The pancreas is a retroperitoneal organ extending across the posterior abdomen in the epigastrium that provides essential endocrine and exocrine functions (Fig. 91-1). In the general population, diabetes is the most common disorder of the pancreas, followed by pancreatitis. Acute pancreatitis is an inflammatory process of the pancreas usually associated with abdominal pain, elevated pancreatic enzymes, and variable involvement of other regional tissues or remote organ systems. Both local and systemic complications may occur. Repeated bouts of pancreatitis from any cause may eventuate in chronic pancreatitis as a result of permanent alterations in function and morphology. Chronic pancreatitis is an ongoing inflammation of the pancreas, which may be interrupted by spells of acute pancreatitis. Pancreatic tumors may develop from the endocrine or nonendocrine structures. These tumors may cause acute pancreatitis, which usually manifest in an indolent fashion. The most common is adenocarcinoma originating from the pancreatic ducts.

The head of the pancreas sits in the loop of the first part of the duodenum, and the tail lies against the hilum of the spleen. The main pancreatic duct (the duct of Wirsung) traverses from the tail through the body to the head of the pancreas where the common bile duct enters the second part of the duodenum through the sphincter of Oddi. Accessory ducts and anomalies are common. Anterior to the pancreas (from right to left) are the transverse colon, the lesser sac of the omentum, and the stomach. Posteriorly lie the bile duct, portal vein, splenic vein, vena cava, aorta, and superior mesenteric artery. To the left are the psoas muscle, kidney, and adrenal gland. Because of their close proximity, inflammation of the pancreas not only may injure these structures but also can mimic a variety of diseases.

The pancreas has both essential exocrine and endocrine functions. Exocrine products include amylase, lipase, trypsin, chymotrypsin, elastase, carboxypeptidase, phospholipase, and other enzymes. In addition, bicarbonate is produced in greatest quantity from this organ. The bicarbonate serves to neutralize gastric acids as well as the enzymes that break down proteins, carbohydrates, and fats. Cholecystokinin, pancreozymin, and secretin, as well as other factors, control secretion of these enzymes. The endocrine functions of the pancreas are managed by insulin, glucagon, pancreatic polypeptide, and somatostatin.

**Principles of Disease**

**Pathophysiology**

Many of the pathobiologic responses that occur in acute pancreatitis, such as edema, inflammation, and parenchymal cell death, are easy to conceptualize. However, knowledge about the exact molecular mechanisms that ultimately lead to these events is still evolving. Intense research to further the understanding of
Acute pancreatitis may be divided into three pathologic phases. The first phase is the local inflammation from obstruction of the pancreatic or bile ducts, direct toxicity of the pancreatic cells, toxins, infections, trauma, or idiopathic causes. Local inflammation subsequently causes premature activation of pancreatic enzymes, such as trypsinogen and zymogen, either in the ducts or in the acinar cells. This activation causes the release of enzymes that are intended to digest dietary proteins and fats; instead they produce cellular breakdown and pancreatic tissue autodigestion.

Initially the inflammatory process is localized, creating focal pancreatic injury and edema. With increasing severity, the inflammation becomes generalized and causes necrosis of the pancreas and spreads to the surrounding fat and tissues. During this second phase of generalized injury, there may be necrosis of the pancreatic ducts as well as the vascular structures, leading to hemorrhage. Necrosis involving more than 30% of the pancreas increases both morbidity and mortality.

Enzyme activation, inflammation, and necrosis cause a variety of complications. For example, fluid collections develop in 30 to 50% of patients with severe pancreatitis. Over time, a fibrinous or granulation wall may form around this fluid collection, creating a pseudocyst. Thus, pseudocysts are not present in the initial phases of pancreatitis but instead develop over 4 to 6 weeks. Fluid collections, necrotic areas, or pseudocysts may become infected in a small number of cases, usually after several weeks. In addition, irritation of the surrounding bowel is common, creating bowel wall edema, ileus, and third-spacing of fluid. Formation of ascites is common and, together with bowel edema, can lead to significant intravascular fluid loss and hypotension.

The final stage of injury occurs with the development of multiorgan damage. Because of the release of inflammatory mediators, the initial localized inflammatory response may cause a systemic immune response syndrome (SIRS), resulting in multiple organ failure. This is a sepsis-like response, and any organ system can be involved, potentially resulting in myocardial depression, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), or renal failure.

Etiology

Pancreatitis has several causes, but the vast majority of cases (80%) will be a result of either gallstones or alcohol, with gallstones the most common cause in most series (approximately 45% vs. 35%) (Box 91-1). The exact pathomechanism of biliary pancreatitis is not clear. Either a stone within the bile duct applies transmural pressure on the pancreatic duct, or a stone in the common channel of the pancreatic duct or common bile duct causes obstruction. Obstruction or pressure on the pancreatic duct causes bile reflux or increased pressure of pancreatic secretions. Either mechanism leads to the activation of pancreatic enzymes, setting off the cascade of pancreatitis. Many cases presumed to be idiopathic probably are caused by small stones, sludge, or crystals that are too small to be detected on ultrasound examination but may be seen on endoscopic retrograde cholangiopancreatography (ERCP). This cause of pancreatitis is potentially correctable; if it is missed, recurrences are likely.

Alcohol is the cause of approximately 35% of pancreatitis cases. As with the other causes of pancreatitis, the mechanism by which alcohol is toxic to the pancreas is not well understood. Possible mechanisms include toxic effects of the ethanol metabolite acetaldehyde, ethanol-related lipid metabolism, or spasm of the sphincter of Oddi. Patients with alcoholic pancreatitis usually have 5 to 10 years of chronic alcohol use before the onset of pancreatitis.

In addition to alcohol, many medications and toxins may cause pancreatitis, including didanosine, pentamidine, oral contraceptives, and selected scorpion venoms (Box 91-2). Pancreatitis can be caused by hypertriglyceridemia, with levels more than 500 mg/dL being implicated. In pregnancy, both gallstones and increased triglyceride levels can cause pancreatitis. When this occurs, both maternal and fetal mortality rates are high.
Blunt and penetrating abdominal trauma can disrupt the ductal system and the pancreatic cells, setting off the enzyme cascade that will result in acute pancreatitis. Pancreatitis also may result from iatrogenic ductal injury in 1 to 10% of ERCP procedures. Likewise, postoperative pancreatitis is well recognized and carries a higher mortality than that associated with other causative disorders. Although both viral and bacterial disorders may precipitate pancreatitis, the two most common viral causes of pancreatitis are mumps and Coxsackievirus B infection. Pancreatitis is more common in patients with human immunodeficiency virus (HIV) infection than in the general population. In addition to the common etiologic risk factors for pancreatitis, this population is at additional risk because of the risk of opportunistic infections, toxicity from HIV-specific medications, and acquired immunodeficiency syndrome (AIDS)–related cancers. Acute pancreatitis is ultimately classified as idiopathic in approximately 10% of cases. Suspected but uncertain causes may include sphincter of Oddi dysfunction and pancreas divisum, which arises from a failure of the dorsal and ventral ducts to fuse. With this entity, most of the pancreatic juice flows through the minor pancreatic duct and papilla. The etiologies of pancreatitis in adults and children are similar, although incidence rates for specific causative disorders are different. Trauma (including child abuse), infection, and idiopathic causes account for 70% of the cases in children. Hereditary pancreatitis is an autosomal dominant trait, with onset frequently

### Box 91-2 Drug-Induced Pancreatitis

<table>
<thead>
<tr>
<th>Possible</th>
<th>Definite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burnetanide</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Azathioprine</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>Cimetidine</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Cyclopentolate</td>
<td>Didanosine</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Estrogens</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Ethyl alcohol</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>Furosemide</td>
</tr>
<tr>
<td>Ethacrynic acid</td>
<td>L-Asparaginase</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Mercaptopurine</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Methyldopa</td>
</tr>
<tr>
<td>Isoretinoin</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Mefenamic acid</td>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Octreotide</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Organophosphates</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Pentamidine</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Ranitidine</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Salicylates</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>Sulfonamides, trimethoprim-sulfamethoxazole, sulfasalazine, sulindac</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Sulindac</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Sulindac</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Sulindac</td>
</tr>
</tbody>
</table>

CMV, cytomegalovirus; DKA, diabetic ketoacidosis; EBV, Epstein-Barr virus; ERCP, endoscopic retrograde cholangiopancreatography; HIV, human immunodeficiency virus; MAI, Mycobacterium avium-intracellulare; TB, tuberculosis.
noted during childhood. Other causes include infections and congenital anomalies.

Clinical Features

Pancreatitis should be suspected in all patients with epigastric abdominal pain, regardless of age. Once the diagnosis has been made, the underlying cause and presence of complications related to the disease should be sought.

Almost all patients with pancreatitis give a history of abdominal pain, most commonly in the midepigastric area; however, the pain also can be in the right or left upper quadrant. If significant inflammation is present, the pain may be diffuse and the patient may have difficulty localizing the discomfort. Typically, onset of symptoms is relatively rapid, increasing in severity over a few hours. The pain generally is described as constant and severe and may radiate to the midback. The degree of pain does not correlate with the severity of disease. Even though gallstones are frequently the cause of pancreatitis, the onset of pain is not usually related to eating. Nausea and vomiting often will accompany the pain. Although the discomfort may be lessened by lying on the side or sitting up, more typically little relief is obtained with position change, moving, eating, vomiting, or bowel movement. Colicky pain or pain that waxes and wanes suggests another diagnosis. Approximately 50% of patients will have a history of similar abdominal pain that may represent a previous episode of biliary colic or mild pancreatitis.

On physical examination, vital signs may be stable but frequently are abnormal. Hypotension, tachycardia, and shock indicate severe disease with complications or an alternate diagnosis. Vital signs also may be influenced by pain (tachycardia, tachypnea, hypertension) or alcohol withdrawal (tachycardia, hypertension, fever). A low-grade fever is present in approximately half of patients with pancreatitis, both at presentation and for the first several days thereafter, even in the absence of infection. A high fever is uncommon during the acute phase of pancreatitis; infection is usually a late complication. Ongoing evaluation should include pulse oximetry because acute hypoxia is an indicator of systemic complications and severe disease.

Patients with pancreatitis generally appear restless and in moderate distress as they search to find a position to relieve their discomfort. They may be jaundiced if an obstructing stone is present. The cardiopulmonary examination may be significant for tachypnea or diminished breath sounds if the patient is hypoventilating from pain or if a pleural effusion (developing more commonly on the left) is present. On inspection, the abdomen may appear normal or may be notably distended. Only rarely will there be evidence of blood within the peritoneum or retroperitoneum resulting from severe hemorrhagic pancreatitis. Presence of blood within these areas is classically manifested as Cullen’s sign (discoloration around the umbilicus) or Grey Turner’s sign (discoloration of the flank). Auscultation of the abdomen may reveal normal, decreased, or absent bowel sounds, depending on whether the patient has a concomitant ileus. Because the pancreas is a retroperitoneal organ, palpation of the abdomen generally reveals epigastric guarding, with rebound tenderness being a less common finding. Murphy’s sign may be present if the pancreatitis is secondary to a biliary source. Very rarely the physician may see evidence of subcutaneous fat necrosis: red nodules most prominent on the extremities. Other physical findings, such as the stigmata of alcoholicism or xanthomas of hyperlipidemia, may help point to the cause of the pancreatitis.

Complications

The patient with acute pancreatitis will often have low grade fever, tachycardia, and leukocytosis; these findings represent three of the four criteria for SIRS. These patients may progress to fulminant sepsis or other severe illness related to the intense localized inflammation of pancreatitis.

Shock may result from volume loss. Fluid sequestration occurs in the pancreas and the bowel lumen and wall. Hemorrhage into necrotic pancreatic tissue also may occur. In addition, release of vasodilator and cardiodepressive substances may occur and worsen hypoperfusion.

Approximately 18 to 30% of patients may have pulmonary complications, including degradation of surfactant by pancreatic phospholipases; pleural effusions (more commonly noted on the left and frequently with elevated amylase levels); hypoxia from atelectasis, hypoventilation, and intrapulmonary shunting; and ARDS. ARDS, caused by the loss of surfactant as well as capillary leak caused by the inflammatory mediators, is rare but carries a 60% mortality rate.

Metabolic complications of pancreatitis include hyperglycemia and hypocalcemia. Hyperglycemia is caused by decreased insulin and increased glucagon. The mechanisms for hypocalcemia are sequestration or saponification of calcium in areas of fat necrosis; hypoalbuminemia, hypomagnesemia, or hyperglucagonemia; and inactivation of parathyroid hormone.

Coagulopathy develops from circulating proteases that affect the coagulation cascade. Acute tubular necrosis can cause acute renal failure and results from the effects of circulating inflammatory mediators or from hypotension and hypoperfusion. Ultimately, multisystem organ failure will occur if the balance of proinflammatory cytokine production overwhelms the anti-inflammatory response, which seeks to restrict the inappropriate movement of proinflammatory agents into the circulation.

Late complications occur after the second week of illness and include involvement of local structures, abscess formation (1–4%), gastrointestinal bleeding from stress ulcers, splenic vein thrombosis, rupture of pancreatic pseudoaneurysms, fistula formation, splenic rupture, venous thrombosis, and right hydronephrosis. Pancreatic pseudocysts develop in 1 to 8% of patients after 4 to 6 weeks and are more common with alcoholic pancreatitis (Fig. 91-2). Long-term complications of acute pancreatitis include recurrent or chronic pancreatitis, diabetes mellitus, and digestive and malabsorption problems.

Figure 91-2. Computed tomography scan showing pancreatic pseudocyst (PP). In this patient the pseudocyst was so large that it compressed the common bile duct, causing obstructive jaundice. GB, gallbladder.
Diagnostic Strategies

Laboratory Tests

The diagnosis of acute pancreatitis and the differentiation from other abdominal disorders depend on careful clinical assessment in conjunction with abnormalities on certain laboratory tests and supportive radiographic findings. Three enzymes are derived from pancreatic acinar cells: amylase, lipase, and the proenzyme trypsinogen. Each has been tested as a biochemical marker of acute pancreatitis.

Amylase Assay. Amylase is an enzyme that cleaves carbohydrates. It is produced primarily in the salivary glands and pancreas, although it also can be found in small amounts in the fallopian tubes, ovary, testis, muscle, intestines, and other organs. Elevations of amylase may be seen in healthy persons, patients with ectopic pregnancy, macroamylasemia, parotitis, renal failure (decreased clearance), mesenteric ischemia, bowel obstruction or infarction, perforated duodenal ulcer, acute peritonitis from other causes, and many other diseases. Pancreatic amylase can be differentiated from other sources of amylase by electrophoresis, a test that is not readily available in the emergency department (ED). Because of the other nonspecific sources of amylase, elevations of amylase lack specificity for the diagnosis of pancreatitis.16 In acute pancreatitis, amylase rises within 6 to 24 hours, peaks in 48 hours, and normalizes in 3 to 7 days. Thus the sensitivity of amylase decreases after the first 24 to 48 hours.16

In addition to the uncertain source of an elevated amylase, several other limitations are recognized for its use in the diagnosis of acute pancreatitis. The application of different assays and the lack of an international standard have led to designation of various measured levels as “normal” or “elevated” across institutions. As expected, the sensitivity and specificity of amylase vary in accordance with the cutoff value selected to make the diagnosis of pancreatitis. Complicating matters is the lack of a universal modality for the diagnosis of pancreatitis; amylase assay, autopsy, computed tomography (CT), and laparoscopy all have been used. The sensitivity of amylase for the diagnosis of pancreatitis ranges widely, depending on the comparative choice of the standard test. In up to 25% of patients with pancreatitis, especially in alcoholics and patients with hypertriglyceridemia (which interferes with the assay) or chronic pancreatitis, the amylase level can be normal. Mild amylase elevations in patients with severe acute abdominal pain of unclear cause, particularly in elders, should raise suspicion for another serious abdominal pathology. Thus the amylase assay, although recognized as an imperfect standard with which to make the diagnosis of pancreatitis, is used by default in some circumstances because of its low cost and rapid availability. However, its precise value is unclear in the initial diagnosis of pancreatitis, particularly in cases with an atypical clinical presentation. Amylase levels alone, whether normal, mildly elevated, or extremely elevated, are not diagnostic for pancreatitis unless accompanied by the appropriate clinical picture.

Lipase Assay. Lipase is a pancreatic enzyme that hydrolyzes triglycerides and has been used both as an adjunctive test and an alternative test for the diagnosis of pancreatitis. Unfortunately, lipase assays are associated with many of the same pitfalls as amylase assays. In the presence of pancreatic inflammation, lipase levels increase within 4 to 8 hours and peak at 24 hours. The levels stay elevated longer than amylase levels, falling over 8 to 14 days,8,16 thus providing greater sensitivity in patients with delayed presentations. Lipase, like amylase, is present in other tissues and tends to be elevated in similar clinical situations. Improved assays have rendered lipase more specific than amylase. Yet, there are still nonpancreatic causes of elevations of lipase, such as duodenal ulcers, bowel obstruction, and idiopathic causes.8,16 Comparisons between amylase and lipase are limited by the lack of a true “gold standard” for the diagnosis of pancreatitis, as well as the choice of cutoff values used for the diagnosis. Despite these limitations, lipase is at least as sensitive as and probably more specific than amylase (specificity of 80 to 99%). At values five times the upper limits of normal, lipase is 60% sensitive and 100% specific. The use of twice the upper limit of normal has been recommended to decrease the possibility of missing the diagnosis of pancreatitis.16 Expert guidelines recommend the use of lipase over amylase in the diagnosis of pancreatitis.17,18

The degree of elevation of amylase or lipase is not a marker of disease severity.5 For example, compared with nonalcoholic patients, alcoholics will frequently have lower amylase levels but may have more severe disease. In a patient with prolonged abdominal pain or a history of pancreatitis, elevated biomarkers for longer than a week may suggest pseudocyst or pancreatic abscess.19 Use of the amylase-to-lipase ratio has not proved helpful in the determination of a specific cause of pancreatitis.14

Other Tests. Several new tests aimed at improving the diagnostic accuracy for acute pancreatitis are under development. Trypsinogen exists in two major forms, with trypsinogen-2 present in high serum concentrations in patients with acute pancreatitis. In a recent study, the sensitivity and specificity for urinary trypsinogen-2 dipstick testing were 93% and 92%, respectively. At present, however, neither this test nor any others have proved useful in standard clinical practice.20

Additional Laboratory Evaluation

In evaluating a patient with abdominal pain, amylase or lipase assays, along with other blood tests, are necessary to narrow the differential diagnosis, detect complications, and determine prognosis. Ranson developed a two-step list of primarily laboratory parameters, performed at hospital admission and after 48 hours, to determine the risk of death from pancreatitis.21,22

With this in mind, additional testing should consist of a complete blood count (CBC), lactate dehydrogenase (LDH) determination, and a comprehensive metabolic panel (including measurement of liver enzymes, calcium, renal function, and glucose). In patients with liver disease, coagulation studies should be performed to determine the degree of liver dysfunction. Arterial blood gas analysis should be done selectively in patients who are acidic or

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### Box 91-3

**Ranson’s Criteria for Pancreatitis-Associated Mortality**

**At Admission**

- Age >55 years
- WBCs >16,000/mm³
- Glucose >200 mg/dL
- LDH >350 IU/L
- AST >250 SF units

**Substitute if Gallstone Induced Admission:**

- Age >70 years
- WBCs >18,000/mm³
- Glucose >220 mg/dL
- LDH >400 IU/L
- AST >250 SF units

Add the total number of signs at 48 hours:

<table>
<thead>
<tr>
<th>Number</th>
<th>Associated Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>1%</td>
</tr>
<tr>
<td>3-4</td>
<td>15%</td>
</tr>
<tr>
<td>5-6</td>
<td>40%</td>
</tr>
<tr>
<td>&gt;7</td>
<td>100%</td>
</tr>
</tbody>
</table>

AST, aspartate transaminase; BUN, blood urea nitrogen; LDH, lactate dehydrogenase; SF, Sigma-Frankel; WBCs, white blood cells.
hypoxic. This information can be used for treatment decisions and to determine prognosis based on Ranson’s criteria. Magnesium should be checked in alcoholic patients and in those patients with electrolyte abnormalities. Both hypocalcemia and hyperglycemia are common in pancreatitis, with the hyperglycemia resulting from glucagon and insulin abnormalities. Calcium is best determined with use of the ionized calcium level. Serum calcium is falsely low in the presence of low albumin levels, as may be seen in patients with pancreatitis. Elevations of creatinine and blood urea nitrogen (BUN) may indicate the presence of hypovolemia or renal involvement, or both. 

Elevation in liver enzymes may result from biliary-induced pancreatitis or from other diseases of the liver or biliary tract. In addition, liver enzyme levels may increase from the pressure on the common bile duct that results from the surrounding pancreatic inflammation. Mild elevations of bilirubin are common in all types of pancreatitis, as well as in many other liver disorders. For the patient diagnosed with pancreatitis, higher elevations of aspartate transaminase (AST) and LDH are related to worse prognosis according to Ranson’s criteria.

When liver enzymes are elevated, the pattern of elevation may help determine the underlying cause of the pancreatitis (Table 91-1). Alanine aminotransferase (ALT) is the best single marker for a biliary cause; levels greater than three times baseline support the diagnosis of biliary pancreatitis.16,22 The higher the elevation of ALT, the greater the specificity and predictive value for gallstones. ALT levels higher than 150 IU/L have 96% specificity, positive predictive value (PPV) of 95%, and 48% sensitivity for gallstone pancreatitis. Significant rises in AST, alkaline phosphatase, and bilirubin also are more likely to be related to biliary pancreatitis but are not as sensitive as ALT.

The CBC may be notable for an elevated white blood cell count; the hematocrit may be either high or low. Early in the disease course, the hematocrit may be elevated because of third-space volume loss. A decrease in hematocrit is a poor predictor of prognosis because it indicates intra-abdominal hemorrhage and severe pancreatitis. An electrocardiogram also should be included early in the workup to determine whether the patient’s abdominal pain may be cardiac in origin.

**Table 91-1**

<table>
<thead>
<tr>
<th>ENZYME AND LEVEL</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT &gt;150 mmol/L</td>
<td>48</td>
<td>96</td>
<td>95</td>
</tr>
<tr>
<td>AST &gt;150 mmol/L</td>
<td>44</td>
<td>95</td>
<td>87</td>
</tr>
</tbody>
</table>
| Alkaline
phosphatase >300 units/L | 24 | 95 | 87 |
| Bilirubin 2.8 mg/dL | 38 | 93 | 89 |


ALT, alanine aminotransferase; AST, aspartate transaminase; PPV, positive predictive value.

**Development of Systemic Complications.** Ranson recognized that the model did not work well for patients with gallstone pancreatitis, so he revised the criteria to reflect the improved mortality. Although Ranson’s criteria have an 89% negative predictive value, the obvious drawback to use of this system in the ED is that the scoring cannot be completed until 48 hours after diagnosis. Furthermore, in patients with AIDS, Ranson’s criteria may not be as accurate because of HIV-induced changes in some laboratory values (such as calcium and LDH).

Although Ranson’s criteria constitute a simple and well-known scoring system, reliance on these criteria alone may result in delayed recognition of illness severity; therefore the Acute Physiology and Chronic Health Evaluation II (APACHE II) system also may be used to judge severity.24,25 This system uses 12 physiologic variables, age, and chronic health status to generate a total point score (Box 91-4). Many online medical calculators are available to allow easy calculation of the APACHE score by summing the weighed values of the measured physiologic parameters. Scoring can be performed on admission and throughout the hospital stay. An APACHE score of 8 or higher indicates severe disease. A score greater than 13 is associated with high likelihood of death. An APACHE III scoring system also has been developed and includes additional physiologic variables, but this system has not proved to be better at predicting outcomes in patients with acute pancreatitis.

C-reactive protein level above 150 mg/L at 48 hours after symptom onset are poor prognostic predictors of disease severity.26 To account for the various factors that indicate the severity of disease in patients with acute pancreatitis, the Atlanta criteria for severity are widely accepted (Box 91-5).27 Finally, a four-variable predictive model that uses BUN, age, LDH, and interleukin-6 has been proposed; initial analysis indicates that it is as accurate as other scoring systems.28 This scoring system will need further validation, however. Given the limitations in the ability to accurately predict severity of illness, patients with acute pancreatitis should initially be treated as though the disease is severe.

**Radiographic Studies**

In pancreatitis, plain abdominal radiographs may reveal an ileus with a sentinel jejunal loop or spasm of the transverse colon and dilation of the ascending colon. Pancreatic calcifications of chronic pancreatitis or gallstones may rarely be seen. The portion of the chest seen as part of the abdominal series may show left-sided or bilateral pleural effusions, atelectasis, or ARDS. Up to 80% of radiographs obtained in patients with pancreatitis will demonstrate some abnormality. Unfortunately, many of these findings are nonspecific, and plain radiography has largely been replaced by more advanced imaging.
### Box 91-5 Atlanta Criteria for Predicting Severe Acute Pancreatitis

<table>
<thead>
<tr>
<th>Criteria for severe acute pancreatitis—one or more of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ranson score 3 or higher on admission (or during the first 48 hours)</td>
</tr>
<tr>
<td>2. APACHE II score 8 or higher at any time during course</td>
</tr>
<tr>
<td>3. Presence of organ failure</td>
</tr>
<tr>
<td>• Shock (systolic blood pressure &lt;90 mm Hg) or</td>
</tr>
<tr>
<td>• Pulmonary insufficiency (Pao2 60 mm Hg or less on room air) or</td>
</tr>
<tr>
<td>• Renal failure (serum creatinine &gt;2 mg/dL after fluid resuscitation)</td>
</tr>
<tr>
<td>4. Systemic complications</td>
</tr>
<tr>
<td>• DIC (thrombocytopenia and hypofibrinogenemia and fibrin split products) or</td>
</tr>
<tr>
<td>• Metabolic complications (serum calcium 7.5 mg/dL or less) or</td>
</tr>
<tr>
<td>5. Presence of one or more local complications (pancreatic necrosis, pancreatic abscess, pancreatic pseudocyst)</td>
</tr>
</tbody>
</table>


### Box 91-6 Differential Diagnosis for Pancreatitis

#### Abdominal Disorders
- Perforated viscus
- Peptic ulcer disease
- Cholecystitis, gallbladder colic
- Cholangitis
- Gastroenteritis
- Nephrolithiasis or pyelonephritis
- Bowel obstruction
- Mesenteric ischemia
- Abdominal aortic aneurysm
- Ectopic pregnancy

#### Cardiopulmonary Disorders
- Myocardial infarction
- Pericarditis
- Pneumonia
- ARDS
- Pleural effusion

#### Systemic Disease
- Sickle cell crisis

ARDS, acute respiratory distress syndrome.

CT and ultrasound imaging are complementary studies in the evaluation of pancreatitis. Magnetic resonance imaging (MRI) offers no significant advantages over CT. Ultrasonography provides more accurate images of the biliary tract than CT; however, the pancreas itself, as well as local complications, are less well visualized by ultrasound. If a biliary cause is suspected, an ultrasound study performed within the first 24 hours of admission may help determine whether gallstones or dilation of the common bile duct is present. In one study that compared the results of CT and initial ultrasonography among patients with pancreatitis, ultrasound findings resulted in a change in treatment in 55% of patients, compared with no changes after CT. CT was 39% sensitive for biliary disease, whereas ultrasonography was 83% sensitive.26,27 In another study, ultrasound imaging was 94% sensitive for gallstones but only 19% for common duct stones and 38% for common duct dilation.28 Because of these limitations, when gallstone pancreatitis is highly suspected, an endoscopic ultrasound study may be more accurate and can help guide the emergency use of ERCP.29 Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive test that may be used to help determine the cause of acute pancreatitis.28 Although ultrasound imaging is more sensitive than CT for investigating biliary causes of pancreatitis, CT may be useful in evaluating for other causes of abdominal pain, the presence of peripancreatic complications (such as hemorrhage, pseudocyst, abscess, or vascular abnormalities), and the extent of any pancreatic necrosis.16,29,30 The Atlanta International Symposium recommended CT in patients with (1) an uncertain diagnosis; (2) severe clinical pancreatitis, abdominal distention, tenderness, fever with temperatures higher than 102°F, C, and leukocytosis; (3) a Ranson score greater than 3 or APACHE score greater than 8; (4) no improvement after 72 hours; and (5) acute deterioration.22 If the diagnosis is clear and evidence of obstruction is lacking, CT or ultrasound imaging can be delayed until after the patient has been admitted to the hospital. The main indication for obtaining a CT in the ED is to exclude other diagnoses; if the patient is significantly ill and can tolerate the procedure, early CT may determine whether complications are already present.

CT also may be used to stage the severity and prognosis of acute pancreatitis. Older studies suggested that both oral and intravenous contrast were appropriate, but with newer CT technology, a discussion with the radiologist may help determine whether oral contrast is needed. The CT severity index is an additional grading system that uses the CT to evaluate how the pancreas looks, as well as evidence of fluid collections or gas adjacent to the pancreas.29 Grades A (no abnormality) and B (focal or diffuse pancreatic enlargement) indicate lower levels of inflammation. Grade C shows mild peripancreatic inflammation and is associated with an increased risk of complications. Grade D (enlarged pancreas with fluid in the anterior pararenal space) and grade E (enlarged pancreas with two or more fluid collections) are associated with significant risk of infection, with mortality rates of up to 15%. Another CT-based scoring system, the extrapancreatic inflammation on CT scan score, is based on the presence of pleural effusion, ascites, and retroperitoneal fluid collection. The initial study was small but showed this system to be superior to the CT severity index in prediction of outcome.30

### Differential Considerations

Pancreatitis should be differentiated from other abdominal processes, cardiopulmonary disorders, and systemic diseases (Box 91-6). A number of acute surgical conditions may mimic pancreatitis in presentation and also may cause elevated biomarkers. Examples are bowel perforation, peritonitis, ischemic bowel, small and large bowel obstruction, and ruptured ectopic pregnancy.

### Management

The management of pancreatitis is primarily supportive; rehydration, pain and nausea control, nutritional supplementation, and monitoring for complications constitute the foundations of care. The supportive care given to the patient with acute pancreatitis has multiple objectives. Because of vomiting and fluid sequestration, most patients with pancreatitis are dehydrated. Fluids should be replaced with normal saline; several liters may be required. Vital signs and urine output should be used to judge the adequacy of volume replacement. Electrolytes should be monitored and replenished.

Abdominal pain associated with pancreatitis is severe and will generally necessitate use of narcotic analgesia. Meperidine has been used historically in pancreatitis and biliary disease. Although
morphine may increase the tone of the sphincter of Oddi, evidence that it worsens the disease process in pancreatitis is lacking.\textsuperscript{24} Patient-controlled analgesia may be the most effective method of pain control. Antiemetics are indicated to control nausea or vomiting.

In the past, patients with pancreatitis were allowed nothing by mouth and nasogastric suctioning was initiated out of concern that oral intake would stimulate the release of pancreatic enzymes. However, randomized clinical trials in patients with mild-to-moderate pancreatitis have shown no benefit from either fasting or use of nasogastric suctioning. Currently, nasogastric suctioning is indicated only in cases of intractable vomiting or ileus, and some enteral feeding should begin as soon as it is tolerable. Some evidence suggests that early enteral nutrition (delivered by feeding tubes placed beyond the ligament of Treitz) may improve outcomes even in severe pancreatitis\textsuperscript{22}; however, if oral feedings are not tolerated or are inadequate, then parenteral feedings should be initiated.

A key management principle is frequent reevaluation for complications of pancreatitis. Hypotension should be corrected with large volumes of normal saline (up to 6 L). In fact, hemodynamic instability in severe pancreatitis results from similar processes seen in sepsis, and management approaches used in septic patients (early goal-directed therapy) are appropriate.\textsuperscript{33} Invasive hemodynamic monitoring may be necessary. Respiratory support is appropriate for respiratory failure or continued shock. Hyperglycemia should be treated cautiously because it may self-correct as the pancreatitis resolves. Hypocalcemia may be the result of decreased albumin or hypomagnesemia; ionized calcium and magnesium levels should be checked before replacement therapy is initiated. If true hypocalcemia is present and the patient is experiencing symptoms, treatment is appropriate. Calcium gluconate should be used if calcium needs to be replenished. The serum potassium should be normalized before calcium replacement, however, because calcium will cause intravascular potassium shifts.

In the case of gallstone pancreatitis, gastroenterology consultation is appropriate to discuss the use of ERCP. Early operative removal of gallstones and the gallbladder has been shown to increase mortality; however, early removal of common bile duct stones by ERCP may reduce morbidity. At present, consensus is lacking regarding the optimal timing of ERCP in the presence of gallstone pancreatitis. Early endoscopic sphincterotomy (in 24–48 hours) and stone removal are recommended in the setting of cholangitis, sepsis, and severe obstructive pancreatitis.\textsuperscript{34} In mild pancreatitis, early ERCP has not consistently been shown to decrease morbidity. In addition, there is approximately a 5% rate of pancreatitis with ERCP and papillotomy, as well as other complications associated with the procedure (bleeding and perforation). In view of the ongoing controversy, it is appropriate to involve the consultant early in the case so that a well-coordinated management plan can be created.

Theoretically, certain medications should moderate the course of pancreatitis; histamine H\textsubscript{2} receptor blockers decrease the release of secretin by inhibition of gastric acid, glucagon directly suppresses pancreatic exocrine secretion, and octreotide inhibits pancreatic secretion. However, these therapies have not been shown to be clinically effective. Other approaches that use inhibitors of inflammatory mediators also have failed to produce clinical improvement. For patients with severe pancreatitis, an H\textsubscript{2} blocker, although not helpful for the acute disease, may decrease stress-induced ulcers.

Use of antibiotics in patients with severe pancreatitis with or without evidence of necrosis of pancreatic tissue is controversial. Prophylactic antibiotics have been reported to be effective in reducing subsequent infection. These positive effects have not been consistently observed, however, and some evidence indicates that use of prophylactic antibiotics in patients with severe pancreatitis may increase the risk of fungal infection.\textsuperscript{35} Two recent studies found no difference with respect to the development of infected pancreatic necrosis with the use of prophylactic antibiotics.\textsuperscript{36,37} The usefulness of early antibiotic treatment remains unclear, although there appears to be a consensus to withhold antibiotics until clear evidence of infection is present.\textsuperscript{9,18,23,32,37}

Surgical intervention or percutaneous drainage may be necessary for cases of infected pancreatic necrosis, infected pseudocyst, or unresolved pseudocyst. Surgery is preferred when percutaneous drainage is not effective or not possible (as with extensive pancreatic necrosis or deteriorating clinical status).

**Disposition**

The course of acute pancreatitis is unpredictable, and complications may occur hours or days after the onset of illness; therefore almost all patients with acute pancreatitis should be admitted to the hospital. Patients with evidence of severe pancreatitis should be admitted to the intensive care unit (ICU), especially if findings include agitation, confusion, rising hematocrit, pulmonary insufficiency, or cardiovascular problems such as hypotension, progressive tachycardia, or poor urine output. Specifically, patients with a score greater than 2 on Ranson’s criteria on admission or other evidence of organ failure, local complications, or significant comorbid illness will also require ICU management.

In hospitals without appropriate intensive care facilities, patients with evidence of severe pancreatitis should be transferred to an appropriate treatment center. If the cause of pancreatitis is suspected or confirmed to be gallstones, discussion with a specialist (gastroenterologist or surgeon) is necessary. Pediatric patients have increased morbidity and mortality from pancreatitis and should be considered for early transfer to a pediatric specialty center.

**CHRONIC PANCREATITIS**

**Principles of Disease**

Chronic pancreatitis is an ongoing inflammatory process leading to irreversible structural damage and impairment of exocrine and endocrine pancreatic function. Normal pancreatic structure is replaced with fibrotic tissue, resulting in pancreatic ducts that are structured in some areas and dilated in others. The incidence is approximately 4 per 100,000.\textsuperscript{38} In 70 to 80% of people, the cause is thought to be chronic alcohol use. The risk increases with the duration and amount of alcohol consumption. The ingestion of more than 150 g of alcohol per day for an average of 5 to 15 years is associated with the development of chronic pancreatitis in 3 to 10% of chronic alcoholics.\textsuperscript{38–41} It is possible that chronic pancreatitis also may develop in persons sensitive to small amounts of alcohol.

Three theories exist as to the mechanisms by which alcohol causes chronic pancreatitis: (1) direct cellular toxicity, (2) alcohol-induced precipitation of proteinaceous fluid in the ductules, which causes obstruction and calcification, and (3) injury caused by recurrent acute pancreatitis leading to irreversible damage and chronic inflammation.\textsuperscript{38,41} Chronic pancreatitis can continue even after the cessation of alcohol use, although it is more commonly associated with alcoholic relapse. Smoking increases the risk of chronic pancreatitis in a dose-dependent fashion, with earlier onset and progression in alcohol-induced pancreatitis.

Other, less common causes of chronic pancreatitis include ductal obstruction, hereditary pancreatitis, cystic fibrosis, trauma, autoimmune, hyperparathyroidism, α\textsubscript{1}-antitrypsin deficiency, hyperlipidemia, and tropical pancreatitis (cassava fruit is implicated).\textsuperscript{36} Idiopathic chronic pancreatitis occurs in approximately
10% of patients. In the 25% of cases of unknown cause, occult alcohol use may be the culprit. In children the most common causes are cystic fibrosis and hereditary pancreatitis.38,42

The pathophysiology of chronic pancreatitis includes chronic calcific pancreatitis, usually seen in alcoholics and characterized by patchy fibrosis, ductal injury, intraductal protein plugs, stones, and chronic inflammatory pancreatitis with diffuse fibrosis and inflammatory changes. As in acute pancreatitis, chronic inflammation can cause local injury resulting in lesions such as pseudoaneurysms, splenic vein thrombosis, pancreatic ascites, or pancreatic fistulae. Pancreatic pseudocyst formation is seen in up to 25% of patients with chronic pancreatitis. Rarely, pseudocysts can erode into vascular structures or can become infected. Narrowing of the bile duct from extrinsic pressure or strictures may lead to elevation of liver enzymes and jaundice. In approximately 5% of patients, duodenal obstruction develops secondary to inflammation around the head of the pancreas. Thus, chronic pancreatitis in an acutely ill patient may be a manifestation of the primary disease or a complication.

The most common endocrine complication is the presence of glucose intolerance in many patients with chronic pancreatitis. Over years, insulin-dependent diabetes develops in 50 to 75% of patients.38,42 Patients with chronic pancreatitis have an increased risk for the development of pancreatic carcinoma of approximately 4%, as do patients with hereditary pancreatitis. In addition, patients with chronic disease have exocrine pancreatic insufficiency with steatorrhea and malabsorption.

Chronic pancreatitis is associated with considerable morbidity in terms of pain and complications. In addition, patients with chronic pancreatitis have an excess mortality of approximately 50% in 20 years.39 However, the cause of death is more likely to be related to other consequences of alcoholism than to pancreatitis.

Clinical Features

Patients with chronic pancreatitis may be in near-constant and intractable chronic pain or may be experiencing complications from chronic pancreatitis or an acute flare of chronic underlying disease. These flares may be severe, and if the patient is relatively well during the interim it may be difficult to distinguish this episode from a recurrent bout of acute pancreatitis. Pain is epigastric, usually radiating to the back and associated with nausea and vomiting. Often the pain is similar to that in previous attacks of acute pancreatitis or flares of chronic pancreatitis. Use of alcohol or eating exacerbates the pain. No correlation has been found between remaining pancreatic function and the degree of pain, although a few studies have shown that the pain may diminish over years of chronic disease. Patients may experience weight loss because of malabsorption or decreased intake secondary to nausea and vomiting or to the recognition that eating may precipitate the pain.

In approximately 15% of patients with chronic pancreatic disease, signs and symptoms of pancreatic exocrine function insufficiency, including malabsorption, diarrhea, steatorrhea, and weight loss, may develop over time. Malabsorption occurs after approximately 90% of the pancreas is nonfunctional. Functional endocrine insufficiency will develop in approximately one to two thirds of patients with chronic disease. The symptoms primarily manifest as hyperglycemia; however, the development of diabetic ketoacidosis is rare. Hypoglycemia is multifactorial in origin, with causes including insufficiency of glucagon, decreased liver glucose stores, malnourishment, and hypoglycemic medications.

On physical examination, patients usually have significant discomfort. They may appear chronically ill from alcoholism, poor nutrition, and malabsorption. On abdominal examination, palpation frequently reveals tenderness without peritoneal signs. The abdomen should be carefully palpated for a mass that may represent a pseudocyst or tumor. Stigmata of chronic alcohol abuse also may be noted; however, jaundice may be from pressure on the common bile duct or from alcohol-related liver injury.

Diagnostic Strategies

The diagnosis of chronic pancreatitis frequently is made clinically rather than on the basis of laboratory testing. The serum levels of amylase and lipase initially are mildly elevated in chronic pancreatitis, but as the disease progresses, these levels normalize. As in acute pancreatitis, the degree of elevation of amylase and lipase is not prognostic. In the patient with the appropriate clinical picture of history of pancreatitis and chronic abdominal pain, normal amylase and lipase levels are consistent with a diagnosis of chronic pancreatitis.

Blood work should include a CBC and complete metabolic profile. The white blood cell count usually is normal. There may be elevations of hepatic enzymes (alkaline phosphatase, bilirubin, or transaminases) either from alcoholic hepatitis or from compression on the biliary duct from pancreatic inflammation or a mass in the head of the pancreas. Elevations in serum glucose also may be seen; hypoglycemia is less common. Decreases in albumin and calcium are common because of the chronic nature of the disease. If the diagnosis is in question, stool may be tested for fecal fat and pancreatic enzymes such as elastase, chymotrypsinogen, and trypsinogen.34,43

Although abdominal radiographs are not necessary, presence of pancreatic calcifications is pathognomonic. Such calcifications are seen in 30 to 50% of patients, usually related to chronic alcohol-induced pancreatitis (Fig. 91-3). Patients with calcifications have had pancreatitis for an average of several years; therefore these patients should be evaluated for long-term complications such as diabetes and malabsorption.

In patients with the clinical manifestations of chronic pancreatitis, including pain, malabsorption, and diabetes, additional corroborating data may be obtained by CT scan, MRCP, ERCP, or endoscopic ultrasound.37,38 In the ED setting, patients with known chronic pancreatitis do not need imaging except when the underlying cause of the pain is in question or if the pain is prolonged, significantly increased, or unresponsive to treatment. CT is 90%
sensitive for chronic pancreatitis and may show dilated intra-
calculi, microcalculi, pseudocysts, or other complications. Although ultrasound imaging is useful in diagnosing the
cause of acute pancreatitis, it is less useful in chronic pancre-
atitis (sensitivity of 75% and specificity of 80-90%). The primary ultrasound findings are pancreatic calcifications and ductal
abnormalities.

Although endoscopic retrograde pancreatography (ERP) is not
an ED procedure, it can be helpful in diagnosing pancreatic duct
abnormalities and measuring pancreatic function. Some gastroen-
terologists consider the ductal abnormalities seen on ERP and
duodenal ultrasound to be pathognomonic for chronic pancre-
atitis. MRCP has an increased role in the evaluation of chronic
pancreatitis.43,44

Differential Considerations

The diagnosis of chronic pancreatitis usually is straightforward in
the alcoholic patient with hyperamylasemia who has chronic
abdominal pain and a history of similar, previous flares of pan-
creatitis. The diagnosis may be more difficult when amylase and
lipase levels are normal. However, the clinician should not forget
that other abdominal processes, unrelated to either the pancreas
or the complications of pancreatitis, are legitimate considerations
in the differential diagnosis (see Box 91-6). In addition, other
chronic abdominal disease such as peptic ulcers, irritable bowel,
gallstones, and endometriosis may manifest with recurrent
abdominal pain. Finally, narcotic-dependent patients in
withdrawal may experience vomiting and abdominal pain that may be
difficult to differentiate from chronic pancreatitis.

Management

The initial management of chronic pancreatitis is supportive.
Depending on the patient’s clinical status and electrolyte values,
replenishment of fluids and electrolytes may be necessary. An
“alcohol cocktail” with thiamine, multivitamins, and folate often
is indicated because patients frequently are malnourished. Anti-
emetics should be used to manage recurrent emesis.

Management of pain is one of the most important and most
difficult aspects of treatment. Laboratory values may be normal
despite significant pain, and patients with chronic pain syndromes
may not exhibit signs of autonomic hyperactivity when experienc-
ing exacerbations of their underlying disease. This lack of correla-
tion may lead to a concern that the expressed need for pain
medication constitutes drug-seeking behavior. Physicians should
err on the side of treatment in most patients, except those with
documented abuse. Nonsteroidal analgesics and acetaminophen
are the preferred drugs for control of pain but often are not
adequate. Either morphine, hydromorphone, or meperidine may
be used and should be titrated to effect. Tramadol (Ultram) also
has been used effectively.44-45 The use of narcotics over extended
periods may be necessary. Non-narcotic modulators of pain, such as
selective serotonin reuptake inhibitors, tricyclic antidepressants,
or gabapentin, may be helpful for chronic pain. In the ideal
medical system, the primary care physician or a pain management
specialist monitors the narcotic prescription because narcotic
dependence may become an issue.

The removal of inciting factors, especially alcohol, is important.
Smoking also plays a role in the development of chronic pancre-
atitis that is independent of alcohol.46 Patients with significant
pain should have nothing by mouth, although, as in acute pancre-
atitis, a nasogastric tube is not indicated. The use of oral pancre-
atic replacement enzymes increases the amount of trypsin in
the duodenum and may decrease stimulation of the pancreas, with
subsequent decrease in pain. Studies of the effectiveness of pan-
creatic enzyme replacement on pain have yielded contradictory
results.41 These enzymes should be used in patients with malab-
sorption or steatorrhea. In theory, proton pump inhibitors or H2
receptor blockers also may reduce pancreatic stimulation; however,
these agents have not been shown to decrease pain or hasten
recovery. Octreotide lowers cholecystokinin levels and may inhibit
pancreatic secretion.41

Beyond ED treatment, helpful adjuncts may include endoscopic
dilation, ductal stone removal, extracorporeal shock wave litho-
tripsy, or stenting of the pancreatic ducts. Common bile duct
stenting also may be necessary, because obstruction occurs in
approximately 5 to 10% of cases.41 Surgery such as pancreatic head
resection, lateral pancreaticojejunostomy, or Whipple pancreatic
duodenectomy is sometimes an option when conservative treat-
ment has failed. One recent study showed improved pain and
physical health summary scores in patients randomized to undergo
surgery rather than endoscopy.46 Pancreatic pseudocysts in chronic
pancreatitis are less likely to resolve spontaneously and should be
drained either endoscopically under ultrasound guidance, percu-
taneously, or in an open procedure. Celiac plexus blocks also have
been used with variable success for pain control.

Disposition

In general, patients with chronic pancreatitis are managed as out-
patients and come to the ED with exacerbations or complications.
Because acute pancreatitis can occur in patients with chronic pan-
creatitis, the same prognostic indicators for severity of acute pan-
creatitis should be considered. Patients with severe disease should
be admitted to the ICU. Patients with dehydration, abdominal
pain unresponsive to medications, or questionabale diagnosis
should be hospitalized for evaluation and treatment. After a
careful ED evaluation, in the absence of dehydration, unstable
vital signs, or uncontrolled pain, the patient may be managed on
an outpatient basis with close follow-up. After hospital discharge,
it is important to stress lifestyle modifications of abstinence from
alcohol and tobacco, as well as intake of frequent, small, low-fat
meals.

PANCREATIC CANCER

Perspective

Pancreatic cancer is a particularly lethal cancer, with a 5-year
survival rate of less than 5% despite aggressive surgery and
advances in chemotherapy. It is the fourth most common cause
of cancer-related death in the United States. The disease is diag-
osed in approximately 11 people per 100,000 per year, and the
incidence has increased threefold over the past 40 years. Because
eyeary symptoms are few, a minority of patients are diagnosed at
an early stage.

Principles of Disease

Little is known about the cause of pancreatic cancer. The most
consistently reported risk factors are smoking, advanced age, a
high-fat diet, and a positive family history. Chronic alcoholism,
chronic pancreatitis, and diabetes have been shown to be risk
factors in some studies.47-50

Ductal adenocarcinomas account for 95% of malignant pancre-
atic tumors. The pancreatic head is the location of origin in 70%
of cases. The tumor extends locally into adjacent structures and
can metastasize by hematogenous or lymphatic spread to liver,
peritoneum, lungs, bones, and brain. Neuroendocrine tumors,
such as gastrinomas, vasoactive intestinal peptide tumors (VIPomas),
and glucagonomas make up the remaining cases.51

These types of tumors carry a better prognosis.
Clinical Features

The presentation of pancreatic adenocarcinoma is variable because progression of the disease is indolent. The tumor usually has been present for several months before the cancer is diagnosed; therefore, presenting complaints may include pain of long duration or one of the many complications of the disease. One of the most common presentations is weight loss, which usually is the result of anorexia rather than malabsorption. The patient may report dull, constant abdominal pain in the epigastrium that may radiate to the back. Alternatively, the patient may have painless jaundice from common bile duct obstruction, and progressive jaundice develops in approximately 75% of patients. When the mass presses on the pancreatic duct, pancreatitis can develop. An enlarged, palpable, but painless gallbladder in the presence of jaundice is most commonly associated with pancreatic cancer (termed Courvoisier’s sign). Glucose intolerance also may develop. As the tumor enlarges, patients may exhibit evidence of bowel obstruction. Pancreatic cancer (as well as other cancers) may render patients hypercoagulable, resulting in thromboembolic presentations. Varices and gastrointestinal bleeding may be caused by compression of the portal system.

Neuroendocrine tumors of the pancreas are rare and manifest with symptoms that reflect the hormones they produce. For example, with insulinomas, the presenting manifestation may be hypoglycemia with weakness, sweating, and tremulousness. Gastrinomas are related to Zollinger-Ellison syndrome and recurrent peptic ulcers. VIPomas (also known as Verner-Morrison syndrome) manifest with extreme watery diarrhea, hypokalemia, and achlorhydria. Glucagonomas manifest with glucose intolerance, stomatitis, and necrotic migratory erythema. Some tumors produce multiple hormones. Carcinoid causes flushing, sweating, and diarrhea. Most tumors produce multiple gastrointestinal hormones but manifest as a dominant clinical syndrome as described earlier. Other, nonfunctional tumors also may be noted incidentally on CT scans as small pancreatic masses. Diagnosis is made by measurement of abnormal levels of hormones and recognition of the appropriate clinical syndrome. Depending on the type, up to 50 to 80% of pancreatic neuroendocrine tumors are malignant.

Diagnostic Strategies

Evaluation of a patient in whom pancreatic cancer is suspected should focus on diagnosis and staging of the disease, assessment of resectability, and palliation of symptoms. CT is the procedure of choice, although pancreatic masses may be seen on ultrasound. MRI also may provide information. Percutaneous ultrasound-guided biopsy, endoscopic ultrasound examination and biopsy, CT-guided biopsy, and laparotomy can be used to obtain tissue specimens for diagnosis. Histologic samples are needed to differentiate ductal adenocarcinoma from islet cell tumors, other metastatic cancers, and lymphoma. Serologic markers have not proved satisfactory for diagnosis or follow-up evaluation, although several oncogenes and tumor markers are under study (for example, CA19-9).

Management

Complete resection of the carcinoma is the only effective treatment. Unfortunately, few tumors (less than 20%) are diagnosed at a stage at which this may be possible. This suggests that even seemingly resectable pancreatic cancer has microscopic systemic spread before operative intervention occurs. Both adjuvant and neoadjuvant therapies have been studied in an effort to improve survival. In patients with unresectable tumors, the median survival period is approximately 6 months. Palliative surgery may be performed to relieve obstruction. Biliary drainage by percutaneously placed or ERCP-placed stents also may help to relieve jaundice. Chemotherapy and radiation therapy may decrease tumor size to ease pain and prolong survival in some patients.

Treatment of neuroendocrine tumors is aimed at limiting tumor growth by both excision and reversal of hormone excess. Patients may be seen in the ED with complications of the cancer such as bowel obstruction, jaundice, or problems with pain control. In view of the grim prognosis for this disease and the significant associated pain, narcotics should not be withheld, and end-of-life issues should be addressed by the oncologist.

KEY CONCEPTS

- Most cases of acute pancreatitis are caused by gallstones (45%) and alcoholism (35%). Other causes include medications, toxins, and trauma.
- The clinical spectrum of acute pancreatitis ranges from mild (epigastric discomfort often associated with vomiting) to life-threatening (severe abdominal pain in the presence of an acute abdomen and hemodynamic instability caused by systemic complications). The mortality rate for severe pancreatitis approaches 30%.
- There is no perfect test for diagnosing acute pancreatitis. The most useful tests include serum amylase and lipase assays. Unfortunately, both tests can yield normal results in up to 25% of cases; mild elevations are not specific for acute pancreatitis and can be seen in many other acute surgical disorders that cause abdominal pain. Both tests are highly specific for pancreatitis when serum levels are elevated five times above the upper limits of normal.
- Emergent abdominal CT should be performed in patients with clinically suspected pancreatitis who appear acutely ill (to exclude peripancreatic complications such as hemorrhage, pseudocyst, or abscess) and in patients with an uncertain diagnosis (to exclude other surgical causes of acute abdominal pain).
- Because the course of acute pancreatitis is unpredictable, most patients require hospitalization for pain control, hydration, observation, and the management of complications. Patients with severe pancreatitis (i.e., those who have more than two of Ranson’s criteria, an APACHE score over 7, or evidence of systemic complications) usually need ICU admission.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.
References