Wolters Kluwer

Clinical manifestations and diagnosis of acute pancreatitis

Author: Santhi Swaroop Vege, MD
Section Editor: David C Whitcomb, MD, PhD
Deputy Editor: Shilpa Grover, MD, MPH, AGAF

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Jun 2020. | **This topic last updated:** Oct 23, 2019.

INTRODUCTION

Acute pancreatitis is an acute inflammatory process of the pancreas. Acute pancreatitis should be suspected in patients with severe acute upper abdominal pain but requires biochemical or radiologic evidence to establish the diagnosis.

This topic will review the clinical manifestations and diagnosis of acute pancreatitis. The etiology, pathogenesis, assessment of severity, and management of acute pancreatitis are discussed separately. (See "Etiology of acute pancreatitis" and "Pathogenesis of acute pancreatitis" and "Predicting the severity of acute pancreatitis" and "Management of acute pancreatitis".)

CLASSIFICATION

Acute pancreatitis is divided into the following:

- Mild acute pancreatitis, which is characterized by the absence of organ failure and local or systemic complications
- Moderately severe acute pancreatitis, which is characterized by transient organ failure (resolves within 48 hours) and/or local or systemic complications without persistent organ failure (>48 hours)
- Severe acute pancreatitis, which is characterized by persistent organ failure that may involve one or multiple organs

The complications of acute pancreatitis are reviewed below. (See 'Natural history and complications' below.)

The classification and predictors of severity are reviewed in more detail elsewhere. (See "Predicting the severity of acute pancreatitis".)

CLINICAL FEATURES

Most patients with acute pancreatitis have acute onset of persistent, severe epigastric abdominal pain [1]. In some patients, the pain may be in the right upper quadrant or, rarely, confined to the left side.

In patients with gallstone pancreatitis, the pain is well localized and the onset of pain is rapid, reaching maximum intensity in 10 to 20 minutes. In contrast, in patients with pancreatitis due to hereditary or metabolic causes or alcohol, the onset of pain may be less abrupt and the pain may be poorly localized. In approximately 50 percent of patients, the pain radiates to the back [2]. The pain persists for several hours to days and may be partially relieved by sitting up or bending forward. (See "Etiology of acute pancreatitis".)

Approximately 90 percent of patients have associated nausea and vomiting which may persist for several hours [3].

Patients with severe acute pancreatitis may have dyspnea due to diaphragmatic inflammation secondary to pancreatitis, pleural effusions, or acute respiratory distress syndrome. (See "Predicting the severity of acute pancreatitis", section on 'Classification of acute pancreatitis' and "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults", section on 'Clinical features'.)

Approximately 5 to 10 percent of patients with acute severe pancreatitis may have painless disease and have unexplained hypotension (eg, postoperative and critically ill patients, patients on dialysis, organophosphate poisoning, and Legionnaire's disease) [4-6]. (See "Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis" and "Definition, classification, etiology, and pathophysiology of shock in adults" and "Organophosphate and carbamate poisoning" and "Clinical manifestations and diagnosis of Legionella infection" and "Unique aspects of gastrointestinal disease in dialysis patients", section on 'Acute pancreatitis'.)

PHYSICAL EXAMINATION

Physical findings vary depending upon the severity of acute pancreatitis. In patients with mild acute pancreatitis, the epigastrium may be minimally tender to palpation. In contrast, in patients with severe pancreatitis, there may be significant tenderness to palpation in the epigastrium or more diffusely over the abdomen. (See "Evaluation of the adult with abdominal pain".)

Patients may have abdominal distention and hypoactive bowel sounds due to an ileus secondary to inflammation.

Patients may have scleral icterus due to obstructive jaundice due to choledocholithiasis or edema of the head of the pancreas. (See "Diagnostic approach to the adult with jaundice or asymptomatic hyperbilirubinemia" and "Choledocholithiasis: Clinical manifestations, diagnosis, and management", section on 'Clinical manifestations'.)

Patients with severe pancreatitis may have fever, tachypnea, hypoxemia, and hypotension. In 3 percent of patients with acute pancreatitis, ecchymotic discoloration may be observed in the periumbilical region (Cullen's sign) or along the flank (Grey Turner sign (image 1)) [7]. These findings, although nonspecific, suggest the presence of retroperitoneal bleeding in the setting of pancreatic necrosis [8]. (See "Evaluation of the adult with abdominal pain in the emergency department", section on 'Physical examination' and 'Disease course' below.)

In rare cases, patients may have subcutaneous nodular fat necrosis or panniculitis (picture 1) [9,10]. These lesions are tender red nodules that frequently occur on the distal extremities but may occur elsewhere.

Patient may also have findings suggestive of the underlying etiology (table 1). As examples, hepatomegaly may be present in patients with alcoholic pancreatitis, xanthomas in hyperlipidemic pancreatitis, and parotid swelling in patients with mumps (picture 2 and picture 3). (See "Etiology of acute pancreatitis" and "Hypertriglyceridemia-induced acute pancreatitis", section on 'Clinical features' and "Mumps", section on 'Clinical manifestations'.)

LABORATORY FINDINGS

Pancreatic enzymes and products — Early in the course of acute pancreatitis, there is a breakdown in the synthesis-secretion coupling of pancreatic digestive enzymes; synthesis continues while there is a blockade of secretion. As a result, digestive enzymes leak out of acinar cells through the basolateral membrane to the interstitial space and then enter the systemic circulation. (See "Pathogenesis of acute pancreatitis", section on 'Intraacinar activation of proteolytic enzymes'.)

Serum amylase — Serum amylase rises within 6 to 12 hours of the onset of acute pancreatitis. Amylase has a short half-life of approximately 10 hours and in uncomplicated attacks returns to normal within three to five days. Serum amylase elevation of greater than three times the upper limit of normal has a sensitivity for the diagnosis of acute pancreatitis of 67 to 83 percent and a specificity of 85 to 98 percent [11].

However, elevations in serum amylase to more than three times the upper limit of normal may not be seen in approximately 20 percent of patients with alcoholic pancreatitis due to the inability of the parenchyma to produce amylase, and in 50 percent of patients with hypertriglyceridemia-associated pancreatitis as triglycerides interfere with the amylase assay [12]. Given the short half-life of amylase, the diagnosis of acute pancreatitis may be missed in patients who present >24 hours after the onset of pancreatitis. In addition, elevations in serum amylase are not specific for acute pancreatitis and may be seen in other conditions (table 2). (See "Approach to the patient with elevated serum amylase or lipase".)

Serum lipase — Serum lipase has a sensitivity for acute pancreatitis ranging from 82 to 100 percent [11]. Serum lipase rises within four to eight hours of the onset of symptoms, peaks at 24 hours, and returns to normal within 8 to 14 days [13].

Lipase elevations occur earlier and last longer as compared with elevations in amylase and are therefore especially useful in patients who present >24 hours after the onset of pain [14]. Serum lipase is also more sensitive as compared with amylase in patients with pancreatitis secondary to alcohol.

However, nonspecific elevations of lipase have also been reported (table 3) [11,15]. (See "Approach to the patient with elevated serum amylase or lipase".)

Other enzymes and products — Trypsinogen activation peptide (TAP), a five amino-acid peptide that is cleaved from trypsinogen to produce active trypsin, is elevated in acute pancreatitis. Since activation of trypsin is likely an early event in the pathogenesis of acute pancreatitis, TAP may be useful in detection of early acute pancreatitis and as a predictor of the severity of acute pancreatitis [16-19]. (See "Predicting the severity of acute pancreatitis", section on 'Other serum markers'.)

Urinary and serum trypsinogen-2 levels are elevated in early acute pancreatitis. However, additional studies are needed to determine their role in the diagnosis of acute pancreatitis [16,18,20-23]. (See "Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis", section on 'Diagnosis'.)

Other pancreatic digestive enzymes that leak into the systemic circulation and are elevated in serum include trypsin, phospholipase, carboxypeptidase, carboxylester lipase, colipase, and pancreatic isoamylase.

Markers of immune activation — Activation of granulocytes and macrophages in acute pancreatitis results in release of a number of cytokines and inflammatory mediators. Acute pancreatitis is associated with elevations in C-reactive protein (CRP), interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor (TNF), and PMN elastase [24]. A CRP

level above 150 mg/L at 48 hours is associated with severe pancreatitis. (See "Predicting the severity of acute pancreatitis", section on 'C-reactive protein'.)

Other laboratory findings — Patients with pancreatitis may have leukocytosis and an elevated hematocrit from hemoconcentration due to extravasation of intravascular fluid into third spaces. Metabolic abnormalities including elevated blood urea nitrogen (BUN), hypocalcemia, hyperglycemia, and hypoglycemia may also occur. (See "Pathogenesis of acute pancreatitis", section on 'Systemic response' and "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis", section on 'Precipitating factors' and "Hypoglycemia in adults without diabetes mellitus: Clinical manifestations, diagnosis, and causes", section on 'Clinical manifestations'.)

IMAGING

Several features may be seen on imaging in patients with acute pancreatitis.

Abdominal and chest radiographs — The radiographic findings in acute pancreatitis range from unremarkable in mild disease to localized ileus of a segment of small intestine (sentinel loop) or the colon cutoff sign in more severe disease. The colon cut off sign reflects a paucity of air in the colon distal to the splenic flexure due to functional spasm of the descending colon secondary to pancreatic inflammation. A ground glass appearance may indicate the presence of an acute peripancreatic fluid collection (table 4). (See 'Local complications' below.)

Approximately one-third of patients with acute pancreatitis have abnormalities visible on the chest roentgenogram such as elevation of a hemidiaphragm, pleural effusions, basal atelectasis, pulmonary infiltrates, or acute respiratory distress syndrome [25].

Abdominal ultrasound — In patients with acute pancreatitis, the pancreas appears diffusely enlarged and hypoechoic on abdominal ultrasound. Gallstones may be visualized in the gallbladder or the bile duct (image 2). (See "Choledocholithiasis: Clinical manifestations, diagnosis, and management", section on 'Transabdominal ultrasound'.)

Peripancreatic fluid appears as an anechoic collection on abdominal ultrasound. These collections may demonstrate internal echoes in the setting of pancreatic necrosis (table 4). (See 'Local complications' below.)

However, in approximately 25 to 35 percent of patients with acute pancreatitis, bowel gas due to an ileus precludes evaluation of the pancreas or bile duct [16]. In addition, ultrasound cannot clearly delineate extrapancreatic spread of pancreatic inflammation or identify necrosis within the pancreas.

Abdominal computed tomography — Contrast-enhanced abdominal computed tomography (CT) scan findings of acute interstitial edematous pancreatitis (image 3) include focal or diffuse enlargement of the pancreas with heterogeneous enhancement with intravenous contrast.

Necrosis of pancreatic tissue is recognized as lack of enhancement after intravenous contrast administration (image 4).

If performed three or more days after the onset of abdominal pain, contrast-enhanced CT scan can reliably establish the presence and extent of pancreatic necrosis and local complications and predict the severity of the disease (table 4). (See 'Local complications' below and "Predicting the severity of acute pancreatitis", section on 'CT scan' and "Predicting the severity of acute pancreatitis", section on 'CT severity index'.)

A common bile duct stone may occasionally be visualized on contrast-enhanced abdominal CT scan. A pancreatic

mass may be seen in patients with an underlying pancreatic cancer, and diffuse dilation of the pancreatic duct or a cystic lesion may be seen in patients with an intraductal papillary mucinous neoplasia or cystic neoplasm. (See "Intraductal papillary mucinous neoplasm of the pancreas (IPMN): Pathophysiology and clinical manifestations", section on 'Clinical presentation' and "Clinical manifestations, diagnosis, and staging of exocrine pancreatic cancer", section on 'Clinical presentation' and "Etiology of acute pancreatitis", section on 'Etiology'.)

Magnetic resonance imaging — On MR T1 weighted images with fat suppression, diffuse or focal enlargement of the pancreatic gland can be seen in patients with acute pancreatitis and the margins of the pancreas may be blurred. Due to pancreatic edema, the signal intensity of the pancreatic parenchyma might be hypointense relative to the liver on T1-weighted images, and hyperintense on T2-weighted images. On contrast-enhanced magnetic resonance imaging (MRI), failure of the pancreatic parenchyma to enhance indicates the presence of pancreatic necrosis.

MRI has a higher sensitivity for the diagnosis of early acute pancreatitis as compared with contrast-enhanced abdominal CT scan and can better characterize the pancreatic and bile ducts and complications of acute pancreatitis [26-28]. Magnetic resonance cholangiopancreatogram (MRCP) is comparable to endoscopic retrograde cholangiopancreatogram (ERCP) for the detection of choledocholithiasis [29]. MRI has the advantage of not requiring radiation, and gadolinium has a lower risk of nephrotoxicity as compared with iodinated contrast [28,30,31]. In addition, in patients with renal failure, a nonenhanced MRI can identify pancreatic necrosis.

However, MRI has the disadvantage of being operator-dependent with consequent variability in quality and technique and its use is limited by the presence of local expertise and availability. In addition, MRI has a longer scanning time as compared with CT scan, making it more difficult to perform in critically ill patients.

(See "Endoscopic retrograde cholangiopancreatography: Indications, patient preparation, and complications" and "Choledocholithiasis: Clinical manifestations, diagnosis, and management", section on 'Imaging test characteristics'.)

DIAGNOSIS

The diagnosis of acute pancreatitis should be suspected in a patient with acute onset of a persistent, severe, epigastric pain with tenderness on palpation on physical examination.

The diagnosis of acute pancreatitis requires the presence of two of the following three criteria: acute onset of persistent, severe, epigastric pain often radiating to the back, elevation in serum lipase or amylase to three times or greater than the upper limit of normal, and characteristic findings of acute pancreatitis on imaging (contrast-enhanced computed tomography [CT], magnetic resonance imaging [MRI], or transabdominal ultrasonography) [32]. (See 'Imaging' above.)

In patients with characteristic abdominal pain and elevation in serum lipase or amylase to three times or greater than the upper limit of normal, no imaging is required to establish the diagnosis of acute pancreatitis.

In patients with abdominal pain that is not characteristic for acute pancreatitis or serum amylase or lipase levels that are less than three times the upper limit of normal, or in whom the diagnosis is uncertain, we perform abdominal imaging with a contrast-enhanced abdominal CT scan to establish the diagnosis of acute pancreatitis and to exclude other causes of acute abdominal pain. In patients with severe contrast allergy or renal failure, we perform an abdominal MRI without gadolinium.

Diagnostic evaluation

Laboratory studies — Elevation in serum lipase or amylase to three times or greater than the upper limit of normal is suggestive of acute pancreatitis. We evaluate levels of serum lipase and amylase. Lipase remains elevated for a longer period of time and has a higher specificity as compared with amylase. (See 'Serum lipase' above and 'Serum amylase' above.)

In addition, a complete blood count, electrolytes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, calcium, and albumin should be obtained to rule out other causes of acute abdominal pain. A pregnancy test should be performed in all women of childbearing age. (See 'Differential diagnosis' below.)

Imaging — The presence of focal or diffuse enlargement of the pancreas on contrast-enhanced abdominal CT or MRI is suggestive of acute pancreatitis. (See 'Abdominal computed tomography' above and 'Magnetic resonance imaging' above.)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of acute pancreatitis includes other causes of epigastric abdominal pain. Acute pancreatitis can be distinguished from these causes based on the clinical features and laboratory studies. However, in some cases if the diagnosis of acute pancreatitis is still in doubt, we perform a contrast-enhanced abdominal computed tomography (CT) scan for further evaluation. (See 'Clinical features' above and 'Physical examination' above and 'Laboratory studies' above and 'Abdominal computed tomography' above.)

- Peptic ulcer disease – Patients may have a history of longstanding epigastric pain that is usually intermittent. The pain does not radiate to the back. Patients may have a history of nonsteroidal antiinflammatory drug (NSAID) use or prior infection with *Helicobacter pylori*. On laboratory testing, patients with peptic ulcer disease have a normal amylase and lipase. (See "Peptic ulcer disease: Clinical manifestations and diagnosis".)

- Choledocholithiasis or cholangitis – Patients with choledocholithiasis and cholangitis may have a history of gallstones or biliary manipulation such as endoscopic retrograde cholangiopancreatography (ERCP). Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations are typically elevated early in the course of biliary obstruction. Later, patients have elevations in serum bilirubin, alkaline phosphatase, exceeding the elevations in serum ALT and AST. Serum amylase and lipase are normal. (See "Acute cholangitis: Clinical manifestations, diagnosis, and management", section on 'Clinical manifestations' and "Choledocholithiasis: Clinical manifestations, diagnosis, and management", section on 'Clinical manifestations'.)

- Cholecystitis – Patients with acute cholecystitis typically complain of abdominal pain, most commonly in the right upper quadrant or epigastrium that may radiate to the right shoulder or back. Unlike patients with acute pancreatitis, patients with acute cholecystitis commonly experience increased discomfort while the area around the gallbladder fossa is palpated and may have an associated inspiratory arrest (Murphy's sign). Mild elevations in serum aminotransferases and amylase, along with hyperbilirubinemia may be seen but amylase or lipase elevations of greater than three times the upper limit of normal are not usually associated with cholecystitis. An abdominal CT scan shows gallbladder wall edema and pericholecystic stranding. (See "Acute calculous cholecystitis: Clinical features and diagnosis", section on 'Clinical manifestations' and "Acute calculous cholecystitis: Clinical features and diagnosis", section on 'Diagnostic approach'.)

- Perforated viscus – Patients with a perforated viscus present with sudden onset abdominal pain and have peritoneal signs with guarding, rigidity and rebound tenderness that are not associated with acute pancreatitis. Patients may have an elevated amylase but elevations are unlikely to be three times the upper limit of normal.

On upright chest film and abdominal films and abdominal CT scan, free air can be seen. Other possible findings on abdominal CT include free fluid, phlegmon, and bowel wall pathology with adjacent inflammation.

- Intestinal obstruction – Patients with intestinal obstruction have abdominal pain with anorexia, emesis, obstipation, or constipation and elevation in serum amylase and lipase. These patients may have a history of prior abdominal surgeries or Crohn's disease. On physical examination, patients may have prior surgical scars or hernias. On abdominal CT scan in addition to dilated loops of bowel with air fluid levels, the etiology and site of obstruction (transition point) may be seen. (See "Etiologies, clinical manifestations, and diagnosis of mechanical small bowel obstruction in adults".)

- Mesenteric ischemia – In patients with mesenteric ischemia, the pain is often periumbilical and out of proportion to findings on physical examination. Patients may have risk factors for mesenteric ischemia including advanced age, atherosclerosis, cardiac arrhythmias, severe cardiac valvular disease, recent myocardial infarction, and intra-abdominal malignancy. Although patients may have elevations in amylase or lipase these are usually less marked than elevations seen in acute pancreatitis. On abdominal CT scan there may be focal or segmental bowel wall thickening or intestinal pneumatosis with portal vein gas. In addition, arterial or venous thrombosis or hepatic or splenic infarcts may be seen. (See "Mesenteric venous thrombosis in adults", section on 'Clinical presentations' and "Nonocclusive mesenteric ischemia", section on 'Clinical features' and "Acute mesenteric arterial occlusion", section on 'Clinical features' and "Overview of intestinal ischemia in adults", section on 'Clinical features'.)

- Hepatitis – Patients have acute right upper quadrant pain, anorexia, and general malaise. Patients may also note dark urine, acholic stool, jaundice, and pruritus. On physical findings, patients with acute hepatitis have scleral icterus and tender hepatomegaly. Laboratory studies are notable for marked elevations of serum aminotransferases (usually >1000 int. units/dL), serum total and direct bilirubin, and alkaline phosphatase with normal amylase and lipase. (See "Hepatitis A virus infection in adults: Epidemiology, clinical manifestations, and diagnosis", section on 'Clinical manifestations' and "Hepatitis B virus: Clinical manifestations and natural history", section on 'Acute hepatitis'.)

In patients who present with an elevated amylase or lipase without abdominal pain, the differential diagnosis is broad (table 2 and table 3). This topic is discussed separately. (See "Approach to the patient with elevated serum amylase or lipase".)

ESTABLISHING THE ETIOLOGY

Once the diagnosis of acute pancreatitis is established, the underlying etiology should be determined (table 1). An approach to identifying the cause of acute pancreatitis is discussed in detail separately. (See "Etiology of acute pancreatitis", section on 'Approach to establishing the underlying etiology'.)

NATURAL HISTORY AND COMPLICATIONS

Patients with acute pancreatitis usually present with acute onset of epigastric abdominal pain and elevated serum amylase and lipase. With supportive treatment, most patients recover without local or systemic complications or organ failure and do not have recurrent attacks. However, a small proportion of patients with acute pancreatitis have necrosis of the pancreas or peripancreatic tissue and complications due to pancreatitis. These patients have a high overall mortality.

Disease course — Approximately 85 percent of patients with acute pancreatitis have acute interstitial edematous pancreatitis characterized by an enlargement of the pancreas due to inflammatory edema [3]. Approximately 15 percent of patients have necrotizing pancreatitis with necrosis of the pancreatic parenchyma, the peripancreatic tissue, or both (table 4).

In most patients with acute pancreatitis, the disease is mild in severity and patients recover in three to five days without complications or organ failure. However, 20 percent of patients have moderately severe or severe acute pancreatitis with local or systemic complications or organ failure. (See 'Local complications' below and 'Systemic complications' below and 'Organ failure' below.)

The overall mortality in acute pancreatitis is approximately 5 percent with a lower mortality in patients with interstitial pancreatitis as compared with those with necrotizing pancreatitis (3 versus 17 percent) [3].

Patients with acute pancreatitis can have recurrent attacks of acute pancreatitis and can also develop chronic pancreatitis [33,34]. In a meta-analysis of 14 studies, which included 8492 patients with acute pancreatitis, the pooled prevalence of recurrent acute pancreatitis and chronic pancreatitis were 22 and 10 percent, respectively [34]. The prevalence of chronic pancreatitis following the first episode and with recurrent acute pancreatitis were 10 and 36 percent, respectively. However, there was significant variability in the pooled prevalence estimates based on the design of the primary studies included in the analysis. In subgroup analysis, the prevalence of chronic pancreatitis in individuals with a history of smoking or alcohol use were 65 and 61 percent, respectively. The risk of progression from acute to chronic pancreatitis was higher in men as compared with women after controlling for age and the severity of acute pancreatitis (odds ratio women 0.12, 95% CI 0.02-0.2).

Local complications — Local complications of acute pancreatitis include acute peripancreatic fluid collection (image 5), pancreatic pseudocyst, acute necrotic collection (image 6), and walled-off necrosis (table 4).

While acute peripancreatic fluid collections and acute necrotic collections may develop less than four weeks after the onset of pancreatitis, pancreatic pseudocyst and walled off necrosis usually occurs >4 weeks after onset of acute pancreatitis.

Both acute necrotic fluid collections and walled off necrosis may become infected. The management of infected pancreatic necrosis (image 7) is discussed in detail separately. (See "Pancreatic debridement", section on 'Infected pancreatic necrosis'.)

Portosplenomesenteric venous thrombosis (PSMVT) develops in approximately 50 percent of patients with necrotizing acute pancreatitis and is rare in the absence of necrosis [35,36]. Complications from PSMVT are rare in patients with acute pancreatitis. In another study that included 45 patients with splanchnic venous thrombosis in patients with acute pancreatitis of whom 17 (38 percent) were treated with anticoagulants, although the use of anticoagulants was not associated with major bleeding, there was also no significant difference in the rates of recanalization [37].

Systemic complications — According to the revised Atlanta classification of acute pancreatitis, a systemic complication of acute pancreatitis is defined as an exacerbation of an underlying comorbidity (eg, coronary artery disease or chronic lung disease) [32].

Organ failure — In the Atlanta classification, organ failure is a distinct entity separate from a systemic complication [32]. Pancreatic inflammation results in the activation of a cytokine cascade that manifests clinically as a systemic inflammatory response syndrome (SIRS). Patients with persistent SIRS are at risk for failure of one or more organs. Organ failure (acute respiratory failure, shock, and renal failure) may be transient, resolving within 48 hours in

patients with moderately severe pancreatitis or persistent for >48 hours in patients with severe acute pancreatitis (table 5). (See "Sepsis syndromes in adults: Epidemiology, definitions, clinical presentation, diagnosis, and prognosis", section on 'Definitions'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute pancreatitis".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Pancreatitis (The Basics)")
- Beyond the Basics topics (see "Patient education: Acute pancreatitis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- The majority of patients with acute pancreatitis have acute onset of severe upper abdominal pain. Patients may have associated nausea and vomiting. On physical examination, patients have abdominal tenderness to palpation. Patients with severe acute pancreatitis may have fever, tachypnea, tachycardia, hypoxemia, and hypotension. (See 'Clinical features' above and 'Physical examination' above.)
- Early in the course of acute pancreatitis, pancreatic enzymes leak out of acinar cells to the interstitial space and then the systemic circulation. Patients with acute pancreatitis may therefore have acute elevations in serum amylase and lipase in addition to other pancreatic enzymes, breakdown products, and inflammatory mediators. (See 'Laboratory findings' above.)
- The diagnosis of acute pancreatitis is defined by the presence of two of the following: acute onset of persistent, severe, epigastric pain often radiating to the back, elevation in serum lipase or amylase to three times or greater than the upper limit of normal, or characteristic findings of acute pancreatitis on imaging (contrast-enhanced computed tomography, magnetic resonance imaging, or transabdominal ultrasonography). (See 'Diagnosis' above.)
- Serum lipase has a slightly higher sensitivity for acute pancreatitis, and elevations occur earlier and last longer as compared with elevations in amylase. Serum lipase is therefore especially useful in patients who present late to the physician. Serum lipase is also more sensitive as compared with amylase in patients with pancreatitis

secondary to alcohol. (See 'Serum lipase' above and "Approach to the patient with elevated serum amylase or lipase".)

- In patients with characteristic abdominal pain and elevation in serum lipase or amylase to three times or greater than the upper limit of normal, no imaging is required to establish the diagnosis of acute pancreatitis.

  In patients with abdominal pain that is not characteristic for acute pancreatitis or a serum amylase and/or lipase activity that is less than three times the upper limit of normal, we perform abdominal imaging with a contrast-enhanced abdominal computed tomography scan to establish the diagnosis of acute pancreatitis and to exclude other causes of acute abdominal pain. (See 'Abdominal computed tomography' above and 'Differential diagnosis' above.)

- Approximately 85 percent of patients with acute pancreatitis have acute interstitial edematous pancreatitis (image 3) characterized by an enlargement of the pancreas due to inflammatory edema. Approximately 15 percent of patients have necrotizing pancreatitis (image 4) with necrosis of the pancreatic parenchyma, the peripancreatic tissue, or both. (See 'Disease course' above.)

- In most patients with acute pancreatitis, the disease is mild in severity and patients recover in three to five days without complications or organ failure. However, 20 percent of patients have moderately severe or severe acute pancreatitis with local or systemic complications or organ failure. (See 'Natural history and complications' above.)

REFERENCES

1. Swaroop VS, Chari ST, Clain JE. Severe acute pancreatitis. JAMA 2004; 291:2865.
2. Banks PA. Acute pancreatitis: Diagnosis. In: Pancreatitis, Lankisch PG, Banks PA (Eds), Springer-Verlag, New York 1998. p.75.
3. Banks PA, Freeman ML, Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006; 101:2379.
4. Lankisch PG, Schirren CA, Kunze E. Undetected fatal acute pancreatitis: why is the disease so frequently overlooked? Am J Gastroenterol 1991; 86:322.
5. Lankisch PG, Müller CH, Niederstadt H, Brand A. Painless acute pancreatitis subsequent to anticholinesterase insecticide (parathion) intoxication. Am J Gastroenterol 1990; 85:872.
6. Kesavan CR, Pitchumoni CS, Marino WD. Acute painless pancreatitis as a rare complication in Legionnaires disease. Am J Gastroenterol 1993; 88:468.
7. Mookadam F, Cikes M. Images in clinical medicine. Cullen's and Turner's signs. N Engl J Med 2005; 353:1386.
8. Dickson AP, Imrie CW. The incidence and prognosis of body wall ecchymosis in acute pancreatitis. Surg Gynecol Obstet 1984; 159:343.
9. Dahl PR, Su WP, Cullimore KC, Dicken CH. Pancreatic panniculitis. J Am Acad Dermatol 1995; 33:413.

10. Bennett RG, Petrozzi JW. Nodular subcutaneous fat necrosis. A manifestation of silent pancreatitis. Arch Dermatol 1975; 111:896.

11. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. Am J Gastroenterol 2002; 97:1309.

12. Fortson MR, Freedman SN, Webster PD 3rd. Clinical assessment of hyperlipidemic pancreatitis. Am J Gastroenterol 1995; 90:2134.

13. Frank B, Gottlieb K. Amylase normal, lipase elevated: is it pancreatitis? A case series and review of the literature. Am J Gastroenterol 1999; 94:463.

14. Gwozdz GP, Steinberg WM, Werner M, et al. Comparative evaluation of the diagnosis of acute pancreatitis based on serum and urine enzyme assays. Clin Chim Acta 1990; 187:243.

15. Treacy J, Williams A, Bais R, et al. Evaluation of amylase and lipase in the diagnosis of acute pancreatitis. ANZ J Surg 2001; 71:577.

16. Dervenis C, Johnson CD, Bassi C, et al. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. Int J Pancreatol 1999; 25:195.

17. Tenner S, Fernandez-del Castillo C, Warshaw A, et al. Urinary trypsinogen activation peptide (TAP) predicts severity in patients with acute pancreatitis. Int J Pancreatol 1997; 21:105.

18. Huang QL, Qian ZX, Li H. A comparative study of the urinary trypsinogen-2, trypsinogen activation peptide, and the computed tomography severity index as early predictors of the severity of acute pancreatitis. Hepatogastroenterology 2010; 57:1295.

19. Khan Z, Vlodov J, Horovitz J, et al. Urinary trypsinogen activation peptide is more accurate than hematocrit in determining severity in patients with acute pancreatitis: a prospective study. Am J Gastroenterol 2002; 97:1973.

20. Kylänpää-Bäck M, Kemppainen E, Puolakkainen P, et al. Reliable screening for acute pancreatitis with rapid urine trypsinogen-2 test strip. Br J Surg 2000; 87:49.

21. Mayumi T, Inui K, Maetani I, et al. Validity of the urinary trypsinogen-2 test in the diagnosis of acute pancreatitis. Pancreas 2012; 41:869.

22. Kemppainen E, Hedström J, Puolakkainen P, et al. Increased serum trypsinogen 2 and trypsin 2-alpha 1 antitrypsin complex values identify endoscopic retrograde cholangiopancreatography induced pancreatitis with high accuracy. Gut 1997; 41:690.

23. Kemppainen E, Hedström J, Puolakkainen P, et al. Urinary trypsinogen-2 test strip in detecting ERCP-induced pancreatitis. Endoscopy 1997; 29:247.

24. Toouli J, Brooke-Smith M, Bassi C, et al. Guidelines for the management of acute pancreatitis. J Gastroenterol Hepatol 2002; 17 Suppl:S15.

25. Ranson JH, Turner JW, Roses DF, et al. Respiratory complications in acute pancreatitis. Ann Surg 1974; 179:557.

26. Lecesne R, Taourel P, Bret PM, et al. Acute pancreatitis: interobserver agreement and correlation of CT and MR cholangiopancreatography with outcome. Radiology 1999; 211:727.

27. Arvanitakis M, Delhaye M, De Maertelaere V, et al. Computed tomography and magnetic resonance imaging in the assessment of acute pancreatitis. Gastroenterology 2004; 126:715.

28. Stimac D, Miletić D, Radić M, et al. The role of nonenhanced magnetic resonance imaging in the early assessment of acute pancreatitis. Am J Gastroenterol 2007; 102:997.

29. Taylor AC, Little AF, Hennessy OF, et al. Prospective assessment of magnetic resonance cholangiopancreatography for noninvasive imaging of the biliary tree. Gastrointest Endosc 2002; 55:17.

30. Morgan DE, Baron TH, Smith JK, et al. Pancreatic fluid collections prior to intervention: evaluation with MR imaging compared with CT and US. Radiology 1997; 203:773.

31. Amano Y, Oishi T, Takahashi M, Kumazaki T. Nonenhanced magnetic resonance imaging of mild acute pancreatitis. Abdom Imaging 2001; 26:59.

32. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013; 62:102.

33. Yadav D, O'Connell M, Papachristou GI. Natural history following the first attack of acute pancreatitis. Am J Gastroenterol 2012; 107:1096.

34. Sankaran SJ, Xiao AY, Wu LM, et al. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. Gastroenterology 2015; 149:1490.

35. Easler J, Muddana V, Furlan A, et al. Portosplenomesenteric venous thrombosis in patients with acute pancreatitis is associated with pancreatic necrosis and usually has a benign course. Clin Gastroenterol Hepatol 2014; 12:854.

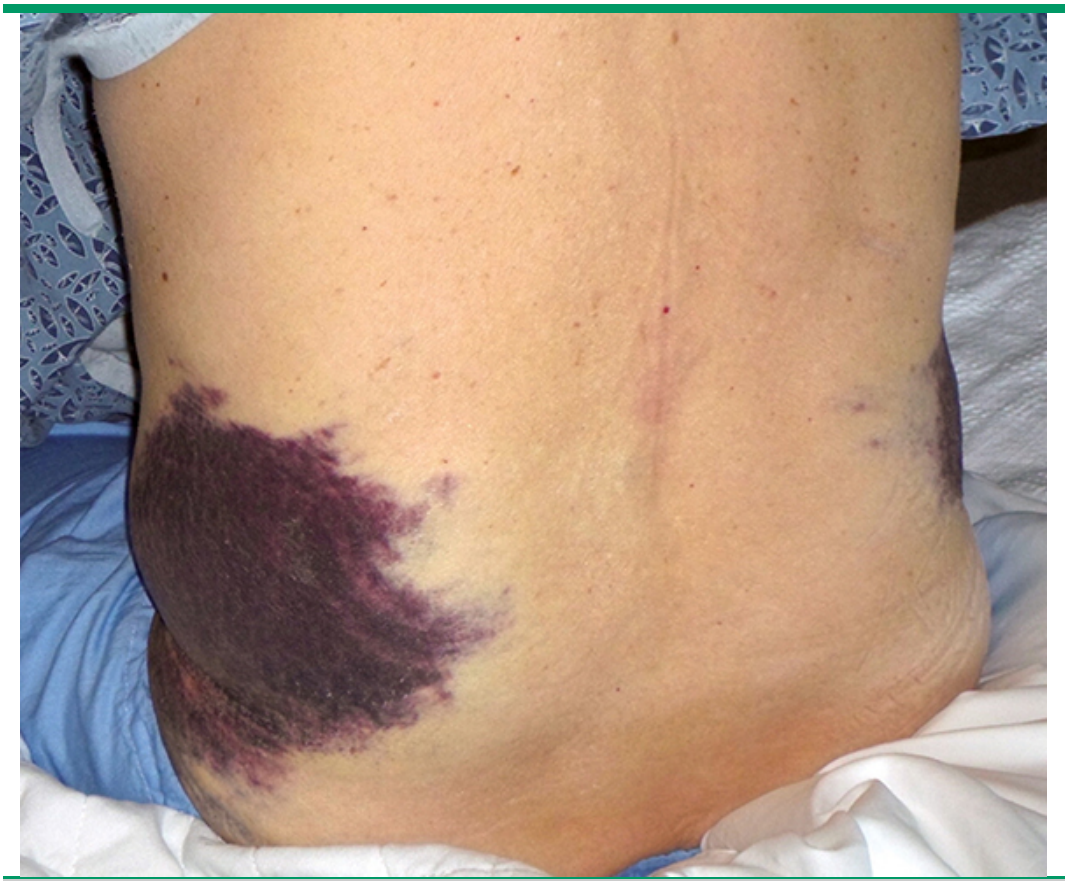
36. Nadkarni NA, Khanna S, Vege SS. Splanchnic venous thrombosis and pancreatitis. Pancreas 2013; 42:924.

37. Harris S, Nadkarni NA, Naina HV, Vege SS. Splanchnic vein thrombosis in acute pancreatitis: a single-center experience. Pancreas 2013; 42:1251.

Topic 5652 Version 37.0

GRAPHICS

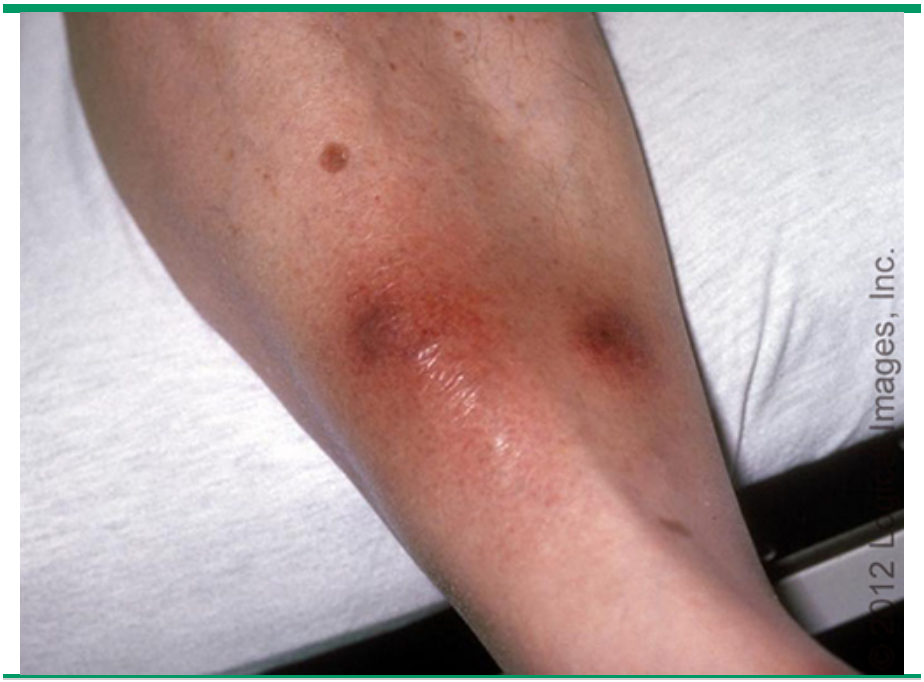
Grey Turner sign



Grey Turner sign refers to flank ecchymoses that result from blood tracking subcutaneously from a retroperitoneal or intraperitoneal source.

Graphic 95719 Version 1.0

Pancreatic panniculitis



Inflammatory nodules on the distal leg.

Graphic 83789 Version 5.0

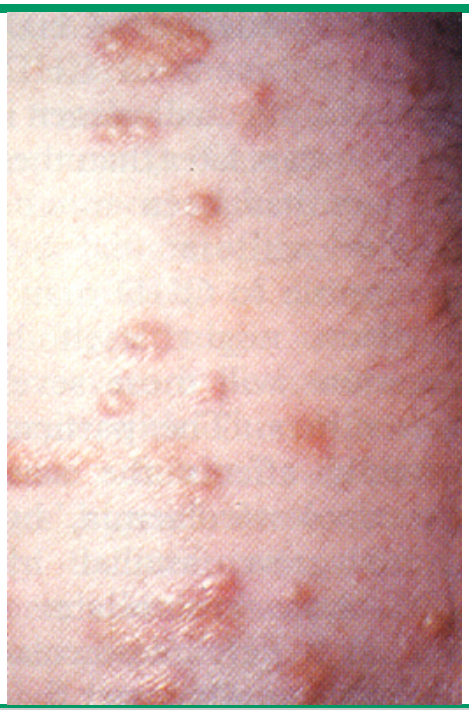
Etiology of acute pancreatitis

Mechanical	Gallstones, biliary sludge, ascariasis, periampullary diverticulum, pancreatic or periampullary cancer, ampullary stenosis, duodenal stricture or obstruction
Toxic	Ethanol, methanol, scorpion venom, organophosphate poisoning
Metabolic	Hyperlipidemia (types I, IV, V), hypercalcemia
Drugs	Didanosine, pentamidine, metronidazole, stibogluconate, tetracycline furosemide, thiazides, sulphasalazine, 5-ASA, L-asparaginase, azathioprine, valproic acid, sulindac, salicylates, calcium, estrogen
Infection	Viruses-mumps, coxsackie, hepatitis B, CMV, varicella-zoster, HSV, HIV
	Bacteria-mycoplasma, Legionella, Leptospira, salmonella
	Fungi-aspergillus
	Parasites-toxoplasma, cryptosporidium, Ascaris
Trauma	Blunt or penetrating abdominal injury, iatrogenic injury during surgery or ERCP (sphincterotomy)
Congenital	Cholodochocele type V, pancreas divisum*
Vascular	Ischemia, atheroembolism, vasculitis (polyarteritis nodosa, SLE)
Miscellaneous	Post ERCP, pregnancy, renal transplantation, alpha-1-antitrypsin deficiency
Genetic	CFTR, PRSS1, SPINK1, and other genetic mutations

*Whether pancreas divisum causes pancreatitis or is an incidental finding is controversial. 5-ASA: 5-aminosalicylic acid; CMV: cytomegalovirus; HSV: herpes simplex virus; HIV: human immunodeficiency virus; ERCP: endoscopic retrograde cholangiopancreatography; PRSS: protease serine; SPINK: serine protease inhibitor Kazal type; SLE: systemic lupus erythematosus; CFTR: cystic fibrosis transmembrane conductance regulator.

Graphic 78423 Version 5.0

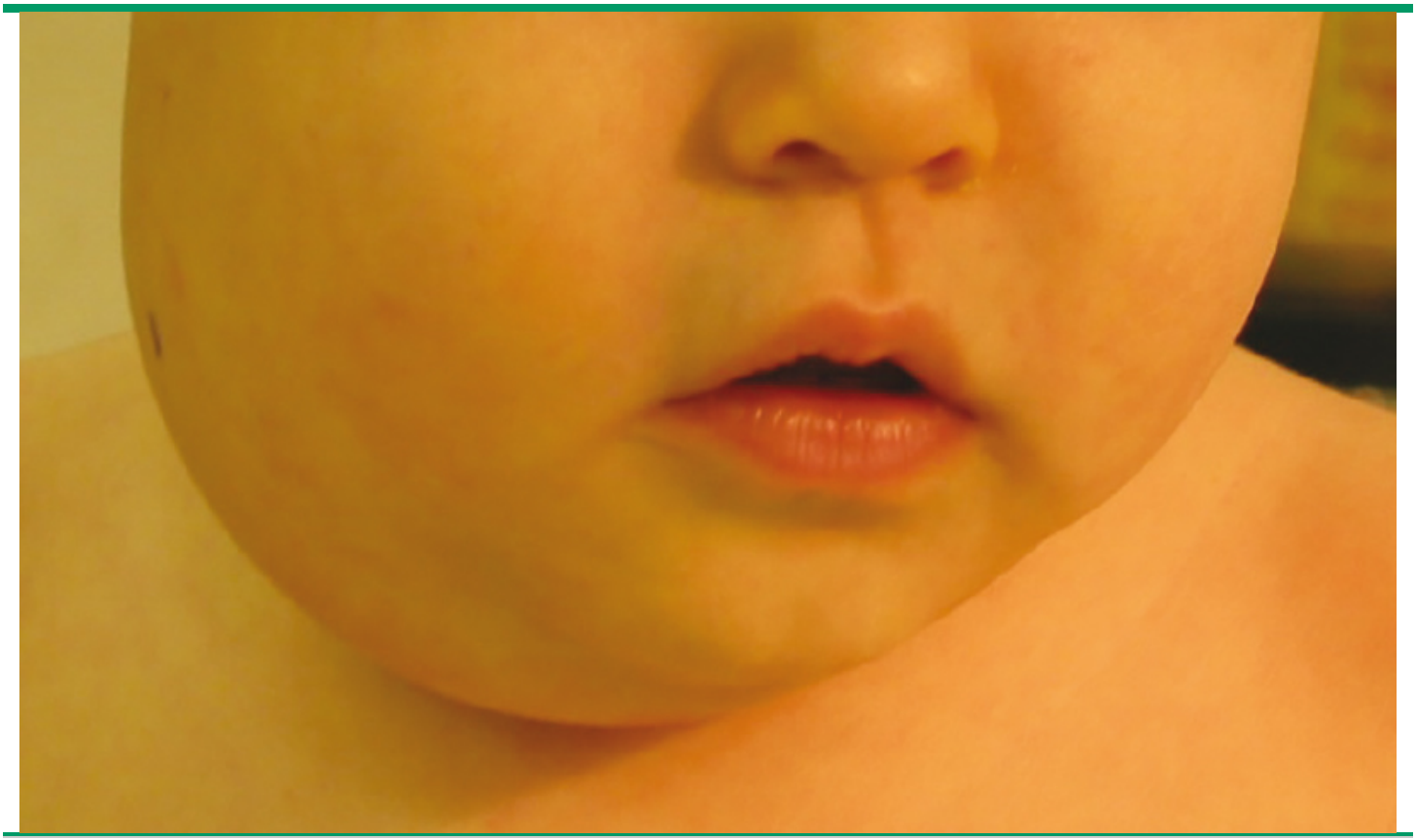
Eruptive xanthomata



Xanthomata are seen on the extensor surface of the forearm in a patient with severe hypertriglyceridemia.

Graphic 82268 Version 2.0

Parotid gland swelling in a young child



There is swelling of the parotid gland anterior and inferior to the auricle, obscuring the angle of the mandible.

Graphic 53503 Version 4.0

Differential diagnosis of hyperamylasemia

Disease	Predominant amylase isoform
Pancreatic disease	Pancreatic
Acute or chronic pancreatitis	
Post-ERCP	
Pseudocyst	
Pancreatic ascites	
Acute cholecystitis	Pancreatic
Intestinal diseases	Pancreatic
Parotitis	
Trauma	
Surgery	
Radiation	
Calculi	
Obstruction	
Infarction	
Malignancy with ectopic amylase production	Salivary
Acidosis or ketoacidosis	Salivary or pancreatic
Renal failure	Salivary and pancreatic
Macroamylasemia	Macroamylase
Fallopian tube diseases	Salivary
Ruptured ectopic pregnancy	
Salpingitis	
Miscellaneous	Salivary and/or pancreatic
Alcoholism	
Anorexia nervosa/bulimia	
Cirrhosis	

Graphic 78538 Version 1.0

Conditions associated with a high serum lipase

Acute pancreatitis
Chronic pancreatitis
Renal failure
Acute cholecystitis
Bowel obstruction or infarction
Duodenal ulceration
Pancreatic calculus
Pancreatic tumors
Type 2 diabetes mellitus
Diabetic ketoacidosis
HIV disease
HCV infection
Macrolipasemia
Post-ERCP/trauma
Sarcoidosis
Celiac disease
Inflammatory bowel disease
Idiopathic
Drugs

HCV: hepatitis C virus; HIV: human immunodeficiency virus; ERCP: endoscopic retrograde cholangiopancreatography.

Graphic 77323 Version 5.0

Revised definitions of morphological features of acute pancreatitis

1. Interstitial edematous pancreatitis

Acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognizable tissue necrosis
Contrast-enhanced computed tomography criteria:

- Pancreatic parenchyma enhancement by intravenous contrast agent
- No findings of peripancreatic necrosis

2. Necrotizing pancreatitis

Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis
Contrast-enhanced computed tomography criteria:

- Lack of pancreatic parenchymal enhancement by intravenous contrast agent, and/or
- Presence of findings of peripancreatic necrosis (see below—acute peripancreatic fluid collection and walled off necrosis)

3. Acute peripancreatic fluid collection (APFC)

Peripancreatic fluid associated with interstitial edematous pancreatitis with no associated peripancreatic necrosis. This term applies only to areas of peripancreatic fluid seen within the first four weeks after onset of interstitial edematous pancreatitis and without the features of a pseudocyst.
Contrast-enhanced computed tomography criteria:

- Occurs in the setting of interstitial edematous pancreatitis
- Homogeneous collection with fluid density
- Confined by normal peripancreatic fascial planes
- No definable wall encapsulating the collection
- Adjacent to pancreas (no intrapancreatic extension)

4. Pancreatic pseudocyst

An encapsulated collection of fluid with a well defined inflammatory wall usually outside the pancreas with minimal or no necrosis. This entity usually occurs more than four weeks after onset of interstitial edematous pancreatitis to mature.
Contrast-enhanced computed tomography criteria:

- Well circumscribed, usually round or oval
- Homogeneous fluid density
- No non-liquid component
- Well defined wall (ie, completely encapsulated)
- Maturation usually requires >4 weeks after onset of acute pancreatitis; occurs after interstitial edematous pancreatitis

5. Acute necrotic collection (ANC)

A collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis; the necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues
Contrast-enhanced computed tomography criteria:

- Occurs only in the setting of acute necrotizing pancreatitis
- Heterogeneous and non-liquid density of varying degrees in different locations (some appear homogeneous early in their course)
- No definable wall encapsulating the collection
- Location—intrapancreatic and/or extrapancreatic

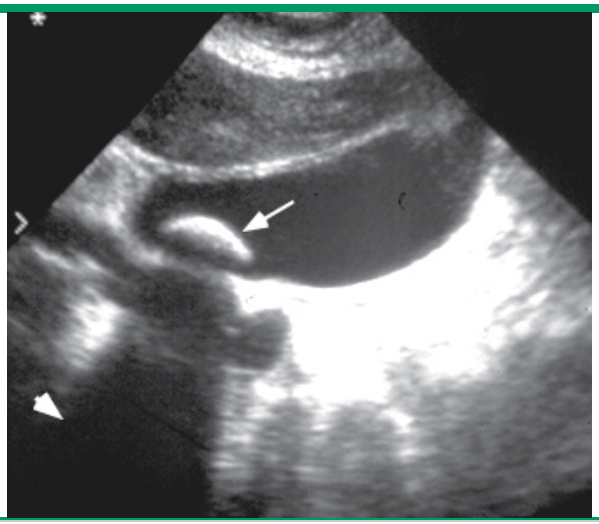
6. Walled-off necrosis (WON)

A mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that has developed a well defined inflammatory wall. WON usually occurs >4 weeks after onset of necrotizing pancreatitis.
Contrast-enhanced computed tomography criteria:

- Heterogeneous with liquid and non-liquid density with varying degrees of loculations (some may appear homogeneous)
- Well defined wall, that is, completely encapsulated
- Location—intrapancreatic and/or extrapancreatic
- Maturation usually requires four weeks after onset of acute necrotizing pancreatitis

Graphic 87683 Version 2.0

Cholelithiasis

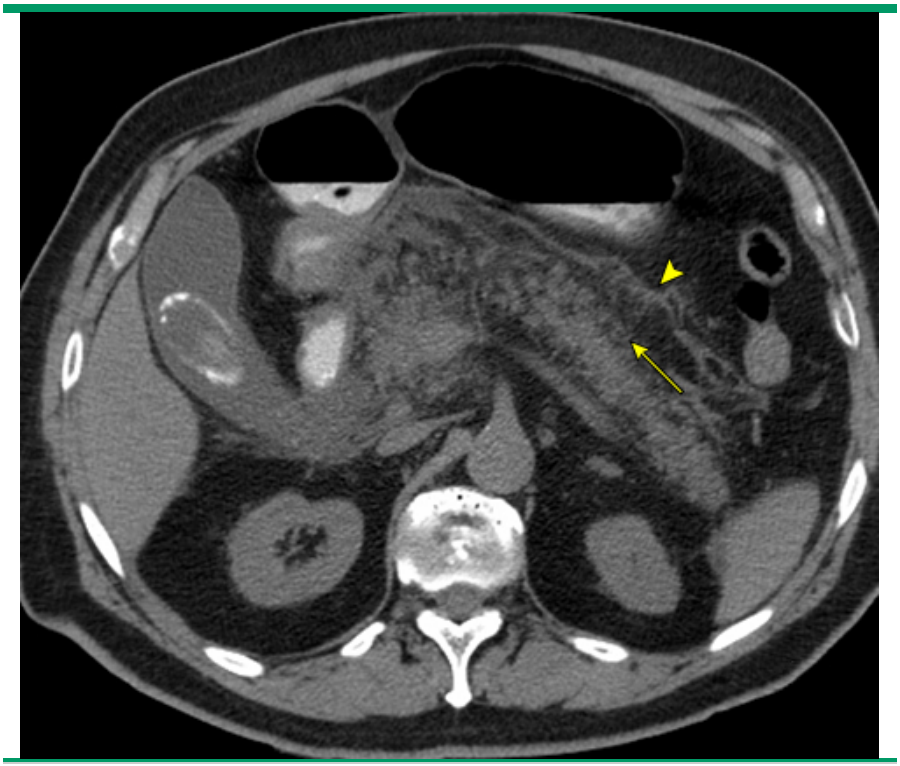


Ultrasound of the gallbladder shows posterior acoustic shadowing (arrowhead) produced by a stone in the lumen of the gallbladder (arrow). There is no gallbladder wall thickening, a finding that may be seen with cholecystitis.

Courtesy of Jonathan Kruskal, MD, PhD.

Graphic 58844 Version 2.0

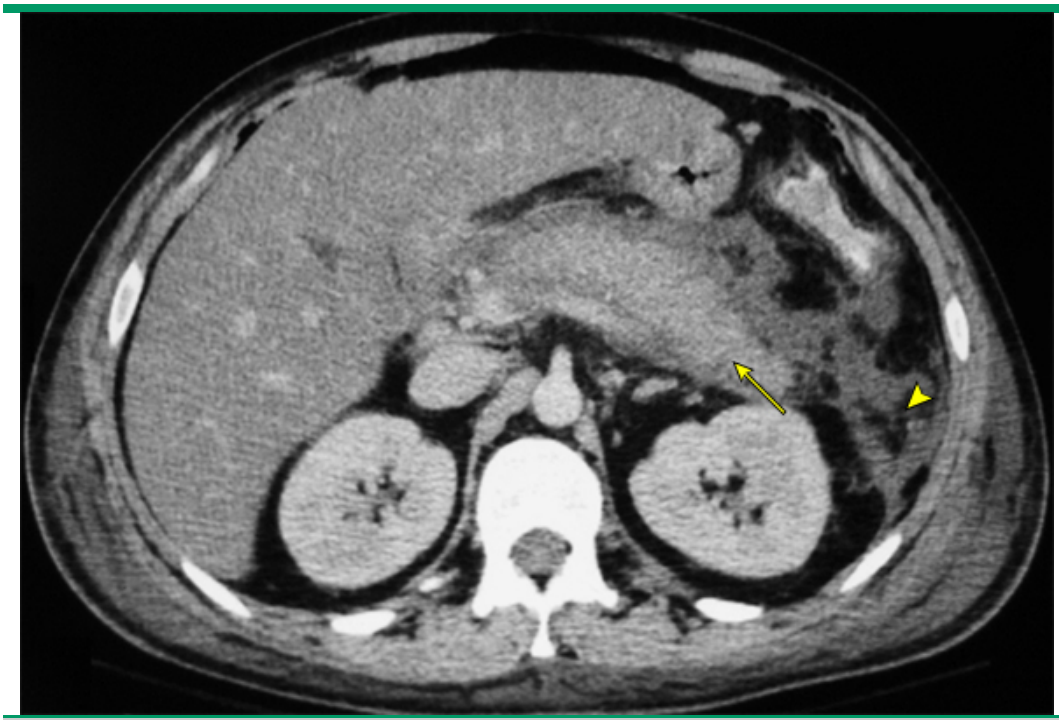
CT scan of acute interstitial edematous pancreatitis



The computed tomography (CT) scan in a 75-year-old man with acute interstitial pancreatitis reveals heterogeneous appearance of the pancreas (arrow) and peripancreatic fat stranding (arrowhead).

Graphic 88430 Version 1.0

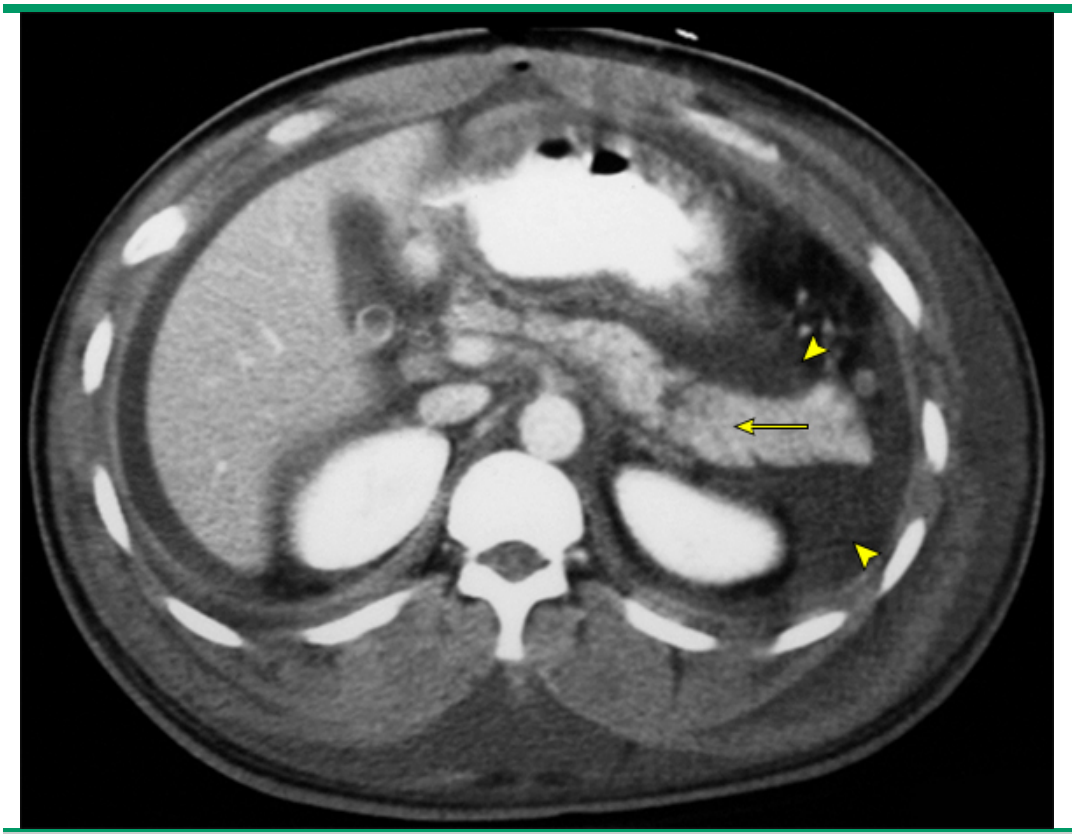
CT scan of necrotizing pancreatitis with peripancreatic necrosis



Computed tomography (CT) scan of a 34-year-old male with acute pancreatitis reveals the pancreas enhances homogeneously (arrow) but there is evidence of peripancreatic necrosis (arrowhead).

Graphic 88432 Version 1.0

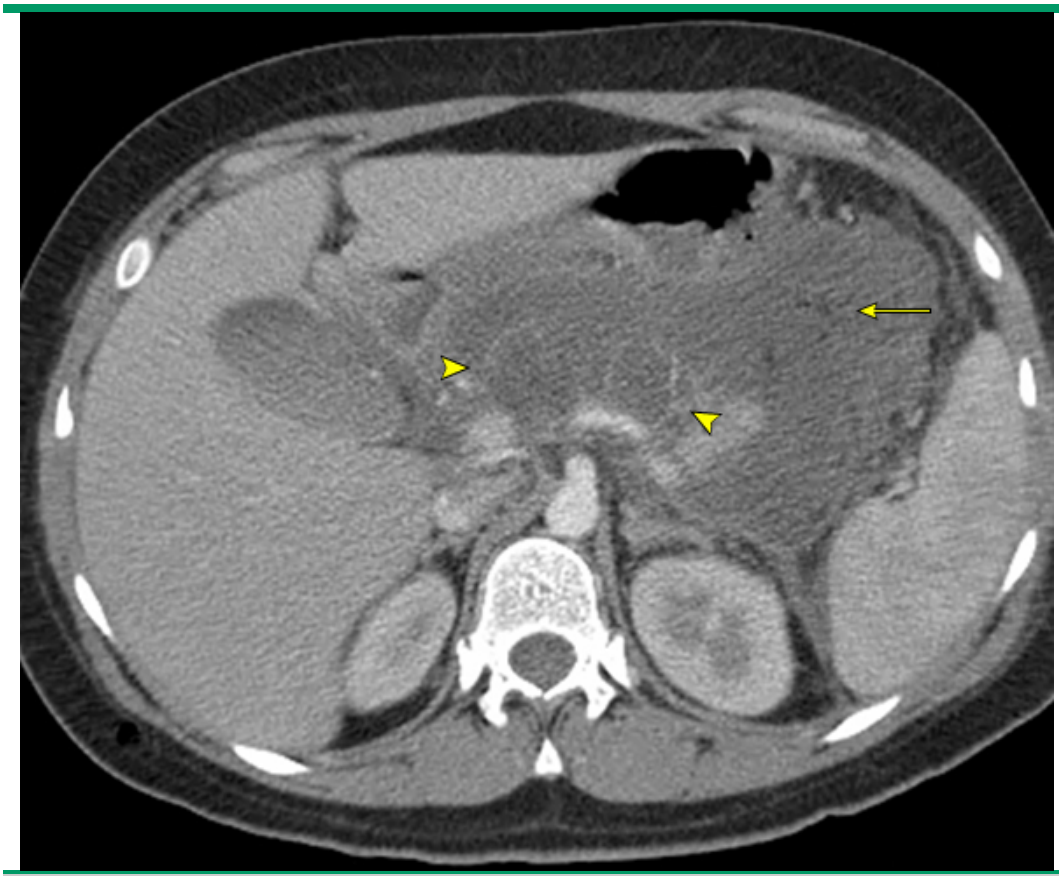
CT scan of acute interstitial pancreatitis with acute peripancreatic fluid collections



Computed tomography (CT) scan reveals acute interstitial pancreatitis with an acute peripancreatic fluid collections (APFC) around the body and tail of the pancreas (arrowheads). There is mild heterogeneity of the enhanced pancreas (arrow).

Graphic 88431 Version 2.0

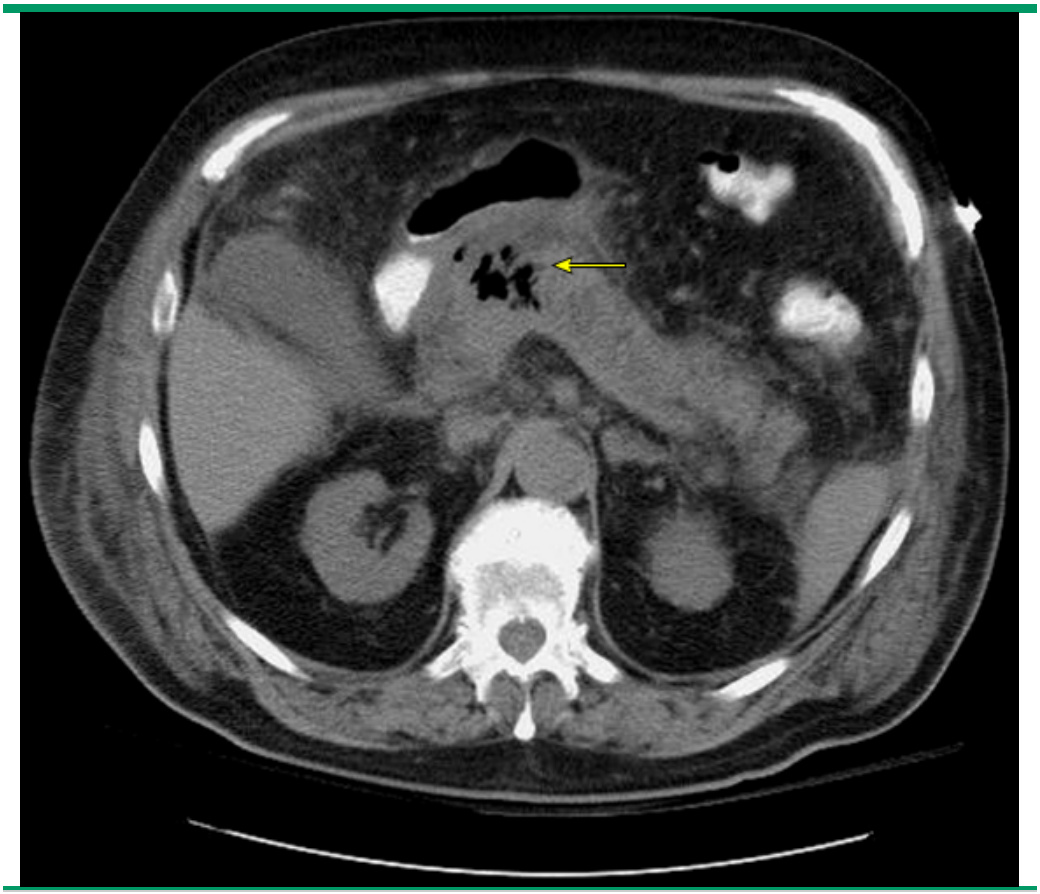
CT scan of acute necrotic collection



Computed tomography (CT) scan reveals an acute necrotic collection in a 20-year-old female with acute pancreatitis. The axial CT image shows pancreatic necrosis with a nonenhancing region in the neck and the body of the pancreas (between arrowheads). In the surrounding anterior pararenal space, there is a large fluid accumulation that contains islands of necrosis (arrow).

Graphic 88434 Version 1.0

CT scan of acute necrotizing pancreatitis complicated by infected pancreatic necrosis



Computed tomography (CT) scan reveals gas bubbles (arrow) within an area of pancreatic necrosis. The presence of gas bubbles is a pathognomonic sign of infection of the necrosis.

Graphic 88436 Version 1.0

Modified Marshall scoring system for organ dysfunction

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO_2/FiO_2)	>400	301-400	201-300	101-200	≤101
Renal*					
(serum creatinine, micromol/L)	≤134	134-169	170-310	311-439	>439
(serum creatinine, mg/dL)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mmHg)¶	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH <7.3	<90, pH <7.2
For nonventilated patients, the FiO_2 can be estimated from below:					
Supplemental oxygen (L/min)	**FiO_2 (percent)**				
Room air	21				
2	25				
4	30				
6-8	40				
9-10	50				

A score of 2 or more in any system defines the presence of organ failure.

* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 micromol/L or ≥1.4 mg/dL.
¶ Off inotropic support.

Graphic 87718 Version 2.0

Contributor Disclosures

Santhi Swaroop Vege, MD Grant/Research/Clinical Trial Support: R 21 NIH trial pentoxifylline completed in August 2017. Consultant/Advisory Boards: Takeda pharmaceuticals; Hightide biopharmaceuticals; Generon (about to sign a contract); Vical. **David C Whitcomb, MD, PhD** Employment: University of Pittsburgh Medical Center. Equity Ownership/Stock Options: Ariel Precision Medicine [genetic testing]. Patent Holder: University of Pittsburgh [US patent 10,174,377 - predicting the risk of developing, or the presence of, recurrent acute pancreatitis and/or chronic pancreatitis]. Grant/Research/Clinical Trial Support: Regeneron [pancreatitis]. Consultant/Advisory Boards: Ariel Precision Medicine [genetic testing]; AbbVie; Abbott; Samsung. **Shilpa Grover, MD, MPH, AGAF** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy