

Acetaminophen poison

When you swallow too much acetaminophen, a poison called NAPQI piles up faster than your liver's shield (glutathione) can grab it. NAPQI sticks to liver cells and kills them.

THE STORY IN ONE SENTENCE

When you swallow too much acetaminophen, a poison called NAPQI piles up faster than your liver's shield (glutathione) can grab it. NAPQI sticks to liver cells and kills them.

“Acetaminophen poisoning kills liver cells when NAPQI overwhelms glutathione. The antidote N-acetylcysteine (NAC) must start within 8 hours—timing saves lives. Doctors use the Rumack-Matthew chart to decide who needs treatment.”

Normal anatomy — the body's job

The liver breaks down acetaminophen using three paths. Two safe paths handle most of the dose: one adds a sugar molecule (glucuronidation), another adds a sulfate group (sulfation). Both turn acetaminophen into harmless waste that leaves in your urine. A tiny third path uses an enzyme system called cytochrome P450 (a chemical machine in liver cells) that makes NAPQI, a toxic molecule. Glutathione, a protective chemical your liver makes, immediately grabs every NAPQI molecule and turns it into harmless waste. This system works perfectly at safe doses because glutathione is always ready and waiting.

BODY'S JOB

The liver's job is to turn chemicals—both helpful and harmful—into forms the body can use or throw away. At normal acetaminophen doses (up to 4 grams a day for adults), the two safe paths handle 90 percent of the drug and the tiny bit of NAPQI gets neutralized instantly. Without this normal job, the cascade of liver failure, bleeding, and confusion seems random instead of predictable and preventable.

1. You swallow acetaminophen. It dissolves in your stomach and small intestine.
2. Acetaminophen enters your bloodstream and travels to the liver.

3. In liver cells, 90 percent flows through the two safe paths (glucuronidation and sulfation). These paths add a tag to the acetaminophen molecule so the kidneys recognize it as waste and throw it out in urine.
4. About 5 to 10 percent flows through the cytochrome P450 path. This path makes NAPQI, a toxic molecule.
5. Glutathione, stored in liver cells, grabs each NAPQI molecule the instant it forms. Glutathione sticks to NAPQI and turns it into a harmless compound that leaves in urine.
6. The liver keeps a reserve of glutathione ready at all times. At safe doses, the reserve never runs out.
7. Result: acetaminophen is cleared from the body, no liver cells die, and you feel no harm.

What breaks

One upstream break—too much acetaminophen overwhelming the safe paths—explains every downstream finding.

CLINICAL TERM

Toxic doses of acetaminophen (more than 7.5 to 10 grams in adults, or more than 150 milligrams per kilogram body weight in children in a single dose, or repeated doses over 4 grams per day for several days) flood and saturate the glucuronidation and sulfation paths. Think of these paths as two lanes on a highway: when traffic is too heavy, both lanes jam. The liver is forced to shunt more acetaminophen through the cytochrome P450 system, the third lane, making huge amounts of NAPQI. Glutathione stores run dry within 8 to 12 hours. Unbound NAPQI sticks permanently to liver cell proteins, especially the mitochondria (the power plants that make energy inside each cell). This kills hepatocytes (liver cells). This is the single upstream break. Every clinical finding—from early nausea to late encephalopathy (brain confusion from toxins the liver cannot clear)—flows from hepatocyte death and loss of the liver's ability to make proteins, clear waste, and process toxins.

How the body compensates

Vital signs and routine labs can look normal in the first 24 hours while liver cell death is already happening. The danger is missing the narrow treatment window before irreversible

liver failure starts. The body tries to hide early damage by making surviving liver cells work overtime, but this mask slips suddenly when too many cells die.

1. {'title': 'Stage 1 (0 to 24 hours): deceptive calm', 'content': 'The patient may feel fine or have only mild nausea and vomiting. Heart rate, blood pressure, oxygen level, and mental status stay normal. Liver enzyme blood tests (AST and ALT) are still normal because not enough cells have died yet to spill enzymes into the blood. This quiet window is the best time to give the antidote, but many patients do not seek care because they feel okay.'}
2. {'title': 'Hidden damage is already happening', 'content': 'Glutathione is draining fast. NAPQI is sticking to liver cell proteins. Cell death has started but takes 12 to 24 hours to show up in blood tests. The poison is working silently.'}
3. {'title': 'Stage 2 (24 to 72 hours): the mask slips', 'content': 'Dying liver cells spill their enzymes—AST and ALT—into the blood. Levels often climb into the thousands (normal is under 40). The liver swells with inflammation and fluid, stretching the tight capsule that wraps it. This causes pain in the right upper belly under the ribs. Nausea may go away, fooling the patient into thinking they are better.'}
4. {'title': 'Compensation tries to hold the line', 'content': 'Surviving liver cells work overtime to make clotting factors, clear bilirubin, and process ammonia. For a while, INR (a measure of how long blood takes to clot) and bilirubin stay near normal. The kidneys concentrate urine to save water. The brain tolerates rising ammonia for a short time. These compensations hide the severity.'}
5. {'title': 'Stage 3 (72 to 96 hours): sudden collapse', 'content': 'Compensation fails when liver cell numbers drop below a critical point—usually losing 70 to 80 percent of functioning cells. The liver stops making clotting factors, so INR shoots up and bleeding happens (coagulopathy, or broken clotting). It stops clearing bilirubin, so skin and eyes turn yellow (jaundice). It stops clearing ammonia, so ammonia crosses into the brain and poisons astrocytes (support cells that feed and protect brain neurons), causing confusion or coma (hepatic encephalopathy, or brain poisoning from liver failure). Dead cells dump lactate and acid that the liver can no longer clear, so blood pH drops (lactic too much acid in the blood (acidosis), or acid piling up). Kidneys shut down from direct toxin damage to the filtering tubes (acute tubular tissue death (necrosis)) and from signals sent by the failing liver that make kidney blood vessels squeeze shut (hepatorenal syndrome).')}
6. {'title': 'Catch it early with the Rumack-Matthew nomogram', 'content': 'Measure blood acetaminophen level at 4 hours after ingestion (or as soon as possible if the patient presents later). Plot the level on the Rumack-Matthew chart. If the level is above the treatment line, start NAC immediately—even if the patient feels fine and liver tests are normal. The chart predicts toxicity risk before liver damage shows up. A level above 150 micrograms per milliliter at 4 hours means high risk of liver failure without treatment.'}

7. {'title': 'Track labs over time to see the slide', 'content': 'Rising ALT and AST show liver cells dying. Rising INR shows clotting function failing. Rising creatinine shows kidney function dropping. Dropping pH shows acid buildup. A patient with normal vitals but rising INR and liver enzymes is getting worse, not stable. The direction and speed of change matter more than one snapshot. An INR above 2 or rising fast signals severe liver injury. ALT or AST above 1,000 is a red flag. Creatinine doubling from baseline means kidney failure is starting.'}
8. {'title': 'The crash point you must not miss', 'content': 'Watch for acute liver failure with impaired blood clotting (coagulopathy) (INR above 1.5), encephalopathy (confusion, sleepiness, or coma), lactic acidosis (acid from oxygen-starved tissues) (pH below 7.3), and acute kidney injury (creatinine rising). This cluster usually appears 72 to 96 hours after overdose. At this point, the patient needs intensive care and liver transplant evaluation. Without transplant, mortality is 50 to 90 percent once encephalopathy and impaired blood clotting appear together.'}

Domino effect

1. Stage 1 (0 to 24 hours): nausea, vomiting, feeling unwell, or no symptoms at all — Acetaminophen is absorbed from the stomach and small intestine into the bloodstream within 30 minutes to 2 hours. It travels to the liver. The liver breaks it down, making NAPQI faster than glutathione can neutralize it. Glutathione stores run out within 8 to 12 hours. NAPQI starts sticking to liver cell proteins, but not enough cells have died yet to spill enzymes into the blood. Liver enzyme tests (AST and ALT) stay normal. The patient feels little or nothing, or has mild nausea from acetaminophen irritating the stomach lining. This deceptive calm is the danger—patients feel okay and delay seeking care, missing the narrow window when the antidote works best.
2. Stage 2 (24 to 72 hours): pain in the right upper belly, rising AST and ALT, sometimes nausea goes away — NAPQI sticks to the mitochondria (the power plants inside liver cells) and other proteins, stopping the cell from making energy. The cell swells, the membrane ruptures, and the cell dies. Dying liver cells spill their enzymes—AST and ALT—into the blood. Levels often shoot up into the thousands (normal is under 40). Right upper belly pain comes from the liver swelling with inflammation and fluid. The tight capsule that wraps the liver stretches, and stretch receptors in the capsule send pain signals. Nausea may go away because the stomach has cleared the drug, fooling the patient into thinking they are recovering. In reality, liver cell death is accelerating.

3. Stage 3 (72 to 96 hours): sudden massive liver failure with yellow skin, bleeding that will not stop, confusion, acid buildup, and kidney shutdown — Huge numbers of liver cells die— often 70 to 90 percent of functioning cells are gone. The liver loses its ability to make things and process waste. It stops making clotting factors (proteins II, VII, IX, X needed for blood to clot), so INR rises and bleeding happens from the nose, gums, gut, or needle sites. It stops processing bilirubin (a yellow breakdown product of old red blood cells), so bilirubin piles up in the blood and skin and eyes turn yellow (jaundice). It stops clearing ammonia (made by gut bacteria breaking down protein), so ammonia crosses the blood-brain barrier and poisons astrocytes (brain support cells that feed and protect neurons), causing confusion, sleepiness, or coma (hepatic encephalopathy). Dead liver cells dump lactate (a waste product from cells dying without oxygen) and the liver can no longer clear it, so lactate and acid pile up in the blood and pH drops (lactic too much acid in the blood (acidosis)). Kidneys fail from two hits: direct toxin damage to the filtering tubes (acute tubular tissue death (necrosis)) and signals sent by the failing liver that make kidney blood vessels squeeze shut, cutting off blood flow (hepatorenal syndrome). The patient is now in multi-organ failure.
4. Stage 4 (4 days to 2 weeks): recovery or death — If NAC was given early and liver cell death is limited (less than 50 to 70 percent of cells lost), the liver can grow back. Liver cells (hepatocytes) can divide and multiply, unlike many other organs. New cells grow and restore function over 1 to 3 weeks. AST and ALT fall, INR normalizes, bilirubin clears, and the patient recovers fully with no long-term damage. If damage is too severe (more than 70 to 80 percent of cells lost), the liver cannot regenerate fast enough. Multiple organs fail— liver, kidneys, brain, clotting system, lungs. Only a liver transplant can save the patient. Without transplant, death comes from brain swelling (cerebral swelling (edema) from ammonia and fluid shifts), bleeding that cannot be stopped, or infection (the liver makes immune proteins, so liver failure leaves the patient defenseless). Mortality without transplant is 50 to 90 percent once encephalopathy and impaired blood clotting (coagulopathy) appear together.
5. None of this is random — Every finding—nausea, rising liver enzymes, bleeding, confusion, kidney failure—traces directly back to glutathione running out and allowing NAPQI to kill liver cells. It is one upstream break cascading downstream in a predictable sequence. Nausea comes from stomach irritation and early toxin signals. Rising AST and ALT come from dying cells spilling enzymes. Bleeding comes from loss of clotting factor production. Confusion comes from ammonia the liver cannot clear. Kidney failure comes from toxins and liver signals shutting down kidney blood flow. Each domino falls because the one before it fell.

6. The body tries to compensate where it can — Early on, surviving liver cells work overtime to keep making clotting factors and processing bilirubin and ammonia, so INR and bilirubin stay normal at first. Kidneys concentrate urine to save water and keep blood pressure up. The brain tolerates low levels of ammonia for a short time by shifting it into other pathways. But these compensations hide the severity until liver cell numbers drop below a critical point—usually 70 to 80 percent lost—and compensation collapses suddenly. INR shoots up, bilirubin climbs, confusion sets in, and kidneys fail all at once. The crash is dramatic because the body was masking the damage until it could not anymore.
7. Trace backward from each finding to the root cause — Every treatment targets one point in the cascade. Activated charcoal (if given within 1 to 2 hours of ingestion) binds acetaminophen in the gut so it cannot be absorbed into the bloodstream. NAC (N-acetylcysteine) refills glutathione stores and gives the liver the building blocks to make more glutathione, so NAPQI gets neutralized. NAC also acts as a direct antioxidant and improves blood flow to the liver. NAC works best if started within 8 hours of ingestion—survival is over 95 percent. If started after 24 hours, survival drops to 60 to 70 percent because too many cells have already died. Liver transplant replaces the organ when cell death is too far gone—usually considered when INR is above 6.5, pH is below 7.3, creatinine is above 3.4, or encephalopathy is grade 3 or 4 (the King's College Criteria for transplant). Treatment logic follows the biology: stop absorption, refill the shield, replace the organ if needed.
8. Timing is everything — Acetaminophen poisoning is one of the most treatable overdoses—if caught early. NAC started within 8 hours prevents liver failure in over 95 percent of cases. After 24 hours, the window narrows. After 48 hours, much of the damage is done. The Rumack-Matthew nomogram helps decide who needs treatment based on blood acetaminophen level at 4 hours after ingestion. A level above 150 micrograms per milliliter at 4 hours means high risk and NAC should start immediately. The nomogram cannot be used for extended-release acetaminophen or for patients who took multiple doses over time (chronic overdose)—these patients need clinical judgment and NAC is often given if any doubt exists. The key teaching: treat early, treat based on the level and the nomogram, and do not wait for symptoms or liver enzyme elevation. By the time AST and ALT rise, glutathione is already gone and liver cells are dying. The antidote works by preventing damage, not reversing it once it has happened.

Symptoms · what the patient feels, and why

- Nausea and vomiting (Stage 1, first 24 hours): Acetaminophen and the pieces your liver breaks it into irritate the lining of your stomach. At the same time, they trigger the area postrema (the brain's vomit switch at the back of the brainstem that watches for poisons in the blood). This double hit makes you feel sick and throw up.

- Feeling better or no symptoms at all (Stage 2, 24 to 72 hours): All the acetaminophen has been soaked up and broken down, so your stomach feels better. Behind the scenes, liver cells are dying, but not enough damage has happened yet to make you feel sick. This quiet window tricks people into thinking they are fine—but the liver is still being destroyed.
- Pain and tenderness in the right upper belly (Stage 2 to 3): Dying liver cells cause the liver to swell with fluid and inflammation. Your liver sits inside a tight bag called the capsule. When the liver swells, it stretches the capsule—and the capsule has pain nerves. The liver cannot expand much inside your ribcage, so the stretching hurts.
- Yellow skin and whites of the eyes (jaundice, Stage 3, 72 to 96 hours): Dead liver cells cannot clean up bilirubin (a yellow waste dye made when old red blood cells break down). Bilirubin builds up in your blood and leaks into your skin and the whites of your eyes, turning them yellow.
- Confusion, extreme sleepiness, or not responding (encephalopathy, Stage 3): The failing liver cannot turn ammonia (made by gut bacteria and when you digest protein) into urea (a harmless waste). Ammonia piles up in the blood, crosses into your brain, and poisons astrocytes (the support cells that feed brain cells). This causes brain swelling and messes up neurotransmitters (the chemical messengers that let brain cells talk), leading to confusion, sleepiness, or even coma.
- Easy bruising, bleeding gums, or bleeding from the stomach or gut (Stage 3): Dying liver cells stop making clotting factors (the proteins that help blood clot), especially the ones that need vitamin K (factors II, VII, IX, and X). A test called INR goes up, meaning blood takes much longer to clot. Even small bumps cause big bruises, and your mouth and gut lining bleed on their own.
- Little or no urine output (oliguria, Stage 3): Your kidneys get hurt two ways. First, a poison made from acetaminophen (called NAPQI) damages the tiny filter tubes in the kidney (acute tubular tissue death (necrosis), meaning the filter tubes die). Second, signals from the failing liver make blood vessels inside the kidney squeeze shut, cutting off blood flow (hepatorenal syndrome). Either way, the kidneys stop making urine.
- Fast heartbeat and low blood pressure (Stage 3 to 4): Massive cell death dumps acid into the blood (lactic too much acid in the blood (acidosis)). Body-wide inflammation (called SIRS—the body's alarm system going off everywhere) and liver failure make blood vessels relax and widen. Blood pools in these floppy vessels instead of flowing. Your heart beats faster, trying to pump enough blood despite the low pressure—like a pump working overtime in a leaky system.
- Belly swelling (ascites, Stage 3 to 4): The failing liver stops making albumin (a protein that holds water inside blood vessels). At the same time, blood backs up in the liver, raising pressure in the portal vein (the big vein bringing blood from your gut). Both forces push fluid out of blood vessels and into your belly cavity, causing swelling.

Focused exam

- **Tenderness in the right upper belly, just under the ribs:** Your liver sits tucked under your right ribs. When too much acetaminophen (Tylenol) kills liver cells, that spot becomes sore when you press it. This tenderness usually shows up 24 to 72 hours after the person swallowed the pills—stage 2 of poisoning, when liver damage is happening fast.
- **Yellow color in the skin and the whites of the eyes (jaundice):** A healthy liver cleans out bilirubin (a yellow waste left over when old red blood cells break down). When poisoning has killed enough liver cells, bilirubin piles up in the blood and stains the skin and eyes yellow. Yellow color means the liver is failing—stage 3 poisoning.
- **New bruises that appear easily, or bleeding that will not stop:** Your liver makes clotting proteins (the things that plug holes in blood vessels so you stop bleeding). When acetaminophen poisoning destroys liver cells, blood cannot clot the way it should. New bruises or bleeding gums are red flags that poisoning has reached stage 3 and clotting has failed.
- **Confused thinking, strange behavior, or extreme sleepiness:** A dying liver cannot clean ammonia (a brain poison) out of the blood. Ammonia fogs the brain, causing confusion, odd behavior, or deep sleepiness (doctors call this hepatic encephalopathy—brain trouble from liver failure). This is stage 3 or 4 poisoning and means the person may need a liver transplant very soon.
- **Nausea, vomiting, and belly pain in the first 24 hours:** In stage 1 poisoning (0 to 24 hours after swallowing), the body sends a warning: nausea, vomiting, sweating, and stomach pain. These are the first clues. The key questions to ask are: What did you swallow? How much? When exactly? These early symptoms often go away by themselves, which tricks people into thinking they are safe—but liver damage is starting silently.
- **Normal belly exam early on, even when the person feels terrible:** Stage 1 acetaminophen poisoning is silent on exam—the patient feels awful but when you press the belly, nothing hurts yet. Stage 2 and 3 bring right upper belly tenderness and liver swelling. Do not miss early cases by thinking a normal exam means the person is safe. The history and blood tests matter more than the exam in the first hours.

Diagnostics · every test answers a question

- **Serum acetaminophen level** → Is the blood level high enough to hurt the liver, based on how many hours have passed since the person swallowed the pills?
- **Liver enzymes (AST and ALT)** → Is the liver already damaged? How much? Is the damage getting worse or starting to heal?
- **PT/INR (prothrombin time and international normalized ratio)** → Is the liver still making clotting proteins, or has it stopped working?

- Total and direct bilirubin → Can the liver still clear waste, or is bilirubin building up and staining the body yellow?
- Serum creatinine and BUN (blood urea nitrogen) → Are the kidneys starting to fail along with the liver?
- Venous or arterial blood gas with lactate → Is the blood becoming too acidic? Are the body's cells starving and dying from lack of oxygen and fuel?
- Blood glucose → Is liver failure causing dangerously low blood sugar?
- Basic metabolic panel (sodium, potassium, chloride, bicarbonate) → Are electrolytes (the salts and minerals in blood) out of balance because the liver and kidneys are failing?

Treatment logic

- NAC (N-acetylcysteine)—the antidote. Oral dosing: 140 milligrams per kilogram loading dose, then 70 milligrams per kilogram every 4 hours for 17 more doses (total 72 hours). IV dosing (preferred in the U.S.): 150 milligrams per kilogram over 1 hour, then 50 milligrams per kilogram over 4 hours, then 100 milligrams per kilogram over 16 hours (total 21 hours; continue longer if liver is still failing). → NAC refills the body's glutathione stores (the natural shield inside liver cells that neutralizes NAPQI, the toxic breakdown product of acetaminophen). Fresh glutathione stops NAPQI from latching onto liver cell proteins and killing the cell. NAC works best when started within 8 hours of swallowing—it prevents nearly 100 percent of severe liver damage if given early. NAC still helps even at 24 hours or later by supporting the liver and reducing inflammation, though it cannot undo damage already done.
- Get a detailed history immediately—What drug did you take? Brand name and any combination ingredients? Exact time swallowed (or best estimate)? Total number of pills or total milligrams? Was it one big dose all at once, or spread over hours (staggered dosing)? Why did you take it—accidental, pain relief, or intentional self-harm? Any alcohol or other drugs taken at the same time? → Knowing the exact dose and time lets you plot the level on the Rumack-Matthew nomogram and decide if NAC is needed. Many over-the-counter cold and pain medicines hide acetaminophen inside (like Nyquil, Percocet, Vicodin)—people often do not realize they took it. Knowing about alcohol or other drugs (especially other liver toxins) tells you if the liver is at higher risk. Knowing intent tells you if the person needs psychiatric evaluation, a safety sitter, and inpatient mental health care after medical treatment.

- Monitor liver function tests (ALT, AST, bilirubin, PT/INR) and creatinine every 12 to 24 hours once NAC is started. If the patient is in stage 2 or 3, check every 6 to 12 hours. Continue NAC until ALT is falling, INR is below 2.0, and the patient is clearly improving. → Watching the numbers over time tells you if NAC is working. Rising ALT and AST mean liver cells are still dying—keep giving NAC. Falling numbers mean the antidote is protecting the cells that are left and the liver is starting to heal. INR returning toward normal means the liver is making clotting proteins again. If numbers keep climbing despite NAC, the patient needs transplant evaluation.
- Contact a liver transplant center early—ideally within 24 hours of hospital arrival—if any King's College Criteria are met: arterial pH below 7.30 after fluids, OR INR above 6.5, OR all three of (1) INR above 3.0, (2) creatinine above 3.4 milligrams per deciliter, and (3) grade 3 or 4 hepatic encephalopathy (deep confusion or coma). → Liver transplant replaces the dying liver with a healthy donor organ and is the only cure once acute liver failure has set in. Early referral saves lives because finding a match, arranging surgery, and transporting the patient take time. The King's College Criteria identify patients whose liver will not recover on its own—waiting too long means death.
- Activated charcoal by mouth—1 gram per kilogram of body weight (maximum 50 grams in adults), given only if less than 1 to 2 hours since swallowing and the person can protect their airway and will not choke → Charcoal is like a sponge—it sticks to acetaminophen still sitting in the stomach and traps it so the drug cannot enter the blood. Less drug absorbed means less NAPQI (the toxic breakdown product that kills liver cells) is made. Charcoal works best within the first hour after swallowing.
- IV fluids (normal saline or lactated Ringer's) to maintain blood pressure and kidney blood flow (perfusion), especially if the patient is vomiting or has low blood pressure → Fluids keep blood flowing to the liver and kidneys, giving them the best chance to heal. Dehydration from vomiting makes kidney injury worse and can tip a sick liver into complete failure. Adequate hydration also helps clear toxins and supports the body while NAC does its job.
- Supportive care for hepatic encephalopathy (brain fog from liver failure)—keep blood sugar above 70 with IV dextrose, correct low sodium, potassium, and phosphate carefully, give lactulose 15 to 30 milliliters by mouth or rectal enema every 6 to 8 hours to lower ammonia, avoid sedatives that deepen coma, and watch for brain swelling (increased pressure inside the skull). → A failing liver cannot remove ammonia from the blood, and ammonia poisons the brain, causing confusion and eventually coma. Lactulose traps ammonia in the gut so it leaves in stool instead of reaching the brain. Fixing sugar and salts protects brain cells while waiting for the liver to heal or for transplant. Avoiding unnecessary sedatives keeps you able to check the neurologic exam and catch worsening early.

Medications

Activated charcoal · Gastrointestinal adsorbent (poison binder)

Activated charcoal works like a powerful sponge in your stomach and intestines. Its surface is covered with millions of tiny holes that trap acetaminophen molecules before they can pass through the gut wall into your blood. Once trapped, the charcoal carries the poison out of your body in your stool. This only works if you give it early—within 1 hour after the person swallowed the pills—because after that, most of the acetaminophen has already been absorbed into the bloodstream.

1. Person swallows too much acetaminophen; pills dissolve in the stomach.
2. Activated charcoal is given by mouth (or through a tube if the person cannot swallow safely).
3. Charcoal's porous surface binds acetaminophen molecules through physical attraction called adsorption—like a magnet pulling metal filings.
4. Bound acetaminophen cannot cross the gut wall into blood.
5. Charcoal moves through the intestines and leaves the body in stool, taking the trapped poison with it.

SAFETY WATCH

Never give activated charcoal if the person cannot protect their airway—meaning they are unconscious, vomiting, or cannot swallow—because it can get into the lungs and cause severe pneumonia (aspiration pneumonitis). · Charcoal causes black stool and sometimes constipation. · Do NOT give charcoal if the person has a hole (perforation) in the gut or a blockage (obstruction). · Charcoal does NOT work for alcohol, lithium, iron, cyanide, or corrosive poisons (acids or alkalis).

N-acetylcysteine (NAC, Acetadote when given IV, Mucomyst when given by mouth) · Antidote (glutathione precursor and direct antioxidant)

N-acetylcysteine is the only antidote that saves the liver from acetaminophen poisoning. Here is how it works: normally, your liver breaks down acetaminophen using two safe pathways (sulfation and glucuronidation, like two clean garbage chutes), but a small amount goes through a third pathway run by an enzyme called CYP2E1 (mainly) and CYP3A4. This third pathway makes NAPQI, a highly toxic chemical. Your liver uses a molecule called glutathione (your body's main trash collector and shield) to immediately grab NAPQI, neutralize it, and flush it out. When you take too much acetaminophen, the safe pathways get overwhelmed, the liver makes much more NAPQI, and glutathione stores run empty—like a bucket with a hole draining faster than you can fill it. Without glutathione, NAPQI attacks and kills liver cells

(hepatocytes) by destroying the proteins and membranes inside them, causing massive cell death (hepatic tissue death (necrosis)). NAC does three powerful things: First, it gives the liver cysteine, the key building block to make fresh glutathione and refill the empty tank. Second, NAC itself can bind directly to NAPQI and neutralize it, acting as a backup shield. Third, NAC improves blood flow (microcirculation) and oxygen delivery to the liver, helping damaged cells survive and repair. The earlier you give NAC, the more liver cells you save—it works best within 8 hours but should be given even days later because it still helps.

- 1.** Person swallows too much acetaminophen; it is absorbed into blood from the gut and travels to the liver.
- 2.** Liver enzymes—mainly CYP2E1 and CYP3A4 (part of the cytochrome P450 system)—convert acetaminophen into NAPQI.
- 3.** Normal glutathione stores are depleted within 8 to 12 hours because NAPQI production is overwhelming the supply.
- 4.** Without glutathione, NAPQI binds covalently (permanently) to liver cell proteins and membranes, causing cell death (hepatocellular tissue death (necrosis)).
- 5.** NAC is given by mouth or IV and enters the bloodstream.
- 6.** NAC is broken down (deacetylated) into cysteine, the rate-limiting building block for glutathione synthesis.
- 7.** Liver cells use cysteine to rapidly rebuild glutathione supplies inside the hepatocyte.
- 8.** Restored glutathione neutralizes remaining NAPQI through conjugation (binding and tagging for removal) and prevents further cell death.
- 9.** NAC also acts as a direct scavenger, using its own sulfhydryl (–SH) group to bind free NAPQI molecules.
- 10.** NAC improves liver blood flow and oxygen delivery (possibly by boosting nitric oxide, a blood vessel relaxer), supporting cell survival.
- 11.** Liver cell death stops or slows; remaining healthy hepatocytes begin regeneration and repair.

SAFETY WATCH

Oral NAC smells and tastes like rotten eggs (sulfur); mix it with juice, soda, or put it in a cup with a lid and straw to help patients tolerate it. Give it cold. · If the person vomits within 1 hour of an oral dose, repeat that dose. If vomiting continues, consider switching to IV NAC or giving an anti-nausea medicine like ondansetron (Zofran) or metoclopramide (Reglan). · IV NAC can cause an allergic-type reaction (anaphylactoid reaction, NOT a true IgE allergy) during the first loading dose—watch for flushing, itching, rash, hives, wheezing, chest tightness, or low blood pressure. This happens in about 6 to 18 percent of patients. · If a reaction occurs, slow or pause the IV infusion and give an antihistamine like diphenhydramine (Benadryl). This is NOT a true allergy, and you should restart NAC at a slower rate because it is life-saving. Rarely, you may need a bronchodilator (albuterol) or epinephrine if the reaction is severe. · Monitor liver enzymes (AST, ALT), INR or PT (clotting test, because the liver makes clotting factors), bilirubin (shows liver's ability to process waste), and creatinine (kidney function, because severe acetaminophen poisoning can hurt kidneys too) daily or more often if the patient is very sick. · Continue NAC until the patient is clinically improving AND INR is below 2.0 AND AST is trending down (going down from its peak). This may take longer than the standard 21-hour IV protocol or 72-hour oral protocol in severe cases—do NOT stop early if the liver is still failing. · If the patient develops acute liver failure (INR above 6.5, severe confusion or coma from hepatic encephalopathy, kidney failure, or too much acid in the blood (acidosis)), contact a transplant center immediately because they may need an emergency liver transplant.

Red flags

- INR greater than 1.5 or liver enzymes (ALT or AST) climbing into the thousands—signals severe liver cell death and loss of clotting proteins
- Confusion, sleepiness, or flapping hand tremor when arms are held out (asterixis)—signs ammonia is poisoning the brain
- Blood lactate greater than 3.5 after giving fluids, or blood pH less than 7.30—means massive cell death and very high risk of dying
- Kidney function worsening (rising creatinine) or urine output dropping below 0.5 mL per kilogram per hour—acute kidney injury on top of liver failure
- Reported swallowing more than 10 grams total (or 150 mg per kg of body weight), or blood acetaminophen level plotting above the treatment line on the Rumack-Matthew nomogram—high risk for liver damage if the antidote NAC is not given quickly

Nursing priorities

1. Start the NAC antidote immediately if the acetaminophen level is above the treatment line on the nomogram, or right away if the patient is confused, jaundiced, or has liver enzymes in the thousands—do not wait for levels if poisoning happened more than 8 hours ago. — NAC donates sulfur groups to rebuild glutathione (the liver shield) and directly grabs onto NAPQI poison before it kills more liver cells. It works best within 8 hours of swallowing acetaminophen, but it still helps even 48 to 72 hours later by reducing inflammation and improving blood flow to dying liver tissue.
2. Draw blood for acetaminophen level at least 4 hours after ingestion, and also send INR (clotting time), ALT and AST (liver enzymes), creatinine (kidney function), and basic metabolic panel with bicarbonate and anion gap. — Levels drawn before 4 hours are still rising in the gut and blood, so they give false low readings. INR above 1.5 and ALT or AST in the thousands mean massive liver cell death. Creatinine rising means acute tubular tissue death (necrosis) (kidney poisoning). Low bicarbonate and high anion gap mean lactic acidosis (acid from oxygen-starved tissues) from cell death.
3. Monitor for anaphylactoid reactions (flushing, itching, hives, wheezing, low blood pressure) during the first IV NAC loading dose, and stop the infusion temporarily if these appear—then restart at a slower rate once symptoms resolve. — The fast IV loading dose releases histamine (an allergy chemical) in about 15 percent of patients, especially in the first 15 to 60 minutes. This is not a true allergy—it is a rate-related reaction. Slowing or pausing the infusion lets histamine levels drop. Do not skip NAC; the benefit outweighs this manageable side effect.
4. Check mental status, hand tremor (hold arms out and watch for flapping), and measure urine output every 2 to 4 hours—report immediately if the patient becomes confused, very sleepy, or makes less than 0.5 milliliters per kilogram per hour of urine. — Confusion and asterixis (flapping hand tremor) signal hepatic encephalopathy—ammonia crossing into the brain because the liver cannot clear it. Dropping urine output means acute kidney injury from direct acetaminophen toxicity or low blood flow. Both require ICU-level care and possible dialysis or transplant evaluation.
5. Place the patient on continuous pulse oximetry and cardiac monitoring, and keep two large-bore IV lines patent with normal saline running. — Severe liver failure causes low blood pressure (loss of albumin and clotting factors causes fluid shifts), lactic acidosis (acid from oxygen-starved tissues) (cells cannot clear lactate), and sometimes acute respiratory distress syndrome (lungs fill with fluid). Two IV lines ensure access for vasopressors (medicines to raise blood pressure), blood products, and continued NAC if one line fails.

6. Hold all non-essential medicines that the liver breaks down, especially opioids, benzodiazepines, and sedatives, unless absolutely needed for pain or agitation. — A failing liver cannot metabolize (break down) most medicines, so they build up to toxic levels in the blood. Sedatives worsen encephalopathy and mask the mental status changes we use to track liver failure. Opioids and benzodiazepines also slow breathing when they accumulate.
7. Keep the patient NPO (nothing by mouth) if they are vomiting, confused, or have an INR above 1.5, and notify the provider to consider a nasogastric tube for oral NAC or switch to IV NAC. — Vomiting prevents oral NAC from staying down long enough to absorb. Encephalopathy raises aspiration risk (vomit going into the lungs). High INR means possible esophageal varices (swollen bleeding veins) from sudden liver failure. IV NAC is safer and just as effective in these situations.
8. Consult the regional poison control center (1-800-222-1222 in the United States) and notify the transplant service early if INR is greater than 2.0, creatinine is rising, pH is less than 7.30, or lactate is above 3.5 after fluid resuscitation. — These are the King's College Criteria that predict more than 90 percent chance of death without liver transplant. Poison control helps manage complex or prolonged NAC protocols. Early transplant consultation speeds evaluation—liver transplant is the only cure once fulminant hepatic failure (sudden total liver shutdown) begins.

Sources

- American Association for the Study of Liver Diseases (AASLD) 2011 Position Paper on Acute Liver Failure
- Rumack-Matthew Nomogram (FDA-endorsed)
- American College of Medical Toxicology (ACMT) NAC dosing guidelines
- Cochrane Database of Systematic Reviews on acetaminophen poisoning management

Last reviewed: 2026-07-07