver damage?
- ALT (alanine aminotransferase) and AST (aspartate aminotransferase), two liver enzymes → Are liver cells breaking open and dumping their insides into the bloodstream?
- INR (International Normalized Ratio), a blood-clotting test → Can the liver still make clotting factors, or has it lost that ability?
- Serum creatinine (a kidney function test) → Are the kidneys failing as a side effect of the liver shutting down?
- Total bilirubin (the yellow pigment test) → Is the liver able to grab bilirubin and get rid of it, or is it backing up?
- Arterial blood gas (ABG) with lactate → Is the blood becoming too acidic because the liver cannot clear lactate and other acids?
- Prothrombin time (PT) or INR at presentation and serially every 4–6 hours if worsening → Is liver synthetic function declining in real time?
- Blood glucose (sugar) check → Can the liver still make and release glucose to keep blood sugar normal?

Treatment logic

- Activated charcoal 1 gram per kilogram of body weight (up to 50 grams total) by mouth or through a nose-to-stomach tube, given only if the person arrives within 1 to 2 hours of swallowing the acetaminophen → Activated charcoal is like a sponge. It sticks to acetaminophen pills still sitting in the stomach and small intestine, trapping them so they cannot be absorbed into the blood. This lowers the total dose that reaches the liver and cuts down how much NAPQI gets made.
- Intravenous N-acetylcysteine (NAC) using the 21-hour protocol: loading dose 150 mg/kg in 200 mL sugar water (D5W) over 1 hour, then 50 mg/kg in 500 mL D5W over 4 hours, then 100 mg/kg in 1,000 mL D5W over 16 hours → NAC refills the liver's supply of glutathione, the bodyguard molecule that grabs and neutralizes NAPQI before it can kill more cells. If started within 8 hours of the overdose, NAC prevents almost all liver damage. Even up to 24 hours, it still helps by stopping further cell death.

- Continue NAC beyond 21 hours if ALT, AST, or INR are still rising or staying high; give another 100 mg/kg over 16 hours and recheck labs every 4 to 6 hours until liver enzymes start falling and INR improves → Some people keep making NAPQI for longer than 21 hours, especially if they took a huge dose or have slow metabolism. Extended NAC keeps glutathione levels high enough to match ongoing toxin production and prevents the injury from getting worse.
- Apply King's College criteria to decide if the person needs a liver transplant: arterial pH below 7.30 after giving IV fluids, OR all three of these—INR above 6.5, creatinine above 3.4 mg/dL (300 μ mol/L), and grade III or IV confusion (hepatic encephalopathy). If criteria are met, immediately call a liver transplant center for evaluation and possible transfer. → These criteria identify people whose own liver is so destroyed it will never recover. Calling a transplant center early puts the person on the list for a donor liver in time to save their life before other organs shut down for good.
- Supportive care: IV fluids (normal saline or lactated Ringer's) to keep blood pressure stable and organs supplied with blood; ondansetron 4–8 mg IV for nausea; dextrose infusion if blood sugar drops below 70 mg/dL; transfuse fresh frozen plasma or give prothrombin complex concentrate only if the person is actively bleeding or needs an urgent procedure and INR is dangerously high → Supportive care keeps the body's systems running while NAC works or while waiting for a transplant. It prevents death from low blood pressure, low blood sugar, brain swelling, or uncontrolled bleeding—all complications of liver failure.
- Psychiatric evaluation and safety planning if the overdose was on purpose (suicide attempt); start inpatient mental health consultation before the person leaves the hospital and arrange outpatient psychiatry follow-up → Psychiatric assessment finds out if the person is still at risk of harming themselves, starts crisis counseling, and sets up ongoing mental health treatment to prevent another attempt.

Medications

Activated charcoal · Gastrointestinal adsorbent (a substance that sticks to toxins)

Activated charcoal is like a super-sticky sponge made of carbon. When you swallow too much acetaminophen (Tylenol), it sits in your stomach and intestines before your body can absorb it into the blood. Charcoal has millions of tiny pores that trap acetaminophen molecules and hold them tight, so they pass out in your stool instead of entering your bloodstream and reaching your liver. It only works if given early—within 1 to 2 hours after you swallow the pills—because after that, most of the drug is already absorbed and the charcoal can't grab it anymore.

1. You swallow activated charcoal mixed with water, usually through a tube or cup.
2. The charcoal spreads through your stomach and upper intestine.

3. Acetaminophen molecules stick to the charcoal's surface like magnets to metal.
4. The charcoal-acetaminophen clump stays in your gut and moves down through your intestines.
5. The whole clump leaves your body in your stool, so the acetaminophen never enters your blood.

SAFETY WATCH

Can cause vomiting—if you vomit and breathe charcoal into your lungs (aspiration), it can cause serious pneumonia (lung infection and inflammation). · Turns your stool black, which is normal and not dangerous. · Can cause constipation or bowel blockage if you are already dehydrated or have slow gut movement. · Do NOT give if you are vomiting uncontrollably, unconscious, or have no gag reflex (can't protect your airway), because of aspiration risk. · Do NOT give if your intestines are blocked, torn, or not working (ileus or perforation).

N-acetylcysteine (NAC) · Antidote and glutathione precursor (a building block that restores the liver's main protective molecule)

When you take too much acetaminophen, your liver tries to break it down using two safe pathways (sulfation and glucuronidation). But in overdose, those pathways get overloaded—like two checkout lanes closing when a huge crowd arrives. The extra acetaminophen is forced through a backup lane called CYP2E1, which turns it into NAPQI, a toxic molecule that acts like bleach inside liver cells. Normally, your liver has a shield called glutathione that neutralizes NAPQI instantly. But in overdose, glutathione runs out, and NAPQI starts killing liver cells. NAC does two lifesaving things: (1) it gives your liver the raw material to make fresh glutathione, restocking the shield, and (2) it directly grabs NAPQI with its own sulfur groups (sulfhydryl groups) and locks it up so it can't hurt cells. Think of NAC as both a repair kit and a cleanup crew.

1. NAC is given through an IV (into your vein) using a three-bag protocol (Prescott protocol).
2. **LOADING** dose: 150 mg per kilogram of your body weight over 1 hour—this floods your blood with NAC fast.
3. **SECOND** bag: 50 mg/kg over the next 4 hours—keeps NAC levels steady.
4. **THIRD** bag: 100 mg/kg over 16 hours—slowly continues the supply. Total time: 21 hours.
5. NAC enters your liver cells and breaks apart into cysteine, the building block of glutathione.
6. Your liver uses cysteine to make new glutathione, restoring the shield.
7. NAC's sulfur groups also bind directly to any NAPQI floating around, neutralizing it before it can damage cells.

8. If your liver enzymes (ALT) or clotting test (INR) stay high after 21 hours, NAC is continued until those numbers improve, meaning liver injury is healing.

SAFETY WATCH

Anaphylactoid reaction (looks like an allergic reaction but isn't true allergy): flushing (red skin), itching, hives, chest tightness, wheezing, low blood pressure. Happens most often during the fast loading dose. If it occurs, slow or pause the infusion, give antihistamines (like Benadryl), and restart NAC slower. · Nausea and vomiting—common, especially with the loading dose. Can give anti-nausea medicine (ondansetron). · Rare: bronchospasm (airway tightening) in people with asthma—watch breathing closely. · Do NOT stop NAC early even if side effects occur—it is the only antidote and must be completed unless life-threatening reaction happens. · Safe in pregnancy—both mother and baby benefit, because NAPQI crosses the placenta and can harm the fetus.

Red flags

- Confusion, asterixis (flapping hand tremor when arms are held out), or altered mental status—warns of hepatic encephalopathy and liver failure happening now
- INR greater than 6.5 or any bleeding without injury (bleeding gums, blood in vomit or stool, large bruises)—shows the blood cannot clot and death risk is very high
- Rising creatinine or low urine output (oliguria) (less than 400 mL of urine per day, about 1.5 cups)—signals acute kidney injury and hepatorenal syndrome
- Lactic acidosis (acid from oxygen-starved tissues) (lactate above 4 mmol/L) or blood pH below 7.3—means the cell's energy system is failing; meets criteria for emergency liver transplant
- Low blood sugar (Hypoglycemia) that does not respond to sugar given through the IV—shows the liver has lost the ability to make glucose; this is late-stage liver failure

Nursing priorities

1. Start the intravenous N-acetylcysteine (NAC) 21-hour protocol immediately: give loading dose 150 mg per kilogram in 200 mL D5W (sugar water) over 1 hour, then 50 mg per kilogram in 500 mL D5W over 4 hours, then 100 mg per kilogram in 1,000 mL D5W over 16 hours. — NAC donates sulfur groups that refill glutathione stores so the liver can detoxify NAPQI before it kills more liver cells. NAC works best when started within 8 hours of ingestion, but it still reduces death even when started late, so never delay—start it while waiting for lab results.

2. Draw blood for acetaminophen level, ALT and AST (liver enzymes), bilirubin, INR and PT (clotting tests), creatinine (kidney test), and basic metabolic panel before starting NAC, then recheck INR, creatinine, ALT, and AST every 12 to 24 hours. — The acetaminophen level at 4 hours after ingestion plotted on the Rumack-Matthew nomogram tells if liver damage will happen. Rising ALT above 1,000 units per liter confirms liver injury. INR above 1.5 shows the liver cannot make clotting factors. Rising creatinine means kidney failure is starting.
3. Assess mental status every 2 to 4 hours using the Glasgow Coma Scale or simple questions like 'What is your name?' and 'Where are you?' and check for asterixis by asking the patient to hold both arms out with wrists bent back for 30 seconds and watching for flapping tremor. — Hepatic encephalopathy happens when ammonia (a toxin normally removed by the liver) builds up in the blood and poisons brain cells. Confusion or asterixis means liver failure is severe and the patient may need intubation (breathing tube) to protect the airway or urgent liver transplant evaluation.
4. Monitor for bleeding by checking skin for new bruises or pinpoint bleeding spots (petechiae) (tiny red or purple dots), inspecting gums and IV sites for oozing, testing vomit and stool for blood, and reporting INR greater than 1.5 or any spontaneous bleeding to the provider immediately. — The liver makes clotting factors II, VII, IX, and X. When the liver fails, INR rises and the blood cannot clot, so patients bleed spontaneously from gums, gut, or IV sites. INR above 6.5 predicts very high death risk and may need fresh frozen plasma (clotting factors) or urgent transplant.
5. Measure and record all urine output every hour, report low urine output (oliguria) (less than 0.5 mL per kilogram per hour or less than 30 mL per hour in most adults), and monitor for dark tea-colored urine. — Acetaminophen and its toxic products can directly damage kidney tubules (the filters inside kidneys). Severe liver failure also drops blood pressure to the kidneys, causing hepatorenal syndrome (kidney failure triggered by liver failure). Low urine output (Oliguria) and rising creatinine warn that kidneys are failing and dialysis may be needed.
6. Watch for anaphylactoid reactions (flushing, itching, hives, wheezing, low blood pressure) during the NAC loading dose, slow or stop the infusion if symptoms appear, give diphenhydramine 25 to 50 mg IV and notify the provider, then restart NAC at a slower rate once symptoms resolve. — NAC is not a true allergy but releases histamine (an inflammatory chemical) in about 15 percent of patients, especially during the fast loading dose. Slowing the infusion stops the reaction. Never abandon NAC completely because it is the only antidote that prevents liver death.

7. Keep the patient NPO (nothing by mouth) if they are vomiting, confused, or have signs of liver failure, place on fall precautions, and pad bed rails if encephalopathy or confusion is present. — Hepatic encephalopathy causes confusion and poor coordination, so patients fall easily. Vomiting risks aspiration (vomit entering the lungs). If mental status worsens, the patient may need intubation to protect the airway before vomit or blood is breathed into the lungs.
8. Prepare for possible transfer to a liver transplant center if INR is greater than 6.5, creatinine is rising above 3.4 mg per deciliter, pH is less than 7.3 on arterial blood gas, or grade III or IV hepatic encephalopathy (confused, drowsy, or unresponsive) develops. — These King's College Criteria predict that the patient will die without a liver transplant. Early transfer to a transplant center improves survival because the sickest patients need evaluation and listing for emergency transplant before multi-organ failure makes surgery impossible.

Sources

- American Association of Poison Control Centers (AAPCC)
- American College of Medical Toxicology (ACMT) 2023 acetaminophen guideline
- Rumack-Matthew nomogram (standard tool for acetaminophen overdose risk)
- King's College Criteria for liver transplant in acute liver failure

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