Acute pancreatitis has an annual incidence of 5 to 40 per 100,000 with an overall mortality of 1.5 per 100,000 (1). The estimated cost of hospitalization for these patients to the US health system is around $2.6 billion annually (2). The clinical course of acute pancreatitis is often self-limited, and usually requires no intervention. Approximately one-third of patients, however, develop pancreatic necrosis, which has an associated mortality rate up to 30% (1,3). Severe acute pancreatitis often demands an extended stay in the intensive care unit (ICU) and a dedicated multidisciplinary care.

Numerous causative factors of acute pancreatitis have been recognized, most commonly secondary to gallstones and excessive alcohol use. The incidence of biliary pancreatitis is increased among white women over the age of 60 years and those with gallstones less than 5 mm in diameter (4,5). Other causes include metabolic derangements such as hypertriglyceridemia, duct obstruction (tumor or pancreas divisum), medications (azathioprine, thiazides, and estrogens), and trauma. About 20% of cases remain idiopathic, although these are expected to become less common as factors of genetic predisposition and environmental susceptibility are elucidated (6).

Trypsin is the key enzyme in the activation of pancreatic zymogens. The inappropriate conversion of trypsinogen to trypsin and a lack of prompt elimination of active trypsin lead to acute pancreatitis (6,7). In addition to further significant tissue damage as a direct result, the inflammatory process may extend beyond the pancreas and result in the systemic inflammatory response syndrome (SIRS), multiorgan failure and, ultimately, death.

Diagnosing acute pancreatitis may be sometimes as difficult as predicting the course or defining the treatment. The best approach may be to elucidate the history of a similar attack or hospitalization and identify associated etiologic factors, most commonly alcohol abuse or biliary tract disease. The recurrence rate of acute pancreatitis is estimated around 30%, and even higher in the alcoholic population. Disease isolated to the head or tail of the pancreas may result in pain localized to the right or left upper quadrant, respectively with or without referred pain to the subcapsular areas due to diaphragmatic irritation. The classic presentation of epigastric pain that radiates to the back may be present in only 50% of patients presenting with acute pancreatitis.

Laboratory Testing

Serum amylase levels that are more than three times the upper limit of normal are often caused by acute pancreatitis given the appropriate clinical presentation (8). Although the serum amylase concentration begins to rise shortly after the onset of the disease, it may return to normal levels in 2 to 4 days. A normal serum amylase level does not exclude the disease. Acute pancreatitis with normal serum amylase levels often occurs in alcoholic patients, and results from a longer duration of symptoms before admission or the inability of an inflamed or chronically diseased pancreas to produce a significant amount of amylase (9). Pancreatitis secondary to biliary tract disease will often present with high serum amylase and elevated alanine aminotransferase (ALT) levels. The latter is the single best predictor of biliary pancreatitis with positive predictive value of 95% in cases of levels greater than three times the upper limit of normal (10). The clinician must remain aware that an elevated serum amylase is not necessarily diagnostic of acute pancreatitis. The differential diagnosis of hyperamylasemia includes perforated or penetrating gastric ulcer, ruptured ectopic pregnancy, and intestinal obstruction or infarction. Measuring urinary amylase, amylase-to-creatinine ratios and amylase isoenzymes have shown no clinical advantage.

An elevated concentration of serum lipase, however, is quite sensitive for the diagnosis of acute pancreatitis secondary to alcohol abuse. Lipase levels tend to remain elevated longer than amylase concentrations. Therefore, an elevated lipase level can be useful information for patients who present later in the course of disease and who may have a normal amylase concentration. Serum lipase levels have no value in predicting severity of disease or pancreatic destruction.

The most reliable serum markers for early prediction of severity of pancreatitis are PMN elastase, albumin, C-reactive protein (CRP) and pancreatic amylase (11). An acute phase reactant, CRP, is the most widely used. Although elevated levels of CRP have been associated with pancreatic necrosis, a 24- to 48-hour latency for CRP to reach optimal predictability limits its use as an early predictor of disease severity (12). Measuring levels of trypsinogen activation peptide and trypsinogen-2 are more specific for acute pancreatitis but are not widely available (13). Interleukin (IL)-6 appears as a promising tool, although further studies are needed regarding its potential use as a clinically relevant predictor of disease severity (14).

Radiologic and Diagnostic Studies

There are numerous radiologic findings suggestive of pancreatitis. These include dilatation of the first portion of the duodenum (duodenal ileus), dilatation of the first loop of the jejenum (jejunal ileus or “sentinel loop”), dilatation of the transverse colon or “colon cut-off” sign (secondary to a
transverse colonic ileus), and elevated hemidiaphragm and pleural effusion, especially on the left side (secondary to diaphragmatic irritation and sympathetic pleural effusions).

Transabdominal pancreatic ultrasound (US) is not sensitive in the diagnosis of acute pancreatitis, often because of gas in the bowel. US frequently provides an incomplete view of the pancreas and the peripancreatic area, especially in obese patients with severe disease. However, it can be helpful in detection of early complications and identification of associated biliary tract disease. Transabdominal US is more sensitive than either computed tomography (CT) or magnetic resonance imaging (MRI) for identifying cholelithiasis and sludge, and for detecting dilatation of the biliary ducts, but is insensitive for the detection of distal biliary duct stones (4). Endoscopic ultrasound (EUS) may be the most accurate test for diagnosing or ruling out biliary causes of acute pancreatitis and may guide the use of endoscopic retrograde cholangiopancreatography (ERCP) (15). Persistent biliary obstruction worsens the outcome, and increases the severity of acute pancreatitis and the risk for ascending cholangitis. ERCP is used with endoscopic sphincterotomy to extract impacted gallstones and drain infected bile in severe acute pancreatitis (16).

In patients with abdominal pain of unclear etiology, CT scan is used to differentiate acute pancreatitis and other intra-abdominal pathologies. The use of radiocontrast is preferred, as contrast-enhanced CT remains the gold standard in the diagnosis of pancreatic necrosis (17). Radiocontrast depicts pancreatic necrosis as focal or diffuse zones of nonenhanced parenchyma. Areas of necrosis may not be present, however, for 48 to 72 hours after presentation. When the use of intravenous radiocontrast material is contraindicated, the diagnosis of acute pancreatitis can be inferred from homogeneous glandular enlargement and the presence of peripancreatic fluid collections (18). In stable patients with contraindication to intravenous contrast, MRI is an alternative method to evaluate the extent of pancreatic necrosis. MRI may also identify early duct disruption that is not visible on CT scan (19). Although contrast-enhanced CT imaging allows the identification of pancreatic necrosis, there is no definitive imaging technique that allows precise identification of infected pancreatic necrosis. The appearance of air in the pancreatic parenchyma usually indicates infection, however may not be always present in patients with infected pancreatic necrosis. Fine-needle aspiration under CT or US guidance with Gram stain and culture of the aspirate is the gold standard for the diagnosis of infected pancreatic necrosis (20). Most series report sensitivity ranging from 90% to 100% and specificity between 96% and 100% (21).

**CLASSIFICATION**

The Marseilles classification recognized four types of pancreatitis: (1) acute pancreatitis, (2) recurrent acute pancreatitis, (3) relapsing chronic pancreatitis, and (4) chronic pancreatitis (22) more comprehensive classification was created in Atlanta in 1992 (23) and then, recently refined to characterize the inflammatory changes and fluid collections (Table 128.1) (24). In this classification, pancreatitis is divided into acute interstitial pancreatitis and necrotizing pancreatitis. The fluid collections are described based on these two types and time at diagnosis. Early (<4 weeks) peripancreatic fluid collections in interstitial pancreatitis are known as acute peripancreatic fluid collections (APFC), whereas in necrotizing pancreatitis, they are called postnecrotic peripancreatic fluid collections (PNPFC). Late (>4 weeks) collections in interstitial and necrotizing pancreatitis are referred as pancreatic pseudocysts and walled-off pancreatic necrosis (WOPN), respectively (Table 128.1) (24).

The degree of severity and outcomes of a patient with acute pancreatitis was described by Ranson et al. (25,26) and included 11 clinical criteria, 5 of which were assessed on admission and 6 after 48 hours (Table 128.2). They are well correlated with morbidity, length of ICU stay, and mortality. The presence of less than 3 of these 11 criteria correlates with a benign course of disease, with 3% mortality rate. The presence of three or more of these parameters on admission or within 48 hours implies a more severe form of pancreatitis, and is associated with high risk of death and major complication. With a single exception, the patients‘ age, these criteria are the result of the statistical analysis of 43 parameters. These parameters were gathered retrospectively from 3 overlapping series comprising 450 patients (25,26). In this series, however, only 21% had acute pancreatitis definitively confirmed by surgery or postmortem examination. Nevertheless, the Ranson scale has been largely used since the 1980s in virtually all studies relating to acute pancreatitis.

A more detailed system, the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system, has also been extensively used and is easily obtained by web-based calculators (Table 128.2). Values equal or greater than 8 are indicators of severe acute pancreatitis. Although cumbersome, it can be measured in a daily basis as opposed to Ranson criteria. The introduction of the Bedside Index for Severity in Acute Pancreatitis (BISAP) score has allowed a simpler prediction of mortality within the first 24 hours of presentation (Table 128.2) (27). Scores greater than 3 are associated with higher rates of mortality and organ failure. BISAP has the

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<th>Table 128.1 Revised Atlanta Classification of Acute Pancreatitis (23,24)</th>
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<td><strong>Morphologic Features</strong></td>
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<td>Fluid collection</td>
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<td>Early (&lt;4 wks) Acute peripancreatic fluid collection</td>
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<td>Late (&gt;4 wks) Pancreatic pseudocyst</td>
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<th>Grades of severity</th>
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<td>• No organ failure</td>
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<td>• No local or systemic complications</td>
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<td>• Organ failure that resolves &lt;48 hrs</td>
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<td>Moderately severe acute pancreatitis</td>
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<td>• Local or systemic complications without persistent organ failure</td>
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<td>Severe acute pancreatitis</td>
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<td>• Persistent organ failure (&gt;48 hrs)</td>
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disadvantage that it cannot easily distinguish transient from persistent organ failure, however its prognostic accuracy is similar to those of the other scoring systems (28). Recent evidence suggests that measurement of IL-6 and CRP may play some role in prediction and assessment of the severity of acute pancreatitis (29). Further scores taking into account these values are forthcoming.

Several scoring systems exist based on CT findings as predictors of disease severity. The Modified CT Scan Index is associated with better correlation of severity and clinical outcomes (Table 128.2) (30). This score classifies disease as mild, moderate, and severe with scores of 0 to 2, 4 to 6, and 8 to 10, respectively (30). In the clinical setting, not all patients undergo immediate CT scan on presentation, thereby making these scores limited in early management.

### TREATMENT OF ACUTE PANCREATITIS

The rationale approach to the therapy for acute pancreatitis includes placing the pancreas “at rest,” supporting the patient’s nutritional and metabolic needs, correcting the acute causes of mortality (i.e., cardiovascular collapse, respiratory insufficiency, and renal failure), and detecting complications of disease that require intervention.

#### Gland Suppression and Nutrition

Suppression of the secretory function of the pancreas has been attempted by elimination of oral fluids, suppression of acid secretion with various H2 and antacids and use of anticholinergics and proteolytic enzyme inhibitors. Calcitonin and somatostatin, which are potent inhibitors of pancreatic enzyme secretion, have also been investigated. Although theoretically beneficial, randomized controlled trials (RCTs) have not shown significant improvement.

Historically, early feeding was associated with increased severity of the disease. Bowel rest, with or without parenteral nutrition, had become the standard of care. It is known that acute pancreatitis results in a hypermetabolic, hyperdynamic SIRS that results in a catabolic state (31). Retrospective evidence suggests that enteral nutrition is not only feasible but may be desirable in such patients. Lack of enteral feeding results in atrophy of the gastrointestinal mucosa, bacterial overgrowth, increased gut permeability, and translocation of bacteria or its products into the circulation (32). Enteral feeding also stimulates lysosomal movement to the cell surface, minimizing the intracellular release of pancreatic enzymes and may, in fact, be therapeutic in acute pancreatitis (31). In addition, enteral nutrition reduces the production of proinflammatory mediators that may also have therapeutic potential in such patients. Enteral nutrition is associated with fewer complications by preserving gut integrity and is more cost effective as compared to total parenteral nutrition (TPN). A meta-analysis of 8 randomized trials involving 348 patients confirmed that enteral tube feeding, as compared with TPN, reduced the rate of infections and mortality among patients with severe acute pancreatitis (33).

The data regarding the timing to initiate enteral nutrition have been heavily investigated, however are nowhere near a consensus. Several nonrandomized studies have shown that nasoenteric tube feeding started within 48 hours of admission, as compared after 48 hours, significantly reduced the rate of major infection and mortality rates (34–37). However, a recently published large multicenter RCT including 208 patients with severe pancreatitis, the PYTHON trial, has shown no significant differences between early feeding (within 24 hours) and oral diet initiated 72 hours after presentation in the rates of major infection or mortality rates (38). These findings challenge the concept of the gut mucosa-preserving of early feeding during acute pancreatitis and question results of prior nonrandomized series.

The route of administration has also been studied. Enteral nutrition can be administered either via gastric or jejunal...
routes. Although the latter is theoretically preferred as it might result in lesser increase in enzyme, bicarbonate, and volume output from the pancreas, this premise has not been proven. Eatock et al. (39) showed no exacerbation of the disease with the nasogastric route as compared to nasojejunal. Though, the jejunal route is advised in patients with gastric atony or duodenal obstruction secondary to pancreatitis and as a result will not tolerate being fed in the stomach.

**Cardiovascular Collapse, Renal Failure, and Respiratory Insufficiency**

The cornerstone of management in early pancreatitis is fluid resuscitation and close monitoring for early manifestations of organ dysfunction. Although a variety of scoring systems, biomarkers, and radiologic findings can help identify patients at risk of organ dysfunction, these do not substitute for frequent clinical assessment and monitoring. Clinical findings including thirst, poor urine output, persistent tachycardia, tachypnea, hypoxemia, altered mental status, and lack of improvement within the first 48 hours are warning signs of impending severe disease (8).

In addition to the frequent assessment of vital signs, the intravascular volume status should be monitored by physical examination and urinary output. Hypovolemia is secondary to increased capillary permeability, relative lymphatic and splanchnic venous obstruction. This accounts for sequestration of up to 40% of circulatory plasma volume in just a few hours, thereby resulting in renal insufficiency. If cardiac output remains low despite adequate filling pressures, inotropic agents should be initiated to improve hemodynamic status.

Early identification of hypoxemia via either pulse oximetry or arterial blood gas measurement is also paramount. Respiratory insufficiency associated with severe pancreatitis is resulted from a decrease in functional residual capacity and shunting, which may be related to elevated paralyzed hemidiaphragms, basilar atelectasis, pleural effusion, empyema, pneumonia, micropulmonary emboli, or alveolar collapse. The latter occurs due to the decrease in pulmonary surfactant, which is degraded by circulating pancreatic enzymes. Positive end-expiratory pressure (PEEP) is required for maintenance of adequate minute ventilation and oxygenation.

Patients with severe acute pancreatitis with hemodynamic instability should be admitted to the ICU, as well as those patients who are at high risk of rapid deterioration such as the elderly (40), patients requiring high-volume resuscitation, renal failure, respiratory compromise, and patients with evidence of substantial pancreatic necrosis (>30%) (16). Obese patients are also at increased risk for developing complications secondary to severe acute pancreatitis (41).

**Therapeutic Peritoneal Lavage**

A meta-analysis of eight randomized clinical trials evaluating the use of continuous peritoneal lavage in patients with pancreatitis indicated that this modality was not associated with any significant improvement in morbidity or mortality (42). This is partially explained by the presence of large volumes of fluid within the peritoneal cavity that may degrade the peritoneal defense mechanisms due to the inability to localize the source of contamination through local fibrinous adhesions between omentum, loops of bowel, and the abdominal wall.

The lavage may, in addition, enhance the absorption of inflammatory mediators into the systemic circulation and remove important local inflammatory mediators, thereby impairing peritoneal defense mechanisms (43,44). The peritoneal mesothelial cells are usually lost in association with peritonitis and their regeneration may be important in the resolution of the inflammation (42). Lavage, with either crystalloid or peritoneal dialysis solutions, inhibits the rate of mesothelial healing (45). Despite a number of early enthusiastic reports, the use of continuous lavage in patients with acute pancreatitis is not supported by the current available evidence.

**Antibiotics**

The natural course of severe acute pancreatitis progresses in two phases (46). The first 14 days are characterized by the release of multiple inflammatory mediators leading to SIRS. The second phase, 2 weeks after the onset of disease, is dominated by an anti-inflammatory state with inhibition of immune system leading to sepsis-related complications and possibly, infected pancreatic necrosis. It occurs in up to 70% of patients with necrotizing pancreatitis and has become the most important risk factor for death. In patients with necrotizing pancreatitis, the proportion of patients with proven infected necrosis at the time of surgery increased from 22% to 24% after the first week, from 36% to 55% after the second week, and up to 72% after the third week. The extent of pancreatic necrosis may also be associated with increased infection rates in patients with more than 50% necrosis of the pancreas (47).

Mortality rates in sterile necrotizing pancreatitis range from 10% to 15% (48), while infected pancreatic necrosis carries mortality rates between 30% and 50% (48). The extent of necrosis in patients with sterile lesions correlates with the presence of organ failure, whereas infected necrosis is associated with organ failure regardless of the extent of necrosis (49).

The bacterial spectrum of infection in acute necrotizing pancreatitis has been described as Enterococci, gram-negative bacteria, and fungi (50). Bacterial translocation from the gut has been demonstrated to play a vital role in necrotizing pancreatitis (51). After the administration of antibiotics with primary efficacy against gram-negative and anaerobic bacteria, the spectrum changes to gram-positive infection (46). These infections do not originate in the gut, but rather are nosocomial infections acquired via venous catheters, urinary catheters, or endotracheal tubes (52). Hospital-acquired infections tend to occur much later (typically after 20 days) while infections with gram-negative organisms occur sooner, usually within 2 weeks of admission (46).

The use of prophylactic in necrotizing pancreatitis has been extensively studied. Most studies utilized a carbapenem, imipenem, as it has high pancreatic tissue concentration and the highest bactericidal activity against most of the organisms in pancreatic infections. The data are anecdotal with reduced mortality and infection rates reported by some studies (53,54) while others have found no significant clinical benefit (55,56). The results vary on inclusion and exclusion criteria, and the focus of each series. A recent meta-analysis demonstrated that the timing of administration may determine the clinical outcome (57). By including only RCTs in which antibiotics were administered early (within 72 hours from the onset of symptoms or hospital admission), the mortality rates (7.4% vs. 14.4%) and incidence of infected pancreatic necrosis (16%
vs. 25%) were significantly reduced in patients receiving prophylactic antibiotics. It was also shown that antibiotic prophylaxis does not result in increased incidence of fungal infections (58). The possibility of concomitant existence of cholangitis in addition to pancreatitis has to be entertained when dealing with biliary obstruction. In such cases, antibiotics have an essential role in the therapy. Our recommendation at this time pending definitive studies is to use carbapenem-based antibiotics early in the disease process.

**SURGICAL MANAGEMENT**

Most episodes of acute pancreatitis are mild and resolve spontaneously within 3 to 5 days. The mortality rate in these patients is less than 1% and they do not routinely require intensive care or surgical management. However, operative intervention is needed in certain cases to prevent recurrences and manage complications (59,60).

**Biliary Pancreatitis**

Occasionally, a common bile duct (CBD) stone may become impacted at the ampulla of Vater, leading to biliary pancreatitis. Typically, the highest serum amylase levels are seen initially, but they return relatively rapidly to normal, as do clinical signs and symptoms. The treatment of gallstone pancreatitis should be guided by the severity of disease. Patients presenting with cholangitis, severe acute gallstone pancreatitis, and obstructive jaundice should undergo urgent ERCP and, if choledocholithiasis is confirmed, endoscopic sphincterotomy should be performed (16). ERCP significantly reduces both the overall complication and mortality rates in patients with severe biliary pancreatitis (54,61). However, ERCP and endoscopic sphincterotomy have no influence on the outcome of mild biliary pancreatitis (61). Should ERCP be considered in a critically ill patient, then it has to be done early in the disease process. ERCP performed after 72 hours of the onset of symptoms will unlikely improve the outcomes.

If there is failure to retrieve the stones during ERCP in a stable patient, bile duct exploration with stone removal needs to be completed at the time of cholecystectomy, and is safely performed laparoscopically in nearly all cases. If ERCP is not previously attempted, CBD stones identified during laparoscopic cholecystectomy by intraoperative cholangiogram can be retrieved by postoperative ERCP. This alternative is preferred if the surgeon is not comfortable in safely performing laparoscopic transcytic CBD exploration. Open cholecystectomy with supraduodenal bile duct exploration is also an option, but should be avoided due to high complication rates (59).

Recurrence of acute pancreatitis in patients with cholelithiasis has been reported in 29% to 63% after hospital discharge without a definitive treatment. The rationale for cholecystectomy and clearance of the CBD is to prevent recurrent biliary pancreatitis. In mild gallstone pancreatitis, cholecystectomy should be performed during the same hospital stay following recovery from the acute event. Patients with mild gallstone pancreatitis should be admitted directly to a surgical service instead of a medical team. Evidence suggests that this results in decreased time for surgery (44 vs. 80 hours), shortened hospital stay (3 vs. 5 days) and lower hospital costs ($11,492 vs. $16,183) (62). In severe gallstone pancreatitis, cholecystectomy should be performed once the inflammatory process has subsided to make the procedure technically feasible and safe. If ERCP and endoscopic sphincterotomy is performed, cholecystectomy should be performed within 6 weeks (63).

MRCP can be used to select patients that might still have CBD stones prior to cholecystectomy. In a study by our group, we found that MRCP had a sensitivity of 100% and an accuracy of 92% in detecting CBD stones in patients recovering from gallstone pancreatitis (64). We advocate that patients with a negative MRCP will not need a preoperative ERCP. Patients with positive MRCP will need a preoperative ERCP to clear the duct. In our opinion, this approach will cut on unnecessary ERCP and will avoid intraoperative issues when dealing with a positive intraoperative cholangiogram (64).

**Vascular Complications**

The systemic vascular effects of acute pancreatitis are related to the release of pancreatic proteases, such as trypsin, which activate complement C5a and precipitate the coagulation cascade, granulocyte aggregation and leukoembolization of vital tissues, such as the lung, kidney, and splanchnic and systemic vascular beds. These events lead to the respiratory distress syndromes, including pulmonary emboli, renal insufficiency, and splanchnic venous thrombosis (65).

Also, there are local arterial and venous complications of pancreatitis. Bleeding from pancreatic pseudocysts and ruptured pseudoaneurysms carries mortality rates of 25% to 40% (66). Bleeding may present as melena from erosion into the proximal gastrointestinal tract or as hypovolemia and abdominal pain if there is rupture into the peritoneal cavity. Diagnosis is usually late or only at postmortem examination. Most patients with gastrointestinal tract bleeding secondary to acute or chronic pancreatitis are alcoholics. Other causes of gastrointestinal bleeding in this population include peptic ulcer disease, gastritis, varices, and Mallory–Weiss tear. The development of pseudoaneurysms is probably related to severe inflammation and enzymatic autodigestion of the pancreatic and peripancreatic arteries. With growth and expansion, pseudoaneurysms may rupture into pseudocysts, adjacent visceria, peritoneal cavity, or pancreatic duct.

The most common vessel involved in splanchnic pseudoaneurysms related to pancreatitis is the splenic artery, followed by the gastroduodenal and the inferior pancreaticoduodenal (67). Pseudoaneurysms may be frequent in up to 10% of patients with chronic pancreatitis, but bleeding rarely occurs unless are associated with pseudocysts. The diagnosis of ruptured pseudoaneurysms requires a high index of suspicion. Diagnostic and therapeutic tools include emergency upper endoscopy, selective visceral angiography, US, and CT scanning. Currently, the best method of assessing a relatively stable patient is CT angiogram with or without a formal angiogram. This provides an accurate diagnosis but also allows, if required, radiologic intervention by embolization of the feeding vessel or the pseudoaneurysm itself (Fig. 128.1) (68). If visceral ischemia distal to the pseudoaneurysm is a concern, a stent may be placed (69). Control can be rendered by either selective arterial vasopressin infusion, angioembolization with Gel foam, detachable intravascular balloons, Gianturco coils, or polymerizing adhesives. Surgical control is only indicated for immediate life-threatening bleeding or failure of interventional
radiology approach or need for management of other coexisting abdominal pathologies (68). However, it is emphasized that control of bleeding from a ruptured visceral aneurysm in the setting of pancreatitis is rarely achieved in the operating room due to the severe inflammatory process. In most cases, the only option available to the surgeon is packing the area and immediate transfer to the radiology suite for embolization.

Hemoductal pancreatitis (or hemosuccus pancreatitis) occurs when a pseudoaneurysm ruptures into the pancreatic duct. It usually encompasses the triad of gastrointestinal bleeding, pancreatitis with epigastric pain, and partial CBD obstruction (70). The diagnosis can be confirmed by selective visceral angiography or ERCP. The treatment of this rare complication requires ligation of the pseudoaneurysm and possible pancreatic resection.

Venous thrombosis of the portal vein is a potential complication of acute or chronic pancreatitis. The clinical course is complicated by acute decompensation, hypotension with sequestration in the vascular bed, acidosis, hepatic enzyme elevation, coagulopathy, and venous infarction of the bowel. Patients who survive this insult develop portal hypertension, and some present months to years later with bleeding esophageal varices. Selective splenic venous thrombosis occurs more frequently, and patients usually present with splenomegaly, unexplained blood loss, pain in the left upper quadrant and subscapular area, and possibly, cardiovascular collapse secondary to the subscapular hematoma. The treatment is splenectomy with preoperative vascular control by angiographic techniques.

During drainage procedures for pancreatic pseudocysts in the presence of associated splenic venous thrombosis, the transgastric approach should be avoided in order to decrease postoperative bleeding from the rich submucosal plexus of high-pressure veins. In the absence of bleeding gastric varices, one may elect to leave the spleen in situ even with splenic vein thrombosis, because not all patients develop bleeding from gastric varices.

**Pancreatic Pseudocyst**

Peripancreatic fluid collections can occur as a result of acute pancreatitis, chronic pancreatitis, surgery (either pancreatic or other abdominal surgery), trauma or neoplasia. With the exception of a cystic neoplasm, peripancreatic fluid collections form either as a result of a disrupted pancreatic ductal system with subsequent fluid leakage or maturation of peripancreatic necrosis. An acute peripancreatic fluid collection (APFC) is located in or near the pancreas; occurs early in the course of acute pancreatitis and always lacks a wall of granulation or fibrous tissue (Table 128.1) (34). APFC is common in patients with severe acute pancreatitis, and more than half of these lesions regress spontaneously.

Pseudocyst is defined as a collection of pancreatic juice that is enclosed by a nonepithelialized wall composed of either fibrous or granulation tissue. It is a frequent complication in acute pancreatitis (10% to 20% of cases) and chronic pancreatitis (20% to 40% of cases) (71). Formation of an acute pseudocyst requires 4 or more weeks from the onset of acute pancreatitis (Table 128.1). It is critical to distinguish a pseudocyst from a pancreatic fluid collection prior to intervention.

The patient usually presents with persistent abdominal or back pain, bloating, early satiety, nausea, vomiting or failure to thrive after an episode of pancreatitis. In few cases, biliary obstruction may ensue if pseudocyst is located in the head of the pancreas. Not uncommonly, a pseudocyst may be asymptomatic and discovered incidentally on imaging studies. The contents are usually rich in pancreatic enzymes and are most often sterile. Bacteria may be present in pseudocysts but often are of no clinical significance. When pus is present, the lesion is termed pancreatic abscess. The distinction between pancreatic abscess and infected necrosis is critical for two reasons: the mortality risk for infected necrosis is double than for pancreatic abscess and specific therapy for each condition may be remarkably different.

Pseudocysts are usually diagnosed by imaging studies, either contrast-enhanced CT scan or US. On CT scan, a pseudocyst appears as a well-circumscribed, rounded lesion with homogeneous fluid density and thickened hyperdense capsule (Fig. 128.2). The initial step in planning intervention is to define the underlying pancreatic ductal anatomy with MRCP.
(or ERCP) and its relationship to surrounding structures. Failure to address pancreatic ductal involvement may result in postoperative failure and recurrence. Distinguishing a pseudocyst from other pancreatic cystic neoplasms is also essential and can be made by initial imaging studies and a detailed history of the patient. The traditional management of pancreatic pseudocyst has been based for decades on a report by Bradley et al. (72) who found spontaneous resolution of the pseudocyst in 24 of 54 patients. This spontaneous resolution occurred most frequently in collections less than 6 cm and/or those resolved within 6 weeks of follow-up. Thus, historically, intervention has been advisable in pseudocysts larger than 6 cm that persist beyond 6 weeks. However, recent experience showed that conservative approach even in these circumstances might be occasionally acceptable.

There are three options for drainage a pseudocyst: percutaneous, endoscopic, and operative. Percutaneous drainage has shown good short-term results, with 84% success rate and 6% recurrence rate (73). However, the prolonged presence of an indwelling catheter, and increased risk for infection and fistula formation remain disadvantages of this technique.

Endoscopic drainage has become the gold-standard method and can be performed either transpanillary or transmurally (cystogastrostomy or cystoduodenostomy). The decision depends on the size of the collection, proximity to the stomach or duodenum, and ability to enter the pancreatic duct and/or reach the area of disruption (74). If pseudocyst communicates with main pancreatic duct, transpanillary drainage can be performed by placing stent across the leak with or without sphincterotomy (75). This approach is useful for collections not accessible transmurally and avoids bleeding and perforation. However, it may lead to scarring the main pancreatic duct. Transmural approach is performed by using electrocautery or needle at a point of extrinsic compression visible endoscopically (74,76). EUS can be used to help demonstrate the collection in cases of difficult access based on CT scan, varices, or absence of extrinsic compression. Resolution can be achieved in nearly 90% of patients, with morbidity rates of 9% to 25% and recurrence rates of 5% to 20% (77,78).

Cystogastrostomy and cystoduodenostomy can also be performed open or laparoscopically, and offers wider drainage and better hemostasis than endoscopic approach. Anterior gastrostomy is performed for access to the posterior gastric wall. Biopsy of the cyst wall is advised in all cases to rule out a cystic neoplasm. Open or laparoscopic Roux-en-Y cystoenterostomies are also used for drainage of a pseudocyst not adherent to the stomach or duodenum. The morbidity rate ranges from 7% to 37% and mortality rates vary from 0% to 6% (79). The recurrence rate with the operative technique is approximately 10% (80). A recent RCT showed equal efficacy of endoscopic and surgical cystogastrostomies regarding recurrence and mortality rates, however shorter hospital stay and lower costs in the endoscopic group (81). The limitation of this study is that the surgical group was composed only by open approach, thereby not taking into account the benefits of laparoscopic surgery. In fact, laparoscopic cystogastrostomy is associated with shorter operating time and hospital stay, and lower morbidity as compared to open drainage (82).

In patients with disconnected pancreatic ducts at the tail of the pancreas, operative intervention with distal pancreatectomy offers better long-term outcomes than cystoenterostomies. At our Institution, patients are initially treated with internal drainage; either transpapillary or transmurally, depending on the ductal anatomy, and surgical drainage is reserved for failure or complication of these methods.

**Biliary Obstruction due to Pancreatic Inflammation**

Biliary obstruction may be found in as many as 25% of cases presenting with acute pancreatitis, and this obstruction, caused by pancreatic swelling, can be confused with a stone lodged at the ampulla. The intrapancreatic portion of the CBD becomes involved in the inflammatory process, but this usually resolves over the course of the disease. If the biliary obstruction does not resolve, a workup including US, ERCP, or transhepatic cholangiography may be necessary to define the anatomy. If the patient develops cholangitis and becomes septic from infected bile in the obstructed duct, ERCP or transhepatic cholangiography is needed for decompression.

**Pancreatic Fistulas**

The inflammatory process of acute pancreatitis may result in disrupted ductal epithelium leading to ductal leak. Leaks are traditionally classified as internal or external. The former present as pancreatic ascites, pleural effusions, pseudocysts, and rarely to small bowel or colon (Fig. 128.3), whereas the latter as pancreaticocutaneous fistulas and are mostly iatrogenic in etiology (83).

The management of pancreatic duct disruptions (PDDs) may be challenging and should include a multidisciplinary team of expert endoscopists, interventional radiologists, and hepatobiliary surgeons. Most of the conditions secondary to PDDs will resolve spontaneously within few weeks with conservative therapy alone. CT scan with pancreas protocol (three phases; arterial, late arterial, and venous) is the initial study of choice. In cases of equivocal findings, MRCP appears as an accurate method.
and noninvasive option to depict ductal anatomy. ERCP is usually avoided in the acute setting due to increased risk of postprocedure pancreatitis and infection via instrumentation. Patients with pleural effusion should be managed with repeated thoracentesis or tube thoracostomy. Initial management includes bowel rest, nutrition support, and possibly octreotide. If conservative management fails, ERCP with stenting is the next step. Stenting is not effective in leaks with complete transection of the main pancreatic duct. For persistent pancreatic pleural fistula, a Roux-en-Y limb pancreaticojejunostomy may be needed to the base of the fistula. Similarly, initial management for pancreatic ascites is conservative, involving large volume paracentesis followed by ERCP with stenting in persistent cases. If no improvement, operative management depends on ductal anatomy: (i) if ductal disruption without pseudocyst, internal drainage with Roux-en-Y limb is the procedure of choice; (ii) PDD in the tail of the pancreas may require distal pancreatectomy; and (iii) ruptured pseudocyst is better managed with drainage procedures via cystogastrostomy or Roux-en-Y cystojejunostomy (83).

Pancreatic Necrosis: Sterile and Infected

The release of activated pancreatic enzymes autodigest the gland and surrounding retroperitoneal tissue and convert acute interstitial edematous pancreatitis to pancreatic necrosis, also termed as necrotizing pancreatitis (Fig. 128.4). Concurrently, venous thrombosis and erosion to the small peripancreatic vessels may lead to hemorrhagic necrotizing pancreatitis. Infected is responsible for late deterioration, organ dysfunction, and mortality rates up to 30% (59). It is rare that septic complications ensue within the first week of presentation, but not unusual after the second week, and they are almost universally present if the patient’s course requires therapy for more than 3 weeks. Clinical signs of abdominal pain, fever, leukocytosis, associated with severe systemic manifestations of hypotension, cardiovascular collapse, pulmonary insufficiency, and renal failure suggest the onset of this complication. Differentiating infected pancreatic necrosis from other sources of systemic illness such as pneumonia, urinary tract, and catheter-related infections may often times be challenging.

Sequential contrast-enhanced CT scan is the best tool available for diagnosis and follow-up. Abscess formation is suspected if air is present in the phlegmon (Fig. 128.5). Percutaneous fine-needle aspiration of the intrapancreatic or peripancreatic fluid collections is routinely advised to confirm bacterial contamination. Conservative management without necrosectomy is the standard approach in cases of sterile necrosis and hemodynamic stability whereas infected necrosis has been historically considered an absolute indication for necrosectomy.

The treatment of sterile necrosis is conservative and expectant. Most patients will improve without intervention. However, urgent intervention and debridement is indicated in a patient that is deteriorating on conservative management. Operative management is warranted in patients that have become unstable or in the presence of symptoms. Severe pain, vomiting, and intolerance to food intake are not uncommon. Drainage and debridement might be necessary in patients with severe pain. Our approach in patients that are not tolerating feedings secondary to vomiting is to insert percutaneous gastrostomy for drainage of the stomach and placing a percutaneous gastrojejunostomy for feeding until the necrosis improve.

The open surgical debridement remains the gold-standard approach for infected necrotizing pancreatitis. However, in the last 20 years, its role is decreasing with the introduction of minimally invasive techniques or, even conservative management with antibiotics alone (84–88). A recent meta-analysis showed that nearly two-thirds of the patients with infected pancreatic necrosis improved with conservative management alone, which included supportive management, antimicrobial therapy with or without percutaneous drainage, and only one-fourth of patients required additional surgical procedures for necrosectomy (89).

Minimally invasive techniques for draining infected fluid and debris include percutaneous, endoscopic, retroperitoneal, or laparoscopic approaches (Table 128.3). There are several available options for percutaneous drainage, including drainage alone, combined aggressive irrigation and drainage, and percutaneous drainage with the use of accessories such as snares and baskets for debridement (90). Early reports on the use of percutaneous drainage of infected pancreatic tissue were not encouraging with 33% mortality and failure rates of...
In patients with respiratory failure, the success rates decrease if the collection is mainly fluid such as an abscess, drainage is quite effective. Van Sonnenberg et al. reported a success rate of 86% when dealing with an abscess and not infected tissue (94). In contrast to drainage alone where no debridement is undertaken, we have proposed percutaneous lavage that consists of active debridement and removal of infected tissue two to three times per week in the radiology suite (95). We reported our results based on 63 consecutive patients with infected pancreatic necrosis. Mortality and overall success rates of this technique were 8% and 77%, respectively (95). Catheters are removed once the drainage becomes minimal and the cavity becomes small. This approach is intensive, time-consuming and is especially suitable for stable patients. In patients with respiratory failure, the success rates decreases to 47% (95). In this population, transporting an intubated patient with organ failure to the radiology suite several times per week is a limitation of the technique. However, when successful, this approach may avoid a major operative debridement. The presence of internal fistulas is another complication of this technique. In our study, 23% of the patients had internal fistula, either to the colon or small bowel (Fig. 128.3). All these fistulas closed spontaneously and posed no clinical significance. The tube feedings were continued in these patients with good tolerance. The utilization of snares and Dormia baskets has also been reported for debridement along with continuous lavage and drainage of infected pancreatic necrosis with success rates ranging from 65% to 100% (96–98). These techniques can aid in the debridement process.

Percutaneous drains can also be placed preoperatively to guide further insertion of a videoscope and allow lavage and removal of necrotic material under direct visualization. This technique is termed “step-up approach.” Initial experience was encouraging with mortality and success rates of 10% and 73%, respectively (99). The technique has improved over the years, including insertion of a videoscope through a port located in a small subcostal flank incision and debridement performed with a long laparoscopic forceps inserted through a second port (100). The so-called videoscopic-assisted retroperitoneal debridement (VARD) has shown success rates from 66% to 80% and mortality rates from 0% to 27% (100–102). Compared to open necrosectomy, VARD reduced complications rates, including new-onset multiorgan failure, enterocutaneous fistula, new-onset diabetes, and bleeding (103). More recently, a single-stage retroperitoneal approach has been introduced. It consists of retroperitoneoscopic anatomical necrosectomy (REAN) in which three trocars are utilized. The perirenal space is entered through the posterior pararenal space. Dissection proceeded from posterior to anterior direction to expose the dorsal side of the perirenal fascia, which is opened to expose peripancreatic abscess (104). Then, necrotic tissue is debrided and catheter drainage is secured. The feasibility and safety of the technique has been reported but further clinical experience is warranted.

Currently, surgery for severe pancreatitis should be deferred as long as the patient continues to respond favorably to conservative management. Early operation directed toward debridement of devitalized tissue to prevent septic complications has proven to increase morbidity. The rationale for delaying surgical therapy is to permit proper demarcation of WOPN to occur, limiting the extent of surgery (39). This approach decreases the risk of bleeding, wound complications, gastrointestinal fistulas, and minimizes the surgery-related loss of vital tissue that predisposes to endocrine and exocrine pancreatic insufficiency. Traditionally, three techniques for open necrosectomy have been used with comparable results: open necrosectomy with closed continuous lavage of the retroperitoneum; open necrosectomy that may or may not be staged with planned re-laparotomies followed by delayed primary closure; and open necrosectomy, often with marsupialization, with open packing and planned re-laparotomies. These approaches are associated with postoperative mortality ranging from 12% to 56%, but there is no trial that prospectively compared these techniques (90,105).

Laparoscopic transgastric necrosectomy has been introduced as a novel approach in attempt to overcome some of complications of open surgery. It may provide adequate

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**TABLE 128.3 Current Therapeutic Approaches for Infected Necrotizing Pancreatitis**

<table>
<thead>
<tr>
<th>Category</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conservative</strong></td>
<td>• May be attractive approach in two settings:</td>
</tr>
<tr>
<td></td>
<td>- As initial management to postpone further intervention in a later stage</td>
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<tr>
<td></td>
<td>- To avoid surgery altogether</td>
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<tr>
<td></td>
<td>• Limited in critically ill patients</td>
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<tr>
<td></td>
<td>• Mortality rates similar to other approaches</td>
</tr>
<tr>
<td></td>
<td>• Limited reported experience</td>
</tr>
<tr>
<td><strong>Percutaneous drainage</strong></td>
<td>High success rates in stable patients (70-80%) and offers low morbidity</td>
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<tr>
<td></td>
<td>• Requires interventional radiology expertise</td>
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<tr>
<td></td>
<td>• Slow and time-consuming</td>
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<tr>
<td></td>
<td>• Limited in critically ill patients with multiple organ failure</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of fistula</td>
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<tr>
<td><strong>Endoscopic</strong></td>
<td>Endoscopic transgastric necrosectomy</td>
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<tr>
<td></td>
<td>• May offer adjunct therapy prior to surgical debridement</td>
</tr>
<tr>
<td></td>
<td>• Suitable in poor risk surgical candidates</td>
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<tr>
<td></td>
<td>• Less risk for fistulas</td>
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<tr>
<td></td>
<td>• Need of repeated procedures</td>
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<tr>
<td></td>
<td>• Need to be anatomically accessible</td>
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<tr>
<td><strong>Surgical</strong></td>
<td>Laparoscopic transgastric necrosectomy</td>
</tr>
<tr>
<td></td>
<td>• Allows wider drainage (lesser sac, paracolic gutter, perinephric, retroduodenal spaces)</td>
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<tr>
<td></td>
<td>• Short term; avoids multiple procedures compared to other noninvasive approaches</td>
</tr>
<tr>
<td></td>
<td>• Risk of intraperitoneal infection transmission rate (30-40%)</td>
</tr>
<tr>
<td></td>
<td>• Pneumoperitoneum not tolerated by critically ill patients</td>
</tr>
<tr>
<td></td>
<td>Open necrosectomy</td>
</tr>
<tr>
<td></td>
<td>• Remains largely performed worldwide but role is decreasing</td>
</tr>
<tr>
<td></td>
<td>- with the introduction of minimally invasive techniques</td>
</tr>
<tr>
<td></td>
<td>• Used after failure of less invasive approaches</td>
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<tr>
<td></td>
<td>• Used in critically ill patients with multiple organ failure</td>
</tr>
<tr>
<td></td>
<td>• Savage procedure</td>
</tr>
<tr>
<td></td>
<td>• Mortality rate: 12–56%</td>
</tr>
<tr>
<td><strong>Combined</strong></td>
<td>Videoendoscopic-assisted retroperitoneal debridement (VARD)</td>
</tr>
<tr>
<td></td>
<td>• Percutaneous followed by minimally invasive retroperitoneal debridement: step-up approach</td>
</tr>
<tr>
<td></td>
<td>• Allows access to endoscopically inaccessible areas</td>
</tr>
<tr>
<td></td>
<td>• Good option in critically ill patients</td>
</tr>
<tr>
<td></td>
<td>• No intraperitoneal infection transmission</td>
</tr>
<tr>
<td></td>
<td>• Lower bleeding risk than endoscopy</td>
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</tbody>
</table>

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Note: The table above lists various therapeutic approaches for infected necrotizing pancreatitis, including conservative, percutaneous drainage, endoscopic, and surgical methods. Each approach has its own advantages and limitations, and the choice of treatment depends on the patient's condition and the extent of the necrosis.
sive technique. Based on large series of patients and randomized clinical trials dedicated multidisciplinary team of endoscopists, interventional radiologists, and surgeons. Further clinical experience based on large series of patients and randomized clinical trials are desirable to define the exact role of each minimally invasive technique.

Key Points

- Acute pancreatitis is a potentially lethal disease with considerable morbidity and mortality.
- The estimated cost of hospitalization for these patients to the US health system is around $2.6 billion annually.
- Acute pancreatitis is divided into acute interstitial pancreatitis and necrotizing pancreatitis.
- Late collections (>4 weeks) in interstitial and necrotizing pancreatitis are referred as pancreatic pseudocysts and WOPN, respectively.
- Endoscopic drainage has become the gold-standard therapy for pseudocysts and can be performed either via cystogastrostomy or cystoduodenostomy.
- Surgical cystogastrostomy and cystoduodenostomy can also be performed open or laparoscopically, and offers wider drainage and better hemostasis than endoscopic approach.
- The management of pancreatic necrosis has suffered a paradigm shift from open surgical debridement to minimally invasive approaches, and selecting the optimal patient is key for success of each technique.
- Surgery for severe pancreatitis should be deferred as long as the patient continues to respond favorably to conservative management. Early operation directed toward debridement of devitalized tissue to prevent septic complications has proven to increase morbidity.

CONCLUSION

Acute pancreatitis is a potentially lethal disease with considerable morbidity and mortality. There are two major types: interstitial and necrotizing. The role of the optimal forms of nutrition and antibiotic regimens are still under debate. The management of pancreatic necrosis has suffered a paradigm shift from open surgical debridement to minimally invasive approaches, and selecting the optimal patient is the key for success of each technique. Currently, these new technologies are only offered in tertiary centers with an experienced and dedicated multidisciplinary team of endoscopists, interventional radiologists, and surgeons. Further clinical experience based on large series of patients and randomized clinical trials are desirable to define the exact role of each minimally invasive technique.

References


