

Acute Cholecystitis

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THE STORY IN ONE SENTENCE

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“Acute cholecystitis means your gallbladder—a small pouch under your liver that stores bile—is blocked, swollen, and infected because a stone got stuck in the exit tube and won't let bile out, so pressure builds and germs grow inside.”

Normal anatomy — the body's job

The gallbladder is a hollow, pear-shaped sac about 3 to 4 inches long that sits tucked under the right lobe of the liver, just below your ribcage. It stores bile—a yellow-green fluid your liver makes continuously—and concentrates it by sucking out water so a little squeeze delivers a strong dose. When you eat fatty food, your intestine releases cholecystokinin (CCK, a hormone that signals the gallbladder to squeeze) into your bloodstream. CCK tells the smooth muscle wall of the gallbladder to contract hard and tells the sphincter of Oddi (the valve where the bile duct meets the intestine) to relax and open. Bile shoots out through the cystic duct, merges with the common bile duct, flows through the sphincter, and empties into the duodenum (the first part of your small intestine). There, bile acts like dish soap—it breaks big fat droplets into tiny ones so digestive enzymes can chop them up and your gut can absorb them. Normal flowing bile also sweeps bacteria backward out of the gallbladder, keeping it flushed clean. The wall is thin—under 3 millimeters—smooth, and pink because blood flows freely through tiny vessels in the mucosa (lining), muscularis (muscle layer), and serosa (outer skin). This cycle—store, concentrate, squeeze, drain, refill—runs smoothly meal after meal, day after day. Keep this normal picture in your head, because every finding in acute cholecystitis is a break from this smooth flow.

BODY'S JOB

The gallbladder's job is to store bile when you are not eating and deliver a concentrated burst of it exactly when your intestine needs help digesting fat. Without the gallbladder, your liver would have to drip weak bile into your gut all day long, and you would struggle to handle a fatty meal—fat would pass through partly undigested, causing greasy diarrhea and poor absorption of fat-soluble vitamins like A, D, E, and K. The cystic duct is the one-way exit tube; if it clogs, the whole system backs up like a blocked drain. Understanding this normal job is the foundation—without it, the disease findings look like a random list instead of a connected story that clicks and makes sense.

1. Your liver makes bile continuously, about 500 to 1,000 milliliters per day, from cholesterol, bile salts, bilirubin (a breakdown product of old red blood cells), and water. Tiny bile channels inside the liver—called canaliculi (KAN-uh-LICK-you-lie), meaning little canals—merge into bigger ducts, like streams joining a river, forming the left and right hepatic ducts (one from each lobe of your liver).
2. The left and right hepatic ducts join to form the common hepatic duct, which carries bile downward toward the intestine.
3. At a fork in the road, some bile flows straight down the common bile duct into the duodenum, and some flows backward up the cystic duct into the gallbladder for storage—like water flowing uphill into a reservoir when the main river is full.
4. Inside the gallbladder, the lining absorbs water and electrolytes (salts like sodium and chloride) back into the bloodstream, concentrating the bile 5 to 10 times stronger. A tablespoon of concentrated bile packs the punch of a cup of weak bile.
5. When you eat fatty food—think butter, cheese, fried chicken, or ice cream—fat hits the cells lining your duodenum. Those cells release cholecystikinin (CCK, a hormone that means gallbladder-mover) into your bloodstream.
6. CCK travels through the blood to the gallbladder and binds to receptors on the smooth muscle cells in the wall, telling them to squeeze. At the same time, CCK relaxes the sphincter of Oddi (the ring of muscle where the common bile duct meets the duodenum), opening the exit door.
7. The gallbladder contracts hard, pushing bile out through the cystic duct. Bile flows down into the common bile duct, through the now-open sphincter of Oddi, and squirts into the duodenum right where food is passing by.
8. In the duodenum, bile salts—the active ingredient in bile—surround fat droplets and break them into tiny micelles (my-SELLS), like dish soap breaking up grease on a pan. This process is called emulsification. Now pancreatic lipase (a fat-digesting enzyme your pancreas makes) can reach the fat and chop it into fatty acids and monoglycerides (simple fats your gut cells can absorb).

9. The gallbladder empties almost completely after a fatty meal, then slowly refills over the next few hours as the liver keeps making bile and the sphincter of Oddi closes again.
10. Normal bile flow keeps the gallbladder flushed clean. Bacteria that drift up from the intestine or land from the bloodstream get washed back out before they can multiply—like a river current sweeping debris away. The constant cycle of fill, squeeze, empty prevents stagnation and infection.

What breaks

One broken thing upstream explains all the weird findings you see downstream. In acute cholecystitis, that one thing is a gallstone or thick bile sludge plugging the cystic duct so bile cannot drain out. Everything that follows—the unrelenting pain, the fever, the swollen wall, the climbing white count, the infection—is your body reacting to that single stuck cork. Trace every symptom backward, and they all point to the same root cause: the exit tube is blocked.

CLINICAL TERM

A gallstone—usually a cholesterol stone (yellow, made of hardened cholesterol crystals) or a pigment stone (black or brown, made of bilirubin and calcium)—or thick bile sludge wedges into the narrow neck of the gallbladder or the cystic duct and blocks it completely. Bile from the liver keeps flowing into the gallbladder, but nothing can escape, so pressure builds inside like water behind a dam. The wall stretches, compressing blood vessels and squeezing capillaries shut. Swelling (Edema) fluid (plasma leaking from vessels) swells the wall, separating the normal layers and making it thick and boggy. Trapped bile is chemically toxic—bile salts and bile acids act like detergent, stripping away the protective mucus layer and killing epithelial cells (the lining cells). Damaged cells release cytokines (chemical alarm signals like interleukin-1, interleukin-6, and tumor tissue death (necrosis) factor-alpha) and prostaglandins (fatty acid signals that make blood vessels leaky), which call for backup. Neutrophils (the first-responder white blood cells) flood into the wall within hours, releasing enzymes and reactive oxygen species (superoxide, hydrogen peroxide) to kill germs and clean up dead cells. Macrophages (cleanup crew white cells) follow, gobbling up debris and releasing more cytokines. This is sterile inflammation—no bacteria yet, just chemical injury and immune response. Within 24 to 48 hours, bacteria—most commonly *Escherichia coli* (E. coli), *Klebsiella* species, *Enterobacter*, *Enterococcus*, and sometimes *Bacteroides* (an oxygen-hating germ from the gut)—migrate up the bile ducts (ascending infection) or seed the gallbladder from the bloodstream (hematogenous spread). Stagnant bile is a perfect growth medium: warm, full of nutrients, and not flowing to wash germs away. Bacteria multiply rapidly, turning sterile inflammation into suppurative cholecystitis (pus-forming inflammation). The gallbladder fills with infected bile and pus—called empyema of the gallbladder. That single upstream blockage—one stuck stone—cascades into all the clinical signs you see: steady right upper quadrant pain, fever, a high white blood cell count (leukocytosis) (high white count), positive Murphy sign, thickened gallbladder wall on imaging, and pericholecystic fluid (fluid around the gallbladder). Read every finding backward to that one plugged tube.

How the body compensates

Vital signs can look stable while the body is working hard behind the scenes to contain the infection. The immune system walls off the gallbladder, and for hours to days heart rate, blood pressure, and oxygen saturation stay in the normal range. That stable window is deceptive and dangerous, because it hides how sick the patient really is—inside, the gallbladder may be dying, pressure may be crushing blood vessels, and bacteria may be spreading. Your job is to spot the crash coming before it arrives by watching trends over time, not just one snapshot. A patient whose vital signs are normal today but whose pain is worse, whose white count is

climbing, or who is starting to look confused or tired is on a downhill slope. Catch the inflection point before it tips into sepsis, gangrene, or perforation.

1. In the first hours to days after the stone blocks the cystic duct, the body tries to contain the infection locally. White blood cells—neutrophils (NEW-tro-fills), then macrophages (MACK-ro-fay-jez, the cleanup crew)—flood the gallbladder wall and surrounding tissue. Blood vessels dilate (widen) to deliver more immune cells and oxygen. The omentum—a fatty, immune-rich apron of tissue that hangs down from the stomach and drapes over the intestines—wraps around the inflamed gallbladder like a blanket, walling off leaked bile or pus and preventing it from spilling into the rest of the belly. At this stage, heart rate, blood pressure, respiratory rate, and oxygen saturation often stay stable because the infection has not spread beyond the right upper quadrant yet and the body's systemic reserves are holding.
2. That stable vital-sign window is deceptive. Vital signs measure the whole body's status—they tell you if the heart, lungs, and circulation are keeping up—but they do not tell you what is happening in one local area. The gallbladder may be quietly dying in the right upper quadrant while heart rate and blood pressure look fine. Pressure inside the gallbladder keeps rising, blood flow to the wall keeps dropping, bacteria keep multiplying, and inflammatory cytokines (alarm proteins like interleukin-1, interleukin-6, and tumor tissue death (necrosis) factor-alpha) keep leaking into the bloodstream. By the time vital signs crash—heart rate climbs above 100 to 110, blood pressure drops below 90 systolic, temperature spikes above 39°C (102°F), respiratory rate climbs above 20—the damage is often severe and much harder to reverse. Early warning signs that compensation is starting to fail include worsening pain (patient reports pain climbing from a 6 to an 8 or 9 out of 10), rising white blood cell count (climbing from 12,000 to 16,000 to 20,000 or higher), new or worsening nausea and vomiting, new confusion or lethargy (a sign of early sepsis or poor blood flow to the brain), and imaging findings that worsen on repeat scan (wall thicker, more fluid around the gallbladder, irregular wall suggesting gangrene).

3. Gangrenous cholecystitis is the first major crash point. Rising pressure inside the gallbladder squeezes the cystic artery shut. When pressure inside exceeds the blood flow (perfusion) pressure of the artery (normally about 70 to 90 millimeters of mercury mean arterial pressure), blood flow stops—starved blood flow (ischemia) begins. Without oxygen, cells switch to burning sugar without oxygen (anaerobic metabolism) and produce lactic acid (the burn you feel in muscles after hard exercise), but they run out of ATP (the cell's energy currency) within hours. Membranes break down, cells swell and burst (necrosis), and tissue turns purple, then black (gangrene). Dead tissue cannot fight infection, cannot heal, and tears easily. On ultrasound you may see an irregularly thickened wall, membranes floating inside the gallbladder (sloughed dead lining), or uneven wall thickening. On CT, look for absent wall enhancement (the wall does not light up with IV contrast because blood is not flowing through it), intramural gas (gas bubbles in the wall, a very specific sign of gangrene), or pericholecystic fluid or stranding (inflammation and fluid leaking into surrounding fat). Gangrenous cholecystitis raises the risk of perforation 3 to 5 times, increases abscess and sepsis rates, and pushes mortality to 15 to 20%. It requires emergency cholecystectomy—ideally within 6 to 12 hours—plus broad-spectrum IV antibiotics covering Gram-negative rods and anaerobes (oxygen-hating germs).
4. Perforation means a hole forms in the overstretched, starved, or dead wall, and infected bile spills out. Perforation occurs in about 3 to 10% of acute cholecystitis cases, usually after 3 to 5 days of untreated or undertreated disease (but it can happen faster in gangrenous or emphysematous cholecystitis). There are two patterns: contained (localized) perforation and free perforation. Contained perforation happens when the omentum, liver, colon, or duodenum walls off the leak, forming a pericholecystic abscess—a pocket of pus and bile next to the gallbladder. Patients have persistent or worsening right upper quadrant pain, high fever (often spiking to 39 to 40°C), rising white count, and a tender, firm mass you can feel under the right ribs. CT shows a fluid collection with a thick, irregular wall next to or around the gallbladder. Treatment is percutaneous drainage (inserting a drain through the skin into the abscess under CT or ultrasound guidance) or emergency surgery, plus IV antibiotics. Free perforation is much more dangerous—the hole is not walled off, so bile and pus spill into the entire peritoneal cavity, causing diffuse peritonitis (widespread infection of the belly lining). Patients develop sudden, severe pain that spreads across the whole belly, rigid abdominal muscles (the belly feels hard as a board—called guarding or peritoneal signs), rebound tenderness (pain when you press and then suddenly let go), fever, fast heart rate (often 110 to 130), low blood pressure (septic shock), and confusion or agitation (brain not getting enough blood). Free perforation is a surgical emergency—mortality is 20 to 30% without immediate laparotomy (open surgery to wash out the belly and remove the gallbladder).

5. Emphysematous cholecystitis happens when gas-forming bacteria invade the starved or dying gallbladder wall. It is rare—about 1 to 3% of acute cholecystitis cases—but much more dangerous. It is more common in older men, diabetics (because high blood sugar feeds bacteria and impairs white cell function), and patients with peripheral vascular disease or chronic kidney disease (both reduce blood flow). The most common culprits are *Clostridium perfringens* (a spore-forming oxygen-hating germ that makes gas rapidly), *Escherichia coli*, and *Klebsiella pneumoniae*. Gas accumulates in the gallbladder wall (intramural gas) or lumen. On ultrasound, gas produces bright echoes with dirty posterior shadowing (a comet-tail or ring-down artifact—bright streaks trailing behind the gas). On CT, gas appears as black pockets or streaks in the wall where only soft tissue should be—this is the most specific sign. Emphysematous cholecystitis progresses to gangrene and perforation much faster than ordinary cholecystitis, often within 24 to 48 hours, and mortality is 15 to 25% even with treatment. It requires emergency cholecystectomy within hours and broad-spectrum IV antibiotics covering anaerobes, such as piperacillin-tazobactam 3.375 to 4.5 grams IV every 6 to 8 hours, or ampicillin-sulbactam 3 grams IV every 6 hours, or meropenem 1 gram IV every 8 hours, or metronidazole 500 milligrams IV every 8 hours plus ciprofloxacin 400 milligrams IV every 12 hours or ceftriaxone 1 to 2 grams IV daily.

6. Sepsis and septic shock are the final crash points, where infection spills from the gallbladder into the bloodstream and triggers a whole-body inflammatory storm. Bacteria and their toxins—endotoxins (lipopolysaccharide fragments from Gram-negative cell walls) and exotoxins (secreted poisons)—activate the immune system everywhere at once. Cytokines (interleukin-1, interleukin-6, tumor tissue death (necrosis) factor-alpha) and complement fragments (pieces of the immune system's attack proteins) flood the circulation, making blood vessels leaky and dilating them (vasodilation), so blood pressure drops. The heart races to compensate (tachycardia, often 110 to 130 or higher). Organs that depend on steady blood flow—brain, kidneys, liver, gut—start to fail: the patient becomes confused or sleepy (brain not getting enough blood), urine output drops below 0.5 milliliters per kilogram per hour (acute kidney injury), liver enzymes and bilirubin climb (liver dysfunction), and lactic acid builds up in the blood (tissue not getting enough oxygen, burning sugar without oxygen). Septic shock is defined as sepsis plus persistent low blood pressure (systolic less than 90 millimeters of mercury or mean arterial pressure less than 65) despite IV fluid resuscitation, requiring vasopressors (norepinephrine, vasopressin—medicines that squeeze blood vessels to keep blood pressure up). Mortality in septic shock from biliary source is 20 to 40% even with ICU care. Watch for early sepsis red flags before full shock arrives: heart rate climbing above 90, temperature above 38°C (100.4°F) or below 36°C (96.8°F) (hypothermia is a very bad sign), respiratory rate above 20 or PCO₂ below 32 (hyperventilating to blow off CO₂), white blood cell count above 12,000 or below 4,000 (leukopenia suggests overwhelming infection), new confusion or altered mental status, or serum lactate above 2 millimoles per liter. Sepsis from cholecystitis requires three things within 1 to 3 hours: source control (drain the infected gallbladder percutaneously or remove it surgically—antibiotics alone cannot fix a blocked, infected closed loop), broad-spectrum IV antibiotics (covering Gram-negatives, Gram-positives, and anaerobes), and aggressive IV fluid resuscitation (30 milliliters per kilogram crystalloid bolus, typically 2 to 3 liters in the first hour for an average adult, then adjust to blood pressure, urine output, and lactate clearance).

7. Always look for trends getting worse, not just a single snapshot. A heart rate that was 85 yesterday and is 98 today and 108 this evening is trending up—compensation is starting to slip. A white count that climbs from 13,000 to 17,000 to 21,000 over 24 hours signals worsening infection, not stable infection. Pain that was a 6 out of 10 and is now a 9, or pain that was stuck in the right upper quadrant and now spreads across the whole belly, suggests progression—maybe starved blood flow (ischemia), gangrene, or early perforation. A patient who was talking clearly yesterday and is confused or sleepy today has early sepsis or inadequate brain blood flow (perfusion) until proven otherwise. Repeat vital signs every 2 to 4 hours in admitted patients and graph the trend. Repeat white count and inflammatory markers (C-reactive protein, procalcitonin if available) daily. Re-examine the belly at least twice a day, looking for new peritoneal signs (guarding, rebound), increasing tenderness, or a new palpable mass. A patient with normal vital signs on a downhill trajectory is not truly stable—they are pre-crash. Catch the inflection point early, escalate care (consult surgery, start antibiotics, get repeat imaging), and prevent the crash before organs fail.

Domino effect

1. A gallstone—or thick bile sludge—wedges into the cystic duct or gallbladder neck and plugs it completely. — The stone acts like a cork jammed in the neck of a bottle. Bile from the liver keeps flowing into the gallbladder at a steady rate (about 20 to 50 milliliters per hour), but nothing can drain out. Pressure inside the gallbladder starts to climb within hours, stretching the wall like air pumped into a balloon. This is the single broken thing upstream—every domino that falls next traces back to this one stuck stone.
2. Steady, unrelenting pain in the right upper quadrant (RUQ) that does not come and go. — The stretched gallbladder wall presses against the parietal peritoneum (the thin, pain-sensitive lining covering the inside of your abdominal wall). Stretch receptors and nociceptors (NO-sih-SEP-torz, pain nerves) fire continuously, sending signals up the intercostal nerves (the nerves between your ribs) and the phrenic nerve (the nerve supplying the diaphragm) to your spinal cord, then to the thalamus (the brain's relay station for sensory signals, deep in the center of your brain), and finally to the somatosensory cortex (the strip of brain that maps body sensation, running ear-to-ear across the top of your head). Unlike biliary colic—where a stone moves in and out, causing waves of crampy pain that come and go over minutes—the pain of cholecystitis is constant because the blockage is fixed. The pain sits in the RUQ because the gallbladder lives under your right ribs, just below the liver. It often radiates (spreads) to the right shoulder tip or right scapula (shoulder blade) because the phrenic nerve—which senses the diaphragm and gallbladder area—shares nerve roots with nerves that supply the shoulder (C3, C4, C5 nerve roots in your neck). Your brain interprets signals from both areas as coming from the shoulder—this is called referred pain.

3. The gallbladder wall swells with swelling (edema) (fluid buildup) and fills with inflammatory cells. — Trapped bile is chemically toxic. Bile salts—like chenodeoxycholate and deoxycholate—and bile acids are detergents. They dissolve the protective mucus layer and punch holes in the lipid membranes of epithelial cells lining the gallbladder, killing them. Dead and dying cells release damage-associated molecular patterns (DAMPs, fragments of broken cells that act like alarm signals) and cytokines (interleukin-1, interleukin-6, tumor tissue death (necrosis) factor-alpha—alarm proteins that call for help). These signals make nearby capillaries (tiny blood vessels) leaky by loosening the tight junctions between endothelial cells (the cells lining the vessel walls). Plasma (the liquid part of blood) leaks out into the tissue, causing swelling (edema)—the wall puffs up and thickens, going from under 3 millimeters normally to 5, 8, 10 millimeters or more. At the same time, neutrophils (the first-responder white blood cells) squeeze out of capillaries—a process called diapedesis (DIE-uh-puh-DEE-sis, meaning cells slipping through gaps)—and flood into the wall. Neutrophils release enzymes (elastase, myeloperoxidase) and reactive oxygen species (superoxide, hydrogen peroxide—bleach-like chemicals) to kill germs and clean up dead cells, but these same chemicals also damage healthy tissue, amplifying inflammation. Macrophages follow hours later, gobbling up debris and dead cells. All this—swelling, neutrophils, macrophages—makes the wall swell, stiffen, and hurt.
4. Bacteria migrate into the stagnant bile and multiply rapidly, turning sterile inflammation into infection. — Normal flowing bile acts like a river current, sweeping bacteria backward out of the gallbladder and down into the intestine. When bile sits still, bacteria—mostly *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Enterococcus faecalis*, and sometimes *Bacteroides fragilis* (an oxygen-hating germ)—drift up from the duodenum through the sphincter of Oddi and common bile duct, or seed the gallbladder from the bloodstream. Stagnant bile is a warm (37°C body temperature), nutrient-rich broth with no flow to flush germs away—it is a perfect culture medium. Bacteria double every 20 to 60 minutes under these conditions. Within 24 to 48 hours, bacterial counts climb into the millions or billions per milliliter. The gallbladder fills with pus—called empyema (em-pye-EE-muh, meaning pus in a body cavity). Bacteria release endotoxins (lipopolysaccharide fragments from Gram-negative cell walls) and exotoxins (secreted proteins) that trigger fever, a high white blood cell count (leukocytosis), and systemic inflammation. Without antibiotics and source control (removing the blockage), infection spreads into the wall—called suppurative cholecystitis (pus-forming inflammation)—and can spill into the bloodstream (bacteremia, sepsis).

5. Fever and a high white blood cell count (leukocytosis) (high white blood cell count) develop.
 - Bacterial endotoxins and cytokines—especially interleukin-1 and interleukin-6 released by macrophages and neutrophils—travel through the bloodstream to the hypothalamus (high-po-THAL-uh-muss, your brain's thermostat, located at the base of your brain just above the pituitary gland). They bind to receptors in the preoptic area of the hypothalamus and trigger the release of prostaglandin E₂ (PGE₂, a fatty acid signal), which resets the thermostat upward. Your brain now thinks 38 to 39°C (100 to 102°F) is normal instead of 37°C, so it makes you shiver to generate heat and constricts blood vessels in your skin to hold heat in—you feel cold and feverish at the same time. Fever speeds up your immune system (white cells move and kill faster at higher temperatures) and slows bacterial growth (most bacteria grow best at 37°C). At the same time, cytokines signal your bone marrow (the spongy tissue inside bones where blood cells are made) to release stored neutrophils from the reserve pool and to crank up production of new white cells. Your white blood cell count climbs above the normal range of 4,000 to 11,000 per microliter, often reaching 12,000 to 20,000 or higher in severe infection. A very high count (above 20,000) or a left shift (seeing immature neutrophils called bands on the blood smear) suggests severe or spreading infection.
6. Positive Murphy sign on physical exam. — You place your fingers under the patient's right ribcage, just below the edge of the liver, and press firmly inward and upward. Then you ask the patient to take a deep breath in. As the diaphragm (the dome-shaped breathing muscle separating chest from belly) pushes down, it pushes the liver and the inflamed gallbladder downward onto your fingers. The swollen, tender gallbladder hits your hand, and sudden sharp pain shoots through the patient—they gasp, stop breathing mid-inhalation, and may grimace or pull away. That involuntary stop is a positive Murphy sign. It happens because the inflamed gallbladder wall is packed with activated pain nerves; pressing on it triggers a flood of pain signals. A positive Murphy sign is about 65% sensitive (it is positive in 65 out of 100 people who truly have cholecystitis) and 87% specific (if it is positive, there is an 87% chance cholecystitis is present), making it a useful bedside clue. If Murphy sign is negative and the patient has no RUQ tenderness at all, cholecystitis is much less likely (high negative predictive value).

7. Ultrasound or CT shows a thickened gallbladder wall—greater than 3 to 4 millimeters, often 5 to 10 millimeters or more. — Swelling (Edema) fluid and inflammatory cells (neutrophils, macrophages, plasma proteins) pack into the wall, swelling it up. On ultrasound, the normal gallbladder wall is a thin bright line less than 3 millimeters thick. In cholecystitis, it looks thick, hypoechoic (dark because fluid does not reflect ultrasound waves well), and sometimes striated or layered—three distinct layers (mucosa, swollen (edematous) muscularis, serosa) separated by fluid, giving a bull's-eye or target sign. On CT with IV contrast, the wall enhances (lights up white) because inflamed vessels are leaky and contrast leaks into the tissue. Wall thickness greater than 4 millimeters is about 50 to 70% sensitive and 80 to 90% specific for acute cholecystitis when combined with other findings. Very thick walls—8 to 10 millimeters or more—or irregular, uneven thickening suggest severe inflammation or early gangrene.
8. Pericholecystic fluid—fluid around the gallbladder—appears on imaging. — Inflammation makes the capillaries and small vessels in and around the gallbladder wall leaky. Plasma and inflammatory fluid seep out into the pericholecystic space (the narrow gap between the gallbladder and the liver or omentum). On ultrasound, fluid appears as a dark (anechoic or hypoechoic) rim or crescent around the gallbladder. On CT, it looks like a bright halo (because fluid is denser than fat on CT). A small amount of pericholecystic fluid is common in acute cholecystitis and just means inflammation is severe. A large amount, especially if loculated (walled off in pockets) or with gas bubbles, suggests localized perforation, abscess formation, or gangrenous cholecystitis.
9. Sonographic Murphy sign during ultrasound—the technician or radiologist presses the ultrasound probe firmly over the gallbladder fundus (the rounded bottom), and the patient feels sudden sharp pain right at that exact spot and stops breathing or says 'Ow, that's the spot.' — It is more accurate than the physical exam Murphy sign because you can see on the screen that you are pressing directly on the gallbladder, not on nearby liver, colon, or muscle. Sonographic Murphy sign is about 85 to 90% sensitive and specific for acute cholecystitis when combined with gallstones and wall thickening.

- 10.** Nausea and vomiting develop. — Pain signals and inflammatory cytokines—interleukin-1 and substance P (a nerve signal that amplifies pain)—travel through sensory nerves, especially the vagus nerve (cranial nerve X, the main nerve connecting the gut to the brainstem), to the chemoreceptor trigger zone (CTZ, a patch of brainstem outside the blood-brain barrier that samples the blood for toxins) and the vomiting center (a cluster of neurons in the medulla, the lower brainstem). The CTZ detects toxins, inflammatory signals, and pain signals in the blood and cerebrospinal fluid and sends an alarm to the vomiting center. The vomiting center coordinates the vomiting reflex: it tells your diaphragm and abdominal muscles to contract forcefully, your stomach to squeeze, and your esophageal sphincter (the valve between esophagus and stomach) to relax, pushing stomach contents upward and out. The vagus nerve also slows gastric emptying (how fast food leaves your stomach), so food and acid sit in your stomach longer, making you feel sick. Nausea and vomiting in cholecystitis are not random—they are direct effects of inflammation signaling the brainstem.
- 11.** If untreated: starved blood flow (ischemia) (too little blood flow), gangrene (tissue death), perforation (hole in the wall), or emphysematous change (gas in the wall) develop. — Rising pressure inside the gallbladder squeezes the cystic artery (the single end artery supplying the gallbladder) and compresses capillaries in the wall, like stepping on a garden hose. When pressure inside exceeds the blood flow (perfusion) pressure in the artery (normally about 70 to 90 millimeters of mercury mean arterial pressure), blood flow stops. Cells run out of oxygen within minutes, switch to burning sugar without oxygen (anaerobic metabolism), and produce lactic acid. ATP (the cell's energy molecule) runs out within hours, ion pumps fail, calcium floods into cells, and cells swell and burst—called tissue death (necrosis). Patches of wall turn dusky, then purple, then black—gangrene. Dead tissue is lifeless, cannot fight infection, cannot heal, and tears easily. If a weak spot opens, the wall perforates, spilling infected bile into the belly. If gas-forming bacteria—*Clostridium perfringens*, *E. coli*, *Klebsiella*—invade the dying tissue, they produce gas as a byproduct of burning sugar without oxygen—emphysematous cholecystitis. All these complications—gangrene, perforation, emphysema—are life-threatening and require emergency surgery. They are the final dominoes in the cascade, all tracing back to that one stuck stone at the beginning.

Symptoms · what the patient feels, and why

- Steady pain in the right upper belly lasting more than 6 hours: A gallstone plugs the cystic duct (the tube that drains bile out of the gallbladder). Bile backs up inside and stretches the gallbladder wall like an overfilled water balloon. The stretched lining sends steady pain signals to your brain.

- Pain shooting to the right shoulder or shoulder blade: The phrenic nerve senses both your diaphragm and your gallbladder, and it also carries feeling from your shoulder. Your brain mixes up the signals and you feel pain in your shoulder even though the real problem is in your belly. Doctors call this mix-up referred pain.
- Fever (temperature above 100.4°F or 38°C): Bacteria trapped in the gallbladder release toxins. These toxins tell the hypothalamus (your brain's thermostat) to turn up your body heat. Higher temperature helps your white blood cells kill the bacteria.
- Nausea and throwing up: Pain signals and inflammation chemicals trigger the vomiting center in your brainstem (the part at the base of your brain that controls basic body functions). The vagus nerve (a large nerve that connects your gallbladder to your stomach) carries the alarm. Your stomach slows down and you feel sick.
- Murphy sign (you gasp and stop breathing when the doctor presses your right upper belly while you breathe in deeply): When you breathe in, your diaphragm pushes down and shoves your swollen, tender gallbladder right onto the examiner's hand. The sudden sharp pain makes you gasp and freeze mid-breath.
- High white blood cell count (above 10,000 cells per microliter): Your bone marrow pumps out extra white blood cells—especially neutrophils (the bacteria-fighting kind)—into your bloodstream to battle the infection inside your gallbladder.
- Loss of appetite: Immune cells release chemical messengers like interleukin-1 and tumor tissue death (necrosis) factor (cytokines that signal danger throughout the body). These messengers tell your hypothalamus (the brain's control center for hunger) to turn off your appetite. Nausea from the irritated gallbladder also makes eating unappealing.
- Yellow skin and eyes (jaundice) in about 10 to 15 out of 100 people: A stone in the cystic duct can squeeze or slip into the common bile duct (the main tube that carries bile from your liver to your intestine). The blockage backs up yellow bile pigment called bilirubin into your blood, turning your skin and eyes yellow.
- Severe pain with a rigid, board-like belly and rebound tenderness (pain when the doctor lets go after pressing): Your gallbladder has torn open (perforated). Infected bile is leaking into your belly cavity and inflaming the lining called the peritoneum. Your belly muscles tighten like armor to guard the area. This is a surgical emergency.
- Confusion, dizziness, or very low blood pressure with a racing heart: The infection has spread into your bloodstream (sepsis). Your body releases chemicals like cytokines and nitric oxide that widen blood vessels all over, dropping your blood pressure. Your heart races to try to keep blood flowing, but your organs—including your brain—are not getting enough oxygen.

Focused exam

- **Murphy sign positive** (patient stops breathing in when you press under the right ribs during a deep breath): The inflamed gallbladder is rubbing against the lining of the belly. When you press and the patient breathes in, the diaphragm (the big breathing muscle under the lungs) pushes the liver and gallbladder down into your hand. If the gallbladder is swollen and angry, that push causes sharp pain and the patient stops breathing mid-breath. This is the single best bedside clue for acute cholecystitis because it tells you the gallbladder wall is swollen from a stone blocking its exit pipe (the cystic duct). It is right 65 times out of 100 when present (65% sensitivity) and rules out other problems 87 times out of 100 (87% specificity).
- **Steady pain in the right upper belly that stays in one spot:** A stone or thick sludge plugs the exit pipe of the gallbladder (the cystic duct), so bile gets trapped inside. Pressure builds, the gallbladder wall swells, and that makes steady, unmoving pain. This is different from biliary colic (pain from a stone sliding through a duct), which comes and goes in waves. Here the stone is stuck, so the pain does not let up. The pain lasts more than 6 hours in acute cholecystitis — shorter pain that goes away on its own is usually simple colic.
- **Fever and high white blood cell count:** Bile trapped behind the blockage becomes a perfect home for bacteria (often *E. coli*, *Klebsiella*, or *Enterococcus* from the intestine). Bacteria multiply, and your immune system fights back by releasing white blood cells and turning up body temperature. Fever above 38°C (100.4°F) and a white count above 11,000 cells per microliter tell you infection has moved in on top of the inflammation. About 70 out of 100 patients with acute cholecystitis have fever or a high white count.
- **Tenderness when you press the right upper belly:** The gallbladder wall is swollen and sensitive. When you press over it, pain shoots through because the tissue is inflamed. Often the belly muscles tighten on their own (called guarding) to protect the sore organ underneath. This reflex tells you the body is trying to shield itself from the pressure. If the belly is rigid all over or the patient has rebound tenderness (pain when you let go after pressing), the gallbladder may have ruptured and spilled bile and pus into the belly — a surgical emergency called perforation.
- **Nausea or vomiting:** The swollen gallbladder irritates nerves in the peritoneum (the thin lining around belly organs). Those nerves send signals up the vagus nerve (a big cable running from belly to brainstem) to the chemoreceptor trigger zone and vomiting center in the medulla oblongata (the part of the brainstem that controls automatic body actions like swallowing and throwing up). This triggers nausea and vomiting. It is a reflex — the gallbladder is not directly touching the stomach, but the brain reads the danger signal and makes you feel sick. Vomiting leads to dehydration and low potassium, which is why IV fluids are needed.

- No yellow color in the skin or whites of the eyes (no yellowing of the skin and eyes (jaundice)): In acute cholecystitis, the stone is stuck in the cystic duct, which only drains the gallbladder — not the common bile duct (the main highway that carries bile from the liver to the intestine). Because that main pipe is still open, bile keeps flowing and bilirubin (the yellow pigment made when old red blood cells are broken down in the spleen and liver) does not pile up in the blood. If you see yellowing of the skin and eyes (jaundice) (yellow skin or eyes, bilirubin above 2 to 3 mg/dL), the problem is likely a stone in the common bile duct (choledocholithiasis) or Mirizzi syndrome (a stone in the cystic duct pressing on the common bile duct from outside), both different emergencies that need ERCP to remove the stone.

Diagnostics · every test answers a question

- Complete blood count (CBC) with differential → Is the white blood cell count elevated, showing that the body is fighting infection or inflammation?
- Comprehensive metabolic panel (CMP) with liver enzymes (AST, ALT, alkaline phosphatase) and total bilirubin → Are the liver enzymes or bilirubin high, hinting that bile ducts beyond the gallbladder are involved? Is the patient dehydrated or having electrolyte trouble from vomiting?
- Right upper quadrant ultrasound → Does the ultrasound show an inflamed gallbladder, stones or sludge inside, and is the main bile duct wide (suggesting a downstream blockage)?
- HIDA scan (hepatobiliary iminodiacetic acid scan using a radioactive tracer) if ultrasound results are unclear → Does the radioactive dye fill the gallbladder, or is the exit pipe (the cystic duct) completely blocked?
- C-reactive protein (CRP) → How intense is the inflammation? Is this patient at high risk for severe complications like tissue death (gangrene) or sepsis?
- Blood cultures (two sets from different arm veins) if fever is high (above 38.5°C or 101.3°F) or patient looks septic (low blood pressure, confusion, fast breathing) → Has infection spilled from the gallbladder into the bloodstream?
- CT scan of the abdomen and pelvis with intravenous contrast if ultrasound is unclear or complications are suspected → Are there complications like perforation (a hole in the gallbladder), abscess (a walled-off pocket of pus), or emphysematous cholecystitis (gas-forming bacteria making bubbles in the gallbladder wall)?
- Lipase level if pain radiates to the back or there is concern for pancreatitis → Is the pancreas also inflamed, suggesting a stone passed through the common bile duct and blocked the pancreatic duct opening?

Treatment logic

- Intravenous fluids (normal saline or lactated Ringer solution) and nothing by mouth (NPO) → IV fluids replace water and salt lost from vomiting, fever, and not drinking. Most patients need 1 to 2 liters in the first few hours, then 100 to 150 mL per hour to keep up with ongoing losses. Keeping the patient NPO stops the intestine from releasing cholecystokinin (a hormone made by I-cells in the duodenum, the first part of the small intestine, when fat or protein arrives). Cholecystokinin tells the gallbladder to squeeze. When you stop that signal, the inflamed gallbladder can rest instead of contracting against a blocked exit, which would spike the pressure inside and worsen pain and swelling.
- Broad-spectrum intravenous antibiotics: ceftriaxone 1 to 2 grams once daily plus metronidazole 500 mg every 8 hours, or piperacillin-tazobactam 3.375 grams every 6 hours (or 4.5 grams every 8 hours for severe infection), or a carbapenem (meropenem 1 gram every 8 hours or ertapenem 1 gram daily) if very sick, septic, or resistant bacteria are suspected → Antibiotics soak into the inflamed gallbladder tissue and bile, killing common bacteria such as *E. coli*, *Klebsiella*, *Enterococcus*, and anaerobes like *Bacteroides fragilis* (bacteria that live without oxygen in the gut). Ceftriaxone is a third-generation cephalosporin that kills gram-negative rods (rod-shaped bacteria) by punching holes in their cell walls; metronidazole kills anaerobes by damaging their DNA. Piperacillin-tazobactam covers both groups in one medicine. This stops infection from spreading into the bloodstream (sepsis), the liver (hepatic abscess), or through the gallbladder wall (gangrenous cholecystitis or perforation). The 2018 Tokyo Guidelines and 2010 Surgical Infection Society guidelines recommend coverage of gram-negative rods and anaerobes for community-acquired infection, and broader coverage (carbapenems or piperacillin-tazobactam) for hospital-acquired or high-risk cases (diabetes, immunosuppression, age over 70).
- Pain medicine (IV ketorolac 15 to 30 mg every 6 hours for up to 5 days, or opioids like morphine 2 to 10 mg IV every 2 to 4 hours or hydromorphone 0.5 to 2 mg IV every 2 to 4 hours) and anti-nausea drugs (ondansetron 4 to 8 mg IV every 8 hours) → Pain medicine blocks pain signals. Ketorolac is an NSAID (nonsteroidal anti-inflammatory drug) that stops cyclooxygenase (an enzyme that makes prostaglandins, the chemicals that send pain and swelling messages), cutting pain and inflammation at the injury site. Use it carefully — no more than 5 days — because it can hurt the kidneys or cause stomach bleeding, especially in older adults. Opioids like morphine and hydromorphone bind to mu-opioid receptors in the spinal cord and periaqueductal gray (a pain-control center in the midbrain), shutting down pain signals before they reach consciousness. Anti-nausea drugs like ondansetron block serotonin (a brain chemical messenger) at 5-HT₃ receptors in the chemoreceptor trigger zone and vomiting center in the medulla oblongata (the brainstem), cutting nausea and preventing more fluid loss from throwing up.

- Laparoscopic cholecystectomy (keyhole surgery to remove the gallbladder) within 72 hours of symptom start → Surgery takes out the entire gallbladder, stones and all, ending the obstruction and infection permanently. The surgeon makes 3 to 4 small cuts in the belly, inflates it with carbon dioxide gas to make room, and uses a camera and long instruments to clip off the cystic duct and cystic artery (the blood vessel feeding the gallbladder), then pulls the gallbladder out through one of the holes. The 2018 Tokyo Guidelines and randomized trials (ACDC 2013, INTACT 2020) show operating within 72 hours (early surgery) shortens hospital stay by 3 to 5 days, lowers complication rates (from 25% to 10%), and cuts readmissions (from 20% to under 5%) compared to waiting 6 to 12 weeks (delayed surgery). After the gallbladder is gone, bile flows straight from the liver through the common hepatic duct (the liver's main drain pipe) into the common bile duct and then the duodenum — you do not need a gallbladder to digest fat; the liver makes bile continuously (about 500 to 1,000 mL per day) and it drips steadily into the gut instead of being stored and squirted in bursts.
- ERCP (endoscopic retrograde cholangiopancreatography) with sphincterotomy and stone removal if imaging or labs suggest a stone in the common bile duct → A flexible camera scope (an endoscope) goes down the throat, through the stomach, and into the duodenum (the first part of the small intestine) to reach the ampulla of Vater (the opening where the common bile duct and pancreatic duct empty into the intestine). The doctor threads a thin wire into the bile duct, injects contrast dye, and takes X-rays to see stones. Then a wire with electric current cuts the sphincter of Oddi (the muscular valve that controls bile and pancreatic juice flow), widening the opening. A tiny wire basket or balloon catheter is used to pull out any stones, restoring bile flow from liver to gut. This prevents ascending cholangitis (infection climbing up the bile ducts into the liver), which causes fever, yellowing of the skin and eyes (jaundice), and confusion (called Charcot triad) and can lead to septic shock. The 2019 American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommend ERCP when total bilirubin is above 4 mg/dL, the common bile duct is dilated above 6 mm on ultrasound (or above 8 mm in older patients or those who had previous surgery), or there is yellowing of the skin and eyes plus very high alkaline phosphatase (above 3 times normal, around 360 U/L).

- Percutaneous cholecystostomy (a drainage tube placed through the skin into the gallbladder under ultrasound or CT guidance) in high-risk patients who cannot safely have surgery right away → A radiologist numbs the skin with lidocaine (a local anesthetic), then pushes a thin catheter through the belly wall into the gallbladder using a needle under live ultrasound or CT guidance. The tube drains infected bile and pus out of the gallbladder into an external bag, bypassing the blocked cystic duct. This drops the pressure inside, controls sepsis (infection in the bloodstream), and buys time to stabilize the patient before delayed surgery 6 to 12 weeks later. The 2018 Tokyo Guidelines recommend this for patients with severe heart or lung disease (ASA physical status class III or higher, meaning serious illness that limits daily activity), septic shock (blood pressure under 90 systolic despite 2 liters of IV fluid), multiple organ failure, or other reasons they cannot survive immediate surgery (like being on a ventilator or having a recent heart attack). About 80 out of 100 patients improve — fever drops and white count falls — within 24 to 48 hours after the tube is placed.
- Ursodeoxycholic acid (ursodiol, 8 to 10 mg per kilogram per day split into 2 or 3 doses, taken by mouth) for patients who refuse surgery or cannot ever have surgery → Ursodeoxycholic acid is a bile acid (a molecule the liver makes from cholesterol to break down fat in the intestine). When you take it as a pill, it makes up a bigger share of your bile, diluting the other bile acids (chenodeoxycholic acid and deoxycholic acid) that are harsher. This makes bile less thick and less likely to form new cholesterol crystals. Over many months (6 to 24 months), it can slowly dissolve small cholesterol stones (under 5 mm) if the gallbladder still squeezes normally. Only 30 to 50 out of 100 patients see stones shrink or disappear, and it works only on cholesterol stones — not pigment stones (stones made from bilirubin, which are brown or black) or calcium stones. Recurrence is common (50 out of 100 patients form new stones) within 5 years once you stop the medicine.

Medications

Intravenous fluids (normal saline or lactated Ringer's solution) · Crystalloid fluid replacement

When you have acute cholecystitis, you cannot eat or drink because your gut needs to rest, and you may throw up a lot. Your body loses water and salt. IV fluids are sterile salt-water mixtures that run through a thin tube placed in a vein. They flow straight into your bloodstream to replace what you lost. They keep your blood pressure steady, help your kidneys flush out waste, and make sure every organ gets enough oxygen-rich blood. Think of it like watering a wilting plant—the water travels through the roots to every leaf, bringing the plant back to life.

1. A nurse places a thin plastic tube (IV catheter) into a vein in your arm or hand.
2. Fluid flows from a bag hanging on a pole, through tubing, and into your vein.

3. The fluid mixes with your blood and spreads through your entire circulatory system.
4. More fluid in your blood vessels raises the total volume, which lifts your blood pressure and improves blood flow to organs (perfusion).
5. Your kidneys filter the fluid, keep water and salts your body needs, and push out waste as urine.
6. Cells everywhere absorb water and dissolved minerals (sodium, chloride, potassium, calcium) so they can run chemical reactions, send nerve signals, and stay alive.

SAFETY WATCH

Too much fluid too fast can overwhelm the heart and make fluid leak into the lungs (pulmonary swelling (edema)), causing shortness of breath and trouble breathing—tell your nurse right away if you feel like you cannot catch your breath. · If you have heart failure or kidney failure, the team will give fluids more slowly and watch your breathing, heart rate, and urine output closely. · Swelling, redness, coolness, or pain at the IV site may mean the catheter slipped out of the vein (infiltration) or the vein is irritated—report it so the nurse can check and move the IV if needed. · Rarely, too much fluid can dilute the salt in your blood (hyponatremia), causing confusion, headache, or seizures—your team monitors blood tests (electrolytes) to prevent this.

Ondansetron (Zofran) · 5-HT₃ receptor antagonist (serotonin blocker, antiemetic)

When the gallbladder is blocked and swollen, pain and irritation in your belly trigger nerve signals that tell your brain to make you vomit. Cells in your gut release a chemical messenger called serotonin (5-HT₃), and that serotonin docks onto special landing spots (5-HT₃ receptors) on the vagus nerve (the main nerve highway running from your gut to your brainstem) and in the chemoreceptor trigger zone (the CTZ, a vomit sensor in the brainstem that reads signals in the blood). When serotonin binds to these receptors, the vomiting control center in your brainstem (the nucleus tractus solitarius) gets the message and tells your stomach muscles to heave. Ondansetron blocks those 5-HT₃ receptors—it sits on them so serotonin cannot land. Without serotonin locking on, the vomit signal never gets loud enough to make you throw up. Think of it like unplugging a fire alarm—the smoke (the nausea signal) is still there, but the bell cannot ring.

1. Inflammation, pain, and stretching in the gallbladder cause enterochromaffin cells (special cells in the gut lining) to release serotonin into the tissue around them.
2. Serotonin normally floats to nearby 5-HT₃ receptors on vagus nerve endings and binds to them, sending a 'nausea' signal up the nerve to the brainstem.
3. Serotonin also travels through the blood and reaches the chemoreceptor trigger zone, where it binds to more 5-HT₃ receptors.

4. Ondansetron is given intravenously (or by mouth before symptoms start) and enters the bloodstream.
5. Ondansetron molecules travel to the gut and brainstem and sit down on 5-HT₃ receptors, blocking the landing spots (competitive antagonism).
6. With the receptors blocked, serotonin cannot activate them, so the nausea signal weakens or stops.
7. The vomiting control center stays quiet, and you feel less nauseated and do not vomit.

SAFETY WATCH

Ondansetron can rarely lengthen the heart's electrical cycle (QT prolongation on an EKG), which can lead to a dangerous fast irregular heartbeat (torsades de pointes)—tell your doctor if you feel your heart racing, pounding, or skipping beats, or if you feel dizzy or faint. · Constipation is common because ondansetron slows gut movement—drink fluids when allowed, and tell your nurse if you have not had a bowel movement in several days. · Headache and dizziness can happen—sit up slowly from lying down, and ask for help if you feel lightheaded when you stand. · Very rare: serotonin syndrome (too much serotonin activity in the brain) if ondansetron is combined with other drugs that raise serotonin (certain antidepressants like SSRIs, SNRIs, MAOIs, or tramadol)—symptoms include confusion, agitation, fast heart rate, high fever, muscle stiffness, twitching, shivering, sweating, and wide (dilated) pupils; report any of these immediately. · Allergic reactions (rash, hives, swelling of the face or throat, trouble breathing) are rare but serious—tell your nurse right away.

Ketorolac (Toradol) · Nonsteroidal anti-inflammatory drug (NSAID)

When the gallbladder is blocked and swollen, damaged cells release an enzyme called cyclooxygenase (COX—comes in two forms, COX-1 and COX-2). COX enzymes take a fatty acid from broken cell membranes (arachidonic acid) and turn it into chemicals called prostaglandins. Prostaglandins make pain nerve endings more sensitive (lower the pain threshold) and increase swelling and heat in the tissue. Ketorolac blocks both COX-1 and COX-2, so fewer prostaglandins get made. With less prostaglandin around, pain nerves send weaker signals, inflammation drops, and you feel less pain. Think of prostaglandins as the volume knob on a loudspeaker broadcasting pain—ketorolac turns the knob down so the signal is quieter.

1. Inflammation and tissue injury in the gallbladder wall cause phospholipase A₂ enzymes to break down cell membranes and release arachidonic acid (a 20-carbon fatty acid).
2. Cyclooxygenase enzymes (COX-1 and COX-2) normally convert arachidonic acid into prostaglandin H₂, which is then turned into active prostaglandins like PGE₂ and prostacyclin (PGI₂).

3. Ketorolac is given by injection (intramuscular or intravenous) and enters the bloodstream quickly.
4. Ketorolac travels to the inflamed tissue in the gallbladder and surrounding area.
5. Ketorolac molecules bind to the active site of both COX-1 and COX-2 enzymes and block them (nonselective, reversible inhibition).
6. With COX blocked, prostaglandin production drops sharply.
7. Lower prostaglandin levels mean pain nerve endings are less excitable and send weaker pain signals to the spinal cord and brain.
8. You feel less pain, and swelling and heat in the tissue decrease.

SAFETY WATCH

Ketorolac can damage the kidneys (acute kidney injury) by blocking prostaglandins that normally keep blood flowing through the kidney filters—the risk is higher if you are dehydrated, have existing kidney disease, or take other drugs that stress the kidneys (like ACE inhibitors or diuretics); your team will check blood tests (creatinine, BUN) before starting and during treatment. · It blocks COX-1 in the stomach and intestine lining; COX-1 normally makes prostaglandins that protect the lining from stomach acid, so ketorolac can cause stomach ulcers, bleeding, or perforation (a hole in the stomach or intestine wall)—tell your doctor immediately if you have black, tarry, sticky stools (melena), vomit that looks like coffee grounds, or severe belly pain. · It interferes with platelet function (the blood cells that form clots), so it can increase bleeding during and after surgery—ketorolac is usually given for no more than 5 days total and is stopped before the operation. · It can raise blood pressure and cause fluid retention, which may worsen heart failure or cause swelling in the legs—avoid in patients with severe heart disease or uncontrolled high blood pressure. · Allergic reactions (rash, hives, swelling of the face or throat, wheezing, trouble breathing) are possible, especially if you are allergic to aspirin or other NSAIDs—tell your team about any allergies before starting. · It can trigger asthma attacks in people with aspirin-sensitive asthma—do not use in these patients. · Rarely, ketorolac can cause liver damage (elevated liver enzymes)—the team monitors liver function if you take it for several days.

Morphine · Opioid analgesic (mu-opioid receptor agonist)

Severe pain from the swollen gallbladder travels up through nerves to the spinal cord and then to the brain, where you consciously feel it. Morphine is a drug that mimics your body's natural pain-relief chemicals (endorphins and enkephalins). It locks onto mu-opioid receptors (special docking proteins) on pain nerve endings in the belly, on relay neurons in the spinal cord, and on neurons in the brain (especially the periaqueductal gray, the thalamus, and the limbic system—the parts that process pain intensity and the emotional suffering it causes). When

morphine activates these receptors, it opens potassium channels (potassium ions flow out of the nerve cell) and closes calcium channels (calcium cannot get in). This makes the nerve less excitable (hyperpolarized), so it is harder for the nerve to fire a pain signal. Morphine also reduces the release of pain-transmitting chemicals (substance P and glutamate) from nerve endings. The result: fewer pain signals leave the belly, fewer reach the brain, and the brain cares less about the signals that do arrive. Think of it like turning down the brightness on a screen—the image (pain) is still there, but it is dimmer and easier to tolerate.

1. Morphine is given intravenously (directly into a vein) or by intramuscular injection, and it enters the bloodstream within seconds to minutes.
2. Morphine travels through the blood and crosses into the central nervous system (brain and spinal cord) and also reaches peripheral pain nerves.
3. Morphine molecules bind to mu-opioid receptors (MOR) on the surface of nerve cells (neurons).
4. Activation of mu-opioid receptors triggers G-protein signaling inside the cell, which opens potassium channels (K^+ ions flow out, making the inside of the cell more negative) and closes voltage-gated calcium channels (Ca^{2+} cannot enter).
5. The nerve becomes hyperpolarized (its electrical charge drops), making it much harder to fire an action potential (the electrical signal that carries pain information).
6. Morphine also reduces the release of excitatory neurotransmitters—substance P and glutamate—from the nerve terminals, so less pain signal is passed to the next nerve in the chain.
7. Pain signals weaken at every stage: fewer signals leave the inflamed tissue, fewer climb the spinal cord, and fewer reach the brain.
8. In the brain, morphine changes how pain is interpreted—it reduces the emotional distress and fear that make pain unbearable, so even if you still feel some sensation, it bothers you much less.
9. You feel significant pain relief and often feel calmer and less anxious.

SAFETY WATCH

Morphine slows breathing (respiratory depression) by reducing the brainstem's response to carbon dioxide—nurses will monitor your oxygen level (pulse oximetry) and breathing rate closely; tell them immediately if you feel very drowsy, confused, hard to wake, or if you are breathing fewer than 8–10 breaths per minute. · It slows movement in the intestines (decreased gut motility), causing severe constipation—almost everyone on morphine needs a stool softener (docusate) and a stimulant laxative (senna or bisacodyl) to prevent hard, painful stools. · Morphine causes the release of histamine from immune cells (mast cells), which can cause itching (pruritus), usually on the face, neck, or chest—tell your nurse; they can give diphenhydramine (Benadryl) to relieve it. · It can cause nausea and vomiting by stimulating the chemoreceptor trigger zone in the brainstem—antiemetics like ondansetron are often given alongside morphine. · Morphine lowers blood pressure (vasodilation) and can slow the heart rate—you may feel dizzy or lightheaded when you sit up or stand; sit up slowly and call for help before walking. · Risk of physical dependence and addiction (opioid use disorder) with prolonged use—in acute cholecystitis, morphine is used for only a few days (until surgery), so this risk is very low in this setting. · Do NOT drink alcohol, take benzodiazepines (like lorazepam, diazepam), or take other sedatives while on morphine—the combination can dangerously slow or stop your breathing. · Older adults and people with lung disease (COPD, asthma) are at higher risk for respiratory depression—morphine is used cautiously and at lower doses in these patients. · Morphine can cause confusion, hallucinations, or vivid dreams, especially in older adults—report any new confusion or strange thoughts.

Piperacillin-tazobactam (Zosyn) · Extended-spectrum penicillin combined with a beta-lactamase inhibitor (beta-lactam antibiotic)

When bile is trapped in the gallbladder, bacteria from the intestines (especially *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus* species, and anaerobes like *Bacteroides fragilis*) can swim backward up the bile ducts and multiply in the stagnant bile, causing infection.

Piperacillin kills these bacteria by breaking their cell walls. Bacteria build their walls out of a tough mesh called peptidoglycan, which is assembled by enzymes called penicillin-binding proteins (PBPs). Piperacillin is shaped like the natural building block of peptidoglycan, so it tricks the PBPs into grabbing it. Once the PBPs bind to piperacillin, they get stuck and cannot finish building the wall. The wall develops holes and weak spots. Water rushes into the bacteria (osmosis), the bacteria swell up like a balloon, and they burst (lysis). Some bacteria fight back by making enzymes called beta-lactamases that cut piperacillin apart before it can work.

Tazobactam is a 'bodyguard' drug—it binds permanently to beta-lactamase enzymes and inactivates them (suicide inhibition). With tazobactam protecting piperacillin, the antibiotic can

kill even bacteria that try to resist it. Together, piperacillin-tazobactam covers a broad range of gram-positive, gram-negative, and anaerobic bacteria.

- 1.** Piperacillin-tazobactam is given intravenously (through an IV) every 6 or 8 hours and enters the bloodstream.
- 2.** It travels throughout the body and concentrates in bile, the gallbladder wall, and inflamed tissue.
- 3.** Piperacillin molecules reach the bacterial cell surface and bind to penicillin-binding proteins (PBPs) on the bacterial cell membrane.
- 4.** PBPs are enzymes that normally cross-link strands of peptidoglycan to build a strong, rigid cell wall; with piperacillin bound, the PBPs cannot finish the job.
- 5.** The cell wall becomes weak, incomplete, and full of gaps.
- 6.** Some bacteria (like many strains of *E. coli* and *Klebsiella*) produce beta-lactamase enzymes that try to chop piperacillin into inactive pieces.
- 7.** Tazobactam enters the bacteria and binds irreversibly to the active site of beta-lactamase enzymes, permanently blocking them (the enzyme 'commits suicide' by grabbing tazobactam and never letting go).
- 8.** With beta-lactamase inactivated, piperacillin remains intact and continues killing bacteria.
- 9.** Water flows into the bacteria through the broken cell wall by osmosis, the bacteria swell, and their membranes burst (osmotic lysis).
- 10.** Dead bacteria release their contents, which your immune system (white blood cells like neutrophils and macrophages) cleans up, and the infection shrinks.

SAFETY WATCH

Allergic reactions: If you are allergic to penicillin or cephalosporins (another class of beta-lactam antibiotics), you may also react to piperacillin—symptoms range from mild rash and hives to severe anaphylaxis (swelling of the face, tongue, or throat; trouble breathing; low blood pressure; fast heart rate). Tell your doctor about any antibiotic allergies before starting. If anaphylaxis occurs, treatment is immediate epinephrine injection and supportive care. · Diarrhea is common because piperacillin kills not only the bad bacteria causing infection but also the good bacteria in your gut that help digest food—this imbalance can cause loose stools. Severe, watery, or bloody diarrhea with cramping and fever may be *Clostridioides difficile* infection (C. diff), a dangerous overgrowth of toxin-producing bacteria; report any severe diarrhea immediately. · Piperacillin-tazobactam can lower your platelet count (thrombocytopenia), which increases bleeding risk—your care team will check a complete blood count (CBC) during treatment; tell your nurse if you notice unusual bruising, tiny red spots on your skin (petechiae), or bleeding that does not stop easily. · It can cause low potassium (hypokalemia), especially if you are also taking diuretics—symptoms include muscle weakness, cramps, and irregular heartbeat; electrolytes will be monitored. · High sodium load: Piperacillin-tazobactam contains a lot of sodium (about 2.35 mEq per gram of piperacillin), which can be a problem if you have heart failure, high blood pressure, or kidney disease—your team will monitor fluid balance and watch for swelling or shortness of breath. · Rarely, it can cause seizures, especially in people with kidney failure or a history of epilepsy, because the drug can build up in the blood—doses are adjusted based on kidney function. · Liver enzyme elevations (transaminitis) can occur—liver function tests (AST, ALT) may be checked if treatment is prolonged. · Interstitial nephritis (kidney inflammation) is a rare allergic reaction that can cause kidney damage—symptoms include fever, rash, and decreased urine output; report these immediately.

Ceftriaxone (Rocephin) plus metronidazole (Flagyl) · Third-generation cephalosporin (ceftriaxone) combined with a nitroimidazole antibiotic (metronidazole)

This is a two-drug combination that together covers the main bacteria causing acute cholecystitis. Ceftriaxone kills aerobic bacteria (bacteria that need oxygen to survive), especially gram-negative rods like *Escherichia coli* and *Klebsiella pneumoniae*, and some gram-positive bacteria like *Streptococcus* species. It works the same way as piperacillin: it binds to penicillin-binding proteins (PBPs) in the bacterial cell wall, blocks them from finishing the peptidoglycan mesh, weakens the wall, and causes the bacteria to burst when water rushes in. Metronidazole kills anaerobic bacteria (bacteria that live in low-oxygen or no-oxygen environments), especially *Bacteroides fragilis* and *Clostridium* species, which are common in bile and gut contents. Metronidazole is a prodrug—it enters the bacteria and is activated by

bacterial enzymes called nitroreductases (which only exist in anaerobic bacteria). Once activated, metronidazole forms toxic free radicals (highly reactive molecules with unpaired electrons) that attack and shred the bacteria's DNA, proteins, and cell membranes. The bacteria's DNA breaks into fragments, the bacteria cannot copy themselves, and they die. Together, ceftriaxone and metronidazole cover almost all the bacteria that cause cholecystitis.

1. Both drugs are given intravenously (through an IV) and enter the bloodstream rapidly.
2. Ceftriaxone travels to the gallbladder, bile, and surrounding tissue, where it binds to penicillin-binding proteins (PBPs) on the cell membrane of aerobic bacteria.
3. Ceftriaxone blocks PBPs from cross-linking peptidoglycan strands, so the bacterial cell wall becomes weak and incomplete.
4. Water flows into the aerobic bacteria by osmosis, they swell, and they burst (lysis).
5. Metronidazole enters anaerobic bacteria in the gallbladder and bile ducts.
6. Inside the bacteria, nitroreductase enzymes (which exist only in anaerobes) add electrons to metronidazole, activating it (reduction reaction).
7. Activated metronidazole forms short-lived toxic free radicals (nitro radical anions) that react with DNA, breaking the double helix into fragments.
8. The bacteria's DNA is destroyed, so they cannot reproduce, and the toxic radicals also damage proteins and lipids in the bacterial cell, causing the bacteria to die (bactericidal effect).
9. Your immune system (neutrophils, macrophages) clears the dead bacteria, and the infection resolves.

SAFETY WATCH

Ceftriaxone: Allergic reactions (rash, hives, itching, swelling, trouble breathing, anaphylaxis) are possible—people with penicillin allergy have about 5–10% chance of also reacting to ceftriaxone (cross-reactivity); tell your doctor about any antibiotic allergies before starting. If anaphylaxis occurs, treatment is immediate epinephrine and supportive care. · Ceftriaxone can cause diarrhea, including *Clostridioides difficile* infection (C. diff), which causes severe watery or bloody diarrhea, cramping, and fever—report any severe diarrhea immediately. · Ceftriaxone can form crystals (precipitates) in the gallbladder (biliary sludge) or kidneys, especially in dehydrated patients or those getting high doses—staying well-hydrated reduces this risk. · Do NOT give ceftriaxone to newborns (especially premature babies or those with yellowing of the skin and eyes (jaundice)) because it can displace bilirubin from protein binding in the blood, leading to kernicterus (brain damage from high bilirubin)—this is not a concern in adults. · Ceftriaxone can rarely cause destroying red blood cells (hemolytic) anemia (red blood cells break apart) or low white blood cell counts—your team may check a complete blood count (CBC) during treatment. · Metronidazole: Do NOT drink any alcohol while taking metronidazole and for at least 48 hours (2 full days) after the last dose—metronidazole blocks an enzyme (aldehyde dehydrogenase) that breaks down alcohol, so alcohol builds up and causes a disulfiram-like reaction: severe nausea, vomiting, flushing (red, hot face), pounding headache, chest pain, fast heartbeat, and trouble breathing. This reaction can be dangerous. · Metronidazole commonly causes a metallic or bitter taste in the mouth and mild nausea—these usually go away after treatment ends. · Rarely, metronidazole causes peripheral neuropathy (nerve damage in the hands and feet) with prolonged use—symptoms include tingling, numbness, burning, or weakness; report any new numbness or tingling immediately, as stopping the drug early may prevent permanent damage. · Very rare: metronidazole can cause central nervous system toxicity (encephalopathy) with high doses or long treatment—symptoms include confusion, trouble speaking, trouble walking (ataxia), seizures, and abnormal MRI findings (lesions in the cerebellum or brainstem); this usually reverses when the drug is stopped. · Metronidazole can darken urine (harmless) and may interfere with certain lab tests (like liver enzyme tests)—tell your lab staff you are taking it. · Metronidazole can interact with warfarin (a blood thinner), increasing bleeding risk—if you take warfarin, your INR (a blood test that measures clotting time) will be checked more often and your warfarin dose may be adjusted.

Red flags

- Rigid belly, rebound tenderness, or guarding—signs the gallbladder may have torn open and bile is leaking into the belly (peritonitis)

- Low blood pressure, racing heart, or confusion—signs of septic shock from infection in the bloodstream
- Gas bubbles in the gallbladder wall on ultrasound or CT (emphysematous cholecystitis)—much higher risk the tissue is dying (gangrene) and will tear open, especially in people with diabetes
- Yellow skin and eyes with high bilirubin level—suggests a stone is blocking the common bile duct or pressing on it (Mirizzi syndrome)
- Severe pain that seems worse than what the physical exam shows—raises concern for dead gallbladder tissue (gangrenous cholecystitis) or blood flow cut off (ischemia)

Nursing priorities

1. Start intravenous normal saline or lactated Ringer solution at 125–150 mL per hour and keep the patient NPO (nothing by mouth). — The inflamed gallbladder needs rest; eating or drinking makes it squeeze and worsens pain and pressure—IV fluids prevent dehydration from vomiting and maintain blood pressure while the patient waits for surgery.
2. Give the first dose of broad-spectrum IV antibiotics within 1 hour: ceftriaxone 1–2 grams plus metronidazole 500 mg, or piperacillin-tazobactam 3.375 grams. — Bacteria (usually *E. coli*, *Klebsiella*, or *Enterococcus*) grow rapidly in trapped bile—early antibiotics stop the infection from spreading into the bloodstream (sepsis) and reduce the chance the gallbladder wall will die (gangrene) before surgery.
3. Assess vital signs every 1–2 hours and watch for fever above 101°F, heart rate above 110, blood pressure below 90 systolic, or oxygen saturation below 94 percent. — Rising fever and heart rate with falling blood pressure signal worsening sepsis or septic shock (infection overwhelming the body)—catching these early lets the team give more fluid, start vasopressors (medicines that raise blood pressure), and move surgery up.
4. Perform a focused abdominal exam every 4 hours: palpate gently for Murphy sign, check for rebound tenderness, guarding, or a rigid belly. — Murphy sign (the patient gasps and stops breathing in when you press the right upper belly during deep inspiration) confirms gallbladder inflammation—new rigidity or rebound means the gallbladder may have perforated and bile is irritating the abdominal lining (peritonitis), requiring emergency surgery.
5. Administer IV pain medicine (ketorolac 15–30 mg every 6 hours or morphine 2–4 mg every 2–4 hours) and an anti-nausea drug (ondansetron 4 mg IV). — Severe pain triggers a stress response that raises heart rate and blood pressure, making the patient sicker—controlling pain also lets you do a better exam because the patient can relax their belly muscles instead of guarding.

6. Monitor intake and output hourly; report urine output below 30 mL per hour or dark, concentrated urine. — Low urine output means the kidneys are not getting enough blood flow from dehydration, sepsis, or low blood pressure—early detection prevents acute kidney injury (sudden kidney failure) and guides how much IV fluid to give.
7. Check the first set of labs: complete blood count (CBC) for white count above 10,000 cells per microliter, comprehensive metabolic panel (CMP) for elevated bilirubin or liver enzymes, and lipase to rule out pancreatitis. — High white count confirms infection; bilirubin above 2 mg per deciliter suggests a stone blocking the common bile duct; lipase above three times normal means pancreatitis (pancreas inflammation) from a passing stone—these results decide if the patient needs ERCP before gallbladder surgery.
8. Prepare the patient for urgent ultrasound of the right upper abdomen, watching for a thickened gallbladder wall, pericholecystic fluid (fluid around the gallbladder), or stones. — Ultrasound is the first imaging test because it is fast, safe, and 95 percent accurate for seeing gallstones and signs of inflammation—a thickened wall (over 4 millimeters) and fluid around the gallbladder confirm acute cholecystitis and help the surgeon plan the operation.

Sources

- Tokyo Guidelines 2018 (TG18)
- American College of Gastroenterology
- World Society of Emergency Surgery 2020
- American College of Surgeons

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