Acute Inflammatory Surgical Disease

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KEYWORDS
- Appendicitis  •  Cholecystitis  •  Cholangitis  •  Pancreatitis  •  Diverticulitis
- Clostridium difficile  •  Colitis

KEY POINTS
- Computed tomography is the most accurate way to diagnose appendicitis and its complications. Abscesses should be percutaneously drained, phlegmon treated with antibiotics, and appendectomy performed in most other cases.
- Immediate laparoscopic cholecystectomy is standard treatment for acute cholecystitis, though percutaneous cholecystostomy is effective in high risk patients. Cholangitis should be treated with endoscopic retrograde cholangiography and sphincterotomy.
- Infected pancreatic necrosis is the primary indication for intervention in pancreatitis. A “step-up” approach beginning with percutaneous or endoscopic drainage and proceeding to surgical debridement when necessary should be used.
- Diverticulitis without abscess or with small abscess should be treated with antibiotics alone. Large diverticular abscesses should be percutaneously drained. In cases of free perforation with peritonitis mandating surgery, primary anastomosis with or without proximal diversion should be considered.
- Subtotal colectomy with end ileostomy is standard surgical therapy for medically refractory Clostridium difficile colitis. There may be a role for ileostomy with antegrade colonic lavage.

Infectious and inflammatory diseases comprise some of the most common gastrointestinal disorders resulting in hospitalization in the United States. Accordingly, they occupy a significant proportion of the workload of the acute care surgeon.

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In 1886, Reginald Fitz of Boston, in his monograph “Diseases of the Vermiform Appendix,” correctly identified the appendix as the primary cause of right lower quadrant inflammation and coined the term appendicitis. Appendicitis is the most common problem of the colon, affecting approximately 300,000 patients a year and some estimate 8% of the Western country population will face appendicitis some time in their lives. In the past, reliance on physical examination and laboratory findings have been the mainstay of diagnosis but in the era of computed tomography and ultrasound imaging, studies are increasingly accepted to assess for appendicitis. The standard treatment has traditionally been open appendectomy, but the number of laparoscopic appendectomies has now surpassed the number of open appendectomies in the United States. Even more recently, there has been a growing debate regarding the nonoperative approach to appendicitis, namely treatment with antibiotics. We review the basic diagnostic options and describe treatment options for acute appendicitis, including the treatment of the perforated appendicitis or delayed presentations.

**Clinical History and Physical Examination**

Appendicitis typically occurs as a result of the obstruction of the appendiceal lumen that subsequently results in ischemia and inflammation. This ischemia and inflammation evolves over several hours and is the cause of early visceral pain that then localizes to the right lower quadrant. The obstruction is typically the result of a fecolith or adenitis. These processes lead to necrosis and perforation of the appendix, which occur usually after at least 48 hours of symptoms. The bacteriology of appendicitis is a mixed enteral flora, including *Escherichia coli*, *Streptococcus viridans*, and *Bacteroides* species.

The clinical history of appendicitis typically includes a 24-hour to 48-hour progression of vague periumbilical pain that migrates and becomes more localized to the right lower quadrant. The tenderness is usually a localized peritonitis with additional manifestations of pain on coughing (Dunphy sign), pain with flexion and internal rotation of the right hip (obturator sign), pain with passive extension of the right hip (psoas sign), or pain in the right lower quadrant during palpation of the left lower quadrant (Rovsing sign). In addition, patients may have tenderness with rectal examination.

The typical laboratory findings include a mild to moderate leukocytosis with a left shift, a urinalysis showing a few white blood cells, and other laboratory findings of inflammation, such as elevated C-reactive protein. The differential diagnosis of right lower quadrant tenderness includes sigmoid diverticulitis (secondary to a redundant sigmoid that reaches across the midline), cecal diverticulitis, retroperitoneal or rectus sheath hematoma, viral enteritis, Crohn disease, perforating colonic carcinoma, and, in women, a number of gynecologic pathologies. A meta-analysis done by Andersen.
found that the history of migration of pain, peritoneal irritation, and elevated laboratory findings suggestive of an inflammatory process were the great predictors of appendicitis. Despite the history, physical findings, and laboratory findings, it is clear that there is no single confirmatory test. The use of physical examination, history, and laboratory values has in the past resulted in negative appendectomy rates of about 15%. One study also attributed $740 million in hospital charges in the 1990s to negative appendectomies. As a result, a number of scoring systems have been developed to improve the positive predictive value of a combination of factors.

The most commonly used and referenced is the Alvarado or MANTRELS scoring system (Table 1). Although the ability of the score, which is a compilation of multiple signs, symptoms, and laboratory values, is better than any individual piece of data, it does not have the power to reliably rule in or rule out appendicitis by itself. A score of 7 to 10 warrants appendectomy and those less than 7 are observed. Using this scoring system, there remains an 11% negative appendectomy rate, albeit improved from the 15% rate that is typical without using the score.

**Radiographic Imaging**

The continued evolution of ultrasound and computed tomography (CT) technology has significantly improved the sensitivity and specificity. Ultrasonography in adults has a sensitivity of approximately 83% with a specificity of approximately 93%. CT scan has a sensitivity of approximately 94% with a 94% specificity. Therefore, whether to use either ultrasonography or CT to rule in or rule out the diagnosis is now an important consideration. The downside to CT is the ionizing energy and cost. The current recommendations of the Surgical Infection Society and Infectious Disease Society of America guidelines is to obtain helical CT with intravenous (IV) contrast as the test of choice when imaging is necessary. Oral and rectal contrast are not necessary components of the imaging. The use of CT scanning has reduced negative appendectomy rates further to approximately 2.6%. A proposed diagnostic algorithm is depicted in Fig. 1.

**Treatment**

Once the diagnosis of appendicitis is made, there are a few options for treatment: (1) appendectomy (open vs laparoscopic), (2) antibiotics, and (3) percutaneous drainage and antibiotics. The open appendectomy, first described by McBurney in 1889, is a classic approach to appendicitis but has for the most part been replaced in the United

<table>
<thead>
<tr>
<th>Table 1 Alvarado score</th>
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<tr>
<td><strong>Variable</strong></td>
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<tr>
<td>Symptoms</td>
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<tr>
<td>Migration</td>
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<td>Anorexia</td>
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<td>Nausea-vomiting</td>
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<tr>
<td>Signs</td>
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<td>Tenderness in right left quadrant</td>
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<tr>
<td>Rebound tenderness</td>
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<tr>
<td>Fever</td>
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<td>Laboratory Values</td>
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<tr>
<td>White blood cells $&gt;10,000/\mu$L</td>
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<tr>
<td>Shift to the left ($&gt;75%$ neutrophils)</td>
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<td>Total Score</td>
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States by laparoscopic appendectomy, first described by Semm in 1983. In 2010, Ingraham and others conducted a study using the American College of Surgeons National Surgical Quality Improvement Program across 222 hospitals. This study found that 76.4% of appendectomies were performed laparoscopically. Overall morbidity and surgical site infections were significantly lower in those who underwent laparoscopic surgery. Although this study supported the use of laparoscopic surgery, there were differences among the groups and they were not randomized. There are a number of randomized trials and in 2010 an update of a Cochrane meta-analysis found that the methodology in the randomized trials was moderate to poor but that there was an increased intra-abdominal infection with laparoscopic appendectomy, whereas open appendectomy had an increased risk of incisional infections. Overall, there is a decreased incidence of surgical infections using the laparoscopic approach; however, given the lack of definitive data, the open technique is still a viable option.

Although the surgical dictum since 1889 has been to remove the inflamed appendix, other inflammatory intra-abdominal processes, such as diverticulitis, have been increasingly treated with antibiotics rather than surgery. There is no question that there are complications associated with surgery for appendicitis and that resolution without surgery has been described. This has led some to consider more routine treatment of appendicitis with antibiotics. In 2006, Styrud and colleagues undertook a randomized controlled trial to evaluate antibiotic treatment versus appendectomy. In 6 hospitals in Sweden they randomized 252 male patients to either antibiotic treatment (2 g IV cefotaxime twice a day for 2 days and 0.8 g tinidazole once daily followed by 10 days of oral ofloxacin) versus appendectomy (open or laparoscopic). Of the 128 randomized to antibiotics, 85% were successfully treated without surgery; 18 of the 128 were operated on within 24 hours and all but one had an acute appendicitis. There were no differences in the number of perforated appendicitis between the 2 groups. The rate of recurrence of symptoms was 14% during the 1-year follow-up. Since

Fig. 1. Algorithm for diagnosis of acute appendicitis. y/o, years old.
then, a follow-up study in Sweden randomized 369 male and female unselected pa-
tients to antibiotics versus surgery, which also demonstrated a 14% recurrence rate
at 1 year. Efficacy of antibiotic treatment was 90%.
In those patients who present with an appendiceal abscess, the diagnosis is
confirmed with CT scan and treatment is typically with a percutaneously placed drain
and antibiotics. A number of studies comparing early appendectomy to percutaneous
drainage and antibiotic treatment in the setting of appendiceal abscess have favored
percutaneous drainage and antibiotics. A treatment algorithm is proposed in Fig. 2.

ACUTE CHOLECYSTITIS/CHOLANGITIS

<table>
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<tr>
<th>Key points</th>
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<tr>
<td>Immediate cholecystectomy is the treatment of choice for acute cholecystitis.</td>
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<td>Cholecystostomy tube is a very effective option for poor-risk patients.</td>
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<td>Immediate endoscopic retrograde cholangiopancreatography (ERCP) is the preferred treatment for cholangitis.</td>
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Acute cholecystitis is the most common inflammatory process of the biliary tree,
occurring in 20% to 30% of patients with symptomatic biliary colic. The inflammatory
process may be calculus or acalculus in origin, most commonly calculus. It is esti-
mated that 20 million people are diagnosed with gallstones, with more than a million
hospitalizations and 700,000 operative procedures per year. By the age of 70,
15% of men and 24% of women have gallstones, and this number increases to
24% and 35%, respectively, by the age of 90. However, two-thirds of those
with gallstones are asymptomatic. The risk of becoming symptomatic is approxi-
mately 1% to 4% per year. Calculous cholecystitis is caused by the acute obstruc-
tion of the cystic duct by a gallstone. Acalculous cholecystitis is an inflammatory
process that is related to stasis and dysfunction of the gallbladder and is most
commonly associated with a systemic critical illness.

Calculus Acute Cholecystitis

Once the cystic duct is obstructed, patients present with increasing right upper quad-
rant pain that often migrates from the epigastrium. This pain may be associated with

![Algorithm for treatment of acute appendicitis.](image)
nausea and vomiting, fever, and malaise. On physical examination the patient will demonstrate right upper quadrant tenderness, which may include a Murphy sign. The Murphy sign is tenderness on inspiration with palpation overlying the gallbladder that causes the patient to arrest their attempt at a full inspiration. It is uncommon for patients to become jaundiced, but they may present with mild jaundice. Often this mild obstructive pattern is the result of a partial obstruction of the right hepatic duct or common bile duct by the inflamed gallbladder (Mirizzi syndrome). Typical laboratory values include a moderately elevated white blood cell count in the range of 10 to 17 cells/mm³, mild elevation of total bilirubin, alkaline phosphatase, transaminases, or amylase.

The diagnosis is usually made by the combination of history, physical examination, and laboratory findings; however, imaging provides important additional information. The most helpful initial imaging study is the ultrasound of the right upper quadrant. This study provides the surgeon with evidence of cholelithiasis with a sensitivity and specificity greater than 95%. It can also demonstrate ultrasonographic signs of acute cholecystitis, including a thickened gallbladder wall (>4 mm), pericholecystic fluid, and a sonographic Murphy sign (more sensitive than the traditional Murphy sign because the probe can be accurately applied directly to the gallbladder). A positive ultrasonic Murphy sign has a sensitivity and specificity of approximately 85% to 95% for acute cholecystitis. This study also provides information regarding the size of the common bile duct (normal <8 mm), although the sensitivity for gallstones in the common bile duct is low due to overlying duodenal air. A hepatobiliary iminodiacetic acid scan is the use of radiotracer that is excreted in the bile. This study is a functional one and will demonstrate a lack of bile flow into the gallbladder, which is suggestive of an obstructed cystic duct; however, this test is not the first-line test for acute cholecystitis due to lack of wide rapid availability and cost. The role of CT scan is limited but may be used in cases in which the ultrasound, serum tests, history, and physical are equivocal and to assess for other potential causes of abdominal pain when the diagnosis is unclear.

The duration of the obstruction and inflammation is related to the severity of gallbladder wall ischemia. The ischemia leads to the spectrum of disease ranging from inflammation, purulent cholecystitis gallbladder, emphysematous gallbladder, to frank necrosis (Fig. 3) and perforation. The gallbladder may become secondarily infected as a result of the stasis of bile with *E coli* and *Klebsiella* being the most common organisms.

**Treatment**

Treatment of acute calculus cholecystitis is supportive with a nasogastric tube if nausea or vomiting persists, nothing by mouth, IV fluids, antibiotics, and cholecystectomy (laparoscopic or open). The timing of the cholecystectomy has drawn some debate over the years, but a few randomized controlled trials have concluded that cholecystectomy within 24 to 72 hours is advantageous compared with delayed cholecystectomy. The conversion rate from laparoscopic to open is similar in these patients and the complication rate is lower in the immediate cholecystectomy groups. Therefore, it is generally recommended to perform a cholecystectomy within 24 hours of the patient’s admission. During this time period, the laparoscopic cholecystectomy is occasionally made easier by planes developed by edema. For patients presenting with 5 or more days of symptoms, some debate still remains whether immediate cholecystectomy is appropriate or is associated with high rates of open conversion and complications. This question has not been directly studied. If the patient is deemed not a surgical candidate, then the gallbladder may be
percutaneously drained. Percutaneous drainage is more than 90% effective and patients usually improve within 24 hours after drainage. If improvement has not occurred by 24 hours, then one may consider the possibility of medical failure and may have to revert to cholecystectomy. The role and timing of percutaneous cholecystostomy has not been clearly defined according to a recent meta-analysis. However, it is clear that particularly in the high-risk elderly that it is an effective and at times definitive treatment. The timing of, need for, and optimal technique for interval cholecystectomy after percutaneous cholecystostomy tube placement has not been definitively studied. We typically perform cholecystostomy tube injection 4 to 6 weeks after drainage. If tube injection shows a persistently occluded cystic duct, we recommend cholecystectomy in all but the most medically infirm patients. If the cystic duct is patent, the risks and benefits of cholecystectomy can be determined on a case-by-case basis. A complete algorithm for management of acute cholecystitis is provided in Fig. 4.

Acalculous Cholecystitis

Only 5% to 10% of all cases of cholecystitis are acalculous. The symptoms are similar to calculous cholecystitis but usually occur in the face of concomitant critical illness. The illness may be medical or traumatic. An underlying sepsis or state of shock is often associated with acalculous cholecystitis and, therefore, early treatment with antibiotics and an intervention are warranted. Most cases are treated with percutaneous cholecystostomy but cholecystectomy is an option. The mortality rate for this condition may be up to 40% because of the associated comorbid conditions.
Acute cholangitis is the result of 2 forces: obstruction and bacterbilia. The bacterbilia is thought be a result of biliary stasis and obstruction. The obstruction causes acute elevations in the biliary pressures leading to rapid bacteremia and sepsis. The 3 typical features of cholangitis (fever, jaundice, and right upper quadrant pain) were described in 1877 by Charcot. The most common cause of obstruction is gallstones; however, benign and malignant strictures, instrumentation, or periampullary cancer have also caused cholangitis.

Patients will present with Charcot triad (described previously); however, severe disease is often accompanied by hypotension and change in mental status with these 5 signs termed Reynold pentad. Fever, often with rigors, is the commonest sign. The laboratory findings are what one might find with a septic patient with an elevated white blood cell count and a left shift. In addition, given the biliary obstruction responsible for the disease, the total bilirubin levels will be elevated with most being direct bilirubinemia along with associated elevations in alkaline phosphatases and transaminases.

Once the diagnosis is made, treatment is initiated immediately with antibiotic administration and fluid resuscitation. An ERCP is performed with stone extraction and sphincterotomy. If the patient presents with severe symptoms, an emergent ERCP is indicated. If the ampulla cannot be cannulated, then a percutaneous transhepatic cholangiocatheter (PTC) may be performed or surgical decompression. ERCP and PTC are less invasive and therefore are the preferred approach in these often unstable patients. Those patients who recover uneventfully should undergo a cholecystectomy if they are not prohibitive surgical candidates. With sphincterotomy, the recurrence rate of biliary complications is decreased from 25% to 5% and therefore may be considered all that is required in patients with multiple other comorbidities.
ACUTE PANCREATITIS

Key points

- Imaging is rarely needed to diagnose acute pancreatitis and should not generally be performed at presentation.
- CT scanning with intravenous contrast should be performed to assess for local complications in patients failing to improve.
- Infected necrosis is the most common indication for surgery in acute pancreatitis, but intervention should be delayed for 4 weeks whenever possible.
- Minimally invasive percutaneous or endoscopic drainage should be the first intervention in infected necrotizing pancreatitis.
- If minimally invasive drainage does not resolve the infected necrosis, surgical debridement is needed.

Acute pancreatitis encompasses a wide range of severity, from mild and self-limited to lethal. In its severe forms, the disease tests the judgment, patience, and tenacity of even the most experienced surgeons. This section answers the most common clinical questions related to care of acute pancreatitis, such as which patients should receive antibiotics, what is the best method of nutrition, which patients require surgery, what is the optimal surgical approach, and others.

Epidemiology and Etiology

Acute pancreatitis is the most common gastrointestinal disorder requiring hospitalization in the United States, with an estimated 274,000 hospitalizations in 2009 and its incidence appears to be increasing. In the United States, cases are evenly distributed between men and women, although alcohol is more commonly the cause in men and gallstones are more commonly the cause in women. The incidence increases with increasing age, although the greatest number of cases occur in patients in the fifth or sixth decade of life. The most common causes of acute pancreatitis are ethanol ingestion and gallstones. Less frequent causes include instrumentation of the bile or pancreatic ducts (ERCP), medications (especially diuretics, antiepileptics, and protease inhibitors), hypertriglyceridemia, hypercalcemia, congenital anatomic or genetic conditions (eg, pancreas divisum or cystic fibrosis transmembrane conductance regulator mutation), mumps, pancreatic neoplasm, and trauma or hypoperfusion. In 10% to 15% of cases a cause is not identified. The overall mortality is 2% to 4%.

Pathophysiology

The pathophysiology of acute pancreatitis is poorly understood. The most common causes of acute pancreatitis can generally be broken down into mechanical (gallstones, ERCP) or systemic (alcohol, medications, hypercalcemia, hypertriglyceridemia). There are 2 suggested mechanisms whereby the mechanical causes result in acute pancreatitis: obstruction of the ampulla, or bile reflux into the pancreatic ductal system. How various systemic agents trigger acute pancreatitis is even less clear.

Most investigators agree that, whatever the inciting mechanism, acute pancreatitis result from activation of trypsin within the pancreatic acinar cells. The pancreas has mechanisms for preventing intracellular trypsin activation and counteracting low levels
of activation, but when these mechanisms are overwhelmed, pancreatic autodigestion ensues, which can progress beyond the gland itself and into the surrounding peri-pancreatic tissues. This local injury can in turn activate a variety of systemic inflammatory mediators (complement, interleukins, phospholipase A2) that may be responsible for the systemic effects seen in severe acute pancreatitis.\textsuperscript{32}

**Diagnosis, Classification, and Severity**

The diagnosis of acute pancreatitis is based on the identification of 2 of the following 3 criteria: (1) clinical: central upper abdominal pain, often with associated nausea and vomiting, and sometimes radiating to the back, (2) laboratory: serum amylase or lipase greater than 3 times the upper limit of normal, (3) radiographic: imaging (usually CT or magnetic resonance imaging [MRI]) characteristic of acute pancreatitis. Imaging is rarely required to make the diagnosis of acute pancreatitis, which can usually be made on the basis of clinical and biochemical parameters alone. Rather, imaging should be used acutely only when the diagnosis is unclear, and is typically more valuable later in the course of disease to better define local complications (discussed later in this article). The etiology of any episode of pancreatitis should be sought, as it may allow prevention of recurrent episodes. When there is no obvious inciting factor, such as heavy alcohol use or recent ERCP, abdominal ultrasound should be performed to evaluate for gallstones as a potential cause.

Terminology has been a frequent source of confusion in acute pancreatitis over the past 2 decades. An international working group recently presented revised definitions that will hopefully provide more uniformity. The severity definitions effectively stratify patients by morbidity and mortality (Box 1). Complex or pancreatitis-specific severity scoring systems (eg, Ranson, Glasgow, Balthazar, APACHE 2) do not perform better than these and need not be calculated. Overall, at least 80% of acute pancreatitis is mild, and 20% is severe or moderately severe.\textsuperscript{33}

**Initial Medical Management**

**Fluid resuscitation**

Patients with severe or moderately severe pancreatitis often manifest systemic signs of inflammation (SIRS). Fluid resuscitation is required in the acute phase and based on the limited data available the fluid of choice is Ringer lactate.\textsuperscript{34} The rate and total amount of

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**Box 1**

**Severity classification in acute pancreatitis**

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<thead>
<tr>
<th>Mild Acute Pancreatitis</th>
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<tr>
<td>• No organ failure</td>
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<tr>
<td>• No local or systemic complications</td>
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<table>
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<th>Moderately Severe Acute Pancreatitis</th>
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<tbody>
<tr>
<td>• Organ failure that resolves within 48 hours and/or</td>
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<tr>
<td>• Local or systemic complication (without persistent organ failure)</td>
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<table>
<thead>
<tr>
<th>Severe Acute Pancreatitis</th>
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<tbody>
<tr>
<td>• Persistent organ failure (&gt;48 hours)</td>
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