Acute cholecystitis: Pathogenesis, clinical features, and diagnosis

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INTRODUCTION — Acute cholecystitis predominantly occurs as a complication of gallstone disease and typically develops in patients with a history of symptomatic gallstones. In a systematic review, it was seen in 6 to 11 percent of patients with symptomatic gallstones over a median follow-up of 7 to 11 years [1]. (See "Uncomplicated gallstone disease in adults", section on 'Natural history'.)

This topic will review the pathogenesis, clinical manifestations, and diagnosis of acute cholecystitis. The management of uncomplicated gallstone disease, acalculous cholecystitis, and the treatment of acute cholecystitis are discussed separately. (See "Uncomplicated gallstone disease in adults" and "Acalculous cholecystitis" and "Treatment of acute calculous cholecystitis".)

DEFINITIONS — The term cholecystitis refers to inflammation of the gallbladder. It may develop acutely in association with gallstones (acute cholecystitis) or, less often, without gallstones (acalculous cholecystitis). It may also develop over time and be discovered histologically following cholecystectomy (chronic cholecystitis).

Acute cholecystitis — Acute cholecystitis refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation that is usually related to gallstone disease.

Acalculous cholecystitis — Acalculous cholecystitis is clinically identical to acute cholecystitis but is not associated with gallstones and usually occurs in critically ill patients. It accounts for approximately 10 percent of cases of acute cholecystitis and is associated with high morbidity and mortality rates [2]. (See "Acalculous cholecystitis".)

Chronic cholecystitis — Chronic cholecystitis is the term used to describe chronic inflammatory cell infiltration of the gallbladder seen on histopathology. It is almost invariably associated with the presence of gallstones and is thought to be the result of mechanical irritation or recurrent attacks of acute cholecystitis leading to fibrosis and thickening of the gallbladder [3-5]. Its presence does not correlate with symptoms since patients with...
extensive chronic inflammatory cell inflammation may have only minimal symptoms, and there is no evidence that chronic cholecystitis increases the risk for future morbidity [6]. Hence, the clinical significance of this entity is questionable. (See "Uncomplicated gallstone disease in adults").

Some authors use the phrase "chronic cholecystitis" when referring to gallbladder dysfunction as a cause of abdominal pain [7]. It is more appropriate in this instance to refer to the condition based on the disorder present, such as pain due to gallstone disease, pain due to biliary dyskinesia (which is attributed to sphincter of Oddi dysfunction), or pain due to functional gallbladder disorder (also called gallbladder dyskinesia). (See "Clinical manifestations and diagnosis of sphincter of Oddi dysfunction" and "Functional gallbladder disorder in adults").

**PATHOGENESIS** — Acute cholecystitis occurs in the setting of cystic duct obstruction. However, in contrast to biliary colic, the development of acute cholecystitis is not fully explained by cystic duct obstruction alone. Studies suggest that an additional irritant (possibly lysolecithin) is required to develop gallbladder inflammation. Once inflammation of the gallbladder begins, additional inflammatory mediators are released, further propagating gallbladder inflammation. In many patients, infection of the biliary system is also involved in the development of acute cholecystitis.

Studies in animals have demonstrated that ligation of the cystic duct alone does not result in acute cholecystitis [8,9]. However, acute cholecystitis can be produced by blocking the cystic duct, followed by deliberate irritation of the gallbladder mucosa (either mechanically with an indwelling catheter or by infusion of an irritant).

One such irritant used in experimental models, lysolecithin, is produced from lecithin, a normal constituent of bile. The production of lysolecithin from lecithin is catalyzed by phospholipase A, which is present in gallbladder mucosa. This enzyme may be released into the gallbladder following trauma to the gallbladder wall from an impacted gallstone [9]. Supporting this hypothesis is the observation that lysolecithin (normally absent in bile) is detectable in gallbladder bile in patients with acute cholecystitis [10].

Inflammatory mediators are released in response to gallbladder inflammation and further propagate the inflammation [11]. Prostaglandins, which are involved in gallbladder contraction and fluid absorption, probably play a central role in this process. In experimental models using human gallbladder tissue, the main prostaglandins synthesized by inflamed human gallbladder microsomes were prostaglandin E2 and 6-keto-prostaglandin F1 alpha, the concentrations of which were increased four times above normal [12]. The prostaglandin hypothesis is supported by the observation that prostaglandin inhibitors relieve biliary colic and can reduce intraluminal cystic pressure [13-15].
Infection of bile within the biliary system probably has a role in the development of cholecystitis; however, not all patients with cholecystitis have infected bile. This observation was illustrated in a study of 467 subjects in whom bile samples were obtained from the gallbladder and common bile duct for aerobic and anaerobic culture [16]. Patients with a variety of hepatobiliary diseases and a healthy control group were included. Patients with gallstones, acute cholecystitis, and hydropic gallbladder had similar rates of positive cultures in the gallbladder and common bile duct, ranging from 22 to 46 percent; cultures were generally sterile in healthy subjects. The main species isolated were Escherichia coli, Enterococcus, Klebsiella, and Enterobacter.

Histologic changes of the gallbladder in acute cholecystitis can range from mild edema and acute inflammation to necrosis and gangrene. Occasionally, prolonged impaction of a stone in the cystic duct can lead to a distended gallbladder that is filled with colorless, mucoid fluid. This condition, known as a mucocele with white bile (hydrops), is due to the absence of bile entry into the gallbladder and absorption of all the bilirubin within the gallbladder.

**CLINICAL MANIFESTATIONS** — The clinical manifestations of acute cholecystitis include prolonged (more than four to six hours), steady, severe right upper quadrant or epigastric pain, fever, abdominal guarding, a positive Murphy's sign, and leukocytosis.

**History** — Patients with acute cholecystitis typically complain of abdominal pain, most commonly in the right upper quadrant or epigastrium. The pain may radiate to the right shoulder or back. Characteristically, acute cholecystitis pain is steady and severe. Associated complaints may include fever, nausea, vomiting, and anorexia. There is often a history of fatty food ingestion one hour or more before the initial onset of pain. The episode of pain is typically prolonged (greater than four to six hours).

**Physical examination** — Patients with acute cholecystitis are usually ill appearing, febrile, and tachycardic, and lie still on the examining table because cholecystitis is associated with true local parietal peritoneal inflammation that is aggravated by movement. Abdominal examination usually demonstrates voluntary and involuntary guarding. Patients frequently will have a positive Murphy's sign. (See 'Murphy's sign' below.)

Patients with complications may have signs of sepsis (gangrene), generalized peritonitis (perforation), abdominal crepitus (emphysematous cholecystitis), or bowel obstruction (gallstone ileus). (See 'Complications' below and "Sepsis and the systemic inflammatory response syndrome: Definitions, epidemiology, and prognosis", section on 'Sepsis' and "Diagnostic approach to abdominal pain in adults", section on 'Peritonitis' and "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults", section on 'Gallstones or foreign body' and "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults", section on 'Clinical presentations'.)
Laboratory evaluation — Patients typically have a leukocytosis with an increased number of band forms (ie, a left shift). Elevation in the serum total bilirubin and alkaline phosphatase concentrations are not common in uncomplicated acute cholecystitis since biliary obstruction is limited to the gallbladder; if present, they should raise concerns about complicating conditions such as cholangitis, choledocholithiasis, or Mirizzi syndrome (a gallstone impacted in the distal cystic duct causing extrinsic compression of the common bile duct) (image 1). (See "Mirizzi syndrome".)

However, there have been reports of mild elevations in serum aminotransferases and amylase, along with hyperbilirubinemia and jaundice, even in the absence of these complications [17]. These abnormalities may be due to the passage of small stones, sludge, or pus.

In patients with emphysematous cholecystitis, mild to moderate unconjugated hyperbilirubinemia may be present because of hemolysis induced by clostridial infection. (See 'Emphysematous cholecystitis' below.)

DIAGNOSIS — Acute cholecystitis should be suspected in a patient presenting with right upper quadrant or epigastric pain, fever, and a leukocytosis. A positive Murphy's sign supports the diagnosis [18]. However, history, physical examination, and laboratory test findings are not sufficient to establish the diagnosis. Confirmation of the diagnosis requires demonstration of gallbladder wall thickening or edema, a sonographic Murphy's sign, or failure of the gallbladder to fill during cholescintigraphy (algorithm 1). In most cases, the diagnosis can be confirmed with an abdominal ultrasound. If the diagnosis remains unclear, cholescintigraphy can be obtained.

Murphy's sign — Patients with acute cholecystitis frequently have a positive "Murphy's sign". To check for a Murphy's sign, the patient is asked to inspire deeply while the examiner palpates the area of the gallbladder fossa just beneath the liver edge. Deep inspiration causes the gallbladder to descend toward and press against the examining fingers, which in patients with acute cholecystitis commonly leads to increased discomfort and the patient catching his or her breath.

In one study, using cholescintigraphy as the gold standard, the sensitivity and specificity of a positive Murphy's sign were 97 and 48 percent, respectively [19]. However, the sensitivity may be diminished in the elderly [20].

Imaging studies — Physical examination alone cannot determine which abdominal viscera is the source of inflammation and pain. Thus, patients presenting with clinical features suggestive of acute cholecystitis should undergo abdominal imaging to confirm the diagnosis. Ultrasonography is usually the first test obtained and can often establish the
diagnosis. Nuclear cholescintigraphy may be useful in cases in which the diagnosis remains uncertain after ultrasonography.

**Ultrasonography** — The presence of stones in the gallbladder in the clinical setting of right upper quadrant abdominal pain and fever supports the diagnosis of acute cholecystitis but is not diagnostic. Additional sonographic features include:

- Gallbladder wall thickening (greater than 4 to 5 mm) or edema (double wall sign) (image 2).
- A "sonographic Murphy's sign" is similar to the Murphy's sign elicited during abdominal palpation, except that the positive response is observed during palpation with the ultrasound transducer. This is more accurate than hand palpation because it can confirm that it is indeed the gallbladder that is being pressed by the imaging transducer when the patient catches his or her breath.

Several studies have evaluated the accuracy of ultrasonography in the diagnosis of acute cholecystitis [18,21-26]. A particularly informative systematic review summarized the results of 30 studies of ultrasonography for gallstones and acute cholecystitis [23]. Adjusted sensitivity and specificity for diagnosis of acute cholecystitis were 88 percent (95% confidence interval [CI] 0.74 to 1.00) and 80 percent (95% CI 0.62 to 0.98), respectively. The sensitivity and specificity of ultrasonography for detection of gallstones are approximately 84 (95% CI 0.76 to 0.92) and 99 percent (95% CI 0.97 to 1.00), respectively [23]. Ultrasonography may not detect small stones or sludge as illustrated by a study that compared ultrasonography with direct percutaneous mini-endoscopy in patients who had undergone topical gallstone dissolution [27]. Ultrasonography was negative in 12 of 13 patients in whom endoscopy demonstrated 1 to 3 mm stones or fragments (picture 1) [27].

In patients with emphysematous cholecystitis, the ultrasound report may erroneously note the presence of "overlying bowel gas making adequate visualization of the gallbladder difficult", when in reality, this reflects air in the wall of the gallbladder. (See 'Emphysematous cholecystitis' below.)

**Cholescintigraphy (HIDA scan)** — Cholescintigraphy using 99mTc-hepatic iminodiacetic acid (generically referred to as a HIDA scan) is indicated if the diagnosis remains uncertain following ultrasonography. Technetium labeled hepatic iminodiacetic acid (HIDA) is injected intravenously and is then taken up selectively by hepatocytes and excreted into bile. If the cystic duct is patent, the tracer will enter the gallbladder, leading to its visualization without the need for concentration. The HIDA scan is also useful for demonstrating patency of the common bile duct and ampulla. Normally, visualization of contrast within the common bile duct, gallbladder, and small bowel occurs within 30 to 60 minutes (image 3). The test is
positive if the gallbladder does not visualize. This occurs because of cystic duct obstruction, usually from edema associated with acute cholecystitis or an obstructing stone (image 4).

Cholescintigraphy has a sensitivity and specificity for acute cholecystitis of approximately 97 and 90 percent, respectively [23,26,28]. Cystic duct obstruction with a stone or tumor in the absence of acute cholecystitis can cause a false positive test. Conditions that can cause false positive results despite a non-obstructed cystic duct include:

- Severe liver disease, which may lead to abnormal uptake and excretion of the tracer.
- Fasting patients receiving total parenteral nutrition, in whom the gallbladder is already maximally full due to prolonged lack of stimulation.
- Biliary sphincterotomy, which may result in low resistance to bile flow, leading to preferential excretion of the tracer into the duodenum without filling of the gallbladder.
- Hyperbilirubinemia, which may be associated with impaired hepatic clearance of iminodiacetic acid compounds. Newer agents commonly used in cholescintigraphy (diisopropyl and m-bromotrimethyl iminodiacetic acid) have generally overcome this limitation [29].

False negative results are uncommon since most patients with acute cholecystitis have obstruction of the cystic duct. When they occur, they may be due to incomplete cystic duct obstruction.

**Morphine cholescintigraphy** — A modified version of the HIDA scan has been described in which patients are given intravenous morphine during the examination. Morphine increases sphincter of Oddi pressure, thereby causing a more favorable pressure gradient for the radioactive tracer to enter the cystic duct. This modification is thought to be particularly useful in critically ill patients, in whom standard HIDA scanning may be associated with false positive results [30,31]. However, the test has not been well standardized and has not gained wide acceptance.

**Magnetic resonance cholangiography** — Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive technique for evaluating the intrahepatic and extrahepatic bile ducts (image 5). Its role in the diagnosis of acute cholecystitis was evaluated in a series that included 35 patients with symptoms of acute cholecystitis who underwent both ultrasound and MRCP prior to cholecystectomy [7]. MRCP was superior to ultrasound for detecting stones in the cystic duct (sensitivity 100 versus 14 percent) but was less sensitive than ultrasound for detecting gallbladder wall thickening (sensitivity 69 versus 96 percent). At the present time, its role in the diagnosis of acute cholecystitis should remain within clinical trials. However, MRCP may be appropriate if there is concern that the patient may have a stone in the common bile duct. (See "Magnetic resonance cholangiopancreatography".)
**Computed tomography** — Abdominal computed tomography (CT) is usually unnecessary in the diagnosis of acute cholecystitis, although it can easily demonstrate gallbladder wall edema associated with acute cholecystitis ([image 6](#image6)). Other CT findings include pericholecystic stranding and fluid, and high-attenuation bile [32,33]. However, CT may fail to detect gallstones because many stones are isodense with bile ([image 7](#image7)) [34,35]. CT can be useful when complications of acute cholecystitis (such as emphysematous cholecystitis or gallbladder perforation) are suspected or when other diagnoses are being considered. (See 'Complications' below.)

**Oral cholecystography** — Oral cholecystography has no role in the diagnosis of acute cholecystitis since it cannot show gallbladder wall edema and requires days to complete. (See "Uncomplicated gallstone disease in adults", section on 'Oral cholecystography'.)

**DIFFERENTIAL DIAGNOSIS** — The greatest initial challenge in the diagnosis of acute cholecystitis is distinguishing it from the more benign condition of biliary colic. Biliary colic is usually caused by the gallbladder contracting in response to a fatty meal, pressing a stone against the gallbladder outlet or cystic duct opening. This then results in increased intra-gallbladder pressure and pain. As in acute cholecystitis, biliary colic causes pain in the right upper quadrant. However, unlike acute cholecystitis, the pain is entirely visceral in origin, without true gallbladder wall inflammation, so peritoneal signs are absent. In addition, patients with biliary colic are afebrile with normal laboratory studies. As the gallbladder relaxes, the stones often fall back from the cystic duct. As a result, the attack reaches a crescendo over a number of hours and then resolves completely. (See "Uncomplicated gallstone disease in adults", section on 'Biliary colic'.)

Most patients who develop acute cholecystitis have had previous attacks of biliary colic, which may further confuse the diagnosis or lead patients to delay seeking medical attention. The following features may help to distinguish an attack of biliary colic from acute cholecystitis. However, such patients usually require imaging studies to help establish the diagnosis:

- The pain of biliary colic typically reaches a crescendo, and then resolves completely. Pain resolution occurs when the gallbladder relaxes, permitting stones to fall back from the cystic duct. An episode of right upper quadrant pain lasting for more than four to six hours should raise suspicion for acute cholecystitis.
- Patients with constitutional symptoms such as malaise or fever are more likely to have acute cholecystitis.

Symptoms that are not suggestive of a biliary etiology include fatty food intolerance not in the form of pain, nausea not in association with pain, pain only a few minutes after a meal, irregular bowel habits, or belching [36,37].
A variety of other conditions can give rise to symptoms in the upper abdomen, which may be confused with biliary colic or acute cholecystitis. These include:

- Acute pancreatitis.
- Appendicitis.
- Acute hepatitis.
- Peptic ulcer disease.
- Nonulcer dyspepsia.
- Irritable bowel disease.
- Functional gallbladder disorder.
- Sphincter of Oddi dysfunction.
- Diseases of the right kidney.
- Right-sided pneumonia.
- Fitz-Hugh-Curtis syndrome (perihepatitis caused by gonococcal infection). Right upper quadrant pain with fever and even a possible positive Murphy's sign in patients at high risk for sexually transmitted diseases should raise this possibility. The HIDA scan is usually negative, but pericholecystic fluid may be confused with acute cholecystitis (image 8).
- Subhepatic or intraabdominal abscess.
- Perforated viscus.
- Cardiac ischemia.
- Black widow spider envenomation [38].

These conditions can usually be differentiated by the clinical setting in which they occur and by obtaining the appropriate diagnostic studies. (See "Differential diagnosis of abdominal pain in adults", section on 'Upper abdominal pain syndromes', and "Diagnostic approach to abdominal pain in adults", section on 'Acute abdominal pain'.)

**COMPLICATIONS** — Left untreated, symptoms of cholecystitis may abate within 7 to 10 days. However, complications are common, so patients with suspected acute cholecystitis require definitive treatment (eg, cholecystectomy). The most common complication is the development of gallbladder gangrene (up to 20 percent of cases) (image 9) with subsequent perforation (2 percent of cases) [39]. (See "Treatment of acute calculous cholecystitis".)

**Gangrene** — Gangrenous cholecystitis is the most common complication of cholecystitis, particularly in older patients, patients with diabetes, or those who delay seeking therapy [39]. The presence of a sepsis-like picture in addition to the other symptoms of cholecystitis suggests the diagnosis, but gangrene may not be suspected preoperatively. (See "Sepsis and the systemic inflammatory response syndrome: Definitions, epidemiology, and prognosis", section on 'Sepsis'.)
Perforation — Perforation of the gallbladder usually occurs after the development of gangrene. It is often localized, resulting in a pericholecystic abscess (image 10). Less commonly, perforation is free into the peritoneum, leading to generalized peritonitis (image 11). Such cases are associated with a high mortality rate. (See "Diagnostic approach to abdominal pain in adults", section on 'Peritonitis'.)

Cholecystoenteric fistula — A cholecystoenteric fistula may result from perforation of the gallbladder directly into the duodenum or jejunum. Fistula formation is more often due to long standing pressure necrosis from stones than to acute cholecystitis [40].

Gallstone ileus — Passage of a gallstone through a cholecystoenteric fistula may lead to the development of mechanical bowel obstruction, usually in the terminal ileum (gallstone ileus) (image 12) [41]. (See "Gallstone ileus" and "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults", section on 'Clinical presentations' and "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults", section on 'Gallstones or foreign body'.)

Emphysematous cholecystitis — Emphysematous cholecystitis is caused by secondary infection of the gallbladder wall with gas-forming organisms (such as Clostridium welchii) (image 13) [42,43]. Other organisms that may be isolated include Escherichia coli (15 percent), staphylococci, streptococci, Pseudomonas, and Klebsiella [43].

Affected patients are often men in their fifth to seventh decade [43], and approximately one-third to one-half have diabetes [43-45]. Gallstones are present in about one-half of patients.

Like other patients with acute cholecystitis, patients with emphysematous cholecystitis usually present with right upper quadrant pain, nausea, vomiting, and low-grade fever. Peritoneal signs are usually absent, but crepitus in the abdominal wall adjacent to the gall bladder may rarely be detected. When such crepitis is present, it is an important clue to the diagnosis. Mild to moderate unconjugated hyperbilirubinemia may be present (caused by hemolysis induced by clostridial infection). The ultrasound report may erroneously note the presence of "overlying bowel gas making adequate visualization of the gallbladder difficult", when in reality, this reflects air in the wall of the gallbladder.

Emphysematous cholecystitis often heralds the development of gangrene, perforation, and other complications [43-45]. In a review of 20 patients with emphysematous cholecystitis, gallbladder perforation occurred in seven, pericholecystic abscess in nine, and bile peritonitis in three [45].

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- Basics topics (see "Patient information: Gallstones (The Basics)" and "Patient information: Gallbladder removal (cholecystectomy) (The Basics)"
- Beyond the Basics topics (see "Patient information: Gallstones (Beyond the Basics)"

**SUMMARY AND RECOMMENDATIONS**

- Acute cholecystitis refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation and is usually related to gallstone disease. (See 'Definitions' above.)
- Patients with acute cholecystitis typically complain of abdominal pain, most commonly in the right upper quadrant or epigastrium. The pain may radiate to the right shoulder or back. Characteristically, acute cholecystitis pain is prolonged (more than four to six hours), steady, and severe. Associated complaints may include nausea, vomiting, and anorexia. (See 'Clinical manifestations' above.)
- Acute cholecystitis should be suspected in a patient presenting with right upper quadrant or epigastric pain, fever, and a leukocytosis. A positive Murphy's sign supports the diagnosis. However, history, physical examination, and laboratory test findings are not sufficient to make the diagnosis. Confirmation of the diagnosis requires demonstration of gallbladder wall thickening or edema, a sonographic Murphy's sign, or failure of the gallbladder to fill during cholescintigraphy (algorithm 1). (See 'Diagnosis' above.)
- Acute cholecystitis must be distinguished from the more benign condition of biliary colic, which presents with the same type of pain. Most patients who develop acute cholecystitis have had previous attacks of biliary colic. The following features may help to distinguish an attack of biliary colic from acute cholecystitis, though such patients usually require imaging studies to help establish the diagnosis (see 'Differential diagnosis' above and "Uncomplicated gallstone disease in adults", section on 'Biliary colic'):
  - The pain of biliary colic typically reaches a crescendo and then resolves completely. Pain resolution occurs when the gallbladder relaxes, permitting stones to fall back from the cystic duct. An episode of right upper quadrant pain
lasting for more than four to six hours should raise suspicion for acute cholecystitis.

• Patients with constitutional symptoms such as malaise or fever are more likely to have acute cholecystitis.

• Patients with biliary colic do not have signs of peritonitis on examination and have normal laboratory tests.

● Left untreated, symptoms of cholecystitis may abate within 7 to 10 days. However, complications are common, so patients with suspected acute cholecystitis require definitive treatment (e.g., cholecystectomy). The most common complication of acute cholecystitis is the development of gallbladder gangrene (up to 20 percent of cases) with subsequent perforation (2 percent of cases). (See 'Complications' above and "Treatment of acute calculous cholecystitis".)

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REFERENCES


Ultrasound from a patient with acute cholecystitis and Mirizzi syndrome

Transabdominal ultrasound from a patient with acute cholecystitis and Mirizzi syndrome. The patient presented with right upper quadrant pain and jaundice. Acute cholecystitis and Mirizzi syndrome are confirmed by the ultrasound findings of a positive sonographic Murphy's sign (pain with compression of the gallbladder by the ultrasound probe), a large shadowing stone impacted in the infundibulum of the gallbladder (white arrow), cholestasis with sludge (yellow arrowhead), and a dilated common hepatic duct (white arrowheads in B). Graphic 86878 Version 1.0
Algorithm for the diagnosis of acute cholecystitis

GB: gallbladder; U/S: ultrasound. Graphic 50032 Version 3.0

Acute cholecystitis with pericholecystic fluid seen on ultrasound

![Algorithm Image]

GB: gallbladder; U/S: ultrasound. Graphic 50032 Version 3.0

Acute cholecystitis with pericholecystic fluid seen on ultrasound
(A) Longitudinal view of the gallbladder showing small shadowing stones in the dependent part of the gallbladder (green arrow). The ultrasound also shows a thickened wall in both the longitudinal projection (white arrow) and transverse projection (B). (B) A small amount of pericholecystic fluid is noted (yellow arrow). (C) The Doppler study shows an increase in blood flow to the wall (red arrow) reminiscent of the hyperemia of an inflammatory process. These findings are consistent with acute calculous cholecystitis. Graphic 83042 Version 2.0

**Percutaneous gallbladder endoscopy showing gallstone**

Percutaneous gallbladder endoscopy shows a small gallstone that was not detected on ultrasonography. *Courtesy of Salam Zakko, MD, FACP.* Graphic 65714 Version 2.0

**Normal HIDA scan**

![Normal HIDA scan](image-url)
This is an example of a normal 99mTc-hepatic iminodiacetic acid (HIDA) scan and shows early filling of the gallbladder at 15 minutes (white arrow) and complete filling by 25 minutes (white arrowhead), indicating a patent cystic duct. Graphic 59241 Version 3.0

**HIDA scan in a patient with acute cholecystitis**

The hepatic iminodiacetic acid (HIDA) scan is abnormal and shows absence of filling of the gallbladder, indicating obstruction of the cystic duct. The duodenum starts to fill with radioisotope at about 20 minutes (white arrow). The radioisotope flows directly into the duodenum (white arrow) starting at 20 minutes. The gallbladder never fills during the course of the 60 minute examination. These findings are consistent with the diagnosis of acute cholecystitis. Graphic 86879 Version 1.0
Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) in a patient with acute cholecystitis

MRI and MRCP images from a patient with acute cholecystitis. Contrast enhanced (A) and fat saturated T2-weighted imaging (B) reveal a hyperemic gallbladder wall (white arrowheads). Multiple small stones are noted lying dependently in the base of the gallbladder (white arrow). The MRCP in the coronal projections (C and D) reveals accumulation of pericholecystic fluid (short yellow arrows). These findings are consistent with the diagnosis of acute cholecystitis Graphic 86864 Version 2.0

Computed tomographic (CT) scan from a patient with acute cholecystitis
The CT scan shows a distended gallbladder with an edematous and hyperemic wall (thick arrow) and inflammatory induration in the fat surrounding the gallbladder (arrowheads). A calcified stone is visible lying dependently at the base of the gallbladder (thin arrow). Graphic 77336 Version 3.0

**Computed tomographic (CT) scan and ultrasound in a patient with acute cholecystitis**

The CT scan (A and B) shows a thick walled and distended gallbladder (thick white arrow) with pericholecystic induration (yellow arrowheads). However, it does not reveal gallstones. The radiologic differential diagnosis includes acute calculous and acalculous cholecystitis. The ultrasound (C and D) confirms the presence of a distended gallbladder (thick white arrow) with stones (black arrow), and the presence of tumefactive sludge (short yellow arrow). The thin white arrow shows a small amount of fluid in the gallbladder fossa. These findings are consistent with acute calculous cholecystitis. Graphic 86866 Version 1.0
Fitz-Hugh Curtis syndrome

A CT-scan image (left) of a young female with Fitz-Hugh Curtis Syndrome. Note the contracted gallbladder in the very center giving the appearance of a gallstone and the large amount of pericholecystic fluid around it. The ultrasound image (right) confirms the contracted gallbladder with the double wall sign. Courtesy of Salam F Zakko, MD, FACP. Graphic 65754 Version 3.0

Gallbladder gangrene on transabdominal ultrasound

Transabdominal ultrasound of a gangrenous gallbladder showing evidence of necrotic and denuded mucosa. The longitudinal view of the base of the gallbladder (A) shows a distended gallbladder, with multiple stones within gallbladder sludge (thin yellow arrow) casting an acoustic shadow (thick yellow arrow). The longitudinal view of the fundus (B) demonstrates denuded mucosa (yellow arrowhead), indicating early necrosis of the gallbladder wall.
Graphic 86863 Version 1.0
Liver abscess complicating acute cholecystitis

Computed tomographic (CT) scan in a patient with acute cholecystitis complicated by perforation and liver abscess formation. (A) The CT scan shows a gall stone (yellow arrow) surrounded by an irregular accumulation of fluid with a hyperemic rim (yellow arrowhead). (B) The fluid can be seen extending from the gallbladder fossa into the liver parenchyma (yellow arrowhead). (C) Percutaneous aspiration of pus confirmed the presence of an abscess and a drain was placed (yellow arrow). Following drainage of the abscess, a small amount of contrast was injected into the decompressed cavity. Graphic 86867 Version 1.0
Contained gallbladder perforation in a patient with acute cholecystitis

Computed tomographic (CT) scan showing a sealed perforation of the gallbladder. Transverse (A) and reformatted coronal projections (B) of the CT scan demonstrate a focal accumulation of fluid near the fundus of the gallbladder (white arrowhead) with significant induration in the pericholecystic fat (yellow arrow). At surgery a necrotic and perforated gallbladder was identified. Graphic 86865 Version 1.0

Gallstone ileus seen on computed tomography (CT) scan

CT scan in a 75-year-old woman with small bowel obstruction due to gallstone ileus. Left panel: Free air is seen in the biliary tree and gallbladder (arrow). Right panel: Dilated loops of small bowel with large gallstone with a calcified rim (arrow) impacted in the terminal ileum. Courtesy of Nezam Afdhal, MD. Graphic 80522 Version 5.0
Emphysematous cholecystitis seen on computed tomographic scan

(A) An axial image of a contrast enhanced computed tomographic (CT) scan demonstrating air within the gallbladder lumen (arrows). (B) A coronal reformat of a contrast enhanced CT demonstrating air within the wall of the gallbladder (arrow).
INTRODUCTION — Acute cholecystitis refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation, which is usually related to gallstone disease (ie, acute calculous cholecystitis). Complications include the development of gangrene and gallbladder perforation, which can be life-threatening. The treatment of acute calculous cholecystitis will be reviewed here. The approach to patients with asymptomatic gallstones, the approach to the pregnant patient with gallstones, and the clinical manifestations and diagnosis of biliary colic, acute cholecystitis and related conditions, such as acalculous and xanthogranulomatous cholecystitis, are discussed separately. (See "Uncomplicated gallstone disease in adults" and "Approach to the patient with incidental gallstones" and "Choledocholithiasis: Clinical manifestations, diagnosis, and management" and "Gallstones in pregnancy" and "Acute cholecystitis: Pathogenesis, clinical features, and diagnosis" and "Acalculous cholecystitis" and "Xanthogranulomatous cholecystitis".)

OVERVIEW OF TREATMENT — Once a patient develops symptoms or complications related to gallstones (biliary colic, acute cholecystitis, cholangitis, and/or pancreatitis), definitive therapy (cholecystectomy, cholecystostomy, endoscopic sphincterotomy, medical gallstone dissolution) is recommended. Without treatment to eliminate the gallstones, the likelihood of subsequent symptoms or complications is high. Complications include the development of gangrene and gallbladder perforation, which can be life-threatening. (See 'Morbidity and mortality' below.)

- In the National Cooperative Gallstone Study, a trial of nonsurgical treatment with chenodiol for biliary tract pain, demonstrated that the risk of recurrent symptoms for untreated patients was approximately 70 percent during the two years following initial presentation [1].
In a cohort study of 25,397 patients from Ontario, Canada with a first episode of uncomplicated acute cholecystitis, 10,304 did not undergo cholecystectomy on their first admission [2]. During a median 3.4 years of follow-up, 24 percent of patients had a gallstone-related event with the majority of events occurring within the first year (88 percent). The risk was highest among 18 to 34-year-old patients. Among the events, 30 percent were for biliary obstruction or pancreatitis.

A review of the United States Medicare database that included 29,818 elderly patients with acute cholecystitis, found a higher risk for mortality over the following two years in patients who were discharged without surgery compared with patients who underwent cholecystectomy in the initial hospitalization (hazard ratio 1.56, 95% CI 1.47-1.65) [3].

Our treatment approach is as follows (algorithm 1):

- Patients with acute cholecystitis should be admitted to the hospital for supportive care, which includes intravenous fluid therapy, correction of electrolyte disorders, and control of pain. Antibiotics may also be indicated. (See 'Supportive care' below.)
- The selection and timing of definitive therapy depends upon the severity of symptoms and the patient's overall risk for cholecystectomy. (See 'Medical risk assessment' below.)
- If gangrene or perforation are suspected, or if the patient develops progressive symptoms and signs such as fever, hemodynamic instability, or intractable pain while on supportive therapy, emergency cholecystectomy or gallbladder drainage may be needed (image 1). (See 'Timing of cholecystectomy' below and 'Indications for surgery in high-risk patients' below.)
- Low-risk patients without emergent indications for intervention generally undergo laparoscopic cholecystectomy preferably during the same admission. (See 'Low-risk patients' below.)
- High-risk patients without emergent indications for intervention are treated with a gallbladder drainage procedure if symptoms do not improve with supportive care. For patients whose medical status can be optimized to allow surgery, cholecystectomy can be considered. (See 'High-risk patients' below.)

SUPPORTIVE CARE — Patients diagnosed with acute calculous cholecystitis should be admitted to the hospital. Patients have often been ill for days prior to seeking medical attention, making intravenous hydration and correction of any associated electrolyte disorders an important initial measure.

Patients should be kept fasting, and although uncommonly needed, those who are vomiting should have placement of a nasogastric tube. (See "Nasogastric and nasoenteric tubes").
**Pain control** — Pain control in patients with acute cholecystitis can usually be achieved with nonsteroidal antiinflammatory drugs (NSAIDs) or opioids. Progression of pain during treatment for acute cholecystitis, despite adequate analgesia, is an indicator of a clinical progression.

We prefer ketorolac (30 to 60 mg adjusted for age and renal function given in a single intramuscular dose) for patients with biliary colic. Treatment usually relieves symptoms within 20 to 30 minutes. Opioids, such as morphine, hydromorphone, or meperidine are appropriate therapy for patients who have contraindications to NSAIDs or who do not achieve adequate pain relief with an NSAID, which may be more common in patients with acute cholecystitis compared with uncomplicated gallstone disease.

It was traditionally thought that meperidine was the opioid of choice in patients with gallstone disease because it has less of an effect on sphincter of Oddi motility than morphine [4-6]. However, a systematic review found that all opioids increase sphincter of Oddi pressure [5]. There are insufficient data to suggest that morphine should be avoided. Morphine has an advantage that it requires less frequent dosing than meperidine, which has a shorter half-life.

**Antibiotics** — Acute cholecystitis is primarily an inflammatory process, but secondary infection of the gallbladder can occur as a result of cystic duct obstruction and bile stasis [7,8]. The rate of empyema and pericholecystic abscess is overall low, but patients can easily develop life-threatening gram negative sepsis from uncomplicated, acute cholecystitis. Thus, antibiotics are commonly administered at the outset to protect against sepsis and wound infection [9]. Studies are conflicting as to whether antibiotics are required for the treatment of uncomplicated, acute cholecystitis [7,8,10-12]. One study of 302 patients showed a lower rate of bacteremia and wound infection, but no difference in the development of empyema of the gallbladder or pericholecystic abscesses with the administration of antibiotics [13]. This is likely due to the obstruction to bile flow that interferes with achieving adequate gallbladder bile concentrations of antibiotics.

Many clinicians routinely administer antimicrobial therapy to all patients diagnosed with acute cholecystitis, which are continued until the gallbladder is removed or the cholecystitis clinically resolves. Others advocate that antimicrobial therapy should only be instituted if sepsis is suspected on the basis of laboratory (more than 12,000 white cells per cubic millimeter) or clinical findings (temperature of more than 38.3°C, <36°C), or in patients with a diagnosis of acute cholecystitis and radiographic findings indicative of gallbladder ischemia or necrosis (eg, air in the gallbladder or gallbladder wall). Routine antibiotics are also recommended in older patients or those with diabetes or immunodeficiency with a diagnosis of acute cholecystitis regardless of these signs [10,14]. (See "Sepsis and the systemic inflammatory response syndrome: Definitions, epidemiology, and prognosis".)
When antibiotic therapy is initiated, the duration of postoperative treatment is generally tailored to the clinical situation. A multicenter trial randomly assigned 414 patients hospitalized for mild or moderate calculous cholecystitis to continue their preoperative antibiotic regimen for five days (2 g amoxicillin plus clavulanic acid, three times daily) or to receive no antibiotics following cholecystectomy [15]. No significant differences in postoperative infection rates (17 versus 15 percent) were found. These results support our current practice of discontinuing antibiotics the day after the cholecystectomy for patients with uncomplicated cholecystitis. Clinical judgement should dictate antibiotic management in more complicated scenarios, such as in the septic postoperative patient.

The need for prophylactic antibiotics at the time of surgery in the absence of clinical symptoms/signs of biliary infection is discussed elsewhere. (See "Open cholecystectomy", section on 'Prophylactic antibiotics' and "Laparoscopic cholecystectomy", section on 'Antibiotics'.)

Empiric antibiotic therapy should include activity against the most common pathogens. In a study of 467 patients, including a control group of 42 with normal biliary trees, positive bile cultures were found in 22 percent of patients with symptomatic gallstones and 46 percent of patients with acute cholecystitis [16]. The most frequent isolates from the gallbladder or common bile duct were Escherichia coli (41 percent), Enterococcus (12 percent), Klebsiella (11 percent), and Enterobacter (9 percent). Empiric antibiotic therapy options and doses are provided in the table (table 1). Antibiotic therapy should subsequently be tailored to culture and susceptibility results when available [7]. Thus, broad-spectrum antibiotics should cover gram-negative organisms and anaerobes. Commonly used regimens are piperacillin-tazobactam, ceftriaxone plus metronidazole, or levofloxacin plus metronidazole.

MEDICAL RISK ASSESSMENT — The American Society of Anesthesiologists (ASA) physical status classification is commonly used to stratify the risk of surgery (table 2) [17]. Other methods to specifically assess cardiac or pulmonary risk are discussed elsewhere. (See "Overview of anesthesia and anesthetic choices" and "Evaluation of cardiac risk prior to noncardiac surgery" and "Evaluation of preoperative pulmonary risk".)

LOW-RISK PATIENTS

Timing of cholecystectomy — Early cholecystectomy, rather than antibiotic therapy and delayed (>7 days after admission) may be preferred among patients who require hospitalization for acute cholecystitis and who are good candidates for cholecystectomy. The bulk of the evidence from large database reviews and randomized trials show that cholecystectomy performed early during the initial hospitalization may be associated with reduced perioperative morbidity and mortality in some patients, and reduces the length of hospital stay and cost [3,18-30]. Early surgery is also easier to perform as local inflammation increases 72 hours past the initial onset of symptoms making dissection less precise,
increasing the severity of surgical complications, and making open conversion more likely. Nevertheless, there are data to suggest that surgery is still safe even after 72 hours of symptom onset [27,31,32].

An early systematic review that included predominantly open, but also laparoscopic cholecystectomy in patients with acute calculous cholecystitis found no significant differences in perioperative morbidity or mortality, but a significantly shorter length of hospital stay for the early surgery group (9.6 versus 5.8 days) [26]. More than 20 percent of patients in the delayed surgery group failed to respond to conservative management or suffered recurrent cholecystitis in the interval period. A coincident Cochrane review (2004) that included five trials limited to laparoscopic cholecystectomy concluded that early laparoscopic cholecystectomy (ranging from immediate cholecystectomy to cholecystectomy within seven days of symptoms) is safe and significantly shortens hospital stay [18]. No significant differences were seen between the groups for the rate of bile duct injury or conversion to open cholecystectomy. An updated Cochrane review (2013) limited to laparoscopic cholecystectomy included two additional trials [28,30], but had similar findings [27]. The incidence of bile duct injury in the early group was 0.4 percent, while that in the delayed group was 0.9 percent, a difference that was not significant. Conversion rates were 19.7 versus 22.1 percent in the early versus late groups, respectively. Among four trials, the total hospital stay was shorter in the early compared with the delayed group (mean difference -4.12 days; 95% CI -5.22 to -3.03). It is important to note that significant complications such as bile duct injury occur rarely, and the included trials (and likely any future clinical trials) were not adequately powered to detect differences in the rates of bile duct injury and other serious complications. Although the Cochrane reviews suggest similar conversion rates for open procedures in patients operated on within seven days, they do not specify how many of the “early surgery” patients were symptomatic for less than 72 hours. Some studies suggest that patients who have surgery more than three days after the onset of symptoms have a higher rate of conversion to open surgery compared with those who have had symptoms for less than three days [33].

A later multicenter trial not included in the Cochrane metaanalyses, the Acute Cholecystitis-early laparoscopic surgery versus antibiotic therapy and Delayed elective Cholecystectomy (ACDC) trial (NCT00447304), randomly assigned patients to surgery within 24 hours of hospital admission (n = 304) or initial antibiotic treatment followed by laparoscopic cholecystectomy delayed more than seven days (n = 314 patients) [23]. The overall rate of morbidity was significantly lower in the immediate compared with delayed cholecystectomy group (11.8 versus 34.4 percent). The rate of conversion to open surgery and mortality did not differ significantly between groups. Mean length of hospital stay (5.4 days versus 10.0 days) and total hospital costs were significantly lower in the immediate cholecystectomy group.
Large database reviews have identified similar benefits for prompt surgical intervention, as well as possible reductions in morbidity and improved late outcomes [22,25,29].

- In a large cohort study from Ontario, Canada, a significantly lower rate of major bile duct injury (0.28 versus 0.53 percent) and shorter length of hospital stay (mean difference -1.9 days) were seen for early compared with delayed cholecystectomy (≥7 days) among 14,220 patients with a first episode of acute cholecystitis [25].
- In a review from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP), those who underwent operation later in the course of admission were more likely to require an open procedure [22].

**Surgical approach** — Laparoscopic cholecystectomy is considered the standard approach for the surgical treatment of acute calculous cholecystitis. Compared with open cholecystectomy, laparoscopic cholecystectomy reduces postoperative pain and significantly shortens hospital length of stay and convalescence, and time away from work, and is preferred by many patients from a cosmetic viewpoint [34-40]. However, the overall serious complication rate in laparoscopic cholecystectomy remains higher than that seen with open cholecystectomy; thus, the threshold for conversion to an open procedure should be low [41,42]. Factors which may lead the surgeon to primarily choose, or convert to, an open approach are discussed in detail elsewhere. (See "Open cholecystectomy", section on 'Indications for open surgery' and "Laparoscopic cholecystectomy", section on 'Intraoperative complications'.)

For selected patients in whom the risk for injury or excessive blood loss is deemed too high to perform cholecystectomy, a cholecystostomy or a subtotal cholecystectomy can be performed. The latter procedure achieves control of the cystic duct at the level of the neck of the gallbladder and leaves the dome of the gallbladder adherent to the liver fossa in situ [43,44]. Biliary leaks can still occur, but these can generally be managed conservatively. (See "Laparoscopic cholecystectomy" and "Complications of laparoscopic cholecystectomy" and "Repair of common bile duct injuries".)

**HIGH-RISK PATIENTS** — Patients categorized as ASA classes III, IV, or V, have perioperative mortality rates ranging from 5 to 27 percent, and are considered high risk for cholecystectomy [17].

For these patients, the risk of cholecystectomy likely outweighs the potential benefits, and an initial nonoperative approach should be undertaken that includes antibiotic therapy and bowel rest. For those who fail to improve, gallbladder drainage should be implemented with the eventual goal of performing cholecystectomy. Once cholecystitis resolves, the patient’s risk for surgery should be reassessed. Patients who have become reasonable candidates for surgery should undergo elective cholecystectomy [45]. Medical management with interval
cholecystectomy only for recurrent acute cholecystitis may be appropriate in some patients [46].

**Gallbladder drainage**—Some form of gallbladder drainage is required for high-risk patients managed conservatively but who show no appreciable improvement and progress to severe symptoms. The goal of drainage is to direct purulent material away from the obstructed gallbladder which also allows for resolution of edema, which often “opens” up the obstructed cystic duct.

Gallbladder drainage can be accomplished via percutaneous, open surgical, or endoscopic approaches. In one retrospective review of 185 patients, 78 percent were treated with percutaneous cholecystostomy, and 22 percent with a tube placed surgically [47]. Over half the patients (57 percent) subsequently underwent laparoscopic cholecystectomy. Regardless of cholecystostomy tube approach, surgical or percutaneous, there were no differences in the proportion of patients who underwent laparoscopic cholecystectomy as definitive treatment.

Percutaneous and endoscopic methods are reviewed in the next sections. Open cholecystostomy is discussed below. (See 'Indications for surgery in high-risk patients' below.)

**Percutaneous**—Gallbladder drainage by percutaneous cholecystostomy in conjunction with antibiotics may be the best initial treatment for very ill patients [48-51]. Percutaneous cholecystostomy is often performed with the intent of delayed cholecystectomy; however, many patients do not actually go on to receive cholecystectomy due to ongoing contraindications [47,52].

A Cochrane review identified only two trials comparing outcomes for patients treated with cholecystostomy for acute cholecystitis [53]. Neither of these trials found any significant differences in mortality for the approaches studied, which included percutaneous cholecystostomy and early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy in one trial, and percutaneous cholecystostomy compared with conservative treatment in the other trial. Although mortality differences have been found in observational studies, in these studies, the healthiest cohort is selected by surgeons for surgical management. As an example, in one retrospective review that included 1918 patients, 30-day mortality after percutaneous cholecystostomy was 15.4 percent, but only 4.5 percent for cholecystectomy [54]. Patients who underwent percutaneous cholecystostomy were older, had a higher ASA classification, more comorbidities, longer hospital stay, more complications, and more readmissions; most ultimately required cholecystectomy. A time-cohort study had similar findings and noted that compared with patients treated with cholecystostomy between 1989 and 1998, a significantly lower
percentage of patients treated between 1998 and 2009 had low ASA classification (zero versus 18 percent) [55].

The technical success of percutaneous cholecystostomy ranges from 82 to 100 percent in various series [48-51]. In a retrospective review, the outcomes of 106 patients with acute cholecystitis (calculous and acalculous) treated by percutaneous cholecystostomy were evaluated over a 10-year period; 67 percent presented to the emergency room and 23 percent were inpatients admitted initially for other conditions [56]. About half in each group had gallstones. After cholecystostomy tube placement, clinical improvement was seen overall in 68 percent, whereas 32 percent showed no improvement or clinically worsened. More patients who presented to the emergency department primarily with acute cholecystitis showed improvement compared with the inpatients (84 versus 34 percent).

Minor complications of percutaneous drainage include bleeding, catheter blockage and dislodgement (10 to 15 percent), and failure to resolve the acute cholecystitis (10 percent) [49,51,57]. In one study, major bleeding complications occurred rarely (0.4 percent) and were no different between patients with and without coagulopathy [57]. Failure is usually related to ineffective drainage due to thick sludge or pus. We generally irrigate the gallbladder contents manually with normal saline through the catheter. If irrigation is ineffective, the percutaneous pigtail catheter can be replaced over a wire with a larger one to achieve more effective irrigation.

Patients who stabilize but continue to be high risk for surgery can be considered for percutaneous gallstone extraction with or without mechanical lithotripsy [58].

**Endoscopic** — Endoscopic transpapillary gallbladder drainage has also been reported in patients with acute cholecystitis in whom percutaneous approaches are contraindicated, or are not anatomically feasible [59,60]. The technique can be technically challenging. In addition, this procedure has all the inherent and occasionally serious complications associated with endoscopic retrograde cholangiography. (See "Endoscopic retrograde cholangiopancreatography: Indications, patient preparation, and complications".)

**Indications for surgery in high-risk patients** — The risk for surgery should be reconsidered once cholecystitis resolves in patients treated conservatively with antibiotics and gallbladder drainage. Patients who have become reasonable candidates for surgery should undergo elective cholecystectomy.

An initial surgical approach may be preferred in some high-risk patients for whom the burden of the ongoing systemic effects of cholecystitis is deemed to be greater than the risk of surgery. A surgical approach may also become necessary if the less-invasive techniques discussed above are not technically feasible, are unsuccessful at providing adequate
drainage, or if the patient does not improve following drainage, which suggests that the gallbladder may have progressed to gangrene.

Laparoscopic cholecystectomy may be the preferred treatment in high-risk patients who require surgery. If cholecystectomy is not feasible, a subtotal cholecystectomy can be performed instead, but if medical risk precludes gallbladder removal, a surgical cholecystostomy tube can be performed through a limited laparotomy in the operating room, or at the bedside in the intensive care unit setting, if necessary. (See "Open cholecystectomy", section on 'Open cholecystostomy tube placement'.)

**MORBIDITY AND MORTALITY** — The overall mortality of a single episode of acute cholecystitis is approximately 3 percent. However, the risk in a given patient depends upon the patient’s health and surgical risk [49]. Mortality is less than 1 percent in young, otherwise healthy patients, but approaches 10 percent in high-risk patients, or in those with complications. Perioperative morbidity and mortality associated with specific treatments are reviewed elsewhere. (See "Open cholecystectomy", section on 'Perioperative morbidity and mortality' and "Laparoscopic cholecystectomy", section on 'Postoperative complications'.)

A study of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database evaluated outcomes following treatment of acute cholecystitis in 5460 patients with and without diabetes [61]. Mortality among 770 patients with diabetes was significantly higher than in the 4690 patients without diabetes (4.4 versus 1.4 percent). The risk for complications including cardiovascular events and renal failure was also significantly increased.

**Prevention of recurrent gallstones** — Following cholecystectomy, or other nonsurgical means to remove gallstones, patients who remain at high risk for developing recurrent gallstones may benefit from certain medical therapies. These are discussed elsewhere. (See "Patient selection for the nonsurgical treatment of gallstone disease", section on 'Prophylaxis in patients at high risk for developing symptomatic gallstone disease'.)

**SUMMARY AND RECOMMENDATIONS**

- Acute cholecystitis refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation, which is usually related to gallstone disease. Once a patient develops acute cholecystitis, definitive therapy aimed at eliminating the gallstones is recommended. Without definitive therapy, the likelihood of recurrent symptoms or complications is high. (See 'Introduction' above and 'Overview of treatment' above.)
- Patients diagnosed with acute cholecystitis should be admitted to the hospital. Initial supportive care includes intravenous fluid therapy, correction of electrolyte disorders, and control of pain. Adequate pain control can usually be achieved with nonsteroidal
antiinflammatory drugs (NSAIDs) or opioids. Patients should be kept fasting and those who are vomiting may need placement of a nasogastric tube. (See ‘Supportive care’ above.)

● Acute cholecystitis is primarily an inflammatory process, but secondary infection of the gallbladder can occur as a result of cystic duct obstruction and bile stasis. Many clinicians routinely administer antimicrobial therapy to all patients diagnosed with acute cholecystitis, which are continued until the gallbladder is removed or the cholecystitis clinically resolves. If sepsis is suspected (laboratory or clinical findings), or radiographic findings are indicative of gallbladder ischemia or necrosis, we suggest empiric antibiotic therapy (Grade 2C). Antibiotic options and doses are provided in the table (table 1). For patients with uncomplicated cholecystitis, we discontinue antibiotics the day after the cholecystectomy. (See ‘Antibiotics’ above.)

● The choice and timing of intervention for acute cholecystitis (cholecystectomy, gallbladder drainage) depends upon the severity of symptoms and the patient’s overall risk of surgery. Drainage options include percutaneous or open cholecystostomy and endoscopic sphincterotomy.

  • Emergent intervention is indicated for patients with:
    - Progressive symptoms and signs such as high fever, hemodynamic instability, or intractable pain in spite of adequate pain medication.
    - Suspicion of gallbladder gangrene or gallbladder perforation

  • For patients without emergent indications for definitive therapy who are low risk for surgery, we recommend cholecystectomy during the initial hospitalization (Grade 1A). Cholecystectomy performed early rather than later in the hospitalization may be associated with reduced perioperative morbidity and mortality. Low-risk patients generally undergo laparoscopic cholecystectomy. Compared with open cholecystectomy, laparoscopic cholecystectomy reduces postoperative pain and significantly shortens the length of hospital stay and convalescence. (See ‘Timing of cholecystectomy’ above and ‘Low-risk patients’ above.)

  • For patients without emergent indications for definitive therapy, and in whom the risk of cholecystectomy outweighs the potential benefits, gallbladder drainage (percutaneous cholecystostomy, endoscopic sphincterotomy, open cholecystostomy) is indicated if symptoms do not improve with supportive care. Once cholecystitis resolves, the patient’s risk for surgery should be reassessed. Patients who have become reasonable candidates for surgery should undergo elective cholecystectomy. Patients who stabilize with a cholecystostomy tube but continue to be at high-risk for surgery can be considered for percutaneous gallstone extraction with or without mechanical lithotripsy. (See ‘Gallbladder drainage’ above.)
Mortality associated with a single episode of acute cholecystitis depends upon the patient's health and surgical risk. Overall mortality is approximately 3 percent, but is less than 1 percent in young, otherwise healthy patients, and approaches 10 percent in high-risk patients, or in those with complications.

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REFERENCES


Treatment of acute cholecystitis

Ruptured gallbladder with biloma
Axial CT scan of the upper abdomen without intravenous but with oral contrast demonstrates a ruptured gallbladder with a collection of bile (biloma) in the gallbladder fossa. Note that there are multiple gallstones that are located outside of the gallbladder. There is also a small amount of fluid around the liver.

*Courtesy of J Pierre Sasson, MD.*

**Graphic 74614 Version 3.0**

**Empiric antibiotic therapy for gram-negative and anaerobic pathogens**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dose (adult)*</th>
</tr>
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<tbody>
<tr>
<td><strong>First choice</strong></td>
<td></td>
</tr>
<tr>
<td>Monotherapy with a beta-lactam/beta-lactamase inhibitor:</td>
<td></td>
</tr>
<tr>
<td>Ampicillin-sulbactam</td>
<td>3 g IV every six hours</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>3.375 or 4.5 g IV every six hours</td>
</tr>
<tr>
<td>Ticarcillin-clavulanate</td>
<td>3.1 g IV every four hours</td>
</tr>
<tr>
<td>Combination third generation cephalosporin PLUS metronidazole:</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone plus</td>
<td>1 g IV every 24 hours or 2 g IV every 12 hours for CNS infections</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500 mg IV every eight hours</td>
</tr>
<tr>
<td><strong>Alternative empiric regimens</strong></td>
<td></td>
</tr>
<tr>
<td>Combination fluoroquinolone PLUS metronidazole:</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin or</td>
<td>400 mg IV every 12 hours</td>
</tr>
<tr>
<td>Levofloxacin plus</td>
<td>500 or 750 mg IV once daily</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500 mg IV every eight hours</td>
</tr>
<tr>
<td>Monotherapy with a carbapenem:</td>
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<tr>
<td>Imipenem-cilastatin</td>
<td>500 mg IV every six hours</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1 g IV every eight hours</td>
</tr>
<tr>
<td>Doripenem</td>
<td>500 mg IV every eight hours</td>
</tr>
<tr>
<td>Ertapenem§</td>
<td>1 g IV once daily</td>
</tr>
</tbody>
</table>

* Antibiotic doses should be adjusted appropriately for patients with renal insufficiency or other dose-related consideration. • *E coli* resistance to Ampicillin-sulbactam is merging in some areas; check local susceptibility data.
Some clinicians use 4.5 g every eight hours for empiric therapy since the percent time above the MIC is similar between the regimens for most pathogens; however, this regimen is NOT recommended for nosocomial pneumonia or *Pseudomonas* coverage. Please refer to UpToDate topics on the "Treatment of hospital-acquired, ventilator-associated, and healthcare-associated pneumonia in adults" and "Treatment of *Pseudomonas aeruginosa* infections". ♦ Fluoroquinolones are generally avoided in pregnant women due to potential fetal toxicity. § Use carbapenems cautiously in patients with immediate-type hypersensitivity to beta-lactams. ¥ Ertapenem lacks activity against *Acinetobacter* and *Pseudomonas* and is not an appropriate choice for severe or nosocomial infection.

**American Society of Anesthesiologists (ASA) Physical Status Classification System**

<table>
<thead>
<tr>
<th>ASA 1</th>
<th>A normal healthy patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA 2</td>
<td>A patient with mild systemic disease</td>
</tr>
<tr>
<td>ASA 3</td>
<td>A patient with severe systemic disease</td>
</tr>
<tr>
<td>ASA 4</td>
<td>A patient with severe systemic disease that is a constant threat to life</td>
</tr>
<tr>
<td>ASA 5</td>
<td>A moribund patient who is not expected to survive without the operation</td>
</tr>
<tr>
<td>ASA 6</td>
<td>A declared brain-dead patient whose organs are being removed for donor purposes</td>
</tr>
</tbody>
</table>

*ASA Physical Status Classification System is reprinted with permission of the American Society of Anesthesiologists, 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573.*