Disorders of the liver, gallbladder, and pancreas are common causes of abdominal pain. In this article, common emergencies related to the liver, gallbladder, and pancreas are reviewed. In each section, a brief discussion of underlying cellular and pathophysiological mechanisms is followed by a review of the emergency department (ED) diagnosis and management of these diseases.

EMERGENCY DISEASES OF THE LIVER

The liver is the largest abdominal organ and performs many complex vital functions, including carbohydrate, protein, and fat metabolism; waste product metabolism and detoxification; destruction of old red blood cells; bile synthesis; and formation of plasma proteins and liver-dependent clotting factors. Most food and drug products pass directly from the gastrointestinal (GI) tract to the liver via the portal venous system. This process allows the liver to clear potentially toxic substances prior to circulation among the other organs of the body. In addition, the hepatocyte is responsible for the synthesis of albumin, as well as clotting factors I, II, V, VII, and X. Thus, albumin levels and prothrombin times can be used as a guide to liver synthetic function.

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Liver injury is often divided into acute and chronic depending on the duration of liver dysfunction. Acute insults may be reversible with the elimination of the offending agent. However, continuous acute liver injury may lead to hepatic fibrosis, the hallmark of chronic liver injury. Progressive fibrosis leads to cirrhosis and liver failure. Mitochondrial dysfunction is the central molecular event in hepatocyte injury.

In the ED, liver disease primarily presents as cholestasis from biliary tract disease, hepatitis, or as a complication of chronic liver disease. With regard to hepatitis, viral infections and alcohol are the most common offending agents. Other etiological factors to consider include acetaminophen, idiosyncratic drug reactions, hepatotoxins, and autoimmune disorders.

Cholestasis and hepatocellular injury/necrosis are the most common pathologic mechanisms for liver disease in the ED. Cholestasis is simply the obstruction of bile flow within the biliary tract. The obstruction may occur as secondary to intrahepatic or extrahepatic processes. Extrahepatic obstruction is covered in the section on gallbladder pathology. Disorders resulting in intrahepatic cholestasis include infection, alcoholic liver disease, pregnancy, infiltrative diseases, sclerosing cholangitis, and primary biliary cirrhosis.

Cholestatic disorders present with variable degrees of jaundice, dark-colored urine, clay-colored stools, and pruritus. Tender hepatomegaly will often be present. A palpable gallbladder indicates extrahepatic cholestasis. Characteristic laboratory findings include significant elevations of bilirubin (total and direct fraction >50%) and alkaline phosphatase. Total bilirubin levels greater than 30 mg/dL make intrahepatic causes of cholestasis more likely than extrahepatic ones. Mild elevations of aminotransferases may occur with progressive disease.

Hepatocellular injury/necrosis results from infection, toxins, and autoimmune processes. The signs and symptoms include nausea, vomiting, anorexia, and fever. Tender hepatomegaly will often be present and splenomegaly may occur. Characteristic laboratory changes include a greater than fivefold increase in aminotransferase levels, mild increase in alkaline phosphatase, prolonged prothrombin time, and variable elevations in bilirubin levels. Continued insults will lead to chronic liver disease, cirrhosis, and liver failure.

The pathophysiology of liver disease relates to both alterations in hepatic anatomy and loss of functioning hepatocytes. Fibrosis is the final common pathway in sustained liver injury. Viral hepatitis results in early periportal fibrosis, whereas alcoholic liver disease causes centrilobular fibrosis. Continued insults by either will lead to panlobular fibrosis, nodule formation, and cirrhosis. Fibrotic changes lead to increased vascular resistance in the portal venous system, with resultant portal hypertension and splanchnic vasodilation and their sequelae. Loss of functional hepatocytes in association with alterations in hepatic circulation leads to decreased protein synthesis (albumin, coagulation factors), decreased detoxification, and changes in carbohydrate and fat metabolism.

Laboratory Abnormalities

Liver function tests and panels include a group of biochemical markers that reflect hepatic function, including markers for hepatocellular injury/necrosis, hepatic synthesis, catabolic activity, and cholestasis. While these tests may be a guide to hepatobiliary activity, one must be aware that extrahepatic diseases can also cause abnormalities in hepatic function tests.

Laboratory tests for hepatocellular injury include aspartate aminotransferase (AST), alanine aminotransferase (ALT), and to a much lesser extent lactate dehydrogenase (LDH). In addition to the liver, AST is found in the heart, muscle, kidney, and brain.
ALT is primarily present in the liver; thus it is a more specific test of hepatic necrosis. ALT is found mostly in the cytosol whereas AST is present in the cytosol and mitochondria. This fact in part explains the increased AST/ALT ratio in alcoholic liver disease where mitochondrial damage is a key factor. In cholestatic disorders, AST increases before ALT, and the levels usually do not exceed a fivefold increase. With viral hepatitis, AST and ALT levels increase over 1 to 2 weeks to levels in the thousands, and return to normal in 6 weeks in uncomplicated cases. Ischemic hepatitis results in a rapid increase to levels greater than 10,000 IU/L [B]. LDH is found in multiple tissues and is extremely nonspecific. However, significant elevation are indicative of ischemic hepatonecrosis.

Tests that evaluate the hepatic synthetic capability include albumin and prothrombin time (PT). Albumin is produced in hepatocytes, with levels decreasing in advancing disease. The half-life of serum albumin is approximately 20 days. Therefore, it is useful in subacute and chronic disease but not acute hepatocellular necrosis. One should bear in mind that albumin levels are also decreased in nephrotic syndrome, cachexia, malnutrition, malabsorption, and various other GI disorders. Coagulation factors I, II, V, VII, and X are synthesized by hepatocytes. In addition, cholestasis impairs vitamin K absorption decreasing the function of coagulation factors II, VII, IX, and X.3 The PT can prolong in as little as 24 hours of liver disease and therefore is much more sensitive than albumin for evaluating hepatic synthetic function.

Bilirubin, alkaline phosphatase, and γ-glutamyl transpeptidase (GGT) are markers for hepatobiliary dysfunction and cholestasis. Bilirubin is a product of the breakdown of heme-containing proteins. Bilirubin is insoluble. In the liver, bilirubin is conjugated to glucuronic acid. Conjugated bilirubin is water soluble and excreted into bile.6 Direct bilirubin measures the level of conjugated bilirubin, whereas indirect bilirubin is the unconjugated fraction. Bilirubin levels are traditionally reported as total bilirubin and direct bilirubin. Direct hyperbilirubinemia indicates hepatocellular dysfunction or cholestasis.3 Indirect hyperbilirubinemia can also be caused by liver disease but also may be due to hemolysis or hereditary diseases, most commonly Gilbert syndrome (a benign genetic defect in bilirubin conjugation).3 Alkaline phosphatase is present in many tissues including bone, placenta, intestine, kidney, and liver. Hepatic alkaline phosphatase is produced in bile duct epithelial cells. Cholestasis stimulates increased production and release of alkaline phosphatase. The half-life of circulating alkaline phosphatase is approximately 1 week.4 Alkaline phosphatase levels are nonspecific and need to be evaluated in context of the clinical scenario and other laboratory values. GGT is also present in biliary epithelial cells, and levels increase in cholestasis. When used in conjunction with alkaline phosphatase, GGT is useful to confirm cholestasis. GGT levels are elevated in chronic alcohol use, due to increased production and decreased clearance. Increased GGT levels are also found in chronic liver disease, on use of certain drugs (anticonvulsants, oral contraceptives), and in various nonhepatic disorders including chronic obstructive pulmonary disease, renal failure, and acute myocardial infarction.

Serum ammonia levels are used in the evaluation of hepatic encephalopathy. Ammonia is a by-product of protein metabolism in the intestines and liver. Ammonia produced by the intestinal flora enters the portal venous system. In the setting of portal hypertension, portal systemic shunting occurs, allowing the ammonia to bypass the liver. The result is increased levels of ammonia crossing the blood-brain barrier. In addition to shunting, hepatic dysfunction is associated with decreased metabolism of ammonia as well as increased levels.
Viral Hepatitis

Viral infections are a common cause of hepatitis. The primary pathogens are hepatitis A (HAV), B (HBV), C (HCV), D (HDV), and E (HEV). Hepatitis D is a defective virus and requires coinfection with HBV. HAV and HEV are transmitted via the fecal-oral route, most commonly through contaminated food and water. Poor hygiene and sanitation are significant risk factors. HAV is most commonly nonfatal and self-limited. However, HAV infection in the setting of preexisting HCV increases the risk of fulminant hepatic failure and death. HEV, similar to HAV, is usually self-limited and nonfatal. However, the clinical course is often more severe than that of HAV. HEV infection during the third trimester of pregnancy is a risk factor for acute fulminant hepatitis and death. In immunosuppressed patients, HEV may progress from acute to chronic hepatitis with persistent inflammation and viremia.

HBV is transmitted through exposure to contaminated blood and body fluids via parenteral or mucosal exposure. During the acute phase, the presentation ranges from asymptomatic to fulminant hepatitis. Ninety-five percent of immunocompetent adults will recover from the acute infection. HBV can seroconvert to chronic hepatitis. In chronic HBV, the clinical presentation ranges from asymptomatic carrier state to cirrhosis. The risk of conversion to chronic HBV is age related and much higher when the infection occurs at a very young age. Chronic HBV is a risk factor for the development of hepatocellular carcinoma.

HDV is also transmitted via blood and body fluid exposure. HDV requires the presence of HBV to replicate, and is only infectious as a coinfection or superinfection on preexisting HBV. HDV portends a more severe course and an increased risk of fulminant hepatitis.

HCV is contracted through blood or body fluid exposure. The acute phase is often asymptomatic or very mild. Whereas fulminant hepatitis is rare in HCV, chronic hepatitis is relatively common. Seventy percent of cases will seroconvert to chronic HCV. Of those with chronic HCV, 15% to 20% will progress to cirrhosis. Chronic HCV, like HBV, increases the risk of hepatocellular carcinoma.

Patients with acute hepatitis will present with varying degrees of weakness, nausea, vomiting, right upper quadrant pain, and jaundice. Diagnosis is made by obtaining hepatitis viral serology. Interpretation of hepatitis viral panels is complex. These measurements can help assess the acuity or chronicity of the infection, as well as immunosuppression. However, this assessment, requiring consideration of the patients’ underlying illnesses and immune status, is beyond the scope of this article. Treatment of acute viral hepatitis in the ED is primarily symptomatic and supportive. Maintaining an adequate fluid and electrolyte balance is the goal of therapy. Admission versus outpatient care is dependent on the severity of the patient’s illness, the ability to maintain adequate hydration, and the absence of complications. If discharged, these patients should be referred for follow-up to monitor recovery and to determine the need for more specific treatments (antiviral, interferon).

Alcoholic Liver Disease

Alcoholic liver disease is a significant source of morbidity and mortality in the United States and worldwide. Alcoholism and its effects rank fifth on the global burden of disease by the World Health Organization. Alcoholic liver disease includes the entire spectrum from alcoholic hepatic steatosis (fatty liver), to alcoholic hepatitis, to fibrosis and cirrhosis. The morbidity and mortality is related to the degree of hepatic fibrosis and dysfunction, and its sequelae.
Alcoholic hepatitis

Alcoholic hepatitis is an acute inflammatory condition of the liver secondary to alcohol use and abuse. In most cases it occurs after many years of significant alcohol abuse. In its mild form the damage is reversible. However, severe cases are potentially lethal, with a mortality rate of up to 40% at 6 months. The most common age group for alcoholic hepatitis is 40 to 60 years. Clinically the presentation ranges from subclinical cases, with only laboratory abnormalities, to severe multisystem dysfunction. The rapid onset of jaundice is a key finding in alcoholic hepatitis. Other findings include right upper quadrant pain, fever, hepatomegaly, weight loss, fatigue, and anorexia. In severe cases, patients may exhibit signs of hepatic decompensation with ascites and encephalopathy. On examination, jaundice and hepatic tenderness are the key findings. In addition, clinical stigmata of chronic alcohol abuse such as spider angiomata, subcutaneous ecchymosis, feminization, and palmar erythema may be present.

The pathogenesis of alcoholic hepatitis is multifactorial, involving gut permeability and endotoxemia, acetaldehyde formation, oxidant stress, and poor nutrition. Ingestion of ethanol alters gut permeability, allowing the absorption of endotoxin into the portal venous circulation. Once in the liver, endotoxin activates the inflammatory cascade leading to the release of inflammatory cytokines, which have local effects on the hepatocytes (injury and necrosis) as well as systemic effects such as fever, anorexia, and weight loss. The metabolism of ethanol in the liver is an additional source of its toxicity, due to by-products of metabolism and oxidative stress. The breakdown of ethanol by alcohol dehydrogenase creates excess reducing equivalents, altering the NADH/NAD⁺ ratio, which subsequently leads to inhibition of fatty acid oxidation and promotes lipogenesis. In addition, ethanol-induced alterations in enzyme activity lead to increased hepatic lipid synthesis, fatty liver, and a decreased rate of fatty acid oxidation. Oxidative stress plays an important role as well. Ethanol ingestion stimulates the activity of cytochrome P450 2E1, which generates reactive oxygen radicals leading to hepatic necrosis. Chronic alcohol abuse also impairs the regenerative capacity of the liver because inflammatory cytokines combined with poor nutrition (lack of metabolic substrates) impairs hepatic cellular replication.

Laboratory findings in alcoholic hepatitis include liver function test abnormalities as well as nonhepatic laboratory changes. Liver function abnormalities include elevations of AST and ALT—up to 7 times the normal. Characteristically the ratio of AST/ALT will be greater than 2:1. The total serum bilirubin is usually greater than 5 mg/dL and the PT is also elevated. Nonhepatic abnormalities include an elevated white blood cell (WBC) count and neutrophil count. The primary management of alcoholic hepatitis is supportive, including the maintenance of fluid and electrolyte balance, glucose supplementation as needed, thiamine, and control of withdrawal symptoms. Abstinence from alcohol is the mainstay of long-term therapy. Abstinence will prevent ongoing liver injury and allow resolution of alcoholic steatosis. Nutritional support is another cornerstone of therapy for alcoholic hepatitis. A large Veteran’s Affairs study found a 100% prevalence of protein calorie malnutrition in these patients; and the degree of malnutrition correlated with the severity of the liver dysfunction. Numerous other agents have been studied for therapy in alcoholic hepatitis. Corticosteroids have shown some benefit in control of the inflammatory cascade, and are currently indicated for severe cases. Pentoxifylline appears to show some promise through reduction of inflammatory cytokines and decreased incidence of subsequent hepatorenal syndrome (HRS). After promising early reports, randomized controlled trials of infliximab and etanercept (direct anti–tumor necrosis factor-α agents) in patients...
with alcoholic hepatitis found them to be associated with increased rates of serious infection and death.\textsuperscript{15,21}

**Complications of Chronic Liver Disease**

In chronic liver disease, complications occur increasingly with rising portal venous pressures and diminishing hepatic metabolic activity. This section focuses on those complications that may present to the ED including HRS, ascites, spontaneous bacterial peritonitis (SBP), and hepatic encephalopathy (HE). Esophageal variceal bleeds are covered in the article elsewhere in this issue on GI hemorrhage.

**Hepatorenal syndrome**

Renal failure is a common complication in patients with liver disease. HRS is the cause in a specific subset of these patients. The combination of liver disease and renal failure portends a poor prognosis and is associated with increased mortality.\textsuperscript{22} HRS is the most common fatal complication of cirrhosis.\textsuperscript{23}

HRS is defined as acute or subacute renal failure in the presence of advanced liver disease and structurally normal kidneys. It is a functional renal failure secondary to severe renal vasoconstriction.\textsuperscript{23} The systemic vascular resistance is markedly reduced, leading to low arterial pressures and subsequent renal vascular constriction.\textsuperscript{24} While this most commonly occurs in patients with cirrhosis and ascites, it can occur in alcoholic hepatitis and in the setting of acute fulminant hepatic failure.\textsuperscript{24} Renal vasoconstriction is the hallmark event in the pathophysiology of HRS. Several theories exist to explain this phenomenon. However, the resulting final common pathway is vasoconstrictor activation, which leads to sodium retention and ascites, water retention and hyponatremia, and renal vasoconstriction and HRS.\textsuperscript{25}

The diagnosis of HRS is complex and is beyond the scope of ED evaluation and management of liver failure patients, because it requires proof that the renal impairment is not due to volume status, shock, infection, nephrotoxic drugs, or acute tubular necrosis.\textsuperscript{26} However, the diagnosis should be suspected in any patient with chronic liver disease and an elevated creatinine.

HRS is classified as type 1 and type 2. Type 1 HRS is characterized by a severe and rapidly progressive renal failure with a doubling of the serum creatinine to greater than 2.5 mg/dL in less than 2 weeks. Type 1 HRS usually develops in the face of an acute precipitant, with SBP the most common insult.\textsuperscript{27} Type 1 HRS is rapidly progressive, and has an extremely high mortality with a median survival of 1 to 2 weeks.\textsuperscript{23} Type 2 HRS is characterized by a slow and gradual increase in serum creatinine with no precipitating events. Refractory ascites is the dominant clinical feature.\textsuperscript{27} It is important clinically to distinguish between types 1 and 2 HRS, because type 1 is an indication for evaluation for liver transplantation.\textsuperscript{23}

The mainstay of ED management of HRS is supportive, although the only definitive therapy is transplantation.\textsuperscript{28} Early therapy should be aimed at correcting any precipitating events such as SBP, infection, and GI bleeding. In type 1 HRS, the underlying precipitating event should be treated aggressively. Early antibiotic support is indicated, because infectious processes are the most common precipitating events.\textsuperscript{23} Diuretics should be discontinued and the intravascular volume should be assessed. Early volume expansion with albumin may improve the renal blood flow.\textsuperscript{23}

**Spontaneous bacterial peritonitis**

Cirrhosis leads to portal hypertension through the obstruction of portal blood flow. This process stimulates a cascade of events, leading to activation of the
renin-angiotensin-aldosterone axis, sodium and water retention, and the development of ascites due to overflow of hepatic lymphocytic fluid into the peritoneal cavity. In addition, increased hepatic sinusoidal hydrostatic pressure and decreased plasma oncotic pressure lead to the excess production of hepatic lymphatic fluid, which ultimately leaks into the peritoneal cavity forming ascites. SBP is an infection of ascitic fluid.

SBP should be suspected in a patient with abdominal pain and preexisting liver disease and ascites. Fever is not always present and the abdominal pain may not be severe. Worsening ascites may be the only early symptom. The patient may also have an altered mental status, GI bleeding, and azotemia. The prevalence of SBP ranges from 10% to 30% in patients with preexisting ascites. While SBP is readily treatable, its development increases the risk of other complications, such as type 1 HRS.

The pathogenesis of SBP involves the translocation of bacteria, most commonly from the GI tract, into the bloodstream. The resulting bacteremia leads to infection of the ascitic fluid through exchange of fluids between the intravascular space and the peritoneal fluid. Escherichia coli is the most common pathogen isolated, with Klebsiella pneumoniae the second most common.

The diagnosis of SBP is relatively straightforward. An abdominal paracentesis should be performed in anyone suspected of having SBP and without contraindications to the procedure. The finding of an ascitic WBC count of greater than 1000 cells/µL and a polymorphonuclear count of greater than 250 cells/µL is diagnostic. A pH of less than 7.35 in the ascitic fluid is supportive of the diagnosis. The ascitic fluid should be cultured, but a positive culture is not necessary to make the diagnosis. Approximately 30% will return a positive culture.

Treatment should be started with the finding of inflammatory ascitic fluid. Third-generation cephalosporins are the treatment of choice. Regarding prevention, treatment with norfloxacin has been shown to be effective at decreasing the incidence of primary SBP as well as recurrence of SBP. The most feared complication of SBP is type 1 HRS, which occurs in up to 30% of patients and carries an exceptionally high mortality. Recurrence of SBP occurs in approximately 70% of patients in 1 year. Long-term prophylaxis with fluoroquinolones has decreased this percentage, but SBP due to quinolone-resistant bacteria is on the increase.

**Hepatic encephalopathy**

HE is a condition in which a patient with liver dysfunction and/or portal-systemic shunting displays neurologic and/or psychological abnormalities without another pathologic condition to explain the findings. HE may present in acute or chronic liver failure. HE is a key feature of fulminant hepatic failure and a is common complication of chronic liver disease. HE includes presentations ranging from mild altered mental status to coma, and neuromuscular abnormalities ranging from tremor and asterixis to decerebrate posturing. The symptoms result from the inability of the liver to detoxify intestinal toxins.

HE is classified into 3 types based on the underlying liver disease. Type A HE occurs in acute liver failure. Type B is caused by portosystemic shunting without intrinsic hepatocellular disease. Type C, the most common form, arises from cirrhosis-induced portal-systemic shunting, and may be persistent or episodic. HE is staged using the West Haven Criteria from stage 0 to 4. Stage 0 shows no change in consciousness and behavior and no neuromuscular changes. Stage 1 involves a trivial lack of awareness with a shortened attention span, and impairment in addition and subtraction abilities. Asterixis and tremor may also begin to appear. Stage 2 involves
lethargy, disorientation, and inappropriate behavior. Slurred speech and asterixis will be present as well. Stage 3 involves gross disorientation and bizarre behavior with a somnolent (but arousable) state. The patient may have muscular rigidity, and asterixis is usually absent. Stage 4 involves a comatose state that may progress to decerebrate posturing.34

The pathogenesis of HE is complex and multifactorial. The key feature is hepatic dysfunction (most commonly cirrhosis-induced portal-systemic shunting) or noncirrhotic portal-systemic shunting leading to the inability of the liver to clear ammonia, γ-aminobutyric acid agonists, and manganese. These substances subsequently cross the blood-brain barrier, leading to altered neurotransmission and neuronal impairment. Neurologic impairment occurs through both direct toxic effects and indirect effects through neuroinhibition. Oxidative stress and inflammatory cytokines play a role as well.7,33,35

The diagnosis of HE requires a thorough history as well as physical and laboratory/radiological evaluation. The diagnosis should be suspected in any patient with known liver disease who presents with altered mental status and neuromuscular abnormalities. However, a thorough evaluation is indicated to rule out other causes of the altered mental status. The differential diagnosis of HE includes, but is not limited to, metabolic encephalopathy (uremia, sepsis, hypoxia, and hypoglycemia), intracranial bleeding, cerebrovascular accident/transient ischemic attack, central nervous system infections or neoplasms, and alcohol withdrawal/intoxication states.36 An elevated serum ammonia is typical of HE. There has been extensive controversy over the years as to whether serum ammonia levels correlated with the severity of HE; however, it appears that if drawn and analyzed appropriately, serum ammonia levels do correlate with the severity of HE.37 Computed tomography (CT) of the head should be performed to rule out structural causes for the altered mental status, and finally the workup should include an evaluation for precipitating causes.36

The management of HE involves simultaneous attention to multiple goals that include general supportive care, treatment of precipitating events, inhibition of ammonia production and absorption, and avoidance of sedatives unless absolutely necessary. General supportive care entails management of the patient’s fluid and electrolyte balance, protection of the airway, and cardiovascular stabilization. Treatment and correction of the precipitating events is extremely important, given that HE will not improve until the precipitant is removed. Common precipitants include gastrointestinal bleeding, infection, renal failure, and dehydration.38 Nonabsorbable disaccharides such as lactulose and lactitol are administered to help decrease the ammonia load from the gut. These medications work by decreasing both the absorption and production of intestinal ammonia, and are considered first-line therapy for HE.39 Antibiotics are administered in HE to decreased ammonia production by decreasing the number of urease-producing bacteria in the gut.39 Oral neomycin has been used for many years although it is potentially ototoxic and nephrotoxic.39 Other antibiotics studied for this purpose include metronidazole, oral vancomycin, and rifaximin.36 Rifaximin has a favorable side effect profile compared with neomycin.39 Finally, recurrent or intractable HE is an indication for evaluation for liver transplantation.38

**EMERGENCY DISEASES OF THE GALLBLADDER**

Biliary tract disease is one of the most common gastrointestinal disorders in the United States, ranging from asymptomatic cholelithiasis to biliary colic, cholecystitis, cholecdocholithiasis, cholangitis, and malignancy. With direct costs of $5.8 billion annually, biliary disease is the second most expensive digestive disease in the United States.40
and accounts for 3% to 9% of hospital admissions for acute abdominal pain. Cholecystitis is the most prevalent surgical disease in industrialized countries. An estimated 700,000 cholecystectomies are performed annually in the United States. The vast majority of biliary tract disease is caused by gallstones. Approximately 20 to 25 million Americans have gallstones, of which 1% to 2% per year become symptomatic. Thus, whereas the annual percentage of patients who develop complications is low, the incidence of acute disease is high because of the high prevalence of gallstones in the population.

Anatomy and Pathophysiology

Hepatocytes secrete bile into the bile canaliculi, which are formed by the cell walls of the hepatocytes. Bile then flows into ductules, which coalesce into successively larger ducts. The hepatic ducts course along with branches of the portal vein and hepatic artery, which together form the portal triad. The right and left hepatic ducts join to form the common hepatic duct. The cystic duct drains the gallbladder and joins the common hepatic duct to form the common bile duct. The common bile duct is usually situated anterior and to the right of the portal vein; it courses caudally behind the first portion of the duodenum, then anterior to the pancreas where it is joined by the pancreatic duct. It drains into the second part of the duodenum at the ampulla of Vater, the orifice of which is controlled by the sphincter of Oddi. Variations in hepatobiliary anatomy are common.

Bile is necessary for proper digestion and absorption of dietary fats and fat-soluble vitamins, as well as the fecal excretion of excess cholesterol and the by-products of red blood cell catabolism. The gallbladder stores bile between meals and also actively concentrates it by removing water and inorganic anions (chloride, bicarbonate). Gallstones are formed when cholesterol and calcium salts precipitate out of supersaturated bile. Bile stasis and a nidus for nucleation/crystallization are also factors. Although most gallstones are composed primarily of cholesterol (cholesterol stones), pigmented stones can also occur. Brown pigmented stones are more common in Asians and with bacterial contamination of the biliary tree, whereas black stones are associated with hemolytic disorders, cirrhosis, cystic fibrosis, and ileal disease. Historically in the United States, up to 10% to 25% of stones were pigmented; however, the percentage of cholesterol stones seems to be increasing as obesity becomes more common. Biliary sludge is a viscous mixture of small cholesterol or calcium bilirubinate crystals that have begun to precipitate; it can lead to the same symptoms and complications as gallstones.

Gallstones become symptomatic when they cause obstruction of the biliary system. When the gallbladder contracts against an obstructing gallstone (typically lodged in the gallbladder neck), biliary colic ensues. If the obstruction is relieved, the pain resolves. Prolonged obstruction leads to increased intraluminal pressure, wall edema, and an acute inflammatory response. If the obstruction continues, the gallbladder wall becomes ischemic and further inflammatory mediators are released. Secondary bacterial infection may result in formation of an abscess or empyema within the gallbladder. Perforation may lead to diffuse peritonitis. Gas-forming organisms may lead to emphysematous cholecystitis.

Bacteria are cultured from the bile of patients undergoing cholecystectomy for uncomplicated gallstone disease in 13% to 32% of patients, and in 41% to 54% of those with acute cholecystitis; healthy individuals do not have bacterial isolates. It is more common to find bacteria in pigment-stone-containing bile than in cholesterol-stone-containing bile (82% vs 26% in one study). Bacteria are more commonly found in the bile of those with biliary obstruction, acute cholecystitis, common duct
stones, cholangitis, and nonfunctioning gallbladders; in males, the elderly, and those with biliary stents. Typical bacterial isolates include enterobacteriaceae (68%), enterococci (14%), bacteroides (10%), and Clostridium species (7%).

Risk factors for cholesterol gallstones are listed in Box 1. Age and gender are the most important risk factors for development of gallstone disease. Gallstones are rare in children, but may be associated with congenital anomalies, Down syndrome, and hemolytic diseases (such as sickle cell disease). By the fifth decade of life, approximately 15% of women have gallstones, increasing to approximately 40% by the ninth decade; the incidence of gallstones increases by 1% to 3% per year in adulthood, depending on risk factors. The female to male ratio of gallstones is approximately 4:1 in those younger than 40 years, and 2:1 in older age groups. More females develop gallstones, so the overall incidence of cholecystitis is higher in females (the overall female to male ratio is 3:1), but a higher percentage of men with gallstones develop cholecystitis.

Patients with previously asymptomatic gallstones have an annual risk of approximately 1% for biliary colic, 0.3% for acute cholecystitis, 0.2% for symptomatic choledocholithiasis, and 0.04% to 0.2% for gallstone pancreatitis. After the first episode of symptoms, the rate of both recurrent symptoms and complications increase, with 1% to 3% per year developing complications.

Clinical Presentation

A wide range of symptoms has been attributed to gallstones. The term “colic,” applied to pain due to biliary disease, can be misleading because it is not paroxysmal, but rather a steady pain that lasts from 15 minutes to more than 12 hours per episode. Colic is perceived in the mid-epigastric region as often as the right upper quadrant. It is typically described as sharp and crampy, and may be precipitated by fatty food intake. It may radiate to the right shoulder or scapula. Associated symptoms may include nausea, vomiting, chills, bloating, belching, acid regurgitation, flatulence,
constipation, and/or diarrhea. Patients frequently have had previous episodes of similar symptoms.58–60

In a prospective cohort study of 233 patients with abdominal symptoms that were suspicious for biliary tract disease, neither classic biliary colic nor any of the described atypical symptoms were sufficiently sensitive or specific to diagnose gallstones. The likelihood ratio for gallstones when biliary pain was present was only 1.34 (95% confidence interval [CI] 1.05–1.71).58 A meta-analysis of 24 publications found similarly poor predictive value for abdominal symptoms. The symptom of biliary colic had an odds ratio of only 2.6 (95% CI 2.4–2.9) in predicting gallstones.59 It is important to be aware that upper abdominal pain has test characteristics similar to right upper quadrant pain,41 so isolated epigastric pain, rather than excluding biliary tract disease, is actually consistent with it. Approximately half of patients who develop acute cholecystitis have a history of biliary colic.56,61

Physical examination may elicit localized right upper quadrant tenderness, but examination will be normal between episodes of biliary colic. Murphy’s sign refers to pain during right upper quadrant palpation during inspiration; as the gallbladder descends into the examiner’s palpating hand, there is sudden inspiratory arrest. Among 100 ED patients with suspected acute cholecystitis (all of whom underwent hepatobiliary scintigraphy, with 53 positive studies), the presence of Murphy’s sign had a sensitivity of 97.2% and specificity of 48.3%.62 A meta-analysis that included data on 565 patients found a positive likelihood ratio of 2.8 (95% CI 0.8–8.6) and negative likelihood ratio of 0.5 (95% CI 0.2–1.0).41 In elderly patients Murphy’s sign is less reliable; the sensitivity has been reported as only 48% with specificity of 79%.63

Courvoisier’s sign refers to a palpable gallbladder in a jaundiced patient. In a case series published in 1890, Courvoisier noted that gallstones rarely lead to persistent gallbladder dilation because they cause obstruction that is intermittent.64 Conversely, the gradual, progressive obstruction caused by malignancy frequently leads to gallbladder dilation. Although cancer of the head of the pancreas is classically associated with Courvoisier gallbladder, there are several other nonmalignant causes.64

No historical features, signs, or symptoms are adequate to rule in or rule out symptomatic cholelithiasis or cholecystitis. After history and physical examination, the differential diagnosis may still be broad and may include acute coronary syndrome, pneumonia, gastritis, peptic ulcer disease, esophageal spasm, pancreatitis, hepatitis, urolithiasis, pyelonephritis, or appendicitis, among others.

Laboratory Evaluation

Laboratory studies are typically normal with episodes of uncomplicated symptomatic cholelithiasis (biliary colic). With acute cholecystitis, there is no single or combination of laboratory abnormalities that has either positive or negative likelihood ratios of sufficient magnitude to rule in or rule out cholecystitis.41 There may be a leukocytosis with left shift, though the WBC count is usually normal. Alkaline phosphatase, liver transaminases, and bilirubin may be normal or mildly elevated. Bile flow is generally not obstructed in acute cholecystitis, so a high bilirubin should prompt consideration of choledocholithiasis. Mirizzi syndrome, when a gallstone impacted in the gallbladder neck or cystic duct compresses the common hepatic duct, can also result in various degrees of biliary obstruction.65 Other laboratory values are nonspecific, but can be useful in ruling out other diagnostic considerations in the differential diagnosis.

Certain clinical and laboratory findings may suggest that acute cholecystitis is more likely than simple biliary colic: history of pain for more than 6 hours, more severe symptoms (pain, nausea, vomiting), pain more localized to the right upper quadrant, fever, Murphy’s sign, leukocytosis, elevated liver enzymes (with greater elevation of alkaline
phosphatase than transaminases), and hyperbilirubinemia. However, because no combination of clinical or laboratory parameters are reliable for the diagnosis of acute biliary disease, the physician’s judgment will be the driving force behind decisions to pursue imaging studies. One estimate is that the physician’s gestalt (after considering clinical and laboratory findings) has a positive likelihood ratio of 25 to 30. Typical imaging studies include ultrasonography, hepatobiliary iminodiacetic acid (HIDA) scan, or CT.

**Diagnostic Imaging Evaluation**

**Ultrasonography**

Ultrasonography of the right upper quadrant should generally be the first-line imaging modality when considering biliary disease. Ultrasonography is considered the most appropriate initial diagnostic imaging study for right upper quadrant pain by the American College of Radiology (ACR). Focused emergency ultrasonography performed by emergency physicians (EPs) is rapid and accurate not only for biliary disease, but also excludes other life-threatening processes such as abdominal aortic aneurysm. Even if used as a screening test with the plan to pursue a formal study regardless of findings, EP-performed ultrasonography may allow earlier interventions (analgesics, antibiotics, surgical consultation) and guide subsequent radiologist-interpreted imaging (eg, the choice of abdominal CT versus ultrasonography performed in the radiology department).

Gallstones appear as bright echogenic foci in the gallbladder lumen; they cast a posterior shadow and are gravity dependent (ie, move with changes in patient position) (Fig. 1). EPs in a wide range of settings have high rates of gallstone identification, with sensitivity of 88% to 96% and specificity of 78% to 96% when compared with radiology department ultrasonography. Minimal training to ensure competence includes at least 25 documented and reviewed cases. False-negative results may occur more frequently with small stones (<1–3 mm), artifact from bowel, and gallstones impacted in the gallbladder neck or cystic duct. Smaller stones may be better visualized with higher frequencies or harmonic imaging. Imaging from different acoustic windows (subcostal, intercostal, and right flank), patient positions (recumbent, decubitus, sitting), and with inspiration if gallstones are suspected but not initially

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**Fig. 1.** In this case of uncomplicated biliary colic, the gallbladder wall is thin. The large stone (open arrowhead) has prominent posterior shadowing (bracket). The portal triad can be located by its position as the “point” of the “exclamation point” formed by the long view of the gallbladder. The classic “Mickey Mouse” transverse view of the portal triad shows the portal vein (asterisk), hepatic artery (arrow), and common bile duct (arrowhead). These structures were verified in real time by using color flow, which demonstrated flow in the artery and vein, but no flow in the bile duct. (Courtesy of Jeremy Smith, MD.)
Higher-quality ultrasound machines may improve diagnostic accuracy of EPs. Given their high prevalence, identification of gallstones does not mean that they are the cause of the patient’s symptoms, so this finding should be correlated with the overall clinical picture.

A sonographic Murphy sign is elicited when maximal tenderness exists when probe pressure is applied directly onto the sonographically visualized gallbladder. Compared with other ultrasonographic findings, it is technically simple to elicit and has high sensitivity in the hands of EPs. In a study of 109 right upper quadrant ultrasonographic examinations performed by EPs, the presence of gallstones and a positive sonographic Murphy sign had a sensitivity of 75% and specificity of 55% for acute cholecystitis. In this study, sensitivity of sonographic Murphy sign in studies performed by technicians and radiologists was lower (45%), but specificity was higher (81%). In another study involving 116 patients using the criterion of both gallstones and sonographic Murphy sign being present, EP-performed ultrasonography was 91% sensitive and 66% specific for acute cholecystitis. Sonographic Murphy sign may not be present in patients with diabetes, gangrenous cholecystitis, or perforation.

Additional sonographic features of acute cholecystitis include gallbladder wall thickening and pericholecystic fluid. These secondary findings are inconsistently detected by EPs, although accuracy likely improves with greater training and experience. Gallbladder wall thickness should be measured at the anterior wall in the transverse plane to avoid edge artifact, posterior acoustic enhancement, or tangent effect. Normal thickness is less than 3 mm; 50% of patients with acute cholecystitis have wall thickening. Conversely, about 50% of patients with wall thickening have a nonsurgical condition such as liver disease, congestive heart failure, renal disease, or the normal contraction seen in a postprandial state.

Gallbladder sludge appears as low-amplitude echoes in the dependent portion of the gallbladder without acoustic shadowing. Occasionally the gallbladder will be completely filled with gallstones, leading to the WES (wall-echo-shadow) sign, in which the gallbladder wall is seen immediately anterior to bright echoes from multiple stones with strong posterior acoustic shadowing. Although rare, gas in the lumen or wall of the gallbladder is an important finding, indicating emphysematous cholecystitis; in this situation, CT may provide additional information. Overall, the ability of EP-performed ultrasonography to diagnose acute cholecystitis is comparably accurate to formal ultrasonography. The radiology literature reports sensitivities ranging from 84% to 98% and specificities ranging from 90% to 99%.

![Fig. 2](image-url) A gallbladder completely filled with stones will lead to the wall-echo-shadow (WES) sign, in which the gallbladder wall (arrow) is seen immediately anterior to bright echoes from multiple stones with strong posterior acoustic shadowing (bracket).
Plain film radiography and CT

Plain radiographs have limited utility in biliary disease, except for evaluating associated ileus or identifying free air associated with emphysematous cholecystitis or perforation. Approximately 20% of gallstones are radiopaque, but a much lower proportion will be seen on plain radiographs. CT scan of the abdomen is much less sensitive than ultrasonography for biliary tract disease, is more expensive, mandates patient movement out of the ED, and exposes the patient to radiation and contrast. The sensitivity of CT for gallstones is approximately 75%. Compared with ultrasonography, one study found CT to have a sensitivity of only 39% and specificity of 93% for acute biliary disease. CT may have a role in biliary disease when ultrasonographic findings are equivocal, or when the complications of perforation or emphysematous cholecystitis are suspected. With equivocal clinical findings and a broader differential diagnosis, the information provided by CT regarding alternative diagnoses may make it a preferable initial imaging modality.

Nuclear medicine hepatobiliary evaluation

Radionuclide cholescintigraphy scans, such as the HIDA scan, can be used when ultrasonographic findings are equivocal, as they have a higher sensitivity (90%–100%) and specificity (85%–90%) for cholecystitis. Cholescintigraphy gives little information about nonobstructing cholelithiasis, and will therefore miss cases of resolved biliary colic after an obstructing stone has spontaneously dislodged from the gallbladder neck. The ACR appropriateness criteria suggest cholescintigraphy as the initial imaging study for suspected acalculous cholecystitis, although this recommendation may be moot because the diagnosis is almost never entertained without a prior ultrasonogram showing gallbladder wall abnormalities and the absence of gallstones. The limited availability and typical delays in obtaining cholescintigraphy render it of only marginal use in the ED.

The study is done after intravenous administration of technetium-labeled derivatives of iminodiacetic acid. These markers are taken up by hepatocytes and are excreted...
into the biliary tree. The gallbladder is normally visualized within 30 minutes of injection and the small bowel within 60 minutes. Nonfilling of the gallbladder is highly suggestive of acute cholecystitis in the proper clinical setting, but nonfilling alone is a nonspecific finding that could also be related to prolonged fasting or severe liver disease. False positives may occur with high bilirubin levels and severe intercurrent illnesses. Scintigraphy is expensive, takes up to 4 hours to complete, and cannot contribute to the diagnosis if the etiology does not concern the biliary tract.

Abdominal magnetic resonance imaging has high diagnostic accuracy for biliary pathology, but the lack of availability, high cost, and time involved limit its use in ED patients. Endoscopic retrograde cholangiopancreatography (ERCP) is useful in the diagnosis and treatment of bile duct obstruction, but is not typically performed in the ED. The diagnostic accuracy of magnetic resonance cholangiopancreatography reaches similar diagnostic accuracy as ERCP, but does not allow for intervention.

### Treatment

During the course of ED diagnostic studies, resuscitative care, volume repletion, antiemetics, analgesics, and bowel rest are indicated. If uncomplicated symptomatic cholelithiasis is diagnosed, referral for scheduled routine cholecystectomy is indicated. Prescriptions for antiemetics and opioid analgesic are typically provided. Nonsteroidal anti-inflammatory drugs (specifically diclofenac and indomethacin) not only ameliorate pain, but may also prevent progression of disease to acute cholecystitis. Diet and nutritional approaches, bile acids to dissolve stones, and lithotripsy can be considered in patients who refuse surgery, but these are not therapeutic options in the ED, and there are high recurrence rates. As previously noted, expectant management of symptomatic gallstones leads to complicated disease (such as acute cholecystitis or pancreatitis) in 1% to 3% of patients per year. However, because the symptoms of biliary colic are so varied and inconsistent, the EP may not be certain whether the patient’s gallstones are an incidental finding or are actually responsible for his or her abdominal symptoms. One literature review found the pooled relief rate of cholecystectomy for “biliary pain” to be 92%, but broader symptomatic indications for cholecystectomy led to much lower corresponding symptom relief rates. Thus, decisions regarding immediate versus outpatient surgical evaluation versus expectant management with follow-up with a primary physician require clinical judgment on a case-by-case basis. Incidentally discovered asymptomatic gallstones are not an indication for cholecystectomy, as the procedure does not improve outcome and has associated morbidity and even mortality.

In addition to the supportive care described, the initial management of acute cholecystitis includes hospital admission and early surgical consultation. Although cholecystitis is predominantly an inflammatory disease, it may be difficult to determine when secondary bacterial infection has occurred, therefore antibiotics should be considered. Typical regimens include ampicillin with gentamycin, ampicillin-sulbactam, piperacillin-tazobactam, a third- or fourth-generation cephalosporin, or a third-generation fluoroquinolone. More severe disease should prompt a broader spectrum of antibiotic coverage. Aside from findings on imaging studies, risk factors for development of complicated disease include advanced age, male sex, diabetes, fever, palpable gallbladder, elevated alkaline phosphatase, and leukocytosis.

Cholecystectomy is the definitive treatment, and should be performed within the first 24 to 48 hours of admission in most cases. The practice of delayed cholecystectomy 4 to 8 weeks after acute inflammation (“cooling off” period) is no longer recommended. Delayed cholecystectomy does not reduce the conversion rate from laparoscopic to
Complications and Special Considerations

The primary cause of cholecystitis is gallstones, but other causes may include primary tumors of the gallbladder or common duct, metastatic lesions, benign gallbladder polyps, parasites, periportal lymph nodes, or foreign bodies (such as bullets or fish bones). Acute acalculous cholecystitis accounts for 5% to 14% of acute cholecystitis cases. Rarely diagnosed in ED patients, it is seen most commonly as a complication in patients admitted to intensive care units. Other risk factors for acalculous cholecystitis include old age, male gender, diabetes, immunosuppression, vascular disease, prolonged fasting, total parenteral nutrition, acute renal failure, and childbirth. Symptoms may be the same as calculous cholecystitis; however, fever may be the only symptom, and up to 75% of cases do not have right upper quadrant pain. Sonographic features are the same as for acute calculous cholecystitis, except that no gallstones are identified (sludge may be present) and sensitivity is lower (29%–92%). A combination of ultrasonography, scintigraphy, and CT may be required to establish the diagnosis. Definitive treatment is cholecystectomy, although critically ill patients may not tolerate the surgical procedure, so percutaneous cholecystostomy may be used as a temporizing measure.

The gallbladder may fistulize with bowel, allowing gallstones to pass directly into the gastrointestinal tract. A large gallstone (usually >2.5 cm) may cause a mechanical obstruction (termed gallstone ileus), typically at the ileocecal junction. Invasion of the gallbladder by gas-forming organisms leads to emphysematous cholecystitis. The gas in the gallbladder lumen or wall may be seen on ultrasonography, CT, or occasionally plain abdominal radiographs. Although classically associated with mortality of 15% or higher, more sensitive ultrasonographic and CT studies now make the diagnosis earlier in the disease process and improve outcomes. Biliary tract gas is a marker of severe disease and should prompt aggressive resuscitative care, broad-spectrum antibiotics, and early surgical intervention.

Approximately 10% to 15% of those with gallstones also have common bile duct stones, which may be asymptomatic, present with the same biliary pain as cholelithiasis, or cause symptoms related to cholestasis. Ductal stones can recur even after cholecystectomy, or may represent retained/residual stones that were not previously identified. Stones in the common bile duct lead to elevations of alkaline phosphatase and GGT levels in more than 90% of patients. Ultrasonography is only 25% to 60% sensitive for detecting bile duct stones, but is very specific (95%–100%). Biliary duct dilation in the presence of gallstones is highly suggestive, but an acutely obstructed bile duct may not be dilated. CT also has low sensitivity (71%–75%) in detecting bile duct stones, but is useful for detecting biliary dilation and excluding other causes (such as a mass lesion) or complications (such as liver abscess). Because of procedure-related risks, ERCP is reserved for those patients at high risk of having bile duct stones and who require therapeutic intervention. Because of the high risk of severe complications such as cholangitis or pancreatitis, therapy for bile duct stones is generally indicated regardless of symptoms.

The most common cause of cholangitis in the United States is choledocholithiasis secondary to cholelithiasis; malignant obstruction rarely causes cholangitis unless...
a biliary procedure has been performed. Charcot’s triad of right upper quadrant pain, jaundice, and fever is found in 50% to 70% of cases of acute cholangitis. Reynolds’ pentad occurs when mental status changes and hypotension are also present (<30% of cases) with more severe disease. In addition to hyperbilirubinemia, leukocytosis is common, and liver transaminases and alkaline phosphatase are elevated. Pancreatic enzyme elevation suggests that bile duct stones caused the cholangitis. Resuscitative care, correction of fluid and electrolyte deficits, correction of coagulopathy (frequently present because of vitamin K deficiency related to prolonged jaundice, or thrombocytopenia from sepsis), and broad-spectrum antibiotics are indicated. ERCP is usually the preferred method of biliary decompression, which is required within 24 to 48 hours (or sooner for more severe disease).

**EMERGENCY DISEASES OF THE PANCREAS**

The pancreas is a retroperitoneal organ that provides both exocrine and endocrine functions, and is divided anatomically into 3 parts. The head is the widest part; located on the right in the curve of the duodenum. The body and tail of the pancreas extend to the left, with the body lying posterior to the stomach and the tail extending to the gastric surface of the spleen and kidney. The tail is in contact with the left colic flexure. The organ is loosely composed of alveolar cells without a distinct capsule. The blood supply is provided by the superior pancreaticoduodenal artery from the celiac trunk and the inferior pancreaticoduodenal artery from the superior mesenteric artery. The endocrine functions of the pancreas are performed by the islets of Langerhans: clusters of cells made up of alpha, beta, and delta cells that produce insulin, glucagon, and somatostatin. The pancreas receives branches of the vagus nerve that help regulate its exocrine functions. Pancreatic amylase, lipase, and proteolytic enzymes are created in the acinar cells and secreted first into the pancreatic duct, and ultimately into the duodenum. The most important of these include trypsinogen, chymotrypsinogen, and procarboxypeptidase, which are cleaved to their active forms inside the duodenum. Acute pancreatitis is an inflammatory condition of the pancreas. Recurrent episodes of acute pancreatitis can lead to chronic pancreatitis and pancreatic dysfunction. Because of the lack of a distinct capsule, injury to the pancreas can cause leakage of pancreatic enzymes into the abdomen, damaging the surrounding organs.

**Epidemiology**

Acute pancreatitis is commonly encountered in the ED, with an estimated incidence of 17 cases per year per 100,000 people. The number of cases appears to be rising according to several studies. One report that reviewed all discharge diagnoses of acute pancreatitis over a 6-year period in the United States from 1997 to 2003 showed an increase of 30%. The investigators noted that the increase may have been secondary to better screening and detection, but there was an increased number of admissions for alcohol abuse and cholecystitis over this time period as well. Patients between the ages of 18 and 64 years account for more than 70% of admissions. Pancreatitis in patients younger than 18 years is exceedingly rare (1.6%). Disease prevalence is equal in women and men (49% and 51%, respectively).

**Risk Factors**

Chronic alcohol use and cholelithiasis account for more than 90% of episodes of acute pancreatitis. Worldwide, gallstones account for the majority of cases, but in the United States the incidence of gallstone and alcoholic pancreatitis is almost equal. In the coming years, there may be a shift toward gallstone disease as the population becomes increasingly obese. The greatest incidence of alcoholic pancreatitis is
between the ages of 45 and 55 years, as it generally takes greater than 10 years of drinking 4 to 5 alcoholic drinks per night to develop pancreatitis. In the younger patient populations, systemic diseases such as cystic fibrosis and hemolytic uremic syndrome are the main pathological conditions. Trauma is a rare cause of pancreatitis, and is seen in about 0.2% of abdominal trauma. Other rare causes include scorpion stings and gila monster bites. The most common infectious causes are mumps and Coxsackie B viruses. Other infectious causes include herpes simplex, varicella zoster, *Mycoplasma*, and *Salmonella typhosa*. Ischemia is a rare cause of pancreatitis, because it has a rich blood supply and generally is secondary to some other systemic condition (such as hypotension, vasculitis, or hypercoagulable disorder). Other risk factors include anatomic abnormalities, autoimmune diseases (lupus), hypercalcemia and hyperparathyroidism, hypertriglyceridemia, hypothermia, drug reactions (such as to tetracycline, valproic acid, metronidazole, thiazides), and postprocedural (ERCP or Whipple procedure) occurrence.

**Pathophysiology**

Whether due to biliary tract obstruction (choledocholithiasis) or pancreatic toxins (alcohol, drugs, and scorpion venom), the central pathophysiologic event in acute pancreatitis is thought to be the premature activation of digestive zymogens within the pancreas. Protective mechanisms normally help to inactivate trypsin and prevent premature activation of the zymogens produced inside the pancreas. In pathologic states, buildup of toxic metabolites and activated trypsin overwhelm these protective mechanisms, causing these and other enzymes (such as chymotrypsinogen and procarboxypeptidase) to be activated within the pancreas. This injury releases inflammatory cytokines that can cause systemic inflammatory response syndrome (SIRS) in 10% to 15% of patients, worsening pancreatic damage and causing multiorgan failure by hypoperfusion. Only 10% of alcoholics develop pancreatitis, and it is unclear why the protective mechanisms fail in these individuals. It is suspected that genetic deficiencies in antitrypsin enzymes may be to blame. In obstructive pathologies such as cholelithiasis, bile refluxes into the pancreatic duct, causing edema and buildup of proteolytic enzymes.

**Clinical Findings**

By far the most common finding in acute pancreatitis is abdominal pain, which can be found in up to 95% of patients and is generally described as a boring pain located in the upper abdomen, radiating in a band-like pain pattern around to the back. The pain is often constant, maximal at onset, and worse with food or drink. It generally lasts for several days and is often associated with nausea and vomiting. The severity of the pain does not correlate with the severity of disease. Patients may also experience dyspnea due to diaphragmatic irritation, pleural effusion, or in severe cases, impaired oxygenation and respiratory function from acute respiratory distress syndrome (ARDS).

Physical examination findings may vary, but in general, increasingly severe pancreatitis is reflected by increasingly pronounced physical findings. In mild disease, the vital signs may be normal or minimally elevated. Abdominal tenderness is generally mild to moderate and is located in the mid-epigastric region. Peritoneal signs will not be present in early disease so that the patient may be actively writhing on the stretcher, similar to patients with renal colic. Bowel sounds may be normal or hypoactive. In moderate disease, the vital signs will become increasingly abnormal with progressive tachycardia and tachypnea. A low-grade fever may develop (50% of cases). Abdominal tenderness usually becomes
increasingly severe. As peripancreatic inflammation progresses, the patient will often lie still with abdominal guarding to minimize peritoneal motion, and may adopt a fetal position to decrease pancreatic stretch. Bowel sounds will often become hypoactive secondary to an ileus. Breath sounds may be decreased in the bases, due to pleural effusions (most commonly on the left). In severe pancreatitis, tachycardia, tachypnea, and hypotension are typical. Peritoneal signs may not develop until late in the course. Crackles and hypoxia may be present, due to ARDS. Cutaneous findings are rare in acute pancreatitis (1.2% in one study), but they portend a complicated hospital course and poor prognosis because they signal the presence of necrosis and hemorrhage. The Grey-Turner sign is ecchymosis located on the flanks, and indicates retroperitoneal bleeding. Ecchymosis located along the inguinal ligament, a finding known as Fox’s sign, also indicates retroperitoneal hemorrhage. Cullen’s sign, ecchymosis located around the umbilicus, is a sign of intra-abdominal bleeding. Livedo reticularis on the abdomen, chest, or thighs, termed Walzel’s sign, is caused by trypsin damage to the subcutaneous veins. None of these signs are specific for pancreatitis, but if found in conjunction with the diagnosis of pancreatitis have been shown to have increased mortality. Cullen’s sign and the Grey-Turner sign also occur in intra-abdominal and retroperitoneal bleeding due to any cause, such as ectopic pregnancy and ruptured aortic aneurysm. Thus these alternative diagnoses should also be considered if these findings are encountered.

**Diagnostic Testing and Imaging**

There is no definitive test for the diagnosis of acute pancreatitis. The diagnosis requires a combination of history, physical examination, diagnostic laboratory studies, and imaging. Traditionally the diagnostic test of choice for acute pancreatitis was serum amylase. Levels above 3 times normal are more specific for the diagnosis of acute pancreatitis. However, amylase is elevated in a variety of conditions, such as pregnancy, renal failure, and esophageal perforation, and can be nondiagnostically elevated in up to 30% of acute pancreatitis cases. Serum lipase has become the primary diagnostic test for acute pancreatitis. It has a sensitivity of 85% to 100% and is more specific than amylase. Other pancreatic enzymes, such as phospholipase A, trypsin, trypsinogen-2, and carboxyl ester lipase, have been evaluated for use in diagnosis, but they have not been proved to be more sensitive or specific than serum amylase and lipase. Leukocytosis is common in acute pancreatitis secondary to the inflammatory cytokines produced, and is rarely indicative of an infectious cause of the disease. AST and ALT may be mildly elevated in alcoholic pancreatitis, but ALT elevations of greater than 150 units/L have been shown to favor the diagnosis of gallstone pancreatitis, with a positive predictive value of 95% in some studied populations.

Though not necessary for the diagnosis, imaging can help to differentiate pancreatitis from other diagnoses and help evaluate for complications of acute pancreatitis. The obstruction series (flat and upright abdominal radiographs with an upright chest film) may occasionally identify a localized ileus or sentinel loop, pleural effusion, pancreatic calcifications, or a calcified gallbladder, but has very low sensitivity and rarely alters the clinical decision regarding whether to obtain a CT if it is available. Due to its retroperitoneal location, ultrasound imaging is rarely helpful in the evaluation of the pancreas, but may be useful in revealing a gallbladder with stones, especially if these are numerous and small (more likely to cause common bile duct obstruction). If visualized, the pancreas may show increased echogenicity, enlargement, or peripancreatic fluid.
CT with both intravenous and oral contrast is the best modality for evaluating pancreatitis and its complications. Routine CT use is not recommended for evaluation of mild episodes of pancreatitis. However, it should be considered for those with moderate or severe pancreatitis or in those for whom another diagnosis (such as aortic aneurysm) is considered. In acute pancreatitis, the gland may appear normal in mild disease. As the severity increases, the pancreas loses its distinct appearance and becomes hazier in appearance. Fluid collections and fat stranding may be seen as severity increases further. CT may also be helpful in visualizing complications such as pancreatic necrosis and pancreatic pseudocyst.101

Mortality and Complications

Overall mortality from pancreatitis is relatively low at approximately 5%, but those with severe pancreatitis can have mortality as high as 25%.95 The problem is in distinguishing low-risk and high-risk patients. Several risk assessment scores have been developed for this purpose including Ranson’s criteria, APACHE II, Imrie score, and CT severity index.102 These scores may be used in conjunction with clinical judgment to help aid in disposition.

Pancreatic necrosis is an important complication of pancreatitis. It carries a mortality of approximately 30% and is responsible for 50% of all deaths from pancreatitis.103 Necrosis is diagnosed on CT by decreased enhancement of the pancreas, and may require percutaneous drainage or laparotomy.

Hemorrhagic pancreatitis is caused by erosion of vasculature by proteolytic enzymes, which can lead to SIRS, diffuse intravascular coagulation, and profound shock. Cullen’s sign and the Grey-Turner sign may herald the presence of this process. Pancreatic pseudocysts are collections of pancreatic enzymes and other debris encapsulated within granulation and scar tissue. Pseudocysts form in approximately 5% to 40% of pancreatitis patients and can be devastating if they rupture. Diagnosis is by CT or abdominal ultrasonography. If the pseudocyst persists past 4 weeks, percutaneous or endoscopic drainage may be required.104

Chronic pancreatitis should be suspected in anyone with recurrent episodes of pancreatitis or epigastric pain. It is most common in patients with a history of alcoholic pancreatitis, and is caused by progressively worsening necrosis, fibrosis, calcification of the pancreas, and destruction of the endocrine and exocrine glands leading to chronic pain, malabsorption, weight loss, steatorrhea, and diabetes mellitus. Chronic pancreatitis is part of a spectrum of disease and is often difficult to diagnose, as serum markers can be normal from chronic destruction of pancreatic tissue.105

Treatment

The mainstay of treatment for acute pancreatitis is supportive care. As always, the ABCs (airway, breathing, circulation) receive priority. Patients with SIRS may develop altered mental status and ARDS from circulating cytokines, requiring supplemental oxygen or even intubation. Patients suffering from acute pancreatitis are generally intravascularly depleted and require aggressive intravenous hydration.94 Urine output should be monitored. Pain, nausea, and vomiting should be controlled.102 Oral intake should be withheld in the acute setting to provide a “rest period” for the pancreas.95 Routine use of antibiotics in pancreatitis is not recommended without a clear infectious cause.103 Surgical intervention may be necessary, so early consultation is advised in the management of severe pancreatitis.103 Initial ERCP is not currently recommended for all patients suspected of having gallstone pancreatitis, but those with signs of cholangitis or worsening jaundice may benefit from early treatment.95
All patients with new-onset pancreatitis should be admitted for further observation and determination of the underlying cause. If pain cannot be controlled with oral pain medications or if oral hydration is unsuccessful, the patient should be admitted for parenteral treatment. Placement in the intensive care unit should be considered in patients with hypotension or hypoxia following aggressive resuscitation. Some patients with recurrent pancreatitis can be safely discharged home in the absence of clinical findings to suggest severe disease.

SUMMARY

Disorders related to the hepatobiliary system and pancreas are common, and EPs should be familiar with their evaluation and management. While much of the care of liver disease is chronic, it is important to bear in mind that acute and life-threatening complications can occur. Hepatic decompensation is often due to an acute precipitant that needs to be identified and treated expeditiously. Biliary disease is highly prevalent. History, physical examination, and laboratory studies can narrow the differential diagnosis, but appropriate imaging studies are necessary for diagnosis. Although most cases are not life threatening, severe complications can occur and progress rapidly, requiring prompt diagnosis and treatment. Finally, although most of the cases of pancreatitis in the ED are not severe, the EP should be alert to the possible presence of hemorrhagic and necrotizing pancreatitis, as well as pancreatic pseudocyst.

REFERENCES


