Inflammatory diseases of the pancreas have a wide range of clinical presentations and disease states. Over the last 10 years, clinical and laboratory investigations have improved our understanding of these diseases, and unlike in the past, when surgical dogma or folklore reigned, basic investigation and clinical trials have provided us with levels of scientific evidence not available previously. In this new era, the surgeon must be knowledgeable about recent advances and exercise sound clinical judgment. For instance, in necrotizing pancreatitis, secondary pancreatic infection was previously considered an absolute indication for immediate pancreatic débridement. Currently, a more circumspect approach is advocated in which the surgeon carefully evaluates an individual patient’s response to the infection while guiding the patient through a series of graded interventions from simple percutaneous drainage through pancreatic débridement (the “step-up” approach). In the surgical treatment of small duct chronic pancreatitis, several centers are actively investigating the applicability of using total pancreatectomy with autologous islet cell transplantation in this setting. Acute and chronic pancreatitis, although rarely present in the same patient (acute or chronic pancreatitis), are two separate disease entities with unique laboratory and radiographic investigations, operations, and postoperative care. For these reasons, this chapter is divided into two independent but sequential sections.

**Acute Pancreatitis**

Acute pancreatitis is a common disease affecting approximately 275,000 patients per year in the United States, and the surgeon is usually contacted to see them in the emergency department or as a surgical consultation on the medical ward. This number has increased steadily over the past 20 years, perhaps due to the obesity epidemic in this country and a corresponding rise in gallstone-related biliary pancreatitis. As a consequence of this escalation, acute pancreatitis is now the most common gastrointestinal discharge diagnosis in US hospitals. Although the overall mortality rate associated with acute pancreatitis is in the range of 2 to 5%, this rate varies greatly depending on the etiology of the pancreatitis, the development of complications of pancreatic necrosis, and the number and severity of comorbid medical conditions. There are four main goals in the treatment of acute pancreatitis: (1) to provide supportive medical care; (2) to minimize or reduce pancreatic necrosis and the associated systemic inflammatory response; (3) to recognize and treat local complications of the disease (i.e., peripancreatic fluid collections, abscess, pseudocysts, biliary and gastric obstruction); and (4) to identify the underlying etiology to prevent subsequent episodes of acute pancreatitis [see Figure 1].

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Financial disclosure information is located at the end of this chapter before the references.

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**INITIAL CLINICAL EVALUATION**

**History**

A careful history is the first step in establishing a correct diagnosis. The pain of acute pancreatitis is characteristically abrupt in onset (occasionally waking the patient from sleep), severe in intensity, boring and constant in character, and upper abdominal (supra umbilical) in location. The pain is frequently described as radiating to the back, chest, flanks, or upper quadrant and is commonly described by patients as “the worst pain [they] have ever experienced.” Nausea and vomiting are prominent associated features related to the accompanying paralytic ileus. Fever is frequently present and reflects the inflammatory nature of the underlying disease state. Although pain is a common finding, it should be emphasized that acute pancreatitis can also occur without abdominal pain in patients who present to the emergency department with shock of unknown origin or mental status changes or in patients who are early in the postoperative period from major abdominal or chest surgery, when postoperative use of intravenous analgesics often masks their symptoms.

The patient's past medical history should be carefully assessed for clues as to the etiology of the disease by inquiring about previous bouts of pancreatitis, previous episodes of biliary colic, hyperlipidemia, parathyroid disease, abdominal trauma, or past endoscopic manipulations (i.e., endoscopic retrograde cholangiopancreatography [ERCP], sphincterotomy, or pancreatic duct stenting). The patient's use of alcohol and tobacco should be elicited. The presence of previous biliary symptoms (e.g., episodic, colicky right upper quadrant abdominal pain associated with fatty food intake) or a previous history of gallstones or cholecystectomy should be sought. Not infrequently, patients with biliary pancreatitis will often admit to previous bouts of biliary colic they wrote off as indigestion. A careful review of the patient’s home medications (medical reconciliation) should be done, focusing carefully on those that have been association with the development of pancreatitis.

**Physical Examination**

After obtaining a history, a careful physical examination should be performed. Inspection of patients often finds them lying in bed in moderate distress. Their mucous membranes are dry and their eyes are sunken. Note the presence or absence of scleral icterus, a manifestation of biliary tract disease. The abdomen is usually mild to moderately distended and symmetrical. Bluish discolorations around the umbilicus (Cullen sign) and a blue-gray discoloration of the abdominal flanks (Grey-Turner sign), although renowned in surgical recall pocketbooks, are rare findings. Auscultation reveals decreased breath sounds at the lung bases (reflective of sympathetic pleural effusions characteristically larger on the left than the right). Typically, an ileus is present, causing...
Gallstone etiology – Laparoscopic cholecystectomy with intraoperative cholangiogram

Admit to hospital - ward bed
- IV hydration
- ± NG tube decompression
- Pain control
- Adequate oxygenation
- Identify etiology of pancreatitis

Patient has suspected acute pancreatitis
Obtain history: focus on past medical history, medication use, and social history to identify possible etiologic factors for acute pancreatitis

Perform physical examination focusing on HEENT, chest, and abdominal examination

Establishing the diagnosis and risk stratification
- Specific blood tests to identify pancreatic inflammation (elevated amylase/lipase, CRP)
- Imaging tests to exclude other diagnoses, confirm the diagnosis of acute pancreatitis, and assess disease severity (CECT)
- Quantitate disease severity (CTSI, APACHE II) and organ dysfunction (SOFA)

Mild Acute Pancreatitis (≈ 80%)
No SIRS, mild reversible organ failure, no necrosis on DPHCT

Acute Pancreatitis Indeterminate Severity (≈ 5%)
Treat like SNP until severity becomes apparent

Severe Necrotizing Pancreatitis (≈ 20%)
SIRS, Organ failure, necrosis on DPHCT

Admit to hospital - ward bed:
- Monitoring lines
- Large-volume resuscitation
- Organ support (cardiac, pulmonary, renal)
- Enteral nutrition
- Pain control
- Antibiotic given on demand
- Identify etiology of pancreatitis

Emergent ERCP ± papillotomy with stone extraction

Evidence of early cholangitis (< 48 hr) with deteriorating clinical course

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Figure 1 Diagnosis and initial treatment of acute pancreatitis. APACHE II = Acute Physiology and Chronic Health Evaluation II; CECT = contrast-enhanced computed tomography; CRP = C-reactive protein; CTSI = Computed Tomography Severity Index; DPHCT = dual-phase helical computed tomography; ERCP = endoscopic retrograde cholangiopancreatography; HEENT = head, ears, eyes, nose, and throat; ICU = intensive care unit; IV = intravenous; NG = nasogastric; SIRS = systemic inflammatory response syndrome; SNP = severe necrotizing pancreatitis; SOFA = Sequential Organ Failure Assessment.
abdominal distention, tympani, and hypoactive bowel sounds. Abdominal examination demonstrates a diffusely tender abdomen with rigidity and involuntary guarding. Palpation of the skin and subcutaneous tissue allows a clinician’s quantification of the degree of volume deficit based on the loss of skin turgor. Occasionally, patients will present in writhing abdominal pain, a rigid abdomen, and accompanying peritoneal signs mimicking an intraabdominal catastrophe.

ESTABLISHING THE DIAGNOSIS

**Laboratory Tests**

Up until this point, the patient’s clinical history, signs, and symptoms are suspicious but not diagnostic of acute pancreatitis and, in fact, are consistent with those of many other common surgical illnesses, such as perforated duodenal ulcer, mechanical small bowel obstruction, volvulus, or acute mesenteric ischemia. The diagnosis of acute pancreatitis requires two of the following three features: (1) abdominal pain suspicious for pancreatic origin, (2) serum amylase and/or lipase activity usually at least three times greater than the upper limit of normal, or (3) characteristic findings on either contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). Laboratory and/or radiologic investigations are not only essential for diagnosis but also provide important information for the stratification of disease severity [see Determining Etiology and Risk Stratification, below].

Serum pancreatic enzyme measurements are the gold standard for identifying acute pancreatitis. Amylase, lipase, elastase, and trypsin are released into the bloodstream simultaneously at the onset of the disease but are then cleared from the blood at different rates. Amylase is cleared most rapidly (<48 hours), whereas lipase and elastase remain elevated for over 96 hours. Differential serum clearance rates make the magnitude of elevation for any specific enzyme dependent on the timing of the blood draw in relation to disease onset. In acute pancreatitis, disease onset is defined as the time that the patient’s abdominal pain began, not when the patient is first evaluated by medical personnel. Many patients have been trying to manage their symptoms of abdominal pain at home for 24 to 48 hours prior to their presentation in the emergency department, placing them well into the initial stages of their disease process. Amylase traditionally has been the serum test of choice for diagnosis, although its overall sensitivity (83%) is limited by extrapancreatic causes of hyperamylasemia [see Table 1], a short serum half-life, and its unreliability in patients with chronic acinar cell damage (chronic pancreatitis). Currently, serum lipase levels greater than three times normal are the most accurate single test (sensitivity 92%) for diagnosing acute pancreatitis.

A complete blood count (CBC) with differential and platelet count, comprehensive metabolic panel, C-reactive protein (CRP) level, arterial blood gas, and serum lactate are appropriate laboratory tests to review. The purpose of these is to assess both the degree of systemic inflammatory response and the corresponding organ dysfunction in patients with acute pancreatitis. Liver function tests (alanine aminotransferase [ALT], aspartate aminotransferase, alkaline phosphatase, bilirubin) are used primarily to distinguish biliary pancreatitis from other causes of acute pancreatitis and to identify patients who may have an impacted stone at the ampulla of Vater resulting in persistent pancreatic and biliary ductal obstruction who benefit from early ERCP [see Clinical course, below]. Although a threefold or greater elevation of ALT is highly predictive of biliary pancreatitis (95% positive predictive value), only half of all patients with known gallstone pancreatitis have significant ALT elevations. CRP levels over 150 mg/L after 72 hours are closely related to necrotizing acute pancreatitis, and these levels can be useful to follow the clinical course of the disease over time.

**Imaging Studies**

Contrast-enhanced CT is the most accurate single imaging test for establishing the diagnosis, quantifying the inflammatory process, and staging the severity of the disease process [see Figure 2]. Precision in terms is essential in describing the morphology of disease states in acute pancreatitis, and this chapter uses definitions and terminology developed at the Atlanta symposium in 1992 [see Table 2]. A good-quality chest x-ray is useful to have early in the clinical course to identify a pleural effusion (poor prognostic factor) and to gauge the degree of capillary endothelial leak and associated interstitial pulmonary infiltrates, which may herald the onset of hypoxemia and pulmonary failure. In patients with known or suspected biliary pancreatitis, a right upper quadrant sonogram is useful in both identifying cholelithiasis and providing supportive evidence for choledocholithiasis based on the findings of intra- and/ or extrahepatic biliary dilatation. MRI and magnetic resonance cholangiopancreatography (MRCP) have been used extensively in Europe to diagnose the disease, but these tests are less commonly used in the United States. The benefits of MRI and MRCP over CT are the lack of ionizing radiation, better definition of solid versus liquid components of necrosis, and delineation of ductal structures. The drawbacks are limited image resolution in critically ill patients who are unable to cooperate with the study, leading to significant motion artifact in the images. Endoscopic ultrasonography (EUS) is the most sensitive imaging modality for detecting cholelithiasis and choledocholithiasis and is not limited like its counterpart, transabdominal ultrasonography, by intestinal gas or body wall edema.

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**Table 1** Nonpancreatic Causes of Hyperamylasemia

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal obstruction</td>
</tr>
<tr>
<td>Intestinal ischemia</td>
</tr>
<tr>
<td>Intestinal perforation</td>
</tr>
<tr>
<td>Common bile duct stone</td>
</tr>
<tr>
<td>Acute cholecystitis</td>
</tr>
<tr>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Macroamylasemia</td>
</tr>
<tr>
<td>Acute appendicitis</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
</tr>
<tr>
<td>Acute salpingitis</td>
</tr>
</tbody>
</table>

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Determining Etiology and Risk Stratification

After establishing the diagnosis of acute pancreatitis, determining the etiology of the disease is important for treatment and to prevent disease recurrence [see Table 3]. Taken together, biliary and alcohol etiologies represent approximately 70% of all cases of acute pancreatitis in the United States.1 Biliary pancreatitis should be suspected if gallstones are identified on a sonogram or CT scan or if the liver function tests are abnormal. Alcohol, along with medications or drugs as possible etiologies, is best assessed by a careful history. Alcoholic binge drinking is a rare cause of acute pancreatitis; more common is a patient with a moderate alcohol intake over a prolonged period of time. Drug-induced acute pancreatitis has been most closely associated with the antimetabolites 6-mercaptopurine and azathioprine; up to 4% of patients taking these drugs will develop acute pancreatitis at some point during treatment.4 Metabolic factors associated with acute pancreatitis include hypertriglyceridermia and hypercalcemia, which are identified during the laboratory evaluation. Although serum triglycerides are commonly elevated (300 to 500 mg/dL) during a bout of acute pancreatitis, in patients who have genetic disorders of lipid metabolism, triglyceride levels above 1,000 mg/dL occur, and these substantial elevations can trigger a bout of acute pancreatitis.13 Less common etiologies include pancreatic duct obstruction (pancreas divisum, sphincter of Oddi dysfunction, intraductal papillary mucinous neoplasm), ERCP-induced pancreatitis, infections, and autoimmune mechanism.

The severity of an episode of AP, as well as the disease-related morbidity and mortality, can be prognosticated using established scoring systems (Acute Physiology and Chronic Health Evaluation II [APACHE II], Glasgow Coma Scale score, Ranson criteria, BISAP score), which are based on a number of measured clinical and laboratory data points.14 A recent observation that obesity is associated with a more severe course of acute pancreatitis led to its inclusion in most scoring systems. Body mass index (BMI) is categorized as normal (score 0), overweight (BMI 26 to 30, score 1), or obese (BMI > 30, score 2). Predicting severity is important for several reasons: (1) it allows patient triage to an appropriate level of hospital care (a surgical ward versus an intensive care unit); (2) it allows objective quantification of disease severity for both clinical trial recruitment; and (3) it allows for comparison of patient outcomes between different clinical series.

Both the Glasgow and Ranson scoring systems are hampered by requiring 48 hours’ worth of data collection prior to calculation and are limited to prognosticating at this one point in time. Both scores have a low positive predictive value (below 50%) for disease severity. The APACHE II scoring has similar sensitivity and specificity to the Glasgow and Ranson systems but a greater than 90% negative predictive value for disease severity in patients with scores less than or equal to 7. Unfortunately, it has a low positive predictive value (50%) for disease severity in patients with

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**Table 2** Definitions from the Atlanta Classification of Acute Pancreatitis10

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pancreatitis</td>
<td>Acute inflammation of the pancreas</td>
</tr>
<tr>
<td>Mild acute pancreatitis</td>
<td>Minimal organ dysfunction and disease that responds to fluid administration</td>
</tr>
<tr>
<td>Severe acute pancreatitis</td>
<td>One of the following:</td>
</tr>
<tr>
<td></td>
<td>• Local complications (pancreatic necrosis, pancreatic pseudocysts, pancreatic abscess)</td>
</tr>
<tr>
<td></td>
<td>• Organ failure10,13</td>
</tr>
<tr>
<td></td>
<td>• ≥ 3 Ranson criteria</td>
</tr>
<tr>
<td></td>
<td>• ≥ 8 APACHE II points</td>
</tr>
<tr>
<td>Acute fluid collections</td>
<td>Fluid collection in or near the pancreas, occurring early in the clinical course, lacking a well-defined wall</td>
</tr>
<tr>
<td>Pancreatic necrosis</td>
<td>Nonviable pancreatic tissue diagnosed by intravenous contrast-enhanced CT scan</td>
</tr>
<tr>
<td>Acute pseudocyst</td>
<td>Fluid collection containing pancreatic secretions (high amylase level) and a well-defined wall</td>
</tr>
<tr>
<td>Pancreatic abscess</td>
<td>Collection of pus, usually near the pancreas, with little or no associated pancreatic necrosis</td>
</tr>
</tbody>
</table>

APACHE II = Acute Physiology and Chronic Health Evaluation II; CT = computed tomographic.

Figure 2  Contrast-enhanced computed tomographic scan done early after the onset of abdominal pain showing inflammation surrounding the pancreas in the retroperitoneum (yellow stars) with extension along Gerota fascia outlining the left pararenal space (white arrows).
scores above 7. Although APACHE II shows significant versatility in that it can be calculated at any time in the clinical course, and sequential scores can reveal trends in the disease state over time, the complexity of this scoring system hinders its general clinical applicability.

The bedside index of severity in acute pancreatitis or BISAP employs a simple five-variable system using BUN (blood urea nitrogen) greater than 25 mg/dL, Impaired mental status (disorientation, lethargy, somnolence, coma or stupor), SIRS (systemic inflammatory response syndrome, characterized by tachycardia, tachypnea, hypocarbia, high or low body temperature, and high or low peripheral white blood cell count), Age greater than 60 years, and the presence of a Pleural effusion. If each variable (BISAP) is given 1 point, mortality ranges from less than 1% of a BISAP score of 0 to 1 to 27% for a BISAP score of 5. The straightforward calculation and ease of use are making this the preferred multivariable scoring system in acute pancreatitis.

In many centers, the multivariable scoring systems have fallen out of favor due to the simplicity and directness of measuring a patient’s SIRS, the degree of organ failure, or the morphologic assessment of the amount of necrosis present in the retroperitoneum. SIRS is defined clinically by two or more of the following clinical criteria: pulse greater than 90 beats/min; rectal temperature less than 36.0°C (96.8°F) or greater than 38.0°C (100.4°F); white blood cell count less than 4,000 or more than 12,000/µL; and respirations greater than 20 breaths/min or carbon dioxide tension (PCO2) less than 32 mm Hg. Organ failure, the physiologic manifestation of an uncontrolled SIRS response, is most easily and reproducibly defined using the Marshall or Sequential Organ Failure Assessment (SOFA) scoring system [see Table 4]. Up to one half of the patients who eventually die of acute pancreatitis do so within the first 7 days of illness from unrelenting multiorgan dysfunction syndrome.15,16

The morphologic severity of acute pancreatitis can be defined by the Computerized Tomography Severity Index (CTSII) developed by Balthazar and colleagues7 [see Table 5]. This system assigns a numeric score to the quantity and location of necrosis and correlates in that the higher the patient’s score, the higher the disease-related morbidity and mortality rates. The most accurate and earliest markers of severity in acute pancreatitis are measuring the SIRS or the inflammatory mediators contributing to the systemic effects that are witnessed, such as granulocyte polymorphonuclear neutrophil elastase, tumor necrosis factor (TNF), interleukin-6, interleukin-8, and CRP. The most useful serum test currently available in clinical practice is CRP, with severe pancreatitis defined by a value greater than 150 mg/L within 72 hours after the onset of disease.17

**Mild acute pancreatitis** Most attacks of acute pancreatitis (80%) are of the mild, edematous variety consisting of an inflammatory disease state in the pancreatic parenchyma that is self-limited, runs its course over a 5- to 7-day period, and results in complete resolution and full constitutional recovery to the structure and function of the pancreas. The clinician’s role in treatment is to provide intravenous fluid hydration, correct electrolyte or blood glucose abnormalities, and provide adequate organ support. Intravascular and interstitial hypovolemia may require 3 to 6 L of a balanced electrolyte solution (9% saline or Ringer lactate) over the first 24 hours to correct the patient’s intravascular volume deficits. A targeted response to volume resuscitation should include lowering the patient’s pulse rate, improvement in the patient’s blood pressure, and producing a urine flow of at least 30 mL/hr. Blood glucose levels tend to rise in acute pancreatitis and may be difficult to control in the initial clinical phases of the disease. Close monitoring and aggressive blood glucose control are essential during the first 24 to 36 hours of a patient’s hospitalization. This aggressive monitoring and control has been shown to improve both morbidity and mortality in hospitalized patients.18 Patients without an underlying history of diabetes will become euglycemic as the acute bouts of pancreatitis resolves and their clinical course improves. Oxygen saturation should be measured continuously and supplemental oxygen given to maintain an arterial saturation greater than 95%. Any evidence of respiratory insufficiency requires a chest x-ray to assess for pulmonary edema, pleural effusions, or acute respiratory distress syndrome (ARDS). Narcotic analgesics are essential in patients with acute pancreatitis, and their parenteral administration ensures adequate delivery in patients during their acute illness and a period of unreliable gastrointestinal absorption. Patient-controlled analgesia is a safe and effective method to achieve pain control in a monitored setting. A nasogastric tube can often be helpful not only in relieving nausea and vomiting but also in helping to improve abdominal symptoms in patients with a paralytic ileus. Chemoprophylaxis for both hemorrhagic gastritis (gastric antisecretory medication) and deep vein thrombosis (antiagulants) is mandatory in all patients.

Patients with mild edematous acute pancreatitis improve quickly over a course of 24 to 36 hours and can then be weaned off their intravenous narcotic medication and placed on either oral narcotic analgesics or nonsteroidal antiinflammatory medication. Their diet can be advanced as tolerated.
Table 4  Organ Failure Scoring Systems Used in Acute Pancreatitis

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Parameter</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marshall scoring system</td>
<td>Respiratory</td>
<td>$P_{O_2}/F_{I_2}$</td>
<td>&gt; 400</td>
<td>301–400</td>
<td>201–300</td>
<td>101–200</td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td>Cr, $\mu$mol/L</td>
<td>≤ 134</td>
<td>134–169</td>
<td>170–310</td>
<td>311–439</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular</td>
<td>SBP, mm Hg</td>
<td>&gt; 90</td>
<td>≤ 90</td>
<td>&lt; 90</td>
<td>&lt; 90</td>
</tr>
<tr>
<td>SOFA scoring system</td>
<td>Respiratory</td>
<td>$P_{O_2}/F_{I_2}$</td>
<td>&gt; 400</td>
<td>≤ 400</td>
<td>≤ 300</td>
<td>≤ 200</td>
</tr>
<tr>
<td></td>
<td>Hematologic</td>
<td>Platelet count $\times 10^9$</td>
<td>&gt; 150</td>
<td>≤ 150</td>
<td>≤ 100</td>
<td>≤ 50</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular</td>
<td>BP, mm Hg</td>
<td>Normal</td>
<td>MAP &lt; 70</td>
<td>Dopamine &lt; 5 (any dose)</td>
<td>Dopamine &gt; 5 Epinephrine ≤ 0.1</td>
</tr>
<tr>
<td></td>
<td>Neurologic</td>
<td>GCS score</td>
<td>15</td>
<td>13–14</td>
<td>10–12</td>
<td>6–9</td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td>Creatinine mg/dL</td>
<td>&lt; 1.2</td>
<td>1.2–1.9</td>
<td>2.0–3.4</td>
<td>3.5–4.9</td>
</tr>
<tr>
<td></td>
<td>Output</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>&lt; 500 mL/day</td>
<td>&lt; 200 mL/day</td>
</tr>
</tbody>
</table>

BP = blood pressure; $F_{I_2}$ = fraction of inspired oxygen; GCS = Glasgow Coma Scale; MAP = mean arterial pressure blood pressure; $P_{O_2}$ = oxygen tension; SBP = systolic blood pressure; SOFA = Sequential Organ Failure Assessment.

Table 5  Computed Tomography Severity Index (CTSI) Grading System

<table>
<thead>
<tr>
<th>CT grade</th>
<th>Definition</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal pancreas</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>Focal, diffuse pancreatic enlargement, mild heterogeneity</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>Intrinsic and extrinsic pancreatic inflammatory changes</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>Prominent peripancreatic inflammatory changes</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>Multiple extrapancreatic fluid collections or abscesses</td>
<td>4</td>
</tr>
</tbody>
</table>

Percent pancreatic necrosis

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Pancreatic necrosis is defined as a focal or diffuse area of diminished parenchymal contrast enhancement (&lt; 50 Hounsfield units)</td>
</tr>
<tr>
<td>&lt; 33%</td>
<td></td>
</tr>
<tr>
<td>33–50%</td>
<td></td>
</tr>
<tr>
<td>&gt; 50%</td>
<td></td>
</tr>
</tbody>
</table>

Total score = CT grading score + necrosis score

0–10

CT = computed tomography.

even if their serum amylase level remains above the normal level as long as they feel hungry and have no nausea or vomiting. At this point in time, identification and treatment of the underlying etiology of pancreatitis (alcohol, biliary, hypertriglyceridemia, hypercalcemia, and medications) become the focus of treatment. Patients in whom hypertriglyceridemia or hypercalcemia are suspected require a full metabolic evaluation. In terms of drug-induced causes of pancreatitis, although most drugs have been associated with this disease, relatively few drugs have been consistently implicated as a cause of acute pancreatitis. The presence of gallstones is confirmed by either transabdominal or endoscopic ultrasonography. Patients with mild biliary pancreatitis benefit from elective laparoscopic cholecystectomy and intraoperative cholangiography after their acute pancreatic inflammation has subsided (roughly 3 to 5 days after onset) but prior to their hospital discharge (roughly 5 to 7 days after disease onset). Patients can safely undergo laparoscopic cholecystectomy in this setting without waiting for complete normalization of their laboratory values or complete resolution of their symptoms. Specific genetic testing for hereditary pancreatitis or endoscopic evaluation of the ampulla of Vater for sphincter of Oddi dysfunction should be considered after the second documented episode of acute pancreatitis (recurrent acute pancreatitis).

Severe necrotizing pancreatitis

Severe necrotizing pancreatitis accounts for the approximately 20% of all episodes of acute pancreatitis and is characterized by glandular destruction, tissue necrosis, leaking pancreatic enzymes, and a SIRS that can lead to organ failure (renal, pulmonary, hepatic, cardiovascular), local and systemic complications, and a significant mortality rate. Newer concepts related to the clinical course of patients with severe necrotizing pancreatitis emphasize that it occurs in two rather distinct clinical phases. The first phase of illness (lasting for approximately 7 days) is characterized by the host’s systemic inflammatory response to tissue injury. In this early disease phase, deaths are attributable to multiple organ dysfunction mediated predominantly by cytokines rather than infection. Aggressive critical care medicine maximizing organ support is the key treatment during this early phase of the
disease process. Volume resuscitation, organ support, enteral nutrition, and the search for a treatable cause of multiple organ dysfunction (e.g., bacteremia, pneumonia, ischemic colitis, and gangrenous cholecystitis) are the main focus of treatment during this disease phase. If antibiotics are used in this setting, they are targeted at active sites of infection (e.g., bacteremia, pneumonia, gangrenous cholecystitis) or started empirically (“on demand”) for a 72-hour course in a critically ill patient who is spiking fevers or deteriorating clinically. Recommended antibiotics include either ciprofloxacin 400 mg twice a day plus metronidazole 500 mg twice a day or meropenem 1g intravenously every 8 hours. A second disease phase occurs after the initial SIRS response has subsided and lasts for approximately 3 weeks (postpancreatitis days 8 to 30). During this second disease phase, patients can progress along several different clinical paths: to disease resolution, stagnation (symptomatic necrosis), or the development of local complications (infected pancreatic necrosis, pancreatic pseudocyst). Morphologic abnormalities of the gland (both parenchyma and ductal system) and peripancreatic tissues predominate during this phase of the disease.

**Clinical course** Some patients progress quickly after their initial presentation to organ failure requiring endotracheal intubation, mechanical ventilation, and cardiovascular and renal support. The complexity of the renal response to severe acute pancreatitis involves decreased renal perfusion (prerenal) and altered renal mechanics with poor tubular function (renal and postrenal), making urine output a poor surrogate for adequate intravascular volume and resuscitation. Oliguria progressing to acute renal failure during this critical time period is often due to underresuscitation rather than intrinsic renal dysfunction. Large volumes of intravenous fluid (5 to 10 L) are sometimes needed early in the course of patients with severe disease, where their administration is often facilitated by central venous access combined with the capability of measuring right heart pressures. Neurologic manifestations of delirium and confusion are often present in the elderly and reflect the underlying consequences of hypoxemia, metabolic disturbances, and hypotension. Cardiovascular support through the use of vasoactive agents is occasionally needed to maintain adequate organ perfusion. The degree of temperature elevations early in the clinical course can often be a gauge as to the severity of the systemic inflammatory response.

Within the first 48 hours of illness, all patients with the diagnosis of severe acute pancreatitis should be evaluated for the possibility of gallstone impaction at the ampulla of Vater. Biliary pancreatitis occurs from gallstone migration from the gallbladder through the cystic and common bile ducts. In certain circumstances, gallstones can become impacted in the distal common bile duct, causing back pressure within the bile duct (acute cholangitis) and pancreatic duct (obstructive pancreatitis). Persistence of this obstruction leads to a severe course, whereas relief of this obstruction may improve the disease course. Despite a number of prospective, randomized clinical trials addressing early ERCP in patients with acute pancreatitis, methodological differences have hampered a general consensus for treatment. Despite this lack of consensus, several points are salient: (1) ERCP with or without endoscopic sphincterotomy (ES) for stone extraction should be carried out in patients with severe acute pancreatitis and evidence of cholangitis (jaundice, fever, leukocytosis, and evidence of biliary tract obstruction, i.e., a dilated common bile duct) and (2) if there is gallstone impaction at the ampulla, ERCP + ES should be done early in the clinical course (< 48 hours after onset) following the onset of acute pancreatitis. Admittedly, the devil is in the details in making this diagnosis. Often in the intensive care unit, considerable uncertainty surrounds the diagnosis of cholangitis, especially in critically ill patients with necrotizing pancreatitis. Nevertheless, careful consideration of this possibility and sound clinical judgment should be used, particularly in those patients who deteriorate following an adequate initial resuscitation.

In patients with severe acute pancreatitis, metabolic expenditure rates are extremely high and nutritional depletion occurs rapidly unless some form of nutrition support is delivered. Nutrition can be provided through both parenteral and enteral mechanisms in these critically ill patients. Total parenteral nutrition (TPN) has been advocated in the past on the belief that patients with a significant ileus from acute pancreatitis did not tolerate enteral nutrients and enteral feeding would stimulate pancreatic secretion and exacerbate trypsin-induced fat and parenchymal digestion, worsening the pancreatitis. These concerns have not been proven in clinical trials, and the use of TPN puts patients at high risk for developing catheter-associated line infections. Furthermore, microcirculatory disruptions of the insuloarterial axis make patients relatively intolerant to the high glucose and fat concentrations delivered in TPN. In contrast, the benefits of enteral nutrition (EN) are substantial; it is less expensive than TPN, maintains gut mucosal integrity, initiates housekeeping functions of the intestine and liver, sets the tone for systemic immunity, and attenuates oxidative stress and the systemic inflammatory response. In the clinical trials done to date in patients with severe acute pancreatitis, EN reduces infections, the need for surgical intervention, and the length of hospital stay more than TPN. Controversy remains over whether EN should be delivered past the ligament of Trietz (~ 40 cm) into the jejunum (nasojugal) or can be instilled directly into the stomach (nasogastric). Until further data are known, distal nasojugal feeding is the safest method, although nasogastric feeding may prove to be simpler, cheaper, and easier to use in patients with severe acute pancreatitis (SAP).

Significant controversy surrounds the use of prophylactic antibiotics in patients with SAP. Despite early, small, uncontrolled trials and a meta-analysis showing a benefit to patients with severe acute pancreatitis treated by prophylactic antibiotics, recent large, prospective, multi-institutional, placebo-controlled, double-blind, randomized trials have failed to show any benefit for antibiotic prophylaxis in preventing infection in pancreatic necrosis. Based on the equivalence in outcome between treatment and control groups in the two most recent well-designed clinical trials using a placebo-controlled group, giving antibiotics “on demand” to critically ill patients in the intensive care unit may be just as effective as giving prophylactic antibiotics in
patients with SAP.28–36 (“On demand” implies used in patients with a proven bacterial infection, a strong suspicion of a bacterial infection, or the beginning stages of SIRS.) Based on the currently available data, there is no evidence to support the routine use of prophylactic antibiotics in SAP.

Following the initial systemic inflammatory response and its associated organ failure (initial phase 1 to 14 days), the clinical course of most patients stabilizes. Their pulmonary and renal dysfunction will often improve, allowing extubation and withdrawal from renal support. Although the initial SIRS response was that of an acute febrile illness, during this phase of the disease process, a patient’s temperature elevations generally diminish or subside. It is critical at this juncture that the patient be provided with adequate EN, pulmonary toilet, and aggressive physical and occupational therapy to improve range of motion and assist with ambulation training. All intravenous lines that are not essential should be removed. Patients with a low volume of necrosis (< 30%), localized to the retroperitoneum, and confluence of necrosis from the tail toward the head (no disconnected segments, i.e., what has previously been termed “central cavitary necrosis”) often go on to resolve their pancreatic necrosis without further intervention.57 In this situation, the necrotizing process may be walled off and isolated by the host. As a result, these patients are asymptomatic (no pain, fever, normal white blood cell count) and able to eat without difficulty, and the necrosis slowly contracts over time. On contrast-enhanced imaging, this necrosis will remain present in its indolent form for months to years. Unlike patients with acute edematous pancreatitis, in whom complete structural and functional restitution occurs, these patients have parenchymal pancreatic loss with persistent structural (pancreatic duct cutoff in the neck/body of the gland) and functional (endocrine or exocrine insufficiency) abnormalities.

Fever spikes or clinical toxicity (tachycardia, hypotension, and leukocytosis) during the second stage of illness (weeks 2 to 4 from initial onset) can represent line infection, urinary tract infection, pulmonary infection, acute cholecystitis, pseudomembranous colitis, and/or infected pancreatic necrosis. All episodes of fever should be carefully investigated with routine blood cultures, urine cultures, stool cultures, chest x-ray, and intravenous line evaluation. If this surveillance fails to identify the source of infection, CT-directed fine-needle aspiration (FNA) with Gram stain and culture of the pancreatic necrosis should be pursued.38 It is critically important at this juncture to ensure that the patient’s clinical decompensation is due to infected pancreatic necrosis rather than a simple line infection as the earlier in the clinical course that one is required to intervene for infected necrosis, the greater the postoperative morbidity and mortality, and the more likely it is that multiple interventions will be necessary for complete resolution of the disease process [see Figure 3]. A positive Gram stain or culture on FNA indicates infected pancreatic necrosis that requires targeted antimicrobial (bacteria and/or fungus) treatment combined with a step-up approach to retroperitoneal intervention.40

The spectrum of antibiotics chosen to treat infected pancreatic necrosis should include coverage for both aerobic gram-negative and gram-positive bacteria and anaerobes [see Table 6]. When choosing appropriate antibiotic coverage, care should be given to consider the classes of antibiotics that have optimal penetration into pancreatic tissue.41

Secondary pancreatic infection in a patient with pancreatic necrosis in the past was considered an absolute indication for open pancreatic necrosectomy.42 Over the last decade, a more nuanced appreciation of the complex relationship between infection, the patient, and the approach and timing of intervention has developed. Currently, in critically ill patients with early-onset secondary pancreatic infection (< 2 weeks), percutaneous drainage and antibiotics can be effective until the patient’s clinical course can be stabilized to allow for definitive necrosectomy.43 A multitude of new minimally invasive techniques are available for necrosectomy, and these can optimally be delayed until the third or fourth week after disease onset, limiting the perioperative morbidity and mortality.44 Although there are scattered reports in the literature of patients with documented secondary pancreatic infections who have been treated successfully by antimicrobial therapy alone,45 most clinicians believe that intervention via a step-up approach is an important adjunct to antimicrobial therapy for optimal source control.46

In those patients considered too unstable to undergo a necrosectomy, broad-spectrum antibiotics combined with percutaneous drainage can be a useful temporizing measure to allow stabilization of a patient’s physiologic status prior to definitive débridement. At the time of necrosectomy, cultures should always be taken for aerobic, anaerobic, and fungal organisms and antibiotics modified based on these results. Cholecystectomy should be considered at the time of necrosectomy in patients with biliary pancreatitis provided that the hepatoduodenal ligament dissection is judged to be safe by the operating surgeon. If they did not have an MRCP or ERCP preoperatively, patients with a presumed biliary etiology for their pancreatitis should also have intraoperative cholangiography to visualize the extrahepatic biliary system and ensure that there are no retained stones in the common bile duct. If this cannot be completed due to inflammation or anatomic distortion in the hepatoduodenal ligament, MRCP should be done. An enteric feeding tube, either a jejunal tube (J tube) or a gastrojejunal tube (GJ tube), should routinely be inserted at the time of intervention to facilitate direct access to the gastrointestinal tract for postoperative alimentation.

Fluid collections in patients with pancreatic necrosis are common. A recent document circulated by the Acute Pancreatitis Classification Working Group, which proposes revisions to the original Atlanta classification nomenclature, suggests that this fluid collection be categorized as either acute peripancreatic fluid collections (APFCs) or acute post-necrotic collections (APNCs).46 APFCs are collections of fluid without associated necrosis and no definable wall and are commonly located in the lesser sac or peripancreatic region. These were previously termed acute fluid collections using the Atlanta classification terminology [see Table 2]. In contrast, APNCs are collections of fluid with necrosis of the pancreatic parenchyma, peripancreatic tissues, or both. APFCs are common during the early clinical course (2 to 4 weeks) of patients following necrotizing pancreatitis and
can be classified as either sterile or infected based on FNA aspirated for Gram stain and culture. The vast majority of these early acute fluid collections are sterile and, as such, are capable of resolution by the body over time. Only when these fluid collections are suspected to be the source of ongoing clinical deterioration or sepsis should they be aspirated for Gram stain with culture; if they are found to be infected, they should be drained. If the acute fluid collections remain asymptomatic, it is important to follow these collections for resolution over time, withholding elective operations such as cholecystectomy until the clinical course of the fluid collections is known. In patients with clinical deterioration and infected acute fluid collections, percutaneous drainage can often be an important temporizing measure to facilitate sepsis control and organ failure stabilization prior to proceeding with pancreatic necrosectomy. In some patients, after 4 weeks of recovery from the acute systemic illness associated with pancreatic necrosis, their

Figure 3  Intervention in necrotizing pancreatitis. CT = computed tomography; FNA = fine-needle aspiration; SIRS = systemic inflammatory response syndrome; VARD = video-assisted retroperitoneal débridement.
clinical progress becomes stagnant and plateau-like. Typically, these patients have a moderately large volume of sterile necrosis, which, although localized and walled off (walled-off pancreatic necrosis), continues to exert subtle physiologic and constitutional derangements such as low-grade fever, mild leukocytosis, inability to eat, and nausea. These clinical symptoms have been termed “persistent unwellness,” a pathologic state in which the volume of retroperitoneal necrosis prevents the patient from returning to his or her premorbid functional status. In these patients, necrosectomy of noninfected necrosis has a role in removing this nidus of devitalized tissue and allowing the body an opportunity to resolve the persistent inflammatory state that this necrotic debris incites. Although intervention in patients with noninfected necrosis remains controversial, after 4 weeks of medical treatment, the necrosis is “mature,” which implies a decrease in the inflammatory vascularity, localization of the necrotic process, and the ability of the operating surgeon to discriminate between live and dead tissue. At this time in the patient’s clinical course, necrosectomy seems warranted as further medical management beyond this point often does not result in symptom resolution.

Reintervention is not infrequent in the clinical course of this complex disease process, and CT-directed drainage is indicated following initial pancreatic necrosectomy for drainage of recurrent fluid collections and/or residual necrosis. Reoperation outside a staged approach should be a rare event and is used for postoperative collections that are either too extensive, thick, or numerous or have failed image-guided percutaneous drainage. These collections often represent areas of continued leakage from the pancreatic duct, a consequence of parenchymal necrosis, and thus are uncontrolled pancreatic fistulae, which, if controlled externally by successful percutaneous drainage or reoperation, allow the patient to recover.

It is gratifying to know that despite the high rate of morbidity and mortality associated with patients who have acute necrotizing pancreatitis and the large amount of both surgical and medical resources required to care for them, their long-term quality of life as assessed by the Short Form-36 Health Survey, once they have recovered fully is similar to that for patients who undergo medical management of chronic pancreatitis or those who have elective pancreatic surgery for ductal abnormalities.

**Chronic Pancreatitis**

Chronic pancreatitis is an inflammatory disorder of the pancreas characterized by glandular fibrosis resulting in permanent structural and functional changes in the organ, ultimately leading to pancreatic endocrine and exocrine insufficiency. Clinical manifestations of this disease are erratic and can range from an asymptomatic state, to circumscribed recurrent bouts of acute pancreatitis (elevated pancreatic enzymes, glandular inflammation), to continuously disabling abdominal pain. Contiguous organ involvement can lead to obstruction of the duodenum (gastric outlet obstruction), distal common bile duct (secondary biliary cirrhosis), or splenic vein (sinistral [left-sided] portal hypertension with isolated gastric varices and hypersplenism). A precise diagnosis can be made only by direct pancreatic biopsy showing fibrosis and a chronic inflammatory cell infiltration. Because of the technical difficulties and potential morbidity associated with direct pancreatic biopsy, provisional diagnoses are made using indirect evidence such as pancreatic duct morphology (Cambridge classification), decreased pancreatic exocrine function (low pancreatic juice HCO₃⁻ level), or clinical criteria (right upper quadrant abdominal pain with radiation to the back) [see Figure 4].

Recently, advances in imaging (EUS) and molecular genetic techniques have permitted the identification of patients who have subtle, early-stage disease or those patients with a genetic predisposition to eventually develop the disease. Overconsumption of alcohol is the primary etiology for chronic pancreatitis in the developed world. Less common etiologies include hereditary pancreatitis, autoimmune pancreatitis, traumatic pancreatitis, post-ERCP pancreatitis, obstructive pancreatitis, tropical pancreatitis, or metabolic conditions such as hypertriglyceridemia or hypercalcemia, rounding out the total population of patients evaluated for this condition. Chronic pancreatitis is a disease treated primarily by medical therapy, with the surgeon’s role limited to the treatment of specific disease complications [see Table 7].
Patient with abdominal pain and suspected chronic pancreatitis

Obtain history: focus on past medical history, alcohol and medication use/abuse and risk factors for chronic pancreatitis

Perform physical examination focusing on HEENT, chest, and abdominal examination

Diagnostic imaging: ductography via MRCP or ERCP; pancreatic gland morphology using cross-sectional imaging (CT scanning or MRI) or endoscopic ultrasonography (EUS)

Functional assessment: secretin-cerulein test, secretin-stimulated magnetic resonance cholangiopancreatography (SS-MRCP), glucose tolerance test

Establish probability of chronic pancreatitis based on evidence (listed by strength of evidence):

1. Pancreatic calcifications
2. Histologic abnormalities
3. Characteristic ductal changes (Marseille classification) on ERCP/MRCP
4. Pancreatic exocrine insufficiency

Low probability of chronic pancreatitis
- Refer to chronic pain specialist

High probability of chronic pancreatitis
- Medical and endoscopic treatment

Inadequate control of symptoms
- Consider surgical treatment

Figure 4  Diagnosis and treatment of patients with chronic pancreatitis. CT = computed tomography; ERCP = endoscopic retrograde cholangiopancreatography; HEENT = heads, ears, eyes, nose, and throat; MRCP = magnetic resonance cholangiopancreatography; MRI = magnetic resonance imaging.
### Table 7  Complications in Chronic Pancreatitis for Which Surgery Is Indicated

<table>
<thead>
<tr>
<th>Complication</th>
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<tr>
<td>Pain</td>
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<tr>
<td>Relapsing pancreatitis (inflammatory mass in the head, pancreatic ductal strictures)</td>
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<tr>
<td>Complicated pancreatic pseudocyst</td>
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<tr>
<td>Biliary obstruction</td>
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<tr>
<td>Duodenal obstruction</td>
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<tr>
<td>Bleeding pseudoaneurysm</td>
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<td>Sinistral portal hypertension with recurrent bleeding</td>
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**INITIAL CLINICAL EVALUATION**

**History**

Abdominal pain is by far the most common complication of chronic pancreatitis for which a patient is referred to a surgeon. Unfortunately, because of the subjective quality of this symptom and our inability to accurately establish causation between a particular patient’s pancreas and his or her abdominal complaints, correctly identifying patients in whom an operation will be beneficial is currently more art than science. Classic abdominal pain syndromes (midepigastric radiating to the back) combined with the morphologic abnormality of the pancreas (e.g., inflammatory mass in the pancreatic head, pancreatic pseudocyst, obstructing stone in the pancreatic duct) are more reassuring than patients who present with atypical pain syndromes combined with “minimal change” in the morphology of their pancreas. Having broadly stated these two disparate manifestations of the same disease process, suffice it to say that these generalizations still suffer from our inexact understanding of the mechanism of pain in this disease process.

Theories as to the pathogenesis of pancreatic pain include high pancreatic tissue or pancreatic duct pressure (compartment syndrome), alteration of sensory nerves with increased transmission due to the loss of their myelin sheath, molecular changes within nerve cells surrounding the pancreas, or a relative increase in the size and number of peripancreatic nerves. Despite these theories of pain pathogenesis, current surgical treatment of chronic pancreatitis relies on empirical results from applying a specific type of operation, either resection or a drainage procedure, to the dominant anatomic abnormality found in an individual patient’s pancreas.35

All patients with chronic pancreatitis should have a complete medical history and physical examination. The history of present illness should focus on the qualities of their pain: type, location, radiation, chronicity, quality (intermittent or constant), temporal relationship to food, and aggregating or alleviating factors. This information is important because when congruent, these clues often lend supporting evidence that can link the identified anatomic abnormality to the patient’s pain. For instance, patients with pancreatic head disease should have midepigastric to right upper quadrant pain syndromes, whereas those with obstructive pancreatitis classically have left upper quadrant pain, which radiates to their backs. In those patients with pancreatic duct strictures, clinical improvement in their pain with successful pancreatic duct stenting (adequate ductal decompression) is generally viewed as presumptive evidence for its pathophysiologic significance. The number of episodes of acute pancreatitis, their severity, whether or not a hospital admission was required, and the frequency of their recurrence should be carefully documented. All patients with chronic pancreatitis should fill out a validated quality of life instrument to objectively document their baseline preoperative status, and these metrics should be periodically readministered (every 6 to 12 months) to objectively quantify the effectiveness of treatment.

In the past medical history, special attention should be made to previous abdominal operations, particularly those involving the upper gastrointestinal tract (liver, bile duct, gallbladder, or pancreas). Careful questioning should be carried out regarding patients’ use of alcohol, prescription drugs (narcotic analgesics), and tobacco. Alcohol abuse, as mentioned previously, is the leading cause of chronic pancreatitis in the Western world. Patients with chronic pancreatitis and chronic abdominal pain often have personality disorders in which substance abuse (alcohol, tobacco, narcotics, and street drugs) is common. Careful documentation of the type, quantity, and frequency of pain medication use should be done. It is critically important that all patients with chronic pancreatitis abstain from alcohol at the time of operation as operative outcomes are notoriously low in the setting of recidivism. Tobacco use is an underrecognized pancreatic toxin in patients with chronic pancreatitis despite the fact that it has been shown to influence both the clinical course and the severity of the disease.36 Family history is important to consider as genetic factors that either increase proteolytic activity (the cationic trypsinogen [PRSS1] gene) or decrease protease inhibition (the pancreatic secretory trypsin inhibitor [SPINK1] gene) can influence the course of recurrent pancreatic inflammation.37 Genetically transmitted impairment of pancreatic duct function (cystic fibrosis transmembrane conductance regulator [CFTR] gene) has also been implicated in the pathogenesis of this disease.

**Physical Examination**

A detailed physical examination should be done with particular focus on the abdomen. Inspection of patients should start with a general assessment of their affect, particularly with regard to depression. Note should be made of their level of family support, as well as identification of abnormal codependency relationships between family members that might enable addictive or maladaptive behaviors. Look carefully for sclera icterus, a sign of distal common bile duct obstruction or advanced liver disease from alcohol abuse. Supraclavicular (deltoid, suprascapular, sternocleidomastoid, bitemporal) muscle wasting is a sign of significant weight loss attributable to poor oral intake, poorly controlled exocrine or endocrine insufficiency, or a combination of these factors. Spider angiomata on the anterior chest wall and palmar erythema are signs of active liver disease. The abdominal examination also often gives clues to the extent of disease. Note the presence or absence of ascites, an enlarged or shrunken liver, or abdominal wall signs of portal venous hypertension (caput medusa); all suggest underlying advanced liver disease. Some patients with chronic abdominal pain syndromes will have hyperpigmented discoloration of their abdomen termed “water bottle stomach” from the repeated applications of warm objects (heating pad, water bottle) to their stomachs to soothe their
abdominal pain [see Figure 5]. Occasionally, an upper abdominal mass may be the physical manifestation of an inflammatory mass or pancreatic pseudocyst. Diffuse abdominal tenderness and mild involuntary guarding during palpation are common physical findings in most patients with chronic pancreatitis.

Laboratory Tests

Whereas patients with acute pancreatitis are identified by hyperamylasemia, patients with chronic pancreatitis rarely have evidence of active pancreatic inflammation unless they are evaluated during an acute episode of pancreatitis (acute or chronic pancreatitis) or have an associated pancreatic pseudocyst. CBC with differential and platelet count, a comprehensive metabolic panel, prealbumin, hemoglobin A1C, and fecal elastase are appropriate laboratory tests to review. The purpose of these studies is to gauge both the overall functional (renal, hepatic) and nutritional status of the patient. Assessment of both the endocrine (hemoglobin A1C) and the exocrine (fecal elastase) function of the pancreas are important at baseline and should be repeated over the course of their treatment. Occasionally, metabolic abnormalities such as hypercalcemia or hypertriglyceridemia are identified as the etiology of recurrent pancreatic inflammation in patients with chronic pancreatitis. The exact role of genetic testing to identify patients with a predisposition to pancreatitis and their ultimate role in evaluation and treatment of patients with chronic pancreatitis are currently being elucidated. The most direct evidence that genetic abnormalities influence pancreatic disease comes from the observation that mutations in codons 29 (exon 2) and 122 (exon 3) of the cationic trypsinogen gene are responsible for the autosomal dominant forms of hereditary pancreatitis. Other mutations, such as the CFTR gene and the pancreatic secretory trypsin inhibitor (SPINK1) gene, although common in the general populations, have been identified with increasing frequency in patients with idiopathic chronic pancreatitis. Although significant progress in the implication of genetic influences on pancreatic diseases has been made, genetic testing should be limited to clinicians who understand the implications of genetic testing, use the obtained information for clinical decision making, and are prepared to provide pretest and posttest counseling to patients (or refer to a genetic counselor) to ensure that testing is done with full informed consent.

Imaging Studies

The role of diagnostic imaging in patients with chronic pancreatitis is twofold: (1) to confirm the diagnosis and (2) to provide precise anatomic information to assist in the application of a specific operative procedure to the identified pancreatic anatomy that gives the highest likelihood of success in relieving the patient’s symptoms. Because both ductal (main and side branch anatomy) and parenchymal (gland structure) information is required to accurately classify patients, imaging of both the pancreatic duct (e.g., MRCP, ERCP) and pancreatic morphology (e.g., CT, MRI) is required for complete evaluation. MRCP or ERCP shows the structural changes to the main pancreatic duct and its side branches. Abnormal findings can be quantified using the Cambridge classification system, which is considered a reference standard for both establishing the diagnosis and grading its severity. Limitations to this grading system arise in those patients who are early in their disease course, where ductal abnormalities may not be readily apparent. Furthermore, it has been shown that structural changes found during ERCP investigations do not correlate well with the level of gland functioning. Parenchymal abnormalities (gland morphology) identified by the cross-sectional imaging of CT or MRI include pancreatic head enlargement or hypertrophy, gland atrophy, ductal dilatation, the presence of calcifications, or evidence of inflammation.

MRI or MRCP with intravenous secretin is a relatively new technique that in one study provides a global assessment of the pancreas, providing information on gland morphology, ductal anatomy, and functional secretory status (pancreatic exocrine function). Secretin is a polypeptide hormone that stimulates the volume of bicarbonate-rich pancreatic secretion with concomitant contraction of the sphincter of Oddi. Using this dual physiologic mechanism during imaging theoretically improves distention of the pancreatic ducts, particularly the small side branch ducts, allowing better visualization during sequence acquisition to

Figure 5  The chronic use of topical thermal treatment by patients with abdominal pain and chronic pancreatitis is sometimes manifest by the classic clinical image of a “water-bottle stomach.”
allow for the radiographic identification of subtle side branch changes in patients with chronic pancreatitis. EUS has become the most sensitive imaging test available to detect small abnormalities of the pancreas. It is useful in identifying both ductal and parenchymal abnormalities that may not be evident on other imaging modalities, but this study lacks the specific anatomic details necessary for proper surgical planning. Because of its high level of sensitivity in detecting subtle parenchymal or ductal abnormalities, most investigators set minimum criteria of at least three distinct parenchymal or ductal abnormalities to make a firm diagnosis of chronic pancreatitis.

**ANATOMIC AND MORPHOLOGIC SUBTYPES OF CHRONIC PANCREATITIS**

Operations directed at patients with chronic pancreatitis can be divided into four basic types: resection, drainage, combined resection and drainage, and denervation. Dominant anatomic abnormalities found in patients with chronic pancreatitis can be broken down into three groups, either large duct, small duct, or minimal change variants based on the anatomic configuration of their main pancreatic duct. Large duct variants have a cross-sectional diameter of their main pancreatic duct of 10 mm, whereas small duct variants have a main pancreatic duct diameter of less than 6 mm. There is some controversy with categorizing patients with pancreatic ducts between 6 and 10 mm into either large or small duct variants. Minimal change pancreatitis is a group of patients who have characteristic symptoms of the disease but little or no anatomic changes in their gland or duct to confirm the diagnosis of chronic pancreatitis.

In the small duct variant of chronic pancreatitis, there are three specific subgroups: large pancreatic head, small pancreatic head, and obstructive pancreatitis. The precise measurements of a large, hypertrophic pancreatic head have not been specifically defined, but enlargement of anteroposterior head measurements greater than 3 cm is generally considered a pancreatic head mass. Obstructive pancreatitis occurs in the setting of a physiologically significant stricture of the main pancreatic duct with associated upstream (toward the spleen) changes in pancreatic duct dilatation, blunted pancreatic side branches, and localized parenchymal inflammation.

**Surgical Treatment Options**

Choosing the correct operation in patients with chronic pancreatitis comes from interpreting the results of published clinical experience when applied to different anatomic and morphologic patient subsets. For instance, the Partington-Rochelle modification of the Puestow procedure has the best results when applied to patients with large (>10 mm) dilated pancreatic ducts and is much less successful when used in patients with small (<6 mm) pancreatic ducts. In contrast, applying a pancreatic head resection to a patient with obstructive pancreatitis would remove the unaffected portion of the gland downstream (toward the duodenum) from the ductal obstruction while leaving the precipitating anatomy untreated. For some anatomic subsets, several different operations can be successfully applied, such as patients with small duct, enlarged head chronic pancreatitis for which either pancreaticoduodenectomy or the Beger- or Frey-type duodenum-preserving pancreatic head resection (DPPHR) can be successfully used depending on the specific patient and surgeon preferences. Below is a brief description of the operations currently available to treat patients with chronic pancreatitis.

![Figure 6](image)

**Figure 6** (a) Large duct pancreatitis—the Puestow or Frey procedure is recommended. (b) Small pancreatic duct—the Whipple, Beger, or Frey procedure is recommended for small ducts with an enlarged pancreatic head, such as (c); the Whipple procedure and/or a total pancreatectomy with islet cell transplantation is recommended for small ducts with no pancreatic head enlargement, such as (d); and distal pancreatectomy is recommended for obstructive pancreatitis in the tail, such as (e). (f) For a duct with minimal change, denervation via thoracoscopic splanchnicectomy is recommended.
Resection Operations

Pancreaticoduodenectomy, either the classic or pylorus-preserving variant, is the traditional resection operation used in patients with chronic pancreatitis. It removes the head of the pancreas, duodenum, and distal common bile duct, a region of the pancreas that has been coined by William P. Longmire, MD, as the “pacemaker” of the disease. This operation is generally applied to small duct variants and has the flexibility to be used in both large and small head subtypes [see Figure 8].

The Beger operation, termed one of the DPPHR procedures, involves transecting the pancreatic neck followed by a subtotal resection of the pancreatic head and removes diseased tissue in the head and uncinate process while preserving the normal relationship and function of the duodenum and distal common bile duct. This operation is applied to patients with small duct chronic pancreatitis and a large, hypertrophic pancreatic head. It has also been selectively used with reported good overall results in patients with small duct chronic pancreatitis and normal pancreatic heads but congenitally small pancreatic duct outflow tracts (e.g., pancreas divisum).

Distal pancreatectomy removes pancreatic parenchyma to the left of the confluence of the splenic vein with the portal vein (body and tail of the pancreas). This operation is used very selectively in patients with obstructive chronic pancreatitis. A high-grade pancreatic duct stricture in the body or tail of the pancreas with upstream (toward the spleen) side branch changes and evidence of localized pancreatic inflammation is the key imaging finding for this diagnosis. Care should be taken to evaluate these strictures for the possibility of pancreatic cancer.

Total pancreatectomy removes the entire pancreas and is extremely limited in its applicability to patients with chronic pancreatitis outside clinical trials using salvage procedures for the pancreatic islets with isolation and reinfusion as an autologous islet cell transplantation. This operation, total pancreatectomy with autologous islet cell transplantation,
is used primarily in patients with small duct or minimal change chronic pancreatitis who have not undergone previous resection of drainage procedures.

**Drainage Operation**

The Partington-Rochelle modification of the Puestow procedure, a longitudinal pancreaticojejunostomy, is the classic operation used to treat patients with large duct pancreatitis by decompressing the entire length of the pancreatic duct (head to tail) into a defunctionalized (Roux-en-Y) limb of jejunum [see Figure 9].

**Combined Resection and Drainage Operation**

The Frey operation is the other procedure termed as a DPPHR, but in contrast to the Beger operation, the pancreatic neck is not transected. The surgeon identifies the pancreatic duct in the neck of the pancreas and then opens the duct longitudinally by following it down into the pancreatic head and out toward the pancreatic tail. In the pancreatic head, the surgeon then cores out pancreatic parenchymal tissue from the pancreatic duct outward, leaving just a thin rim of tissue and pancreatic capsule around the head of the pancreas contiguous with the duodenum. A defunctionalized limb of jejunum (Roux-en-Y) is then anastomosed side to side to the pancreatic duct in the body and tail and to the remaining rim of pancreatic tissue in the head to effect complete drainage of the entire gland. This operation is perhaps the most versatile as it can be applied to patients with either small or large duct chronic pancreatitis as well as patients with either enlarged or normal-sized pancreatic heads [see Figure 10].

**Denervation Operation**

Bilateral thoracosopic splanchnicectomy is a minimally invasive approach to splanchnic denervation used to treat pain in patients with chronic pancreatitis. Candidates are
generally patients with no other surgical targets (i.e., minimal change pancreatitis) who have been shown to have a splanchnic-mediated pain pathway based on their response to a differential epidural anesthetic. Although pancreatic denervation operations over the last 50 years have had periodic surges in enthusiasm, their general applicability to patients with chronic pancreatitis has been limited.

Clinical Results

In measuring the results of surgery in patients with chronic pancreatitis, long-term success is typically defined by a thorough clinical follow-up of at least 5 years’ duration. When restricting data to long-term outcome measures, the results for pancreatic head resections are shown in Table 8. In a recent meta-analysis, DPPHRs have been shown to be equivalent in outcome to pancreaticoduodenectomy in the outcome variables of pain relief, overall morbidity, and incidence of postoperative endocrine insufficiency. In this same analysis, DPPHRs were judged to be superior to pancreaticoduodenectomy in terms of operative time, postoperative hospital stay, and overall quality of life measures. When one compares the two most common DPPHRs, the Beger operation and the Frey operation, there are no significant differences in a randomized, controlled clinical trial when patients were followed for over 8 years [see Table 9].

The outcomes of patients with chronic pancreatitis treated by longitudinal or lateral pancreaticojejunostomy (drainage operation) are shown in Table 10. After a mean follow-up of 79 months, 72% of patients experienced either complete or partial pain relief following operation, with a mean perioperative mortality rate in this group of patients of only 1%. A surgical denervation procedure as exemplified by
Figure 10 The Frey operation is a combination resection (coring out of the pancreatic head) followed by drainage into a longitudinal pancreaticojejunostomy.

bilateral thoracoscopic splanchnicectomy is a minimally invasive treatment of chronic pancreatitis with low perioperative morbidity and mortality rates. Based on currently available data, complete or partial pain relief is achieved in only 50% of patients during moderately long-term clinical follow-up [see Table 11].

Pancreatic Pseudocysts
Complicated pseudocysts commonly occur in patients with acute or chronic pancreatitis in association with an underlying pancreatic duct abnormality, and their surgical treatment should take this fact into account. The majority of patients with pseudocysts and chronic pancreatitis should

<table>
<thead>
<tr>
<th>Measured Variable</th>
<th>DPPHR</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain relief</td>
<td>Equivalent outcomes</td>
<td></td>
</tr>
<tr>
<td>Overall morbidity</td>
<td>Equivalent outcomes</td>
<td></td>
</tr>
<tr>
<td>Endocrine insufficiency</td>
<td>Equivalent outcomes</td>
<td></td>
</tr>
<tr>
<td>Operative time</td>
<td>+++</td>
<td>–</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Quality of life</td>
<td>++</td>
<td>–</td>
</tr>
</tbody>
</table>

DPPHR = duodenum-preserving pancreatic head resection; PD = pancreaticoduodenectomy. + = quantitatively better.

Table 8 Comparison of Duodenum-Preserving Pancreatic Head Resection of Both the Frey and Beger Types with Pancreaticoduodenectomy

<table>
<thead>
<tr>
<th>Measured Variable</th>
<th>Frey Operation (n = 36)</th>
<th>Beger Operation (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life</td>
<td>1.35 (0–100)</td>
<td>1.7 (0–100)</td>
</tr>
<tr>
<td>Pain score</td>
<td>11.25 (0–99.75)</td>
<td>11.25 (0–75)</td>
</tr>
<tr>
<td>Exocrine insufficiency</td>
<td>78%</td>
<td>88%</td>
</tr>
<tr>
<td>Endocrine insufficiency</td>
<td>60%</td>
<td>56%</td>
</tr>
<tr>
<td>Late mortality</td>
<td>32% (8/25)</td>
<td>31% (8/26)</td>
</tr>
</tbody>
</table>

*Median follow-up = 102 months.

Table 9 Long-Term* Comparison of the Frey and Beger Operations in Patients with Chronic Pancreatitis

*Scientific American Surgery
not be treated by cyst drainage alone, as is often the case in patients with a pseudocyst following a bout of acute pancreatitis, as the underlying ductal abnormality, if left untreated, will result in continued symptoms. In these patients, in addition to pseudocyst drainage, some form of pancreatic duct drainage and, occasionally, parenchymal resection should be added to the operation to address the underlying anatomic abnormality that contributed to the formation of the pancreatic pseudocyst. Attention should be paid to subtle complications such as fibrotic strictureing of adjacent organs, including biliary stricture (elevated alkaline phosphatase, transaminases, and a dilated common bile duct) or the duodenum (early satiety, weight loss, inability to eat). Once identified, complications can be addressed at the time of operation by the judicious application of one of the aforementioned operative procedures. Pseudoaneurysms occur as a consequence of severe inflammation and are commonly related to a pseudocyst. Bleeding into a pancreatic pseudocyst is heralded by the acute exacerbation of abdominal pain and confirmed by cross-sectional imaging showing a density increase in the fluid contained within the pancreatic pseudocyst (blood) [see Figure 11]. Angiographic embolization for immediate control is generally the initial treatment of choice [see Figure 12]. Following successful control of the acute episode of hemorrhage, formal resection of the involved pancreas can be carried out with direct ligation of the affected artery (gastroduodenal, pancreaticoduodenal, splenic).

### Table 10
Outcomes of Longitudinal/Lateral Pancreaticejjunostomy in Patients with Chronic Pancreatitis

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Complete or Partial Pain Relief (%)</th>
<th>Mortality (%)</th>
<th>Mean Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greenlee et al⁴⁶</td>
<td>86</td>
<td>80</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>Adloff et al⁴⁶</td>
<td>105</td>
<td>93</td>
<td>2</td>
<td>65</td>
</tr>
<tr>
<td>Adams et al⁴⁶</td>
<td>85</td>
<td>55</td>
<td>0</td>
<td>76</td>
</tr>
<tr>
<td>SIELEZNEFF et al⁴⁶</td>
<td>57</td>
<td>84</td>
<td>0</td>
<td>65</td>
</tr>
<tr>
<td>Sakorafas et al⁴⁶</td>
<td>120</td>
<td>81</td>
<td>0</td>
<td>96</td>
</tr>
<tr>
<td>Mean results</td>
<td>453</td>
<td>72</td>
<td>1</td>
<td>79</td>
</tr>
</tbody>
</table>

### Table 11
Outcome of Bilateral Thoracoscopic Splanchnicectomy in Patients with Chronic Pancreatitis

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Complete or Partial Pain Relief (%)</th>
<th>Mean Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moodley et al⁴⁶</td>
<td>17</td>
<td>94</td>
<td>12</td>
</tr>
<tr>
<td>Ihse et al⁴⁶</td>
<td>21</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>Buscher et al⁴⁶</td>
<td>44</td>
<td>46</td>
<td>36</td>
</tr>
<tr>
<td>Howard et al⁴⁶</td>
<td>55</td>
<td>35</td>
<td>32</td>
</tr>
<tr>
<td>Hammonds et al⁴⁶</td>
<td>20</td>
<td>60</td>
<td>15</td>
</tr>
<tr>
<td>Mean results</td>
<td>157</td>
<td>50</td>
<td>30</td>
</tr>
</tbody>
</table>

**Figure 11** Splenic artery pseudoaneurysms associated with a chronic pancreatic pseudocyst seen on contrast-enhanced computed tomography seen as a hypodense area in the pancreatic tail associated with some distortion of the splenic artery (yellow arrows).

**Figure 12** Angiographic embolization of a splenic artery pseudoaneurysm associated with a pancreatic pseudocyst prior to definitive treatment by distal pancreatectomy and splenectomy.

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References