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Wolters Kluwer

Acute cholangitis: Clinical manifestations, diagnosis, and management

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INTRODUCTION

Acute cholangitis is a clinical syndrome characterized by fever, jaundice, and abdominal pain that develops as a result of stasis and infection in the biliary tract. It is also referred to as ascending cholangitis. Cholangitis was first described by Charcot as a serious and life-threatening illness; however, it is now recognized that the severity can range from mild to life-threatening [1].

This topic will review the clinical features, diagnosis, and management of acute cholangitis. The approach to patients with primary sclerosing cholangitis, the management of common bile duct stones, and the endoscopic management of malignant biliary obstructions are discussed in detail elsewhere. (See "[Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis](#)" and "[Primary sclerosing cholangitis in adults: Management](#)" and "[Endoscopic management of bile duct stones](#)" and "[Endoscopic stenting for malignant biliary obstruction](#)".)

EPIDEMIOLOGY AND RISK FACTORS

The most frequent causes of biliary obstruction in patients with acute cholangitis without bile duct stents are biliary calculi (28 to 70 percent), benign biliary stricture (5 to 28 percent), and malignancy (10 to 57 percent) [2]. Malignant obstruction may be due to the presence of tumor

in the gallbladder, bile duct, ampulla, duodenum, or pancreas. Benign biliary strictures may be congenital, post-infectious (eg, AIDS cholangiopathy) or inflammatory (eg, primary sclerosing cholangitis). (See ["AIDS cholangiopathy"](#) and ["Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis"](#).)

Acute cholangitis can also occur following endoscopic retrograde cholangiopancreatography (0.5 to 1.7 percent), particularly therapeutic endoscopic retrograde cholangiopancreatography following stent placement, or postoperatively due to bile duct injury, or a strictured biliary-enteric anastomosis (pancreaticoduodenectomy, liver transplantation, liver resection, and Roux-en-Y hepaticojejunostomy). Rarely, the distal common bile duct may be obstructed by food, stones, or debris in patients with a biliary-enteric anastomosis (Sump syndrome) [3].

Other rare causes of obstruction leading to acute cholangitis include extrinsic compression of the bile duct due to a duodenal periampullary diverticulum (Lemmel syndrome), inflammation secondary to acute pancreatitis, or an impacted stone in the cystic duct or neck of the gallbladder (Mirizzi syndrome). Intrinsic causes of biliary obstruction include blood clots, and parasitic infections (mainly liver flukes and the roundworm *Ascaris*). Retained worm fragments can serve as a nidus for biliary stones and cause recurrent pyogenic cholangitis. (See ["Recurrent pyogenic cholangitis"](#), section on 'Etiology'.)

PATHOGENESIS

Acute cholangitis is caused primarily by bacterial infection in a patient with biliary obstruction. The organisms typically ascend from the duodenum; hematogenous spread from the portal vein is a rare source of infection [4].

- **Mechanism of bacterial entry into the biliary tract** – Mechanisms to prevent entry of bacteria into the biliary tract include the sphincter of Oddi, which acts as an effective mechanical barrier to duodenal reflux and ascending bacterial infection. In addition, continuous flushing action of bile, plus the bacteriostatic activity of bile salts, helps maintain bile sterility. Secretory IgA and biliary mucous probably function as anti-adherence factors, preventing bacterial colonization.

Bacteria are able to enter the biliary tract when the normal barrier mechanisms are disrupted. This occurs after endoscopic sphincterotomy, choledochal surgery, or biliary stent insertion. Acute cholangitis frequently develops after endoscopic or percutaneous manipulation with incomplete biliary drainage or as a late complication of biliary stent blockage. Biliary obstruction raises intrabiliary pressure and leads to increased

permeability of bile ductules, permitting translocation of bacteria and toxins from the portal circulation into the biliary tract [2]. Elevated pressure also favors migration of bacteria from bile into the systemic circulation, increasing the risk of septicemia [4]. In addition, increased biliary pressure adversely affects a number of host defense mechanisms including Kupffer cells, bile flow, and IgA production [4]. (See "[Infectious adverse events related to endoscopic retrograde cholangiopancreatography \(ERCP\)](#)", section on 'Acute cholangitis'.)

Bacteria can also pass spontaneously through the sphincter of Oddi in small numbers. The presence of a foreign body, such as a stone or stent, can then act as a nidus for bacterial colonization. Bile taken from patients without obstruction is sterile or nearly sterile [5]. By comparison, approximately 70 percent of all patients with gallstones have evidence of bacteria in the bile [5,6]. Patients with common bile duct stones have a higher probability of bile culture positivity than those with gallstones in the gallbladder or cystic duct [5].

- **Microbiology** – Culture of bile, ductal stones, and blocked biliary stents are positive in over 90 percent of cases of acute cholangitis, yielding a mixed growth of gram-negative and gram-positive bacteria. The most common bacteria isolated are of colonic origin [7]. *E. coli* is the major gram-negative bacterium isolated (25 to 50 percent), followed by *Klebsiella* (15 to 20 percent) and *Enterobacter* species (5 to 10 percent). The most common gram-positive bacteria are *Enterococcus* species (10 to 20 percent). Anaerobes, such as *Bacteroides* and *Clostridia*, are usually present as part of a mixed infection, but their frequency is underestimated by standard culture techniques. Recovery of anaerobes appears to be more common after repeated infections or surgery on the biliary tree.

CLINICAL MANIFESTATIONS

The classic presentation of acute cholangitis is fever, abdominal pain, and jaundice (Charcot's triad), although only 50 to 75 percent of patients with acute cholangitis have all three findings [8]. The most common symptoms of acute cholangitis are fever and abdominal pain, which are seen in approximately 80 percent of patients. Jaundice is seen in 60 to 70 percent of patients [9].

In addition to fever, abdominal pain, and jaundice, patients with severe (suppurative) cholangitis may present with hypotension, and mental status changes (Reynolds pentad). Hypotension may be the only presenting symptom in older adults or those on glucocorticoids.

Patients with acute cholangitis can also present with complications from bacteremia, including hepatic abscess, sepsis, multiple organ system dysfunction, and shock.

DIAGNOSTIC APPROACH

Clinical suspicion and evaluation — Acute cholangitis should be suspected in patients with fever, abdominal pain, and jaundice. (See "[Choledocholithiasis: Clinical manifestations, diagnosis, and management](#)".)

- In patients with fever, abdominal pain, jaundice (Charcot's triad), and abnormal liver tests, we proceed directly to endoscopic retrograde cholangiopancreatography (ERCP) to confirm the diagnosis and provide biliary drainage. (See '[Choice of procedure](#)' below and '[Endoscopic drainage](#)' below.)
- In all other patients with suspected acute cholangitis, we perform a transabdominal ultrasonography to look for common bile duct dilatation or stones. An abdominal computed tomography (CT) is performed in patients with abdominal pain and in patients with suspected acute cholangitis who have a normal abdominal ultrasound.

If the transabdominal ultrasound and CT are normal in a patients with suspected acute cholangitis, we perform a magnetic resonance cholangiopancreatography (MRCP) ([image 1](#)) [10,11]. For patients who cannot undergo MRCP but have conjugated hyperbilirubinemia suggestive of biliary obstruction, we proceed with ERCP. If the liver tests are normal or if the patient is pregnant or at high risk for complications from ERCP, we perform an endoscopic ultrasound to look for evidence of bile duct stones or obstruction. If the results of ERCP or EUS are negative for biliary tract disease, alternative etiologies should be considered. (See '[Differential diagnosis](#)' below.)

Laboratory tests — Laboratory evaluation to establish the diagnosis and grade the severity include a complete blood count, electrolytes, comprehensive metabolic panel, prothrombin time (PT), and PT-international normalized ratio. A pregnancy test should be performed in all women of childbearing age. Blood cultures should be performed in all patients in whom cholangitis is suspected to help direct antibiotic therapy. Cultures should also be obtained from bile or stents removed at endoscopic retrograde cholangiopancreatography [12]. (See '[Assessment of disease severity](#)' below and '[Endoscopic drainage](#)' below.)

Laboratory tests in patient with cholangitis typically reveal an elevated white blood cell count with neutrophil predominance, and a cholestatic pattern of liver test abnormalities, with elevations in the serum alkaline phosphatase, gamma-glutamyl transpeptidase, and bilirubin (predominantly conjugated) concentration [9]. However, a pattern of acute hepatocyte necrosis can be seen in which the aminotransferases may be as high as 2000 IU/L [13]. This pattern

reflects microabscess formation in the liver. (See '[Clinical manifestations](#)' above and "[Pyogenic liver abscess](#)", section on '[Clinical manifestations](#)'.)

Imaging

- **Abdominal ultrasound** – Features suggestive of acute cholangitis include biliary dilation or evidence of the underlying etiology. Abdominal ultrasound has a high specificity for bile duct dilation and bile duct stones (94 to 100 percent), but the sensitivity for the detection of dilated bile ducts and biliary obstruction ranges from 38 to 91 percent [[14-16](#)]. Ultrasound has the advantage of being a noninvasive test that can be performed at the bedside in critically ill patients. However, it is operator-dependent and can be negative either when only small stones are present in the bile ducts (which occurs in 10 to 20 percent of cases) or with acute obstruction when the bile duct has not yet had time to dilate ([image 2](#)).
- **Abdominal CT scan** – CT imaging has a high sensitivity to identify bile duct dilatation and can identify biliary stenosis (eg, biliary carcinoma, pancreatic cancer, or sclerosing cholangitis) but conventional CT has a low sensitivity for bile duct stones (25 to 90 percent) [[17-20](#)]. Helical CT has shown improved performance over conventional CT for choledocholithiasis, with 65 to 88 sensitivity and 73 to 97 percent specificity [[21](#)]. Disadvantages of a CT scan include a higher cost as compared with abdominal ultrasound and radiation exposure.
- **Magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/MRCP)** – MRI/MRCP are used for imaging when a diagnosis is unclear despite abdominal ultrasound or CT. MRCP can clearly delineate the bile duct without the use of contrast and has higher diagnostic accuracy in identifying the cause of biliary obstruction as compared with CT and abdominal ultrasound [[22](#)]. Imaging findings in acute cholangitis include an increase in signal intensity around the bile duct on T2-weighted images and heterogeneous enhancement of the bile duct wall on contrast-enhanced T1-weighted images [[23](#)].
- **Endoscopic ultrasound of bile ducts** – EUS is occasionally used as a diagnostic tool for evaluating suspected choledocholithiasis in patients who cannot undergo MRCP and can be therapeutic. (See '[Endoscopic drainage](#)' below.)

Diagnosis — A diagnosis of acute cholangitis is made if a patient has evidence of systemic inflammation with one of the following:

- Fever and/or shaking chills.

- Laboratory evidence of an inflammatory response (abnormal white blood cell count, increased serum C-reactive protein, or other changes suggestive of inflammation).

and both of the following:

- Evidence of cholestasis: Bilirubin ≥ 2 mg/dL or abnormal liver chemistries (elevated alkaline phosphatase, gamma-glutamyl transpeptidase, alanine aminotransferase, or aspartate aminotransferase, to >1.5 times the upper limit of normal).
- Imaging with biliary dilation or evidence of the underlying etiology (eg, a stricture, stone, or stent).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of acute cholangitis includes other etiologies of right upper quadrant abdominal pain and fever. Acute cholangitis can be distinguished from most of these based on the clinical history (eg, a bile leak should be considered following laparoscopic cholecystectomy), physical examination, laboratory studies, abdominal imaging, and endoscopic retrograde cholangiopancreatography. (See ['Imaging'](#) above.)

- **Acute cholecystitis** – Patients with acute cholecystitis may present with fever and abdominal pain. However, patients with acute cholecystitis should not have a significantly elevated bilirubin or alkaline phosphatase unless there is a secondary process causing cholestasis. In addition, abdominal imaging in acute cholecystitis typically reveals a normal common bile duct, gallbladder wall thickening, and a sonographic Murphy's sign. (See ["Acute calculous cholecystitis: Clinical features and diagnosis"](#), section on ['Diagnostic approach'](#).)
- **Biliary leak** – Biliary leaks are a complication of bile duct injury, usually as a complication of laparoscopic cholecystectomy. Patients present with fever and abdominal pain and/or bilious ascites. On abdominal imaging, patients usually have contained, loculated collections in the gallbladder fossa ([image 3](#)) or around the liver, or can have frank, diffuse biliary peritonitis. (See ["Complications of laparoscopic cholecystectomy"](#), section on ['Bile leaks \(type A, C, D injury\)'](#).)
- **Acute pancreatitis** – Patients with pancreatitis usually present with acute onset of epigastric abdominal pain. In some patients, the pain may be in the right upper quadrant. Patients with acute pancreatitis have elevation in serum lipase or amylase to three times or greater than the upper limit of normal, and focal or diffuse enlargement of the pancreas on contrast-enhanced abdominal computed tomography (CT) or magnetic

resonance imaging. (See "[Clinical manifestations and diagnosis of acute pancreatitis](#)", [section on 'Diagnosis'](#).)

- **Liver abscess** – Patients with a liver abscess can present with right upper quadrant pain, transaminitis, or hyperbilirubinemia. Ultrasound and CT can differentiate between a liver abscess and acute cholangitis. (See "[Pyogenic liver abscess](#)", [section on 'Diagnosis'](#).)

MANAGEMENT

Assessment of disease severity

Severe (suppurative) cholangitis — Acute cholangitis is considered severe if it is associated with the onset of dysfunction in at least any one of the following organs/systems:

- Cardiovascular dysfunction – Hypotension requiring [dopamine](#) ≥ 5 micrograms/kg per min, or any dose of [norepinephrine](#)
- Neurological dysfunction – Disturbance of consciousness
- Respiratory dysfunction – PaO₂/FiO₂ ratio < 300
- Renal dysfunction – Oliguria, serum creatinine > 2.0 mg/dl
- Hepatic dysfunction – Prothrombin time-international normalized ratio > 1.5
- Hematological dysfunction – Platelet count $< 100,000/\text{mm}^3$

Moderate acute cholangitis — Acute cholangitis is defined as moderate if it is associated with any two of the following:

- Abnormal WBC count ($> 12,000/\text{mm}^3$, $< 4,000/\text{mm}^3$)
- Fever 39°C (102.2°F)
- Age (≥ 75 years)
- Hyperbilirubinemia (total bilirubin ≥ 5 mg/dl)
- Hypoalbuminemia

Mild acute cholangitis — Mild acute cholangitis does not meet the criteria for moderate or severe cholangitis at initial diagnosis.

General measures

Supportive care — Patients diagnosed with acute cholangitis should be admitted to the hospital. Based on the severity, patients with acute cholangitis require intravenous hydration and correction of associated electrolyte disorders, and analgesics for pain control. In addition, patients require close monitoring for organ dysfunction and septic shock. (See "[Sepsis](#)

syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis".)

Antibiotics — In general, empiric regimens for intra-abdominal infections include antimicrobials with activity against enteric streptococci, coliforms, and anaerobes. The choice of antibiotics should take into consideration whether the infection is community-acquired versus healthcare-associated, as well as individual risk factors for infection with resistant bacteria and risk for adverse outcomes ([table 1](#)). We recommend the following antibiotic regimens for patients with acute cholangitis based on their individual risk category [24]:

- For patients with community-acquired acute cholangitis of low to-moderate risk ([table 2](#)). Low-risk community-acquired intra-abdominal infections are those that are of mild to moderate severity in the absence of risk factors for antibiotic resistance or treatment failure. Such risk factors include recent travel to areas of the world with high rates of antibiotics-resistant organisms, known colonization with such organisms, advanced age, immunocompromising conditions, or other major medical comorbidities.
- For patients with community-acquired acute cholangitis of high risk ([table 3](#)). High-risk community-acquired intra-abdominal infections are those that are severe or in patients at high risk for adverse outcomes or antimicrobial resistance.
- For patients with healthcare-associated acute cholangitis ([table 4](#)).

The chosen antimicrobial agents should subsequently be tailored to culture and susceptibility results when they become available. The duration of antibiotics depends on the adequacy of control of infection and the clinical stability of the patient [7,24]. Once the source of infection is controlled, antimicrobial therapy for patients with acute cholangitis is continued for an additional duration of four to five days. Antibiotic therapy for intra-abdominal infections, including acute cholangitis and the duration of therapy, are discussed in detail elsewhere. (See "[Antimicrobial approach to intra-abdominal infections in adults](#)", section on 'Empiric antimicrobial therapy'.)

Biliary drainage

Timing based on disease severity

- 70 to 80 percent of patients with acute cholangitis respond to initial management with antibiotic therapy. In patients with mild to moderate cholangitis, biliary drainage should be performed within 24 to 48 hours [2,25,26]. (See '[Assessment of disease severity](#)' above.)

- Patients with mild to moderate cholangitis that fail to respond to conservative management for 24 hours, and patients with severe (suppurative) cholangitis require urgent (within 24 hours) biliary decompression. (See ['Assessment of disease severity'](#) above.)

Choice of procedure — Endoscopic sphincterotomy with stone extraction and/or stent insertion (depending on the cause of the obstruction) is the treatment of choice for establishing biliary drainage in acute cholangitis ([image 2](#)). However, occasionally endoscopic retrograde cholangiopancreatography (ERCP) is not technically feasible, or it fails to establish biliary drainage. In such cases, biliary drainage can often be achieved by EUS-guided biliary drainage. Percutaneous transhepatic cholangiography or surgical decompression are rarely performed and are reserved for cases when endoscopic drainage fails or is unavailable. (See ["Endoscopic management of bile duct stones"](#) and ["Endoscopic stenting for malignant biliary obstruction"](#) and ["Percutaneous transhepatic cholangiography in adults"](#) and ["Surgical common bile duct exploration"](#).)

Endoscopic drainage — Common bile duct stones can be removed successfully in 90 to 95 percent of patients after sphincterotomy. Endoscopic drainage is associated with significantly lower overall rates of mortality and morbidity compared with surgical decompression (mortality rates of 4.7 to 10 percent versus 10 to 50 percent) [[27-30](#)].

Stone extraction is usually accomplished with balloon extractor catheters or a wire basket. Large or impacted stones require mechanical lithotripsy or cholangioscopy with electrohydraulic or laser lithotripsy for fragmentation prior to removal. Prior to injection of contrast, many endoscopists aspirate the bile duct to remove bile and pus in an attempt to decompress the biliary system and reduce the risk of inducing bacteremia with contrast injection. Occlusive cholangiography should not be performed in patients with acute cholangitis since it can promote the development of septicemia ([picture 1](#)). (See ["Endoscopic management of bile duct stones"](#).)

Placing a stent within the bile duct without first performing a sphincterotomy appears to permit adequate drainage and may be another option for patients with coagulopathies [[31](#)]. Placement of a nasobiliary catheter is another option in patients with underlying coagulopathies that prevent sphincterotomy, in those in whom drainage is inadequate due to the presence of large stones, or in those who are too ill to leave the intensive care unit and undergo the procedure with fluoroscopy. This procedure permits active decompression of the common bile duct by aspiration, and provides a route for irrigation of the biliary system [[32,33](#)]. However, the catheters may inadvertently be dislodged.

Another alternative to ERCP for biliary drainage is EUS-guided cholangiopancreatography with biliary drainage and stent placement in patients at high risk for complications with ERCP and where ERCP has failed or was not possible due to altered surgical anatomy or obstructing duodenal or ampullary tumors. (See ["Therapeutic endoscopic ultrasound", section on 'EUS-guided cholangiopancreatography'](#).)

Percutaneous drainage — Percutaneous transhepatic biliary drainage is performed when endoscopic drainage is unavailable or unsuccessful (eg, Roux-en-Y anastomosis or Whipple resection or duodenal narrowing). Percutaneous transhepatic cholangiography (PTC) involves transhepatic insertion of a needle into a bile duct, followed by injection of contrast material to opacify the bile ducts. PTC permits a number of therapeutic interventions, including drainage of infected bile, extraction of biliary tract stones, dilation of benign biliary strictures, or placement of a stent across a malignant stricture. However, percutaneous transhepatic biliary drainage requires a dilated biliary system and is more invasive as compared with ERCP. (See ["Percutaneous transhepatic cholangiography in adults"](#).)

Another alternative to ERCP for biliary drainage is placement of a percutaneous cholecystostomy tube in patients with an intact gallbladder.

Surgical drainage — Surgical drainage for acute cholangitis is reserved for patients in whom other methods of biliary drainage cannot be performed or have failed. For patients who have acute cholangitis due to an obstructing stone, biliary decompression can be accomplished with open or laparoscopic common bile duct exploration, with choledocholithiasis removal, with or without placement of a T tube. In hemodynamically stable patients with gallstones, a cholecystectomy can be performed at the same time (see ["Surgical common bile duct exploration"](#)). For patients who have acute cholangitis due to a malignant biliary obstruction, surgical options include resection (eg, Whipple or bile duct resection), bypass (eg, hepaticojejunostomy), and T tube drainage (see ["Bile duct resection and reconstruction"](#)). For patients who have iatrogenic bile duct injury/obstruction, surgical repair (eg, hepaticojejunostomy) is indicated (see ["Repair of common bile duct injuries"](#)). However, it is rare in contemporary practice that acute cholangitis would require surgical drainage.

Addressing the underlying predisposing cause — In addition to antimicrobial therapy and biliary drainage, management of the underlying cause is warranted to prevent recurrence.

- In patients with gallstones, elective cholecystectomy after the resolution of cholangitis is recommended in order to prevent future attacks of biliary colic and complications of gallstone disease. Rates of recurrent cholangitis are high even after a sphincterotomy has been performed [21]. (See ["Laparoscopic cholecystectomy", section on 'Indications'](#).)

- In patients with a benign biliary stricture, as a consequence of bile duct injuries, endoscopic therapy or surgical repair may be required. (See ["Repair of common bile duct injuries"](#), section on 'Repair options' and ["Endoscopic management of postcholecystectomy biliary complications"](#), section on 'Biliary stricture'.)
- In patients with recurrent pyogenic cholangitis, regular endoscopic surveillance may be required to remove as many stones as possible and/or surgical resection of the affected hepatobiliary segment with a biliary-enteric anastomosis. (See ["Recurrent pyogenic cholangitis"](#), section on 'Prevention of long-term complications'.)
- In patients with malignant stenoses, management is typically with stent placement at the time of endoscopic biliary drainage. The specific type chosen will depend on the patient's life expectancy and the likelihood of stent occlusion. (See ["Endoscopic stenting for malignant biliary obstruction"](#).)

Patients who are pregnant — In general, women with acute cholangitis who are pregnant are managed the same way as patients who are not pregnant, with antibiotics and biliary drainage. However, antibiotic choices should take into account potential fetal toxicity. In addition, fetal shielding should be used during fluoroscopy and exposure time should be minimized. (See ["Gallstone diseases in pregnancy"](#), section on 'Choledocholithiasis/cholangitis' and 'Antibiotics' above.)

PROGNOSIS

Reported mortality rates for acute cholangitis are highly variable, ranging from 2 to 65 percent [2]. Studies of patients with severe cholangitis who were treated in the 1970s found mortality rates that exceeded 50 percent [34,35]. With advances in treatment, the mortality rate for cholangitis has dropped, with mortality rates in more recent studies of 11 percent or less [28,36-40]. However, while improved, mortality rates for patients with severe acute cholangitis remain high (20 to 30 percent) [30,41].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See ["Society guideline links: Cholecystitis and other gallbladder disorders"](#) and ["Society guideline links: Intra-abdominal infections in adults"](#) and ["Society guideline links: Biliary infection and obstruction"](#).)

SUMMARY AND RECOMMENDATIONS

- **Clinical presentation** – The classic presentation of acute cholangitis is fever, abdominal pain, and jaundice (Charcot's triad), although only 50 to 75 percent of patients with acute cholangitis have all three findings. The most common symptoms of acute cholangitis are fever and abdominal pain. Confusion and hypotension can occur in patients with severe cholangitis (Reynolds pentad). Hypotension may be the only presenting symptom in older adults or those on glucocorticoids. Patients with acute cholangitis can also present with complications including hepatic abscess, sepsis, multiple organ system dysfunction, and shock. (See '[Clinical manifestations](#)' above.)
- **Diagnosis** – Acute cholangitis should be suspected in patients with fever, abdominal pain, and jaundice.

A diagnosis of acute cholangitis requires evidence of systemic inflammation with one of the following:

- Fever and/or shaking chills.
- Laboratory evidence of an inflammatory response (abnormal white blood cell count, increased serum C-reactive protein, or other changes suggestive of inflammation).

and both of the following:

- Evidence of cholestasis: Bilirubin ≥ 2 mg/dL or abnormal liver chemistries (elevated alkaline phosphatase, gamma-glutamyl transpeptidase, alanine aminotransferase, or aspartate aminotransferase, to >1.5 times the upper limit of normal).
- Imaging with biliary dilation or evidence of the underlying etiology (eg, a stricture, stone, or stent).

- **Initial evaluation**

In patients with fever, abdominal pain, jaundice (Charcot's triad), and abnormal liver tests, we proceed directly to endoscopic retrograde cholangiopancreatography (ERCP) to confirm the diagnosis and provide biliary drainage. (See '[Choice of procedure](#)' above and '[Endoscopic drainage](#)' above.)

In all other patients with suspected acute cholangitis, we perform a transabdominal ultrasonography to look for common bile duct dilatation or stones. An abdominal computed tomography (CT) scan is performed in patients with abdominal pain and in

patients with a normal abdominal ultrasound to exclude other causes. If the transabdominal ultrasound and CT are normal in a patient with suspected acute cholangitis, we perform a magnetic resonance cholangiopancreatography (MRCP) ([image 1](#)). For patients who cannot undergo MRCP but have conjugated hyperbilirubinemia suggestive of biliary obstruction, we proceed with ERCP. If the liver tests are normal or if the patient is pregnant or at high risk for complications from ERCP, we perform an endoscopic ultrasound to look for evidence of bile duct stones or obstruction.

- **Supportive care** – Patients suspected of having acute cholangitis should be admitted to the hospital for evaluation and management. Management of acute cholangitis includes monitoring for and treating sepsis, providing antibiotic coverage, and establishing biliary drainage. (See '[Management](#)' above.)
- **Antibiotics** – The choice of antibiotics should take into consideration whether the infection is community-acquired versus healthcare-associated, as well as individual risk factors for infection with resistant bacteria and risk for adverse outcomes ([table 1](#) and [table 2](#) and [table 3](#) and [table 4](#)). Once blood culture results are available, therapy should be tailored. Once the source of infection is controlled, antimicrobial therapy for patients with acute cholangitis is continued for an additional duration of four to five days. (See '[Antibiotics](#)' above.)
- **Biliary drainage**
 - **Timing based on disease severity** – Biliary drainage is required in all patients with acute cholangitis. The timing of biliary drainage depends on disease severity. In patients with mild to moderate cholangitis, biliary drainage should be performed within 24 to 48 hours. Patients with mild to moderate cholangitis that fails to respond to conservative management for 24 hours and patients with severe (suppurative) cholangitis and require urgent (within 24 hours) biliary decompression. (See '[Assessment of disease severity](#)' above.)
 - **Choice of drainage procedure** – We recommend endoscopic sphincterotomy with stone extraction and/or stent insertion for establishing biliary drainage in acute cholangitis rather than treatment with antibiotics alone (**Grade 1B**). If endoscopic decompression is not technically feasible or fails to establish biliary drainage, biliary drainage can often be achieved by percutaneous transhepatic cholangiography. Surgical decompression for acute cholangitis is more morbid and only reserved for

patients in whom other methods of biliary drainage cannot be performed or have failed. (See '[Biliary drainage](#)' above.)

- **Management of the underlying cause** – In addition to antimicrobial therapy and biliary drainage, management of the underlying cause is warranted to prevent recurrence. In patients with gallstones, this includes elective cholecystectomy after the resolution of cholangitis to prevent future attacks of biliary colic and complications of gallstone disease. (See '[Addressing the underlying predisposing cause](#)' above.)

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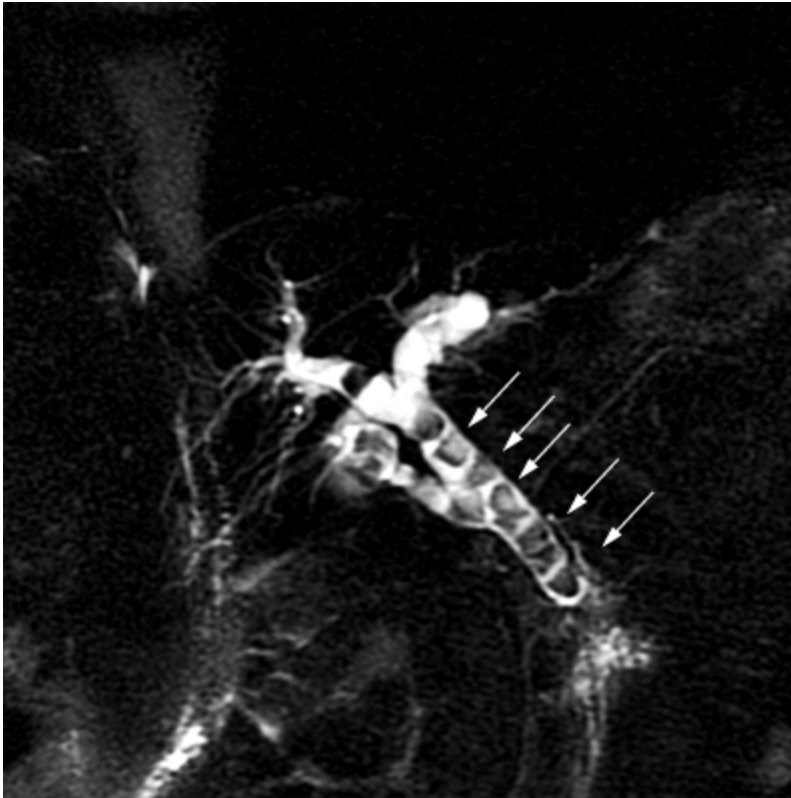
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Topic 658 Version 28.0

GRAPHICS

Acute cholangitis MRCP

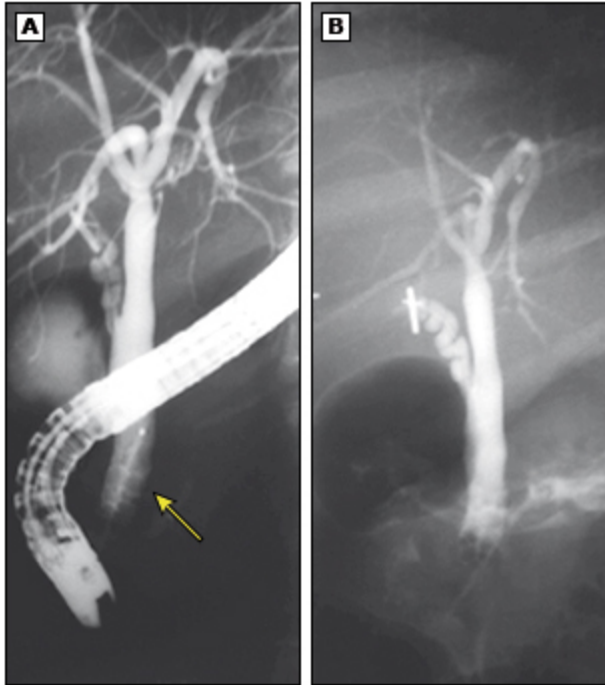


A 64-year-old man presented to the emergency department complaining of severe right upper quadrant abdominal pain, nausea, vomiting, and fevers. Laboratory data revealed an elevated white blood cell count with a left shift, elevated liver function tests including bilirubin, and elevated pancreatic enzymes. A right upper quadrant ultrasound revealed a dilated bile duct with possible stones in the bile duct and gallbladder. Magnetic resonance cholangiopancreatography (MRCP) was performed and revealed multiple filling defects in the common bile duct and cystic duct (arrows).

Courtesy of Andres Gelrud, MD.

Graphic 57884 Version 2.0

ERCP in acute cholangitis



Diagnosis and treatment of acute cholangitis with ERCP.

(A): Multiple small stones in the lower common bile duct (arrow). Ultrasonography had shown borderline dilatation of the common bile duct but no stones.

(B): After sphincterotomy and stone extraction, the common bile duct is free of stones.

ERCP: Endoscopic retrograde cholangiopancreatography.

Courtesy of Nezam Afdhal, MD.

Graphic 62967 Version 3.0

Bile leak following cholecystectomy on US



A transverse ultrasound image through the gallbladder bed following cholecystectomy shows a complex fluid collection (arrow).

US: ultrasound.

Graphic 91310 Version 1.0

Risk factors that warrant broad empiric antimicrobial coverage for intra-abdominal infections

Factors associated with mortality
Age >70 years
Medical comorbidity (eg, renal or liver disease, presence of malignancy, chronic malnutrition)
Immunocompromising condition (eg, poorly controlled diabetes mellitus, chronic high-dose corticosteroid use, use of other immunosuppressive agents, neutropenia, advanced HIV infection, B or leukocyte deficiency)
High severity of illness (ie, sepsis)
Extensive peritoneal involvement or diffuse peritonitis
Delay in initial intervention (source control) >24 hours
Inability to achieve adequate debridement or drainage control
Factors associated with infection with antibiotic-resistant bacteria
Health care-acquired infection
Travel to areas with higher rates of antibiotic-resistant organisms* within the few weeks prior to infection onset or if antibiotics were received during travel
Known colonization with antibiotic-resistant organisms

* High rates of antibiotic resistance have been reported from southeast Asia, east Asia, the Middle East, and Africa.

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Graphic 105865 Version 3.0

Empiric antibiotic regimens for low-risk community-acquired intra-abdominal infections in adults

	Dose
Single-agent regimen	
Piperacillin-tazobactam*	3.375 g IV every 6 hours
Combination regimen with metronidazole*	
One of the following:	
Cefazolin	1 to 2 g IV every 8 hours
or	
Cefuroxime	1.5 g IV every 8 hours
or	
Ceftriaxone	2 g IV once daily
or	
Cefotaxime	2 g IV every 8 hours
or	
Ciprofloxacin	400 mg IV every 12 hours or 500 mg PO every 12 hours
or	
Levofloxacin	750 mg IV or PO once daily
Plus:	
Metronidazole¶	500 mg IV or PO every 8 hours

For empiric therapy of low-risk community-acquired intra-abdominal infections, we cover streptococci, Enterobacteriaceae, and anaerobes. Low-risk community-acquired intra-abdominal infections are those that are of mild to moderate severity (including perforated appendix or appendiceal abscess) in the absence of risk factors for antibiotic resistance or treatment failure. Such risk factors include recent travel to areas of the world with high rates of antibiotics-resistant organisms, known colonization with such organisms, advanced age, immunocompromising conditions, or other major medical comorbidities. Refer to other UpToDate content on the antimicrobial treatment of intra-abdominal infections for further discussion of these risk factors.

The antibiotic doses listed are for adult patients with normal renal function. The duration of antibiotic therapy depends on the specific infection and whether the presumptive source of infection has been controlled; refer to other UpToDate content for details.

IV: intravenously; PO: orally.

* When piperacillin-tazobactam or one of the combination regimens in the table cannot be used, ertapenem (1 g IV once daily) is a reasonable alternative.

¶ For most uncomplicated biliary infections of mild to moderate severity, the addition of metronidazole is not necessary.

Graphic 106948 Version 13.0

Empiric antibiotic regimens for high-risk community-acquired intra-abdominal infections in adults

	Dose
Single-agent regimen	
Imipenem-cilastatin	500 mg IV every 6 hours
Meropenem	1 g IV every 8 hours
Doripenem	500 mg IV every 8 hours
Piperacillin-tazobactam	4.5 g IV every 6 hours
Combination regimen with metronidazole	
ONE of the following:	
Cefepime	2 g IV every 8 hours
OR	
Ceftazidime	2 g IV every 8 hours
PLUS:	
Metronidazole	500 mg IV or orally every 8 hours

High-risk community-acquired intra-abdominal infections are those that are severe or in patients at high risk for adverse outcomes or antimicrobial resistance. These include patients with recent travel to areas of the world with high rates of antibiotics-resistant organisms, known colonization with such organisms, advanced age, immunocompromising conditions, or other major medical comorbidities. Refer to the UpToDate topic on the antimicrobial treatment of intra-abdominal infections for further discussion of these risk factors.

For empiric therapy of high-risk community-acquired intra-abdominal infections, we cover streptococci, Enterobacteriaceae resistant to third-generation cephalosporins, *Pseudomonas aeruginosa*, and anaerobes. Empiric antifungal therapy is usually not warranted but is reasonable for critically ill patients with an upper gastrointestinal source.

Local rates of resistance should inform antibiotic selection (ie, agents for which there is >10% resistance among Enterobacteriaceae should be avoided). If the patient is at risk for infection with an extended-spectrum beta-lactamase (ESBL)-producing organism (eg, known colonization or prior infection with an ESBL-producing organism), a carbapenem should be chosen. When beta-lactams or carbapenems are chosen for patients who are critically ill or are at high risk of infection with drug-resistant pathogens, we favor a prolonged infusion dosing strategy. Refer to other UpToDate content on prolonged infusions of beta-lactam antibiotics.

The combination of vancomycin, aztreonam, and metronidazole is an alternative for those who cannot use other beta-lactams or carbapenems (eg, because of severe reactions).

The antibiotic doses listed are for adult patients with normal renal function. The duration of antibiotic therapy depends on the specific infection and whether the presumptive source of infection has been controlled; refer to other UpToDate content for details.

IV: intravenous.

Graphic 106949 Version 12.0

Empiric antibiotic regimens for health care-associated intra-abdominal infections in adults

	Dose
Single-agent regimen	
Imipenem-cilastatin	500 mg IV every 6 hours
Meropenem	1 g IV every 8 hours
Doripenem	500 mg IV every 8 hours
Piperacillin-tazobactam	4.5 g IV every 6 hours
Combination regimen	
ONE of the following:	
Cefepime	2 g IV every 8 hours
OR	
Ceftazidime	2 g IV every 8 hours
PLUS:	
Metronidazole	500 mg IV or orally every 8 hours
PLUS ONE of the following (in some cases*):	
Ampicillin	2 g IV every 4 hours
OR	
Vancomycin	15 to 20 mg/kg IV every 8 to 12 hours

For empiric therapy of health care-associated intra-abdominal infections, we cover streptococci, enterococci, Enterobacteriaceae that are resistant to third-generation cephalosporins and fluoroquinolones, *Pseudomonas aeruginosa*, and anaerobes. We include coverage against methicillin-resistant *Staphylococcus aureus* (MRSA) with vancomycin in those who are known to be colonized, those with prior treatment failure, and those with significant prior antibiotic exposure. Empiric antifungal coverage is appropriate for patients at risk for infection with *Candida* spp, including those with upper gastrointestinal perforations, recurrent bowel perforations, surgically treated pancreatitis, heavy colonization with *Candida* spp, and/or yeast identified on Gram stain of samples from infected peritoneal fluid or tissue. Refer to other UpToDate content on treatment of invasive candidiasis.

If the patient is at risk for infection with an extended-spectrum beta-lactamase (ESBL)-producing organism (eg, known colonization or prior infection with an ESBL-producing organism), a carbapenem should be chosen. For patients who are known to be colonized with highly resistant gram-negative bacteria, the addition of an aminoglycoside, polymyxin, or novel beta-lactam combination (ceftolozane-tazobactam or ceftazidime-avibactam) to an empiric regimen may be warranted. In such cases, consultation with an expert in infectious diseases is advised.

When beta-lactams or carbapenems are chosen for patients who are critically ill or are at high risk of infection with drug-resistant pathogens, we favor a prolonged infusion dosing strategy. Refer to other UpToDate content on prolonged infusions of beta-lactam antibiotics.

The combination of vancomycin, aztreonam, and metronidazole is an alternative for those who cannot use other beta-lactams or carbapenems (eg, because of severe reactions).

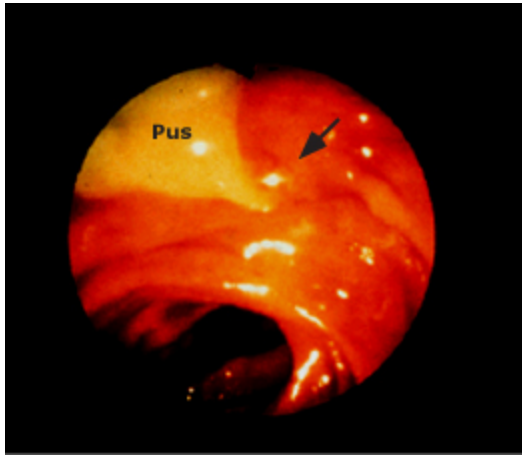
The antibiotic doses listed are for adult patients with normal kidney function. The duration of antibiotic therapy depends on the specific infection and whether the presumptive source of infection has been controlled; refer to other UpToDate content for details.

IV: intravenous.

* We add ampicillin or vancomycin to a cephalosporin-based regimen to provide enterococcal coverage, particularly in those with postoperative infection, prior use of antibiotics that select for *Enterococcus*, immunocompromising condition, valvular heart disease, or prosthetic intravascular materials. Coverage against vancomycin-resistant enterococci (VRE) is generally not recommended, although it is reasonable in patients who have a history of VRE colonization or in liver transplant recipients who have an infection of hepatobiliary source.

Graphic 106950 Version 12.0

Suppurative cholangitis



Endoscopy in a patient with suppurative cholangitis shows pus coming out of the ampulla of Vater (arrow).

Graphic 69133 Version 1.0

