

APAP Toxicity

A plain-English guide for you and your family

WHAT IS HAPPENING

Normally, your liver breaks down acetaminophen through two safe pathways that turn it into harmless waste you pee out. A tiny bit goes through a third pathway that makes NAPQI, a poisonous chemical. Your liver keeps a supply of glutathione—a natural protector that grabs NAPQI and turns it into something safe—so that tiny bit of NAPQI never hurts you. In overdose, the two main safe pathways get completely full and can't handle any more acetaminophen. Your liver is forced to push most of the drug through the third pathway, which makes a flood of NAPQI. Within a few hours, NAPQI uses up every bit of glutathione your liver has. Now the poison has nothing to stop it, so it sticks to your liver cells and kills them. The tricky part is timing. In the first 24 hours, you feel fine or just a little sick to your stomach—no warning that your liver is being destroyed. Between 24 and 72 hours, you get pain under your right ribs because your liver is swelling, and blood tests show sky-high liver enzyme numbers because cells are dying and spilling their insides into your blood. Between 72 and 96 hours, so many liver cells are dead that your liver stops doing its jobs: it can't make the proteins that clot your blood, so you bleed and bruise easily; it can't clean ammonia out of your blood, so ammonia builds up and poisons your brain, making you confused or even unconscious; and your kidneys start to fail because they depend on a healthy liver to keep blood flowing to them. After 96 hours, you either start to recover—because your liver can grow new cells to replace the dead ones—or you die from liver failure unless you get an emergency liver transplant. Every step follows logically: NAPQI overwhelmed glutathione, liver cells died, and your body's backup systems collapsed one by one. NAC (the antidote) works by giving your liver the building blocks it needs to make fresh glutathione. If you get NAC within 8 hours, it almost always stops the damage before it starts. After 24 hours, it's less effective, but it still helps by protecting the cells that are left and calming down inflammation. None of this is random—each symptom is your body's direct response to running out of the tools it needs to detoxify acetaminophen.

What you might feel

- Nausea and vomiting (first 24 hours)

- Right upper quadrant pain—sharp or aching pain under the right ribs (24–72 hours)
- Yellowing of the skin and eyes (Jaundice)—yellowing of the skin and whites of the eyes (48–96 hours)
- Confusion, sleepiness, or coma—hepatic encephalopathy (72–96 hours)
- Easy bruising, bleeding gums, or blood in vomit or stool (72–96 hours)
- Decreased urine output and dark urine (72–96 hours)
- Rapid breathing and severe fatigue (72–96 hours)
- Low blood sugar (Hypoglycemia)—shakiness, sweating, and confusion from low blood sugar (72–96 hours)

Call the doctor right away if...

- 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

What the care team will do

- 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.
- 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.
- 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.

- 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.
- 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.
- 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.
- 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.
- 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.

Medicines you may be given — and why

Activated charcoal

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.

N-acetylcysteine (NAC)

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.

Where this information comes from

- 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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