CONDITION

Acetaminophen and codeine overdose

Learn how acetaminophen and codeine overdose affects breathing and the liver, which symptoms require emergency care, and how poisoning is diagnosed and treated.

WHAT IT IS
Poisoning from excess acetaminophen and codeine

BODY SYSTEM
Liver, nervous system and breathing

MAIN SYMPTOMS
Severe sleepiness, slowed breathing, nausea or vomiting, upper right abdominal pain

WHAT CAUSES IT
Taking too much acetaminophen and codeine

HOW IT IS DIAGNOSED
Blood acetaminophen level, liver tests, clinical opioid assessment

MAIN TREATMENT
Antidotes and breathing support

CAN IT BE CURED?
Sometimes - early treatment improves outcomes

IS IT AN EMERGENCY?
Yes, with any suspected overdose

LONG-TERM OUTLOOK
Generally better with early treatment, potentially poor with severe liver injury

Overview

Acetaminophen and codeine are combined in some prescription pain medicines. Acetaminophen reduces pain and fever. Codeine is an opioid like oxycodone or morphine , a type of medicine that changes how the brain and nervous system respond to pain.

An overdose can happen when someone takes too much of the combination product at one time or over several hours or days. It may be accidental or intentional. A person may also overdose by taking several products that contain acetaminophen without realizing they share the same ingredient.

The two medicines cause different forms of poisoning. Too much codeine can slow or stop breathing. Too much acetaminophen can damage the liver. Serious liver injury may develop even when the person initially feels well.

A suspected overdose is a medical emergency. Do not wait for symptoms. In the United States, call 911 for trouble breathing, severe sleepiness, collapse, or inability to wake. For any suspected overdose, contact Poison Control at 1-800-222-1222 or use the official webPOISONCONTROL service . Outside the United States, contact the local emergency service or poison center.

Symptoms

Codeine effects often appear earlier than signs of acetaminophen-related liver injury. However, timing varies with the amount taken, the formulation, other substances, and the person's health.

Signs of opioid poisoning from codeine may include:

Acetaminophen poisoning may cause few or no symptoms during the first day. Early symptoms, when present, can include nausea, vomiting, sweating, poor appetite, tiredness, or abdominal discomfort. These symptoms do not show how severe the poisoning is.

Over the next one to three days, liver injury may become clearer. Symptoms can include worsening nausea, pain or tenderness in the upper right abdomen, confusion, yellowing of the skin or eyes, dark urine, unusual bleeding, or extreme weakness. Some people briefly feel better before liver problems become apparent.

Call emergency services immediately if the person cannot be awakened, has slow or absent breathing, has a seizure, collapses, or develops blue or gray skin or lips. If naloxone is available, give it according to its package instructions while help is on the way. Naloxone can reverse opioid effects, but it does not treat acetaminophen poisoning.

- Unusual sleepiness or inability to wake
- Slow, shallow, irregular, or stopped breathing
- Snoring, choking, or gurgling sounds in someone who cannot be awakened
- Very small pupils
- Limpness, confusion, or loss of consciousness
- Pale, bluish, or gray lips, fingertips, or skin
- Nausea or vomiting

Causes and risk factors

An overdose may occur after one large ingestion. It can also result from repeated doses that add up to too much acetaminophen, especially when more than one medicine is involved. Acetaminophen may appear on labels as "APAP," and it is found in many prescription and nonprescription pain, fever, cold, and flu products.

Common situations linked with overdose include taking extra tablets because pain continues, taking doses too close together, confusing product strengths, or combining medicines without checking their ingredients. Medication errors may occur when several people are caring for the same child or adult.

Alcohol, sedatives, and other opioids can increase codeine's effects on breathing and alertness. Examples include benzodiazepines like diazepam or lorazepam , sleep medicines, and some muscle relaxants. A person who has not recently used opioids may have less tolerance and may be affected by a smaller amount than someone with opioid tolerance.

Codeine must be converted by a liver enzyme into morphine to produce much of its opioid effect. Genetic differences can cause some people to convert codeine into morphine more rapidly than expected, increasing the risk of dangerous breathing problems. This variability is one reason codeine can affect people differently.

The risk of acetaminophen-related liver injury may be influenced by delayed treatment, repeated excessive dosing, prolonged fasting or poor nutrition, heavy alcohol use, and certain medicines that affect liver enzymes. Existing liver disease can complicate assessment, although the level of risk depends on the person's specific condition and exposure.

Children can be poisoned by an adult's medicine. Older adults and people with breathing disorders may also be more vulnerable to opioid-related complications. Any possible ingestion by a child requires immediate advice from a poison center or medical professional.

Diagnosis

Clinicians begin by supporting breathing and circulation. They do not need to wait for test results before treating dangerous opioid effects or starting time-sensitive acetaminophen care.

Information about the exposure is important. The care team may ask for the product name, tablet strength, estimated number taken, time of ingestion, and whether doses were taken all at once or over time. They will also ask about alcohol, other medicines, medical conditions, and whether the exposure may have been intentional. Bringing the package or a photograph of the label can help.

A blood acetaminophen level is a key test. After a single ingestion at a known time, a level

drawn at least four hours later can be plotted on a treatment chart called the Rumack-Matthew nomogram. The chart estimates the risk of liver injury and helps guide treatment.

The nomogram cannot be used in the same way when the time is unknown, doses were spread out, or repeated excessive doses were taken. In these situations, clinicians consider the acetaminophen level, symptoms, liver tests, and exposure history together. An early level taken before four hours may need to be repeated because it may not yet reflect the peak concentration.

Other tests may include liver enzymes, bilirubin, blood-clotting measurements, kidney function, glucose, electrolytes, and blood acid levels. Severe liver injury can interfere with clotting and blood sugar control. Tests may be repeated to follow the direction of the illness.

Codeine or morphine blood levels are not usually needed to guide urgent care. Diagnosis of opioid poisoning is mainly based on breathing, alertness, examination findings, and response to naloxone. Oxygen monitoring, heart monitoring, and an electrocardiogram may be used. Routine urine drug screens have limitations and do not rule an overdose in or out.

Treatment and management

Treatment takes place in an emergency department and may require hospital admission. The main goals are to restore breathing, prevent liver injury, and monitor for complications.

For codeine poisoning, clinicians provide oxygen and support the airway. Assisted ventilation may be needed if breathing is inadequate. Naloxone blocks opioid effects and can restore breathing. Because naloxone may wear off before codeine or its active metabolites do, repeated treatment or a continuous infusion may sometimes be necessary. The person must be observed for returning sleepiness or slowed breathing.

For acetaminophen poisoning, the antidote is N-acetylcysteine, often called NAC or acetylcysteine. It helps the liver safely process a toxic acetaminophen byproduct. NAC is most effective when started early, but it can still help after liver injury has begun. Clinicians may start it before all results are available when treatment would otherwise be delayed.

NAC can be given by mouth or through a vein. The route and length of treatment depend on the situation and the hospital's protocol. Blood tests help determine when treatment can safely stop. Reactions such as flushing, rash, or wheezing can occur with intravenous NAC; medical teams can usually manage these reactions while continuing necessary treatment.

Activated charcoal may be considered soon after some ingestions because it can reduce medicine absorption. It is not appropriate for every patient, especially someone who is very sleepy and cannot protect their airway. It should only be given under poison-center or medical

guidance. Do not induce vomiting or use home remedies.

People with severe liver injury receive close monitoring and supportive care. This may include treatment for low blood sugar, bleeding problems, kidney injury, brain swelling, or infection. Early consultation with a liver transplant center may be needed if acute liver failure develops.

If the overdose was intentional or occurred during a mental health crisis, treatment also includes a safety and mental health assessment. This is part of routine overdose care and helps plan safe support after the immediate medical danger has passed.

Complications

Codeine can cause respiratory failure, meaning breathing becomes too weak to supply the body with oxygen. Possible consequences include cardiac arrest, aspiration of vomit into the lungs, pneumonia, and brain injury from lack of oxygen.

Acetaminophen can cause acute liver injury or acute liver failure. Acute liver failure may lead to confusion from toxin buildup, abnormal bleeding, low blood sugar, kidney failure, acid buildup in the blood, and failure of several organs. A small group of severely affected patients may need a liver transplant.

Repeated vomiting, prolonged unconsciousness, or combining the medicine with alcohol or sedatives can add further risks. Outcomes are generally better when the overdose is recognized and treated early, but treatment may still be beneficial after a delay.

Follow up

Follow-up depends on the amount and pattern of exposure, test results, symptoms, and treatments received. Some people can leave the hospital after an appropriate observation period and reassuring tests. Others need repeated blood tests, longer monitoring, or specialist care.

After discharge, attend all scheduled appointments and laboratory testing. A clinician may need to confirm that liver tests, kidney function, and blood-clotting measurements are improving. Do not restart medicines containing acetaminophen, codeine, or other opioids until the treating clinician says it is appropriate.

A routine medication review can help prevent another accidental overdose. This should include prescription medicines, nonprescription pain relievers, and cold or flu products. Patients and caregivers can ask a pharmacist to identify products that contain acetaminophen or cause sedation.

Seek emergency care after discharge for new or worsening trouble breathing, inability to stay awake, confusion, fainting, repeated vomiting, yellow skin or eyes, severe abdominal pain, unusual bleeding, or markedly reduced urination. These are not symptoms to save for a routine appointment.

If the overdose was connected to self-harm, follow the safety plan made with the care team. Urgent help is appropriate if thoughts of self-harm return or the person may not remain safe.

Sources

- Dart RC, Mullins ME, Matoushek T, et al. Management of acetaminophen poisoning in the US and Canada: A consensus statement . JAMA Network Open . 2023;6(8):e2327739.
- American College of Medical Toxicology. ACMT position statement: Duration of intravenous acetylcysteine therapy following acetaminophen overdose . Journal of Medical Toxicology . 2016;12:213-215.
- National Library of Medicine, DailyMed. TYLENOL with Codeine-acetaminophen and codeine phosphate tablet prescribing information .
- National Library of Medicine, MedlinePlus. Acetaminophen and codeine overdose . U.S. Department of Health and Human Services.
- Centers for Disease Control and Prevention. Lifesaving naloxone . National Center for Injury Prevention and Control.
- Fontana RJ, Liou I, Reuben A, et al. AASLD practice guidance on drug, herbal, and dietary supplement-induced liver injury . Hepatology . 2023;77(3):1036-1065.