144

# PANCREATITIS

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## ACUTE PANCREATITIS

### DEFINITION

Acute pancreatitis, which is a discrete episode of cellular injury and inflammation in the pancreas, is triggered by the release of activated digestive enzymes into the pancreas and peripancreatic tissues. Acute pancreatitis usually presents with symptoms of abdominal pain, nausea, and vomiting

accompanied by an elevation in serum levels of amylase, lipase, or both and by radiographic evidence of pancreatic inflammation, edema, or necrosis. Although pancreatic morphology and function may recover after such an episode, complete recovery is unlikely if the initial damage is substantial, particularly if the original episode is associated with significant pancreatic necrosis. With repeated episodes, there can be a shift from acute inflammation, necrosis, and apoptosis to a milieu of chronic inflammation, the activation of pancreatic stellate cells, continued tissue destruction, and ultimately the fibrosis characteristic of chronic pancreatitis. About 25% of patients with acute pancreatitis will have recurrence, and about 10% will develop chronic pancreatitis.[1]

## EPIDEMIOLOGY

Acute pancreatitis, which is the most common cause of hospitalization for a gastrointestinal condition in the United States,[2] accounts for approximately 275,000 hospitalizations yearly. This rate of hospital admissions has doubled over the past 2 decades. The incidence of acute pancreatitis ranges from 13 to 45 per 100,000 population. The total cost of caring for these patients is substantial, with estimates of $6 billion annually. The incidence of acute pancreatitis is increasing in the United States and in many other countries, perhaps because of heightened clinical suspicion for the diagnosis, the more widespread use of serum-based and radiologic testing, and an increasing incidence of gallstones in the midst of the obesity epidemic.

The risk of acute pancreatitis increases fourfold between ages 25 and 75 years. The risk is two- to threefold higher among the black population in the United States compared with whites. Increased abdominal adiposity but not body mass index increases the risk of acute pancreatitis approximately twofold.

## PATHOBIOLOGY

The mechanisms that lead to acute pancreatitis include exposures to potential disease triggers and genetic polymorphisms that predispose to acute pancreatitis. Acute pancreatitis is characterized by premature activation of pancreatic digestive enzymes within the pancreas. In many models of pancreatitis, abnormal calcium signaling and the activation of specific protein kinases lead to the generation of inflammatory mediators, the activation of enzymes within the acinar cell, misdirected exocytosis, and ultimately the cellular injury and death that characterize acute pancreatitis.[3] The activation of trypsinogen to trypsin may be a critical initial step, with trypsin having the capacity to activate other proteases within the gland. These activated enzymes produce cellular injury and death. Necrosis may involve not only the pancreas but also surrounding fat and structures, leading to fluid extravasation into the retroperitoneal spaces ("third-space" losses). Although some degree of microscopic necrosis may be present in most cases of acute pancreatitis, more substantial necrosis (visible on an enhanced contrast computed tomography [CT] scan) is termed *acute necrotizing pancreatitis* and is distinguished from the milder *acute interstitial pancreatitis*, in which necrosis is not visible on a CT scan.

In addition to local damage within and around the pancreas, acute pancreatitis may be associated with distant organ system failure. The release of inflammatory cytokines and activated digestive enzymes into the systemic circulation can produce a systemic inflammatory response syndrome (SIRS; Chapters 106 and 108) and associated organ system failure. The most common manifestations of this process in severe acute pancreatitis include hypotension, renal failure, and respiratory failure. Gallstones and alcohol account for about 70% to 80% of all cases of acute pancreatitis, and the cause remains unknown in about 10% of cases (Table 144-1).

**TABLE 144-1 CAUSES OF ACUTE PANCREATITIS**

| ETIOLOGY | EXAMPLES | COMMENTS |
|---|---|---|
| Gallstones | Gallstones<br>Microlithiasis | Best detected by EUS |
| Drugs and toxins | Ethyl and methyl alcohol<br>Tobacco<br>Azathioprine, 6-mercaptopurine, pentamidine, didanosine, sulfonamides, thiazides, aminosalicylates, valproic acid, and others<br>Scorpion venom<br>Insecticides | <br><br>Usually idiosyncratic<br><br>Caused by hyperstimulation of pancreatic secretion |
| Metabolic | Hypertriglyceridemia<br>Hypercalcemia | Usually requires triglyceride level >1000 mg/dL |
| Trauma | Post-ERCP<br>Blunt or penetrating trauma<br>Postoperative | Risk varies with indication and may be reduced by rectal NSAIDs and pancreatic duct stents |
| Obstruction of the pancreatic duct | Benign pancreatic duct stricture<br>Benign ampullary stricture (e.g., celiac disease, diverticulum)<br>Ampullary adenoma or adenocarcinoma<br>Pancreatic ductal adenocarcinoma<br>Intraductal papillary mucinous neoplasm<br>Pancreas divisum<br>Sphincter of Oddi dysfunction | <br><br><br><br><br>Controversial<br> |
| Infections | Cytomegalovirus, mumps, rubella, Coxsackie B<br>*Candida*, histoplasmosis<br>Ascaris | |
| Genetics | *PRSS1* mutations<br>*CFTR* mutation<br>*SPINK1* mutation<br>Others (chymotrypsin C, calcium sensing receptor, claudin-2, others) | Mutation sufficient to cause disease<br>Mutations or polymorphisms predispose to pancreatitis |
| Autoimmune pancreatitis | Type 1<br>Type 2 | Elevations in serum levels of IgG4 may be seen in Type 1 |
| Idiopathic pancreatitis | | |

ERCP = endoscopic retrograde cholangiopancreatography; EUS = endoscopic ultrasonography; NSAID = nonsteroidal anti-inflammatory drug.

### Gallstones and Obstruction

Passage of a gallstone through the ampulla of Vater, with transient obstruction of the pancreatic duct, is the initiating event for gallstone pancreatitis. Only about 5% of all patients with gallstones develop pancreatitis, and patients with smaller gallstones (≤5 mm), which can pass the cystic duct and reach the ampulla, are at highest risk. Microlithiasis describes very tiny gallstones that are not easily visible on standard transabdominal ultrasonography but may cause gallstone pancreatitis.

In addition to gallstones and microlithiasis, pancreatic duct obstruction owing to pancreatic ductal adenocarcinoma (Chapter 194), ampullary adenoma or carcinoma, or intraductal papillary mucinous neoplasm can cause acute pancreatitis. Benign strictures of the ampulla may cause acute pancreatitis, owing to duodenal diseases such as celiac disease and periampullary diverticula. Sphincter of Oddi dysfunction, defined by high pressures of the pancreatic sphincter, and pancreas divisum, in which the larger dorsal pancreas drains through the smaller minor papilla, are controversial causes of acute pancreatitis because patients with them often have coexistent underlying genetic mutations that contribute to this disease.

### Alcohol

Long-standing use of substantial alcohol (Chapter 33), usually more than 5 years of intake averaging more than 5 to 8 drinks daily, is required before pancreatitis develops. Even then, the absolute risk of pancreatitis is only 2% to 5%, thereby emphasizing important cofactors such as a high-fat diet, genetic variability, and smoking. Interestingly, binge drinking does not appear to be a risk factor for pancreatitis, and many patients develop their first episode of pancreatitis several days after stopping drinking. The mechanism by which alcohol causes pancreatic injury is uncertain but likely involves a mixture of direct toxicity, oxidative stress, and alterations in pancreatic enzyme secretion.

### Drugs, Toxins, and Metabolic Factors

Serum triglyceride levels greater than 500 mg/dL and usually greater than 1000 mg/dL can cause acute pancreatitis (Chapter 206). The mechanism is

not known. Pancreatitis also can be precipitated by the administration of estrogens, which can exacerbate underlying hypertriglycideremia. Hypercalcemia is an exceedingly rare cause of acute pancreatitis. Drug-induced pancreatitis is rare and is generally an idiosyncratic event. Implicated drugs include 6-mercaptopurine and azathioprine (up to a 4% attack rate), didanosine, pentamidine, valproic acid, furosemide, sulfonamides, and aminosalicylates. Toxins that may cause acute pancreatitis include methyl alcohol (Chapter 110), organophosphate insecticides, and venom from certain scorpions (Chapter 359).

### Trauma

Iatrogenic trauma to the pancreas and pancreatic duct during performance of an endoscopic retrograde cholangiopancreatography (ERCP; Chapter 134) is a common cause of pancreatitis. The risk of acute pancreatitis ranges from less than 5% for patients with simple common bile duct stones or malignancy to as high as 20% for patients with suspected sphincter of Oddi dysfunction.[4] Penetrating trauma and blunt trauma, ranging from a contusion to the gland to a severe crush injury and even transection of the gland, can also cause acute pancreatitis. Ischemic injury to the gland can occur after surgical procedures, especially in patients who undergo cardiopulmonary bypass.

### Infections

*Ascaris lumbricoides* (Chapter 357) may cause pancreatitis by obstructing the pancreatic duct as the worms migrate through the ampulla. A number of viruses may infect the pancreatic acinar cells directly, including cytomegalovirus (Chapter 376), Coxsackie B virus (Chapter 379), Echovirus (Chapter 379), and mumps virus (Chapter 369). Fungal infections of the pancreas are exceedingly rare but may be seen in the setting of immunosuppression.

### Genetic and Autoimmune Causes

Mutations in several genes predispose to the development of acute and chronic pancreatitis.[5] Most patients with these mutations will not develop pancreatitis, but those who do often develop relapsing acute pancreatitis and ultimately chronic pancreatitis.

Gain-of-function mutations in the cationic trypsinogen gene (*PRSS1*) predispose to hereditary pancreatitis with such a high penetrance that nearly all affected individuals will ultimately develop chronic pancreatitis (see later) and have a more than 35-fold lifetime risk of developing pancreatic ductal adenocarcinoma (Chapter 194) by age 70 years. Mutations in the cystic fibrosis conductance regulator (*CFTR*; Chapter 89), serine protease inhibitor Kazal type 1 (*SPINK1*), chymotrypsin C (*CTC*), calcium-sensing receptor gene, and claudin-2 genes predispose to both relapsing acute and chronic pancreatitis. With the exception of *PRSS1*, these mutations are best viewed as cofactors that interact with other risk factors and disease modifiers to cause pancreatitis.

Two forms of autoimmune pancreatitis, classically presenting as chronic pancreatitis (see later), have been identified.[6] Type 1 is a systemic disease that affects the salivary glands, retroperitoneum, biliary ducts, kidneys, and other organs and rarely presents as acute pancreatitis. Type 2 only affects the pancreas and may occasionally present as unexplained acute pancreatitis.

## CLINICAL MANIFESTATIONS

Abdominal pain, nausea, and vomiting are the hallmark symptoms of acute pancreatitis. The abdominal pain is usually in the epigastric region and often radiates to the back. The pain is steady, reaches its maximum intensity over 30 to 60 minutes, and persists for days. These characteristic symptoms may be masked in patients who present with delirium, multiple organ system failure, or coma.

The physical examination usually reveals tachycardia, and more severe cases often present with or develop hypotension, tachypnea, and fever. Confusion, delirium, and even coma may occur. The abdomen is often distended with diminished bowel sounds. Tenderness to palpation of the abdomen, which may be epigastric or more diffuse, is typical, and rebound and guarding are observed in more severe cases. Dullness to percussion in the lower lung fields may be noted owing to a pleural effusion. Rare physical findings include ecchymoses of the flank (Grey Turner sign) or umbilicus (Cullen sign), which occur when fluid and blood track into these spaces from the retroperitoneum. Jaundice may be present if there is biliary obstruction by a stone.

The presence of dyspnea, tachypnea, oxygen desaturation, hypotension, or tachycardia portends a worse prognosis. Severe acute pancreatitis is defined by the presence of organ system failure (usually cardiovascular, renal, or pulmonary) or by the presence of pancreatic complications such as pancreatic and peripancreatic necrosis (Table 144-2).[7]

**TABLE 144-2 COMPLICATIONS OF ACUTE PANCREATITIS**

| COMPLICATION | EXAMPLES |
|---|---|
| Systemic complications | Hypotension and shock<br>Adult respiratory distress syndrome<br>Acute renal failure<br>Disseminated intravascular coagulation<br>Hypocalcemia<br>Hypertriglyceridemia<br>Hyperglycemia<br>Encephalopathy and coma |
| Gastrointestinal bleeding | Stress ulceration<br>Pseudoaneurysm |
| Local complications | Acute peripancreatic fluid collection<br>Pseudocyst<br>Pancreatic necrosis (infected or sterile)<br>Acute necrotic collection<br>Walled-off pancreatic necrosis<br>Duodenal or biliary obstruction |

## DIAGNOSIS

The diagnosis of acute pancreatitis requires the presence of two of three primary features: abdominal pain, elevations in serum amylase or lipase levels, and imaging studies consistent with acute pancreatitis. Accurate diagnosis also requires that other conditions that can mimic acute pancreatitis, such as intestinal infarction or small bowel obstruction, be excluded. It is equally important to define the most likely cause and the severity of pancreatitis because both strongly influence management.

### Laboratory Tests

#### *Amylase and Lipase*

Nearly all patients with acute pancreatitis have an elevation in serum levels of amylase or lipase within a few hours after the onset of symptoms. Elevation more than three times the upper limit of normal is the recommended cutoff for diagnosing acute pancreatitis. Lipase remains elevated longer than amylase. Amylase and lipase levels may be normal in rare patients with acute pancreatitis, particularly if the measurement is delayed for several days after the onset of symptoms. In addition, marked hypertriglyceridemia can interfere with the accurate measurement of amylase and lipase. Both enzymes are cleared by the kidney, and renal failure can raise the level of these enzymes up to five times the upper limit of normal in the absence of pancreatitis. Both amylase and lipase can be elevated in a variety of other conditions, some of which may mimic acute pancreatitis. These include intestinal ischemia and infarction (Chapter 143), bowel obstruction (Chapter 142), cholecystitis (Chapter 155), and choledocholithiasis (Chapter 155). In addition, amylase may be elevated from ectopic pregnancy, acute salpingitis, and a variety of extraabdominal conditions such as parotitis (Chapter 369), lung cancer (Chapter 191), head trauma (Chapter 399), and others. In some patients, only amylase or lipase levels may be elevated. Given its improved specificity, equal cost, and equal sensitivity, lipase is preferred over amylase as a single diagnostic test.[8] Frequent serial measurements of amylase or lipase levels in patients with acute pancreatitis are not helpful in clinical decision making.

#### *Other Laboratory Tests*

In addition to amylase and lipase levels, all patients should have blood testing for renal function, liver chemistries, electrolyte concentrations, and levels of calcium and triglycerides. In severe pancreatitis, leukocytosis, hemoconcentration, and azotemia may be seen. Hyperglycemia, hypocalcemia, and mild hypertriglyceridemia can develop in more severe cases. Liver chemistries may be elevated in patients with gallstone pancreatitis. Elevations in alanine aminotransferase levels more than three times the upper limit of normal are most suggestive of gallstones as the cause of pancreatitis, although any significant elevation in liver chemistries should raise the possibility of gallstones (Chapter 155).

### Imaging Studies

Imaging studies are used not only in establishing the diagnosis but also in determining the etiology and prognosis. In most patients, ultrasonography,

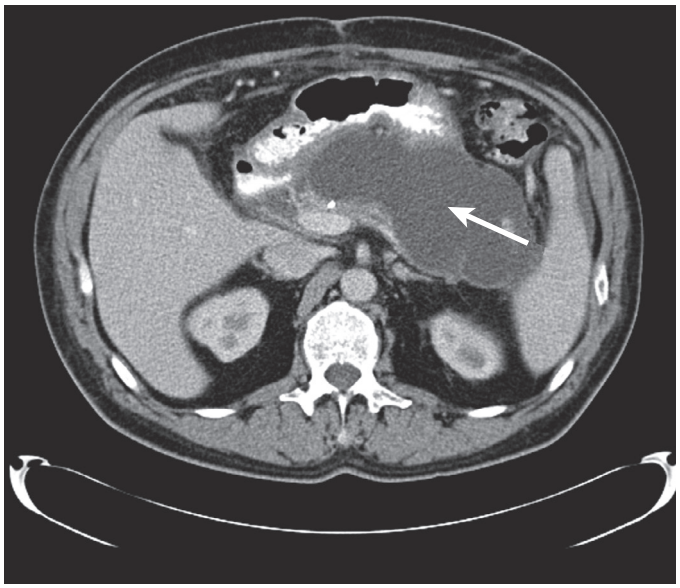

**FIGURE 144-1.** A computed tomography scan demonstrating a large area of pancreas that does not enhance with intravenous contrast *(arrow)*, consistent with pancreatic necrosis.

CT, or magnetic resonance imaging (MRI) are used in a complementary fashion.[9]

*Abdominal ultrasonography* can confirm the presence of acute pancreatitis by documenting pancreatic enlargement, edema, or associated peripancreatic fluid collections. Visualization of the pancreas may be inadequate owing to body habitus or overlying intestinal gas. Ultrasonography is accurate in identifying a ductal gallstone as the definitive cause of acute pancreatitis. Alternatively, gallstones in the gallbladder or a dilated common bile duct strongly suggests gallstones as the cause of acute pancreatitis.

*Computed tomography* is more accurate than ultrasonography for confirming the diagnosis of acute pancreatitis and for documenting the presence of pancreatic necrosis and peripancreatic fluid collections. CT is also particularly helpful in excluding some of the intraabdominal conditions that can mimic acute pancreatitis. However, CT is less accurate than ultrasonography in identifying gallstones. On contrast-enhanced CT, the pancreatic parenchyma that opacifies with intravenous contrast is considered still viable, but the parenchyma that does not opacify is necrotic (Fig. 144-1). The amount of pancreatic necrosis has some prognostic importance, but the degree of necrosis cannot be accurately identified on CT until 3 or more days after the onset of the disease. CT scans are not routinely required in patients with acute pancreatitis but should be performed in patients with a first attack, with severe disease, with disease that is slow to improve, or when the diagnosis is not clear.[10]

*Magnetic resonance imaging* is equivalent to CT in its ability to document the presence of acute pancreatitis, identify the presence of necrosis, and document nonpancreatic diseases that could mimic acute pancreatitis. In addition, *magnetic resonance cholangiopancreatography (MRCP)* is much better than CT in identifying the presence of gallstones and in assessing abnormalities of the pancreatic duct, such as pancreas divisum or a disrupted pancreatic duct. MRI is more difficult than CT to perform in critically ill patients.

*Endoscopic procedures,* including ERCP and endoscopic ultrasonography, are important in both diagnosis and therapy of acute pancreatitis. Endoscopic ultrasonography, which is primarily used to establish the cause when the initial evaluation is unrevealing, is particularly accurate in identifying underlying malignancy, premalignant lesions such as ampullary adenoma, and small gallstones or microlithiasis. ERCP is never used as a diagnostic test but may be used to evaluate rare causes of pancreatitis, such as pancreas divisum or sphincter of Oddi dysfunction, in patients with unexplained relapsing pancreatitis.

## Determining Etiology

To identify the cause of acute pancreatitis, the history should focus on alcohol and tobacco use, previous biliary colic, drug history, family history, and recent trauma. Alcohol use may need to be corroborated with family members. All patients should undergo transabdominal ultrasonography, with CT or MR considered for patients who have a first attack or a severe attack, who fail to rapidly improve, or who do not have a clear diagnosis. Gallstones should be suspected if stones are seen on ultrasonography, CT, or MRI or if liver chemistries are abnormal, particularly if liver chemistries improve or normalize over a few days. If these initial studies are unrevealing, endoscopic ultrasonography is usually performed to assess for small gallstones, microlithiasis, or underlying malignancy, particularly in patients older than age 40 years. More specialized investigations such as ERCP, sphincter of Oddi manometry, or genetic testing are usually reserved for patients seen in referral centers after multiple attacks of pancreatitis.

On initial evaluation, about 25% of patients do not have an identified cause, but surreptitious alcohol use and microlithiasis are probably the most common underlying causes in these patients. After a detailed evaluation, approximately 10% of patients are ultimately diagnosed with idiopathic pancreatitis.

## Determining and Predicting Severity

Severe pancreatitis is defined as organ system failure that persists for more than 48 hours or by local pancreatic and peripancreatic complications such as necrosis, acute fluid collections, or pseudocysts. Moderately severe pancreatitis is characterized by transient organ failure for less than 48 hours, by a local complication, or by a systemic complication owing to worsening of an underlying comorbid disease. Mild acute pancreatitis implies the absence of these features.

Organ failure can be single or multiple, early or late in onset, and progressive and persistent or transient. Patients may exhibit altered mental status, hypoxia, tachypnea, massive third space fluid loss, and intravascular volume depletion. In severe acute pancreatitis, renal failure, pulmonary failure, and circulatory failure most commonly occur as part of the SIRS response. Multiple organ system failure, particularly if it persists beyond 48 hours after admission, is associated with prolonged hospitalization, intensive care unit (ICU) admission, need for surgery, and death.

Local pancreatic and peripancreatic complications help define the severity of acute pancreatitis. The degree of pancreatic necrosis, which is defined on contrast-enhanced CT as areas of pancreas that do not enhance with intravenous contrast infusion, correlates with a worse outcome, particularly if infection develops in the devitalized necrotic tissue. Fluid collections may also accumulate around the pancreas in various retroperitoneal and peritoneal spaces. Much of this inflammatory fluid usually resolves, but some may form into a more circumscribed *pseudocyst* over several weeks. However, some fluid collections seen on contrast-enhanced CT may initially be termed *pseudocysts* when in reality they contain solid necrotic material as well as fluid and actually represent *walled-off pancreatic necrosis* that will require a different therapeutic approach than simple pseudocysts.

# TREATMENT

## General Supportive Care

The majority of patients will recover within several days, but it is usually not possible to identify these patients accurately at the time of admission. Patients initially should not be given any oral food or fluids. In patients with more severe pancreatitis, admission to an ICU is appropriate.[11] Pain control usually requires parenteral narcotics (e.g., hydromorphone 1-2 mg every 4-6 hours initially or via patient controlled analgesia). Antiemetic agents (Table 132-5) are often required. Early and aggressive hydration (e.g., ≥250 cc/hr or even more) in the first 12 to 24 hours may be necessary to normalize the blood urea nitrogen (BUN), hematocrit, and vital signs and to generate adequate urine output.[12] Lactated Ringer solution may be preferred over normal saline. Care must be taken to ensure patients receive sufficient volume but not enough to cause fluid overload or the development of an abdominal compartment syndrome.

Patients can begin to be fed, beginning with a low-fat solid diet, when bowel sounds have returned and nausea has resolved, without necessarily waiting until all abdominal pain has resolved. Early nasoenteric feeding is no better than an oral diet started 72 hours after admission, with enteral feeding reserved for those who cannot tolerate oral feeding. Enteral nutrition with an elemental or semi-elemental formula is associated with fewer complications and less cost compared with total parenteral nutrition.

## Treatment of Complications

Most patients who develop acute gallstone pancreatitis have already passed the offending gallstone into the duodenum, but those with a

persistent or multiple stones are at higher risk of developing cholangitis and possibly more severe pancreatitis. Early ERCP is recommended in patients with gallstone pancreatitis and concomitant cholangitis (fever, jaundice, right upper quadrant pain) and in patients who have strong evidence of a persistent bile duct stone at 48 hours after admission based on a visible persistent stone on an imaging study, jaundice, a persistently dilated bile duct, or worsening liver chemistries. By comparison, early ERCP is not recommended for patients with severe pancreatitis, as evidenced by early and progressive organ system failure, but without cholangitis or suspicion of a persistent bile duct stone.[■] When unsure, endoscopic ultrasonography or MRCP can help identify persistent bile duct stones before consideration of ERCP.

The systemic complications that develop in patients with severe acute pancreatitis are similar to those commonly encountered in other ICU patients, as well as specific metabolic issues that occur in the setting of severe pancreatitis. Hyperglycemia, which develops particularly if parenteral nutrition is used, contributes to higher rates of infections. Hypocalcemia is common in severe pancreatitis, but ionized calcium levels are usually normal and treatment is not needed in the absence of signs of hypocalcemia (Chvostek's sign or Trousseau sign; Chapter 245). Hypertriglyceridemia is usually mild, but even levels greater than 1000 mg/dL usually drop promptly when the patients do not eat. However, occasional patients with sustained severe hypertriglyceridemia may require plasmapheresis.

Acute peripancreatic fluid collections are common in acute pancreatitis, and most fluid collections will resolve spontaneously. Some, however, will mature into an encapsulated, fluid-filled pseudocyst outside of the confines of the pancreas. A pseudocyst also does not require therapy unless it causes abdominal pain or obstruction of a hollow viscus or it is associated with infection or bleeding; in these situations, endoscopic therapy is preferred.[■] Arterial bleeding from a pseudoaneurysm caused by a pseudocyst may be massive and require an emergent CT scan for diagnosis followed by embolization.

In addition, patients with necrotizing pancreatitis may develop infected pancreatic necrosis. Infection of preexisting necrosis typically occurs 2 to 3 weeks into the illness and is heralded by fever, leukocytosis, and worsening abdominal pain. The responsible organisms are usually gram-negative rods and other intestinal flora, but *Staphylococcus aureus* is an important agent as well. If infected necrosis is suspected, a contrast-enhanced CT scan should be obtained to identify the extent of necrosis and assess for indirect evidence of infected necrosis (i.e., gas in the necrotic collection). A CT-directed fine-needle aspiration of the necrotic area for culture and Gram stain can allow antibiotic therapy to be tailored; otherwise, broad-spectrum empiric antibiotics should counter possible infective agents (Table 108-2). Prophylactic antibiotics to prevent infection in patients with preexisting sterile pancreatic necrosis is not recommended, although many patients with severe or necrotizing pancreatitis may ultimately receive antibiotics for treatment of various hospital-acquired infections. Ideally, conservative therapy is continued for at least 4 weeks to allow the infected necrotic material to demarcate, begin to liquefy, and become encapsulated so it can be more easily drained. Percutaneous, endoscopic, or minimally invasive surgical draining procedures are as effective and safer than early open surgical debridement,[■] which is reserved for very rare patients with progressive clinical deterioration.

Any hospital-acquired infection (Chapter 282) dramatically worsens prognosis. Common infections include urinary tract infections (Chapter 284), pulmonary infections (Chapter 97), line infections, and *Clostridium difficile* (Chapter 296).

### Prevention

The use of a rectal nonsteroidal anti-inflammatory drug suppository (e.g., indomethacin 100 mg or diclofenac 100 mg) placed either just before or just after ERCP reduces the risk of post-ERCP pancreatitis by about 50%.[■] Placement of a temporary pancreatic duct stent provides equivalent protection. By comparison, preventing recurrent acute pancreatitis is more challenging. Abstinence from alcohol (Chapter 33) and tobacco (Chapter 32), which can be achieved in many patients, can reduce recurrent attacks[■] and should be strongly encouraged. Cholecystectomy (Chapter 155) prevents subsequent attacks of gallstone pancreatitis and should be undertaken within a few weeks of discharge, at the latest. In patients who are not surgical candidates, endoscopic sphincterotomy provides reasonable protection from subsequent attacks. Control of serum lipids (Chapter 206) prevents subsequent attacks of hyperlipidemic pancreatitis. Therapy of lesions that obstruct the pancreatic duct such as strictures, ampullary adenomas, and possibly sphincter of Oddi dysfunction and pancreas divisum may also prevent recurrences.

## PROGNOSIS

The case-fatality rate for acute pancreatitis has decreased over time and now averages approximately 1% to 2%. More than 80% of all patients with acute pancreatitis recover promptly and are discharged within a few days. In patients with severe acute pancreatitis, however, the mortality rate is between 10% and 20%. The mortality rate may even approach 30% in patients with more severe and numerous comorbid conditions and in patients who develop pancreatic necrosis, particularly infected necrosis, or organ system failure.

A number of scoring systems and other methods have been developed in an attempt to help guide clinicians predict prognosis, but none has been documented to be superior to experienced clinical judgment. The Ranson criteria, which are of historical interest only, have been replaced by APACHE (Acute Physiology and Chronic Health Evaluation) II and by more simplified systems using multiple-factor scoring. Practice guidelines suggest a cutoff of greater than 8 APACHE II points as the definition of severe disease, but this cutoff has a high false positive rate. An elevated BUN or hematocrit that does not return to normal with fluid therapy is associated with increased mortality rates. A C-reactive protein level greater than 150 mg/L at 48 hours is as accurate as many multifactorial scoring systems at predicting poor outcome. The BISAP score (BUN >25 mg/dL, impaired mental status, SIRS, age >60 years, and pleural effusion) has a possible score of 0 to 5, depending on the number of criteria present. Mortality ranges from less than 1% for a BISAP score of 0 or 1 up to 27% for a BISAP score of 5. For patients with alcoholic pancreatitis, the risk of progression to chronic pancreatitis is about 14% in patients who stop drinking and smoking after the first episode of acute pancreatitis but greater than 40% in those who do not change these behaviors.

# CHRONIC PANCREATITIS

## DEFINITION

Chronic pancreatitis, which is a syndrome with multiple predisposing risk factors, culminates in a final common pathway of irreversible and permanent pancreatic damage characterized by chronic inflammation, destruction of normal cellular (acinar) structures, and fibrosis. Chronic pancreatitis usually evolves after episodes of acute pancreatitis, some of which may have been subclinical, but the transition between acute and chronic pancreatitis may be difficult to identify.

## EPIDEMIOLOGY

The prevalence of symptomatic chronic pancreatitis in Western countries is about 50 per 100,000 population, with an estimated incidence of five to 12 cases per 100,000. In the United States, chronic pancreatitis accounts for about 125,000 outpatient visits and 25,000 hospitalizations yearly. Interestingly, the prevalence of histologic evidence of chronic pancreatitis in autopsy studies approaches 5%. Many people apparently develop chronic damage to the pancreas as a consequence of normal aging, other diseases, or exposure to toxins (e.g., social consumption of alcohol) but do not develop any symptoms or signs of chronic pancreatitis during life.

## PATHOBIOLOGY

Multiple episodes of acute inflammation, whether clinical or subclinical, eventually change the inflammatory milieu of the pancreas, with a shift to chronic inflammation, cellular loss, and the activation of pancreatic stellate cells with production of fibrosis. This process becomes self-sustaining and produces the characteristic histologic features in which a chronic fibrosis gradually replaces the acute inflammation.

The pathophysiology of pain, the most common symptom of chronic pancreatitis, is complex, involving both local pancreatic nociception as well as central nervous system responses. Chronic pancreatitis associated pain produces visceral, spinal cord, and central hyperalgesia, and the pain may become self-perpetuating even if therapy on the pancreas is successful.

### Alcohol and Tobacco

Alcohol causes about 40% of all cases of chronic pancreatitis in the United States and other developed countries.[13] As with acute pancreatitis, which clinically or occasionally subclinically will precede chronic pancreatitis, substantial and prolonged ingestion of alcohol is usually required, on the order of 5 to 8 drinks daily over more than 5 years. The risk of chronic pancreatitis is only 2% to 5% in patients who consume this much alcohol, pointing to important cofactors such as host genetics and cigarette smoking. There is also evidence that tobacco alone can cause chronic pancreatitis, and smoking alone may be responsible for up to 25% of cases. The combination of alcohol and tobacco is synergistic in causing chronic pancreatitis.

### Genetics

Hereditary pancreatitis is an autosomal dominant disease characterized by early onset of acute and chronic pancreatitis, the development of exocrine and endocrine pancreatic insufficiency, and a very high risk of pancreatic

ductal adenocarcinoma (Chapter 194). Mutations in the trypsinogen (*PRSS1*) gene appear to cause a gain in function in which the mutant trypsinogen, once activated to trypsin, is difficult to inactivate. This trypsin, if present in an amount that overwhelms normal protective mechanisms, can activate other pancreatic enzymes and lead to pancreatic damage and eventually to chronic pancreatitis. One of the protective mechanisms is a trypsin inhibitor called SPINK1. Loss of function mutations in *SPINK1* mutations may predispose to chronic pancreatitis, but unlike PRSS1 mutations, are not sufficient alone to cause chronic pancreatitis. Major mutations in the cystic fibrosis conductance regulator (CFTR) lead to cystic fibrosis (Chapter 89), which may be associated with chronic pancreatitis and pancreatic atrophy. Some mutations in CFTR predispose to chronic pancreatitis without causing the sinopulmonary features of cystic fibrosis. Combined mutations of SPINK1 and CFTR may place patients at particularly high risk for chronic pancreatitis. Other mutations and polymorphisms associated with chronic pancreatitis include chymotrypsin C and the calcium-sensing receptor gene. Polymorphisms of claudin 2, an X-linked gene, work synergistically with alcohol and may partially explain the increased risk of alcoholic chronic pancreatitis in men.

### Other Causes

*Autoimmune pancreatitis* most often presents as a mass-like lesion with obstructive jaundice, mimicking cancer. It may also present as chronic pancreatitis and rarely as acute pancreatitis. Type 1 autoimmune pancreatitis, which usually occurs in the fifth or sixth decade of life, is characterized by focal or diffuse swelling of the pancreas, elevations in serum IgG4, and involvement of other organs. Biliary strictures, salivary gland inflammation, retroperitoneal fibrosis, and renal lesions are commonly seen. Histology shows infiltration of these organs by chronic inflammatory cells and especially by plasma cells bearing IgG4 on their surfaces. The target of the autoimmune process is not known. Type 2 autoimmune pancreatitis is limited to the pancreas and occurs in a broader age group, including children.

*Tropical pancreatitis* is seen primarily in southern India. Characteristic features include childhood onset, exocrine insufficiency, diffuse pancreatic calcifications, and inevitable diabetes. There is a strong genetic component (SPINK1 and others), but cofactors such as malnutrition and dietary toxins have been suggested. In southern India, this disease is becoming rarer and is being replaced by alcohol and tobacco as the most common cause of chronic pancreatitis.

*Recurrent or severe acute pancreatitis*, particularly a severe acute attack that causes substantial pancreatic necrosis, can destroy enough of the gland to produce exocrine and endocrine insufficiency. In addition, diseases that cause repeated attacks of pancreatitis can lead to chronic pancreatitis. One example is *hypertriglyceridemia*, which causes acute pancreatitis but commonly leads to chronic pancreatitis.

## CLINICAL MANIFESTATIONS

The most common symptom of chronic pancreatitis is pain. The pain may be episodic or constant and is generally felt in the epigastrium with radiation to the back. If pain is episodic, the patient may be labeled as having acute pancreatitis or an acute flare of chronic pancreatitis. When pain is severe, nausea and vomiting may occur. Pain may worsen, improve, or remain stable over time. Pain is the symptom that is most responsible for medical care and the symptom that most detracts from quality of life. A small percentage of patients do not have pain and instead present with exocrine (steatorrhea, weight loss) or endocrine (diabetes) pancreatic insufficiency.

Most patients present initially with an episode of acute pancreatitis but then develop evidence of chronic pancreatitis; others have obvious chronic pancreatitis at their first presentation. The disease tends to be progressive over time even if the original cause (e.g., alcohol) is removed.

## DIAGNOSIS

The diagnosis may be suspected based on the clinical features but must be confirmed by tests that identify either structural damage to the pancreas or derangements in pancreatic function (Table 144-3). Chronic pancreatitis is a slowly progressive disease, and visible damage to the gland (e.g., on a CT scan) and functional failure (e.g., steatorrhea or diabetes) may not be apparent for years. All diagnostic tests are most accurate when the disease is far advanced, and all are far less accurate in the early stages of disease. Early diagnosis, when pain may be severe but imaging study results are normal or equivocal, is difficult.

No clear cause is found in a significant number of patients with chronic pancreatitis. In modern studies from referral centers, almost half of women and about 25% of men are labeled as having *idiopathic chronic pancreatitis.* Some have underlying genetic mutations that put them at particular risk, but gene testing may not be feasible or possible. Even if genetic testing is performed, many commercially available screens (e.g., for CFTR) only test a small percentage of all known mutations, and management will not necessarily be affected. Genetic testing for *PRSS1* is recommended if the family history is suggestive of an autosomal dominant disorder. Others may be surreptitiously using alcohol or may be smokers.

### Tests of Pancreatic Structure

Plain abdominal radiographs may demonstrate diffuse or focal pancreatic calcification in patients with advanced chronic pancreatitis. Although specific for chronic pancreatitis, these findings are quite insensitive.

Abdominal ultrasonography is of limited accuracy owing to its inability to visualize the entire pancreas. A dilated pancreatic duct, pancreatic calcifications, gland atrophy, or changes in echotexture are seen in about 60% of patients.

Computed tomography is the most widely used diagnostic test for chronic pancreatitis. High-quality images can be obtained of the pancreas and pancreatic duct. Characteristic findings include a dilated pancreatic duct, ductal or parenchymal calcifications, and atrophy (Fig. 144-2). These structural changes take years to develop, so CT is not as accurate in early or less advanced chronic pancreatitis. Similar to CT, MRI allows detailed images of the pancreas, and the addition of MRCP allows even better assessment of pancreatic duct morphology. At some centers, secretin is administered at the time of MRCP to allow better visualization of the pancreatic duct.

Endoscopic retrograde cholangiopancreatography provides the most detailed images of the pancreatic duct. Changes in the duct include dilation,

**TABLE 144-3 DIAGNOSTIC TESTS FOR CHRONIC PANCREATITIS**

| STRUCTURAL | FUNCTIONAL |
|---|---|
| Biopsy | Hormonal (secretin) test |
| Endoscopic ultrasonography | Using an oroduodenal tube |
| Endoscopic retrograde cholangiopancreatography | Using an endoscope |
| Magnetic resonance imaging with magnetic resonance cholangiopancreatography | Fecal elastase |
| Computed tomography | Serum trypsin |
| Ultrasonography | Fecal fat |
| Plain radiography | Blood glucose |

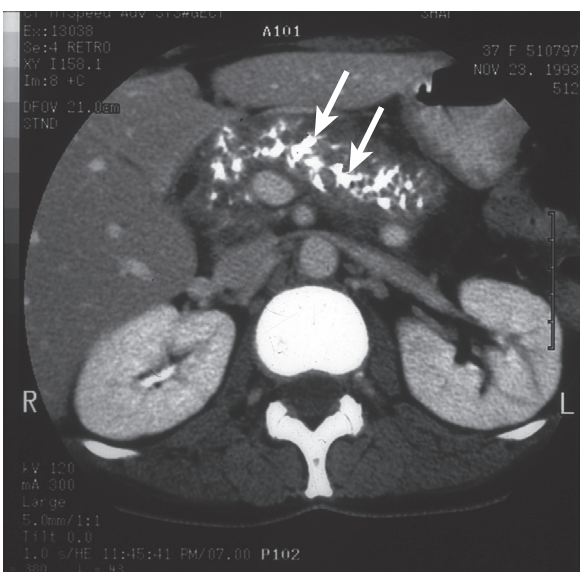


**FIGURE 144-2.** A computed tomography scan demonstrating diffuse pancreatic calcification in a patient with long-standing chronic pancreatitis *(arrows)*.

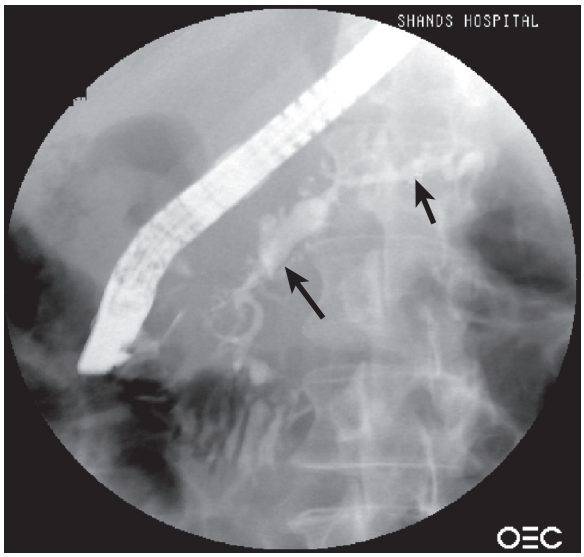


**FIGURE 144-3.** Endoscopic retrograde cholangiopancreatography demonstrating a very irregular pancreatic duct with areas of dilation and structuring in a patient with chronic pancreatitis *(arrows)*.

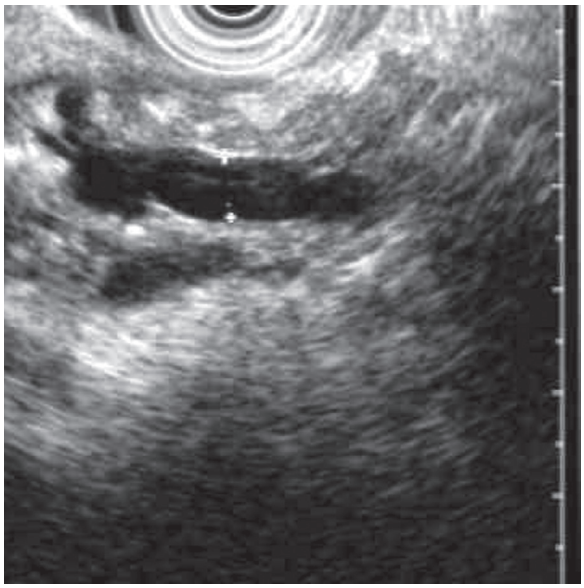

**FIGURE 144-4.** Endoscopic ultrasonography in a patient with chronic pancreatitis, demonstrating a dilated pancreatic duct (*marks* on margin of main duct).

irregularity, ductal stones, and strictures (Fig. 144-3). These findings are not completely specific for chronic pancreatitis and can be seen in other situations, including pancreatic cancer, after a pancreatic duct stent, and in very elderly individuals. Because of its risk, ERCP should be undertaken only when therapy involving the pancreatic duct is appropriate. Endoscopic ultrasonography allows very detailed images of pancreatic parenchyma and duct (Fig. 144-4) without the risk of ERCP. Normal endoscopic ultrasound results exclude chronic pancreatitis, but very abnormal endoscopic ultrasound results are highly consistent with chronic pancreatitis. However, many endoscopic ultrasound studies show intermediate findings, which are not specific for chronic pancreatitis.

### Tests of Pancreatic Function

Serum trypsinogen is abnormally low in patients with far advanced chronic pancreatitis. Levels below 20 ng/mL are seen in patients with chronic pancreatitis that is sufficient to cause functional failure (e.g., steatorrhea). Serum levels of amylase and lipase are of little diagnostic utility for chronic pancreatitis. Serum glucose is elevated in those with endocrine insufficiency.

Quantification of fat in stool during a 72-hour collection while on a high-fat diet can be used to document steatorrhea but is rarely performed. Qualitative analysis of fat with Sudan staining of a stool specimen has poor sensitivity and specificity. Fecal levels of pancreatic elastase are diminished in patients with advanced chronic pancreatitis and steatorrhea. Fecal elastase below 100 mcg/g stool is consistent with advanced chronic pancreatitis. The test can be performed while patients are taking pancreatic enzyme therapy.

One pancreatic function test involves passing an oroduodenal tube and administering a supraphysiologic dose of secretin. Pancreatic secretions are collected over the course of 1 hour and analyzed for their bicarbonate concentration. A normal study is defined by a peak bicarbonate concentration of greater than 80 mEq/L. This test result becomes abnormal earlier in the disease process than any other test but is not widely available. An alternative, using endoscopy instead of a tube, is slightly less sensitive.

### Diagnostic Approach

As the disease advances, typically over years, the structural and functional damage accumulate to the point that essentially all diagnostic test results are positive. In most patients, the diagnosis can be or will have been established by routine tests such as CT or MRI. Endoscopic ultrasonography and ERCP are rarely needed for diagnostic purposes in patients with long-standing chronic pancreatitis. The diagnostic challenge lies with patients who present with a severe pain syndrome suggestive of chronic pancreatitis but who have normal CT or MRI results. In these patients, endoscopic ultrasonography is the best choice unless the patient can have access to a secretin-based pancreatic function test. ERCP should not be used for purely diagnostic purposes because of the risk of complications, especially post-ERCP pancreatitis.

## TREATMENT Rx

### Abdominal Pain

Pseudocysts, obstruction of a surrounding hollow organ (e.g., duodenum or bile duct), and superimposed carcinoma cause chronic pain. A good-quality CT or MRI is usually sufficient to exclude these possibilities and to help choose appropriate therapy. Patients who have a dilated (generally >5 mm) pancreatic duct are candidates for endoscopic and surgical decompression therapy to relieve pain. Patients without ductal dilation are generally not appropriate for endoscopic and surgical therapy and must rely instead on medical therapy (Table 144-4).

Medical therapy starts with vigorous and structured attempts to assist patients in stopping alcohol and tobacco, if applicable. Most patients require analgesics. It is appropriate to start with the less potent agents first (e.g., tramadol, 50 mg four times daily), although many patients require more potent agents (Table 30-4) and may benefit from an adjunctive agent (e.g., gabapentin, pregabalin, selective serotonin-reuptake inhibitors, or tricyclic antidepressants; see Table 30-3 in Chapter 30) to potentiate the narcotic effect. Antioxidants (mixtures of selenium, vitamins E and C, β-carotene, and methionine) have been studied in two large randomized trials, with mixed results. Pancreatic enzyme therapy (see later) may have some beneficial effect on pain.[14]

Endoscopic retrograde cholangiopancreatography can be used to dilate ductal strictures and place stents. Ductal stones, if they are not too large and are not impacted, may also be removed. Lithotripsy of larger stones is usually required to reduce the stone to manageable fragments. This approach is technically successful in more than 80% of carefully selected patients, with pain relief in 70% to 80% of patients. Unfortunately, only a subset of patients with chronic pancreatitis has ductal anatomy that is amenable to this type of therapy.

Endoscopic ultrasound-guided celiac plexus block, which uses a local anesthetic and a steroid, or neurolysis, which uses absolute alcohol, can reduce the pain of chronic pancreatitis for weeks to months. However, the durability of those approaches has not been demonstrated, so they should be viewed as temporizing measures at best.

Surgery to decompress the pancreatic duct can provide more effective and durable long-term outcomes than endoscopic therapy for chronic pancreatitis. The most commonly performed procedure involves a longitudinal incision of the pancreatic duct from the body of the pancreas to as close to the duodenum as possible, and this "filleted" duct is overlaid with a defunctionalized Roux limb. At the time of surgery, ductal strictures can be incised and ductal stones can be removed. The procedure is relatively simple in those with a dilated pancreatic duct (>5 mm) and preserves maximal pancreatic parenchyma. Pain relief in the short term is good (>80%), with about 50% obtaining long-term relief of pain. Alternative surgical procedures for pain include partial pancreatic resection, typically the head of the gland. More ambitious procedures, including pancreaticoduodenectomy and total pancreatectomy, usually coupled with autotransplantation of harvested islet cells, are performed as a last resort at a small number of specialized centers.

**TABLE 144-4** TREATMENT FOR PAIN ASSOCIATED WITH CHRONIC PANCREATITIS

| TREATMENT | EXAMPLES |
|---|---|
| Medical therapy | Alcohol and tobacco cessation<br>Analgesics and adjunctive agents<br>Antioxidants<br>Non–enteric-coated enzymes |
| Neurolysis | Celiac plexus block or neurolysis<br>EUS guided<br>CT guided |
| Endoscopic therapy | Stent<br>Stone removal, lithotripsy |
| Surgical therapy | Pancreaticojejunostomy (modified Puestow operation)<br>Partial pancreatic resection (Whipple operation, duodenum preserving pancreatic head resection, others)<br>Total pancreatectomy with islet cell autotransplantation |

CT = computed tomography; EUS = endoscopic ultrasonography.

**TABLE 144-5** ENZYME THERAPY FOR EXOCRINE PANCREATIC INSUFFICIENCY*

| PRODUCT | AVAILABLE STRENGTHS | COMMENTS |
|---|---|---|
| | *USP lipase units/capsule or tablet* | |
| Zenpep | 3000; 5000; 10,000; 15,000; 20,000; 25,000 | Enteric-coated capsule |
| Creon | 3000; 6000; 12,000; 24,000; 36,000 | Enteric-coated capsule |
| Pancreaze | 4200; 10,500; 16,800; 21,000 | Enteric-coated capsule |
| Ultresa | 13,800; 20,700; 23,000 | Enteric-coated capsule |
| Pertzye | 8000; 16,000 | Enteric-coated capsule with bicarbonate |
| Viokace | 10,440; 20,880 | Non–enteric-coated tablet |

*For the treatment of pain, non–enteric-coated preparations are used. For exocrine insufficiency, cotreatment with acid-reducing medications is necessary when using non–enteric-coated preparations.

## Exocrine Insufficiency

Steatorrhea and maldigestion do not occur until approximately 90% of pancreatic enzyme secretion is lost usually after at least 5 to 10 years of chronic pancreatitis. Patients may note weight loss and oily stools but often do not complain of diarrhea. Patients with chronic pancreatitis and exocrine insufficiency maldigest fat, protein, and carbohydrates, but fat maldigestion is most severe. In addition to weight loss, malabsorption of fat-soluble vitamins, particularly vitamin D, is common. A formal 72-stool fat analysis, which is the most accurate method to document steatorrhea and to gauge effectiveness of therapy, is rarely done. Instead, the clinical features and a fecal elastase less than 100 mcg/g stool, coupled with an appropriate response to enzyme replacement therapy, is the best substitute for 72-hour fecal fat testing.

Pancreatic enzymes (Table 144-5) include both enteric-coated (capsules) and non-enteric-coated (tablets) preparations. Non–enteric-coated preparations are the agents of choice if the goal is to treat pain. They can also be used to treat exocrine insufficiency, although the enteric-coated preparations are used more frequently for this indication. No generic products are currently available. The goal of enzyme therapy, which is to administer at least 10% of normal pancreatic output with each meal, translates to approximately 90,000 USP units of lipase with each meal. Because most patients are still producing some digestive enzymes and have a compensatory increase in gastric lipase, it may not be necessary to prescribe the full dosage of 90,000 USP units with each meal. An initial starting dosage of 50,000 to 70,000 units of lipase per meal, with subsequent assessment of the clinical response, is reasonable.

If non–enteric-coated preparations are used, then cotreatment with an H2-blocker or proton pump inhibitor (Table 138-1) is required to prevent acid denaturation of enzymes, a critical point of emphasis. Enzymes should be administered during and immediately after the meal. Supplementation with vitamin D and calcium is appropriate because osteoporosis and osteopenia are very common. Supplementation with other fat- and water-soluble vitamins may also be needed.

Successful enzyme replacement therapy is generally defined as weight gain, absence of visible oil in the stool, and normalization of fat-soluble vitamin levels. Failure of enzyme therapy is most often caused by an inadequate dose. Increasing the dose up to the full 90,000 USP units with meals and encouraging compliance is appropriate as a first step. In patients using a non–enteric-coated preparation, the dose of the H2-blocker or proton pump inhibitor can be increased to reduce the acid destruction of enzymes. Some patients may not respond because a second disease, such as small intestinal bacterial overgrowth (Chapter 140), is contributing to the malabsorption.

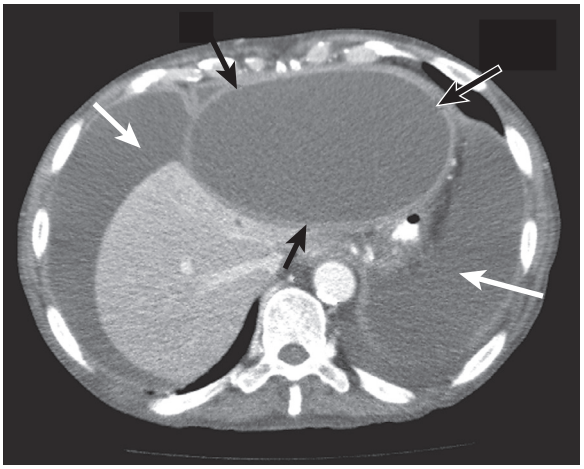

**FIGURE 144-5.** On computed tomography, a large pseudocyst is seen *(black arrows)*. In addition, ascites surrounding the liver *(white arrow)* is caused by a leak from the pseudocyst (pancreatic ascites).

## Endocrine Insufficiency

Diabetes mellitus (Chapter 229) is a very late complication of chronic pancreatitis. Some patients will develop type 2 diabetes, some develop type 3C diabetes in which there is a loss of both insulin and glucagon secretion.[15] In such patients, overly aggressive therapy may lead to hypoglycemia, which cannot be reversed by the usual natural glucagon surge. Treatment-induced hypoglycemia can be fatal in these patients, especially if they are also malnourished. As a result, treatment should avoid exceedingly tight glucose control.

## Complications

Pseudocysts, when they are discovered in patients with chronic pancreatitis, are generally mature and have a visible capsule surrounding them. As in acute pancreatitis, pseudocysts in chronic pancreatitis do not require therapy if they are not producing symptoms and are not rapidly enlarging. By comparison, symptomatic pseudocysts require drainage by endoscopic, percutaneous, or surgical procedure.

Pseudocysts may leak into the peritoneal compartment (pancreatic ascites) or track into the chest (pancreatic pleural effusion). Patients usually present with abdominal distention or dyspnea, respectively, rather than abdominal pain. Amylase level in the fluid is usually greater than 4000 U/L. Endoscopic therapy with stent placement across the connection between pseudocyst and pancreatic duct is highly effective in this situation (Fig. 144-5).

Cystic neoplasms require resection. Features that suggest a cystic neoplasm include a cyst with a thick wall or nodules in the wall, a cyst with multiple internal septations, or a cyst occurring in a patient who does not have a history of pancreatitis.

Chronic pancreatitis is also a strong risk factor for pancreatic ductal adenocarcinoma (Chapter 194), with a lifetime risk of about 4% to 5%. The risk is much higher in patients with hereditary pancreatitis and in patients who smoke. Equally important, it may be very difficult to distinguish cancer from benign disease, particularly in those with autoimmune pancreatitis.

## PREVENTION

There is not currently any reliable method to prevent chronic pancreatitis, although patients who have fewer episodes of acute pancreatitis are less likely to develop chronic pancreatitis. Patients at risk for chronic pancreatitis and patients with recurrent episodes of acute pancreatitis should avoid alcohol and tobacco. Patients with autoimmune pancreatitis should be treated with steroids (see earlier) to reduce the risk of progression.

## PROGNOSIS

The prognosis of chronic pancreatitis is heavily influenced by its cause, as well as by concurrent smoking and ongoing alcohol use. With prolonged follow-up of 10 to 20 years, the majority of patients will develop exocrine or endocrine

insufficiency. The survival rate of patients with chronic pancreatitis is lower than in age-matched control participants. Death is usually not attributable to pancreatitis itself but rather to malignancy, postoperative complications, and complications of tobacco and alcohol.[16] Overall, the 10-year survival rate approximates 70% and the 20-year survival rate is 45%. Patients who are older, smoke, or have alcohol as the cause are at highest risk of mortality.

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## REVIEW QUESTIONS

**1.** A 52-year-old man is admitted with presumed acute alcoholic pancreatitis. On admission, his blood pressure is 111/60 mm Hg, pulse is 110 beats/min, respiration rate is 18 breaths/min, and temperature is 37.8° C. His initial physical examination is notable for a tender abdomen without rebound but is otherwise normal. Initial laboratory results include a WBC of 14,000/μL, Hgb 14.1, normal electrolytes, BUN of 26, creatinine of 1.2, and lipase of 720. Liver tests, calcium, and the triglyceride level are normal. Ultrasonography in the emergency department notes a normal gallbladder and bile duct. A computed tomography scan obtained in the emergency department notes some peripancreatic fluid and haziness of the peripancreatic fat. He is admitted to an intermediate care unit and treated with vigorous fluid resuscitation, antiemetics, and analgesics. On day 2, his blood pressure and pulse have normalized, but he has developed a low-grade fever of 38.1° C. He continues to have significant pain and some nausea. A CT scan obtained on day 3 now reveals that 40% of the pancreas is necrotic; there is no gas in the necrotic area. Fever continues with a maximum temperature of 38.2° C, the WBC is still 14,000/μL with a left shift. What would you recommend now?

A. Initiate imipenem.
B. Perform a fine-needle aspiration (FNA) and culture of the necrotic collection.
C. Place a percutaneous drain in necrotic collection.
D. Obtain a surgical consultation.
E. Continue the current conservative therapy.

**Answer: E** The patient has moderately severe acute pancreatitis with necrosis. Prophylactic antibiotics are not recommended. Infection of the necrosis usually occurs after 1 to 2 weeks of disease, and the clinical features and imaging are not suggestive of infection; as a result, FNA is not needed. The necrosis is not yet walled off or liquefied, so placement of a drain in the collection would be harmful. There is no indication for surgery in this patient. Conservative therapy, which could include placement of a nasoduodenal tube to initiate nutrition, should be continued.

**2.** A 42-year-old woman is seen in the emergency department with abdominal pain, nausea, and vomiting over the past 12 hours. On physical examination, she is in obvious pain. She is tachycardic, but her vital signs are otherwise normal. Her general physical examination results are normal; her abdomen is mildly distended and tender to palpation without rebound. Laboratory results include amylase of 4500, AST of 220, ALT of 170, alkaline phosphatase of 200, total bilirubin of 1.8, WBC of 12,000/μL, and Hgb of 12; the remaining blood test results are normal. Abdominal ultrasonography reveals several small stones in the gallbladder; the common bile duct is 7 mm. A CT scan reveals interstitial pancreatitis. She is admitted and treated with intravenous fluid, antiemetics, and analgesics. On the following day, her AST is 140, ALT is 160, total bilirubin is 1.6, and WBC is 11,000/μL. She remains afebrile. What would you recommend now?

A. Initiate antibiotics
B. Urgent endoscopic retrograde cholangiopancreatography
C. Repeat ultrasonography now
D. Endoscopic ultrasonography now
E. Continue current conservative therapy

**Answer: E** This patient has gallstone pancreatitis, which is resolving. There are no features to suggest concomitant cholangitis, and liver chemistries are improving. Urgent ERCP is not required. Prophylactic antibiotics are likewise not indicated. There is no reason to repeat the ultrasonography, and the liver chemistries are improving. An EUS is not needed because there is no clinical concern for microlithiasis. Continued conservative management is appropriate.

**3.** You see a 58-year-old man who was recently discharged after a 2-week admission for acute pancreatitis. The cause of the pancreatitis is not known, his liver chemistries and triglycerides were normal, and his abdominal ultrasonography revealed no gallstones. He does not drink but does smoke; he was on no medications known to cause pancreatitis. He is now feeling well. A CT scan during the hospitalization revealed enlargement of the head of the pancreas with peripancreatic fluid and stranding but no necrosis. What would you recommend now?

A. Serum IgG4 level
B. Endoscopic ultrasonography
C. Genetic testing
D. ERCP
E. No further testing unless a second attack occurs

**Answer: B** This patient with an unexplained episode of pancreatitis and at an age older than 40 years must be evaluated for the possibility of malignancy underlying his unexplained pancreatitis. Endoscopic ultrasonography (EUS) provides the most effective method to search for underlying malignancy and to exclude microlithiasis. Genetic testing might be considered if his EUS results are negative. The patient might have autoimmune pancreatitis, but this is a diagnosis of exclusion.

**4.** A 28-year-old woman is evaluated as an outpatient for chronic abdominal pain. This is her first visit with you, and she reports that she has chronic pancreatitis. The pain is continuous, epigastric, without radiation, and has been present for 2 years. She has not lost weight, does not smoke or drink, and has no family history of pancreatic disease. She is currently treated with oxycodone four times daily, with little relief of pain. You obtain previous medical records, which include several emergency department visits; on one of these visits, her amylase was elevated to 156 (normal <140). Results of several CT scans obtained during these visits were normal. Her physical examination result is normal. Results of laboratory tests, including amylase, lipase, liver chemistries, and triglycerides, are normal. What would you recommend now?

A. ERCP
B. EUS
C. Celiac plexus block
D. Initiate gabapentin
E. Fecal elastase

**Answer: B** This patient has a chronic pain syndrome but does not have sufficient evidence of chronic pancreatitis. ERCP is not indicated as a diagnostic procedure. Celiac plexus block would only be considered if a diagnosis of chronic pancreatitis was confirmed and even then only in rare circumstances. Gabapentin as an adjunctive agent is reasonable but again only after an accurate diagnosis is made. Fecal elastase would be normal in this patient; even if she has chronic pancreatitis, it is not far enough advanced for fecal elastase to be abnormal. EUS provides the best method to assess this patient for chronic pancreatitis.

**5.** A 52-year-old man with an 8-year history of chronic pancreatitis attributable to alcohol and tobacco is evaluated for weight loss. He has chronic pain that is managed with tramadol. He has also been treated with pancreatic enzymes and is currently taking 20,000 units of an enteric-coated lipase preparation with each meal. He notes a 20-lb weight loss over the past 6 months. He reports a normal appetite but does have some loose stools. His physical examination is notable for evidence of weight loss. Laboratory testing includes a normal CBC, amylase, and lipase. A CT scan reveals a dilated pancreatic duct with diffuse pancreatic calcifications. Fecal elastase is 85 mcg/g of stool. What would you recommend now?

A. Empiric treatment for small intestinal bacterial overgrowth
B. Add a proton pump inhibitor
C. Increase pancreatic enzyme dosage
D. Pancreatic duct stent
E. Refer for pancreatic surgery

**Answer: C** This patient has exocrine insufficiency and is on an inadequate dose of enzymes (which should be at least 50,000 units of lipase with each meal and up to 90,000 units). Small intestinal bacteria overgrowth might be considered if he fails to respond to an appropriate dose of enzymes. Acid suppression is not needed with enteric-coated preparations. Placement of a pancreatic duct stent or surgery might be considered for intractable pain, but this patient has pain manageable with simple medical measures.